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The Editorial Board of the Middle East Journal of Anesthesiology dedicates this issue of the MEJA to the Children of Qana
THE WATER OF QANA IS TURNED INTO BLOOD

Qana (modern spelling is “QANA” is a little village in South Lebanon which was blessed by the presence of our Lord and Saviour, Jesus Christ, his Holy Mother and his disciples. Qana is the Village where Christ performed his first miracle by changing the water into wine at the marriage feast (John 2: 1-11). Thus, Qana is deeply rooted in our Christian history.

Unfortunately, in modern times and due to the Middle East conflict, Qana has been the victim of Israeli aggression twice: once in April 1996, when an Israeli rocket killed 105 Lebanese men, women and children. And second, on Sunday morning, July 30, 2006, when a Israeli rocket killed 60 people, including 37 children. The stated figures illustrate this indiscriminate killing of children, which is against the Geneva Convention, the United Nations Charter and all laws of civilized nations.

An editorial from an article written by His Eminence Metropolitan PHILIP Primate, Antiochian Orthodox Christian Archdiocese of North America July 31, 2006.
THE QAHA MASSACRE

EDITORIAL
Editorial...

A PRESIDENT'S BEIRUT DIARY*

JOHN WATERBURY**

For most of the nine years that I have served as President of the American University of Beirut, I have frequently said that 90 percent of what I do would be familiar to the president of any American higher-education institution, and the remaining 10 percent reflects the peculiarities of doing business in Lebanon and the broader region. Sometime on July 12, 2006, those percentages reversed to something like 30/70. I have been a student, scholar, and resident of this region for over 45 years, but nothing I have learned in that time is adequate preparation for the 70 percent that I now face.

I have kept a detailed diary since early July in which I have tried to balance my instincts as a political scientist firmly pinned to a small dot on the world’s map which happens to be – or seems to be as I write – a fulcrum for a major turning point in international politics, and my instincts as a university president looking to the long-term survival of a great institution. Some excerpts:

July 9: After our commencement ceremonies on June 24, my wife, Samah, and I leave Beirut for New Jersey. Those were my ninth commencement exercises, and it is gratifying to realize that I have graduated well over 10,000 students. (AUB has more than 7,000 students and 640 full-time-equivalent faculty members). I spent the days after graduation working with a committee on the components of a strategic plan, doing annual performance reviews of the people who report directly to me, and reviewing candidates’ files for a number of senior positions.

** President of the American University of Beirut.
July 12: Sarah and I celebrate our third wedding anniversary. We visit the sculpture garden near Trenton, N.J., and have lunch there. This evening we learn from the news that Hizbollah has taken two Israeli soldiers prisoner in a cross-border raid and killed some others. Such events are always fraught with danger but not out of the ordinary.

July 14: Speaking by cellphone with AUB’s chief of campus protection, Saadallah Shalak, and provost, Peter Heath, I learn that the Israelis have bombed the Beirut airport, including the fuel depot. That comes as news to me because, at the invitation of an AUB trustee, Sarah and I have flown to San Francisco to attend an annual meeting at Bohemian Grove, which has no television or cellphone coverage – I have had to briefly leave the premises to contact the campus.

Obviously the Israelis’ response is more than expected, reminiscent of a similar episode in 1999 when they bombed two power plants near Beirut. Saad Shalak is nervous. He was an internal-security officer throughout the civil-war years, and he expects a ground invasion from Israel. He tells me that the Hizbollahis want it and are ready for it. He is already anticipating a flood of refugees into Beirut. Peter Heath is unfappable. (And he remains so throughout the next three weeks).

July 16: I give a previously scheduled breakfast talk on Lebanon at the Grove, attended by a large crowd that includes the journalist and presidential adviser David Gergen and Supreme Court Justice Stephen Breyer. I had planned to speak about political Islam, but the drama unfolding in Lebanon demands that I focus on the current crisis. People seem to appreciate my remarks, but I feel as if I were commenting on a Lebanon as far away as Mars.

July 17: Back at my computer, I sent out a mass of e-mail messages that I have queued up. I should have reviewed them beforehand. One, dated July 11, asked the Dean of Engineering and the Dean of Arts and Sciences to start planning for the annual football (soccer) match between the two faculties’ student teams. Coming in the midst of Israeli air assaults and sea bombardments, my message seems uncaring – if not demented – until they notice the send date.
July 22: I must get back to Beirut. The fighting is worsening; Israel is attacking all over Lebanon. I have agreed with the Provost and with the Vice President for Administration that we will bring all essential personnel to the campus and house them in our dormitories or in nearby hotels. That allows us to maintain hospital care, the power plant, network services, payroll, and other finance functions at close to full strength.

(Eventually we house more than 700 people, many of whom had been left homeless from the destruction in the south). We back up all basic documentation in case our servers go down. American and other non-Lebanese faculty and staff members are being evacuated. There is a fear that as the fighting intensifies, the refugee problem in Beirut may become unmanageable, and our campus might have to absorb part of the flood. Summer classes are suspended. Our Faculties of Medicine and of Health Sciences put in motion a number of initiatives to provide medical care to the refugees. A trickle of war-wounded people find their way to our emergency room, but most are stuck in the south with no or very little medical attention. Nearly all roads and bridges are cut, and any vehicle out in the open appears to be fair game.

It is Saturday, and I am in our New York offices to interview a candidate for the position of vice president for finance. Remarkably, none of the candidates has pulled out. It is hot, humid, and rainy. At about 5 p.m., I find a text message on my cellphone asking me to call CNN. When I do, I am told: “We want you to be on Larry King Live”.

“When?”

“Tonight”.

I plead no. I am in a shirt and slacks. I am sweaty and unkempt. Hardly presidential. But I am told that it doesn’t matter, and, at the end of the 9 p.m. broadcast, I appear on Larry King Live. He asks me some questions about Hizbollah that I answer carefully but honestly.

July 27: It has become abundantly clear that the looming crisis for Lebanon is the shutting down of its major public-sector power plants—all dependent on imported fuel oil which must come by ship. If the fuel runs out (and we believe there is about a two-week supply at normal levels of...
consumption), then the power goes off, the hospitals lose their life-
support systems, and the cities cannot pump water.

I spend two days in Washington, D.C., pounding around the Hill and
the State Department lobbying for help to persuade the Israelis to allow
fuel deliveries through their sea blockade (still in effect as I write). We
see Under Secretary of State for Political Affairs, R. Nicholas Burns;
Assistant Secretary of Defense for International Security Affairs, Peter
Rodman; and Greg Le Gerfo, director for Israel, Palestinian Affairs, and
Jordan at the National Security Council. We also meet with senior staffer
Mary Locke of the Senate Foreign Relations Committee and several
senior officials of the U.S. Agency for International Development’s
Office of U.S. Foreign Disaster Assistance. (I like to think that such
efforts eventually paid off, although the first tanker did not come through
the blockade until August 18. I know that U.S. Ambassador to Lebanon
Jeffrey Feltman and members of his staff were working on this around the
clock).

**August 2:** It has taken me some time, but I have gotten an orange
light from the AUB Board Chair to head back to Beirut via Amman. It is
risky, as Israel has bombed heavily the road from Damascus and has
begun to hit the northern border crossings as well. It is a little spooky
flying directly in to Amman through Israeli airspace, seeing the flat coast
near Tel Aviv, then the hills around Jerusalem, then the north end of the
Dead Sea before touching down in Amman. I am on the right side of the
airplane. Lebanon is on the left.

**August 5:** Still in Amman. As usual, I wake up around 2 a.m., pulse
pounding, insides churning, and a fevered caravan of worst-case scenarios
parading across my mental monitor. It has been like this for quite a while.
I envision refugees pouring onto the campus in an orgy of looting and
destruction of anything that smacks of America. (In fact, the refugees
everywhere in Lebanon are exemplars of good behavior – there is no
looting, violence, or invasion of private property. Beirut is not Baghdad).
Or Hizbollah falls back on Beirut, inviting Israel into urban warfare.
Hizbollah uses the campus to launch rockets against Israeli forces, so the
campus becomes a target for Israel. Or, Israel seizes the campus as a staging area in the battle for Beirut, and AUB becomes a target for Hizbollah.

For years my diary has been littered with concerns regarding Hizbollah. The University has students and employees, maybe even some faculty members, although I don’t know them, who are sympathizers. We have never had a major problem with Hizbollah, the Party of God, yet I worry about the objective incompatibility between its ideals and ours. Can we coexist? Sometimes I think not, but then I think about the historic role of universities, often embodying a counterculture, an alternative, that some forces in society, including governments, do not like or respect. I try to remember that the great universities on the eastern seaboard of the United States carried on in a society that tolerated and legalized slavery. It’s 5 a.m. I am feeling better.

August 6: AUB’s Vice President for Finance, John Bernson, has come out to Amman over land from Beirut, heading to the United States to take up a long-planned move to be chief financial officer at Sarah Lawrence College. He and I spent a morning going over financial scenarios for the University. The worst case, losing the entire fall semester, could cost us in the neighborhood of $30-million. The longer-term concern is what the war will do to our painstaking progress over the past decade in re-establishing our role as a regional institution of choice, recruiting students from all over the Arab world and beyond. Although AUB’s student body remains primarily Lebanese, in recent years, the number of undergraduates from the United Arab Emirates, Saudi Arabia, Jordan, Syria, Kuwait, and other countries has increased steadily. What will the war do to our equally successful efforts in recruiting non-Lebanese faculty members? It looks as if a lot of our hard work over several years may have gone out the window.

August 8: Here we go! I have hired a private car and driver to take me from Amman through Damascus and up to the northern border between Syria and Lebanon at Abboudiyeh. Nael, a Palestinian, is a chain smoker. I ask him how many trips he has made to Beirut. “This is my 15th
since July 12”, he says. “It beats what I did before. I used to drive Amman-Baghdad”.

We cover the distance fast, fill up at the last gas station before the crossing, and enter Lebanon. Nael takes my passport and residence card into the Lebanese authorities. He comes back with a Lebanese security officer who allegedly wants to make sure that I belong to the papers that he has just seen. He smiles at me and says in English, “Welcome back to Lebanon, Mr. Waterbury”.

AUB security chief Saad Shalak is waiting for me as we clear customs, and he, Nael, and I proceed to Beirut in about two hours. Just over the border, there is a culvert and low bridge that the Israelis have bombed the day before. We drive carefully around the crater.

August 9: The Israelis bomb the exact spot again the next day.

August 10: We hold our regular weekly meeting of the Board of Deans, going over the status of new professors, the whereabouts of continuing faculty members, what to do about research support for summer projects, energy-conservation measures, and so forth. I also meet with the crisis-response team, chaired by Acting President, George Tomey, whose long and often painful experience of the civil war stands us in good stead in the present situation. He is instrumental in procuring fuel for our power plant on the informal market, although if Electricité Du Liban shuts down for want of fuel, our backup capacity will carry us only a few days.

August 13: A cease-fire appears to be near at hand. I am heading up the mountains to Beit Mery, overlooking Beirut, to have lunch with Ghassan Tueni. Ghassan is the doyen of Lebanon’s journalists and publishers, a former cabinet minister, the father of Jibran Tueni (the managing editor of Al-Nahar newspaper and an outspoken critic of Syria who was assassinated last December), and a trustee emeritus of AUB. As we lunch overlooking Beirut, we hear a series of terrific explosions that we soon learn have taken place in the area of Imam Hasan School in the Dahiyeh (south Beirut) and on Hajjaj Street in Shiyah, a mixed neighborhood of Muslims and Christians that had not been targeted
before. Shadia Tueni, Ghassan’s wife, asks us, “Do you imagine the human beings down there when you hear these explosions, or do you just hear the noise and imagine the rubble?” No one answers. (The next day, we learn that more than 20 people, civilians of all ages, perished in those attacks – indeed the heaviest since the beginning of the war – after Israel had accepted the cease-fire).

**August 17**: A fragile cease-fire is holding. At the Deans’ meeting, we decide to resume our summer classes on August 28 and to begin our new academic year on September 27. Moueen Salameh, the Registrar, reports that some 450 out of around 5,900 undergraduates have requested copies of their transcripts – which may indicate the maximum number of them contemplating registration elsewhere. Not too terrible. I send e-mail letters to every new and continuing student, telling them the start dates and that I hope to see them back with us soon.

**August 18**: The first fuel tanker is allowed through the Israeli sea blockade to unload at the Zouq power plant. We don’t have to turn out the lights just yet.

**August 29**: Our summer classes resumed yesterday with something like 90 percent of our 3,000 summer students present. That is encouraging.
ANESTHETIC CONSIDERATIONS FOR OUTPATIENT COLONOSCOPY

RAMZI DAKOUR*, AMIR BALUCH*, OMAR SALEH*, RIKIN PATEL**, ALAN KAYE***, AND ELIZABETH FROST****

Introduction

Gastrointestinal (GI) procedures are administered in multiple settings such as the intensive care unit, emergency room, hospital operating room, or in an ambulatory unit. One of these procedures, colonoscopy, is a popular tool for monitoring, preventing, and diagnosing a variety of gastrointestinal diseases ranging from inflammation of the GI tract to colon cancer. A coordinated effort between the anesthesiologist and the gastroenterologist is essential to maximize patient safety and efficiency.

Indications and Contraindications

The decision to perform colonoscopy must take into account the cost, risk, and accuracy of diagnostic alternatives. In the United States, the fulfillment of these criteria may differ from that in foreign countries, where resources and/or perceptions relating to colonoscopy are population specific. Indications for colonoscopy can be classified as diagnostic vs. therapeutic, high-risk vs. low-risk, and high-yield vs. low-yield.

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** Medical Student, University of Texas Health Science Center, San Antonio, Texas, USA.
*** MD, PhD, Professor and Chairman, Department of Anesthesiology, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA.
**** MD, Department of Anesthesia, Mount Sinai Medical Center, New York, New York, USA.
Indications for Colonoscopy Use

The diagnostic use of colonoscopy is mainly reserved for obtaining biopsied material, since the procedure gives optimum exposure to mucosal tissue from the anal canal to the terminal ileum. If a biopsy is not deemed necessary, there are more cost-effective methods of diagnosis, including barium enemas and virtual colonoscopy. The indications for therapeutic use of colonoscopy (i.e. polypectomy) are more widely accepted since the cost, morbidity rate, and mortality rate of this procedure are lower than the alternative of surgery. It is important to note that age, diet, and family history all may influence risk stratification for cancer or other pathophysiological processing of the GI tracts.

Before performing the colonoscopy, the patient should be identified as being at high or low risk for perforation, and a risk-benefit analysis should be assessed. Examples of indications that are high risk include decompression of acute colonic pseudoobstruction, polypectomy of large polyps, stent placement, and dilation of colonic strictures. In contrast, when physicians employ colonoscopy for screening purposes of asymptomatic average-risk persons, the risk of perforation is extremely low.

Furthermore, indications for colonoscopy should be classified according to their expected yield for diseases such as neoplasia. Rectal and colonic bleeding is among the highest-yield indication for colorectal cancer. Conversely, many screening procedures as well as postpolypectomy and ulcerative colitis surveillance are considered to be relatively low-yield indications. [Table 1].

A study in 1993 evaluated seven major indications for colonoscopy including rectal bleeding, polyp follow-up, iron deficiency anemia, cancer follow-up (21%), abdominal pain (38.2%), abnormal bowel habit, and colitis to analyze the diagnostic yield of the procedure. Of significance, rectal bleeding, polyp follow-up and iron deficiency anemia produced the highest diagnostic yields of 69.1%, 53.3% and 47.7% respectively, whereas, cancer follow-up (21%), abdominal pain (38.2%) and abnormal bowel habit (46.8%) produced much lower yields. It is important to note,
however, that the yield of colonoscopy increases with age. The frequency of polyps is higher and there is a higher incidence of colorectal cancer. In a 2002 study, gender was also shown to have an effect on colorectal cancer, as the frequency rates of large polyps and colorectal cancer were found to be significantly lower in females than in males.

Table 1

<table>
<thead>
<tr>
<th>Indication</th>
<th>Procedures to detect Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two Consecutive positive FOBT, not rehydrated</td>
<td>2.7</td>
</tr>
<tr>
<td>Rectal bleed, nonemergency</td>
<td>8.9</td>
</tr>
<tr>
<td>Acute lower GI hemorrhage</td>
<td>11.8</td>
</tr>
<tr>
<td>Iron-deficiency anemia</td>
<td>13</td>
</tr>
<tr>
<td>Positive FOBT, rehydrated</td>
<td>45</td>
</tr>
<tr>
<td>Screening average-risk males ≥60 yrs</td>
<td>64</td>
</tr>
<tr>
<td>Surveillance after cancer resection, anastomotic recurrence</td>
<td>74</td>
</tr>
<tr>
<td>Surveillance after cancer resection, metachronous cancer</td>
<td>82</td>
</tr>
<tr>
<td>Screening average-risk people ≥50 yrs</td>
<td>143</td>
</tr>
<tr>
<td>Screening positive family history, prospective studies only</td>
<td>286</td>
</tr>
<tr>
<td>Postpolypectomy surveillance</td>
<td>317</td>
</tr>
</tbody>
</table>

FOBT, fecal occult blood test


Bleeding indications for colonoscopy are associated with a high prevalence of early stage cancer, and therefore early intervention can improve survival rates. Generally, patients who present with positive fecal occult blood tests and are 40 years or older undergo a full colonoscopy. Recent studies have also demonstrated the cost-effectiveness of distal colon visualization followed by full colonoscopy for patients suffering from rectal bleeding who are in their twenties and thirties.

Additional indications for colonoscopy are associated with other diseases besides neoplasia. If a patient presents with chronic diarrhea, a
biopsy should be performed to check for collagenous or lymphocytic colitis. The yield for this type of disease is 5-15%, with an increased prevalence in older females. When bleeding does not accompany abdominal pain, illness is usually not associated with colorectal cancer. However, colonoscopy is indicated in a patient with abdominal pain coupled with chronic diarrhea to exclude the presence of Crohn's disease. Moreover, positive findings on radiographs and sigmoidoscopy could be indications for the diagnostic use of colonoscopy. Examples of these findings include filling defects seen with barium enemas and virtual colonoscopy, colonic strictures seen in radiographic imaging, and colonic thickening viewed on abdominopelvic CT scans (which could signify a tumor).

As previously mentioned, one of the major uses for colonoscopy in the United States is for colorectal cancer screening. Of importance, special guidelines exist for patients with a family history of familial adenomatous polyposis (FAP), hereditary nonpolyposis colon cancer (HNPPC), and inflammatory bowel diseases. The colon cancer alliance indicates that screening should begin during puberty, at age 21, and 8 years after the onset of pancolitis, or 12-15 years after the onset of left-sided colitis for these diseases, respectively. According to the 2000 guidelines as outlined by the American College of Gastroenterology, colonoscopy is listed as the most effective screening tool for colorectal cancer, assuming the proper resources and professional expertise are available to correctly perform the procedure. In a recent study published in The New England Journal of Medicine comparing a barium enema and colonoscopy in their sensitivity to detecting early signs of colorectal cancer, it was found that the barium enema detected polyps in only 39% of cases that were detected by colonoscopy.

Contraindications

Before performing a colonoscopy, the health professional must verify that the patient exhibits no contraindications to the procedure. Contraindications to colonoscopy can be classified as either absolute
or relative. Toxic megacolon, fulminant colitis, and a perforated viscus open to the peritoneal cavity are absolute contraindications, and these should nullify any type of colonoscopy. Relative contraindications are ones in which risk to the patient is significantly increased. Examples of relative contraindications that should be considered are acute diverticulitis, recent myocardial infarction or pulmonary embolism, and pregnancy [Table 2].

Table 2

<table>
<thead>
<tr>
<th>Colonoscopy Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Toxic megacolon</td>
</tr>
<tr>
<td>Fulminant colitis</td>
</tr>
<tr>
<td>Perforated viscus</td>
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<td></td>
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</tbody>
</table>

Preparation

The colon must be adequately cleansed before a colonoscopy can be performed to improve the accuracy of diagnosis and reduce the risk of complications. Efficient colon cleansing is also cost effective according to a recent study of 400 colonoscopies by Rex et al. This report concluded that the extra time involved in suctioning and washing to satisfactorily expose the mucosa of patients with inadequate bowel preparations led to more aborted exams and earlier repeat surveillance. In monetary terms, the average cost increased by 12% and 22% in the university and public hospitals studied, respectively.

Early methods of colon preparation were modeled after barium enema preparations and modified for colonoscopy. Currently, three major options exist for colon preparation: diet and cathartic regimen, gut lavage, and phosphate preparations. Regardless of the method used, the patient must be thoroughly instructed on the cleansing procedure and must adhere precisely to the guidelines in order for the preparation to be effective.
Dietary methods for colon cleansing include a 48-72 hour regimen of clear liquids, laxatives, and enemas. In a 1984 study, this regimen was compared to another regimen which involved a minimum-residue diet which the patient undertook 24-72 hours before the exam\(^2\). The study showed that the cleansing efficacy of the minimum-residue diet was better than that of the clear liquids/laxatives/enemas regimen and has since become standard. Concerning cathartic methods of cleansing, a solution of magnesium citrate and senna X-prep was shown to have good cleansing efficacy and was acceptable to most patients\(^2\). The combination of magnesium citrate and bisacodyl has also been utilized and was found to be more effective in colon cleansing than castor oil\(^2\).

The main solution used for the gut lavage method of colon preparation is a polyethylene glycol electrolyte lavage solution (PEG-ELS). The benefit of this solution is that it does not significantly alter fluid and electrolyte balance when compared to saline or electrolyte preparations\(^3\). Although the efficacy rate of PEG-ELS reaches a high level, there is still scientific debate concerning its benefit relative to the third type of preparation, sodium phosphate\(^4,5\).

A recent study comparing the cleansing efficacy of two types of PEG solutions with a sodium phosphate preparation showed that the sodium phosphate solution has a slightly less cleansing efficacy than one of the PEG solutions\(^6\). However, other studies comparing sodium phosphate with PEG\(^7\) and a PEG-bisacodyl solution\(^8\) indicated opposite results, concluding that the sodium phosphate solution was superior to the PEG solutions in cleansing efficacy and patient tolerance. Furthermore, before administering a regimen of sodium phosphate for colon cleansing, certain contraindications must be taken into account. The FDA warns of increased risk to patients who have congestive heart failure, renal insufficiency, gastrointestinal obstruction, bowel perforation, colitis, megacolon, ileus, dehydration, ascites, gastric retention, inability to take fluid orally, or patients taking medications/diuretics that might affect electrolyte balance\(^9\).
Although rare, incidences of bacterial infection caused by colonoscopy do exist. The main concerns for infection during this procedure are bacteremia caused by endogenous bacteria and infection spread to the patient by contaminated equipment. Bacterial infections transmitted by endoscopes are extremely rare if proper procedures for disinfection are performed beforehand. Postprocedural bacteremia caused by endogenous bacteria or other factors is uncommon as well. In fact, only 2.2% of colonoscopies have recorded this type of infection, and even in the case of infection, complications are seldom observed.

While infection rates are considered uncommon, sparse data concerning the issue of infection risk and colonoscopy cause ambiguity in this area and have prompted the American Heart Association to create guidelines for antibiotic prophylaxis to be used for specific indications to help prevent against bacterial endocarditis. In addition to preventative measures, a careful cost-benefit analysis should be performed for each case before deciding to use antibiotic prophylaxis.

Anticoagulant considerations

Management of anticoagulants and antiplatelet agents must be emphasized during colonoscopy. Decisions must be made about when to stop and resume anticoagulation therapy during the procedure. The risks associated with discontinuing the therapy include thromboembolic complications, and must be weighed against the risk of gastrointestinal hemorrhage related to the procedure. Before any guidelines were published, a 1996 survey of 1269 American Society of Gastrointestinal Endoscopy (ASGE) members found that anticoagulation was routinely stopped before colonoscopy by 71-82% of physicians, and all restarted the therapy immediately after the procedure. In 2002 the ASGE updated guidelines for the management of anticoagulation based on classifying endoscopic procedures as either high or low risk [Table 3].
Table 3

ASGE Guidelines

<table>
<thead>
<tr>
<th>High procedural risk</th>
<th>Low Risk of Thromboembolism</th>
<th>High Risk of Thromboembolism</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Discontinue warfarin 3-5 days</td>
<td>Discontinue warfarin 3-5 days</td>
</tr>
<tr>
<td></td>
<td>before colonoscopy, reinstitute</td>
<td>before colonoscopy. Consider</td>
</tr>
<tr>
<td></td>
<td>after procedure</td>
<td>heparin while INR is below</td>
</tr>
<tr>
<td></td>
<td></td>
<td>therapeutic level</td>
</tr>
<tr>
<td>Low procedure risk</td>
<td>Delay elective procedures</td>
<td>Delay elective procedures</td>
</tr>
<tr>
<td></td>
<td>while INR is in</td>
<td>while INR is in</td>
</tr>
<tr>
<td></td>
<td>supratherapeutic range, no</td>
<td>supratherapeutic range, no</td>
</tr>
<tr>
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<td>change in anticoagulation</td>
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Adapted from Waye JD, Rex DK, Williams CB. Colonoscopy: Principles and Practice. Malden, MA: Blackwell Publishing Ltd; 2003, 225.

In conclusion, no controlled studies have been published concerning the risks of either continuing or discontinuing anticoagulation therapy before colonoscopy. However, there have been case studies published of patients who developed thrombosis after anticoagulation therapy was discontinued for a short period of time\(^\text{36}\). Furthermore, in a 2002 review of 109 previously performed colonoscopies in which patients discontinued their warfarin for three days prior to the procedure, only one case involving hemorrhagic complications was recorded\(^\text{37}\).

Preanesthetic Testing

Frequently no tests are required. Any laboratory studies should be requested only after a history and physical examination have been completed and the anesthesiologist has reason to believe that the results will alter his management strategy (eg, patient has been bleeding recently, Hb level is 8 gm and the decision is made to transfuse preprocedure).

Sedation Plans

Although there is debate about whether sedation is obligatory for
colonoscopy, studies indicate that patients desire sedation even though it may not be necessary. Proper sedation can contribute positively to patient comfort, satisfaction and improve recovery.38

Small doses of midazolam and meperidine potentiate the effects of propofol, an ultrashort-acting hypnotic agent, thereby allowing careful and efficient sedation during endoscopic examinations39. In a study conducted in 2003, propofol was tested against midazolam/fentanyl for outpatient colonoscopy. On average, propofol was administered to a total dose of 277 mg whereas midazolam and fentanyl were given at 7.2 mg and 117 µg, respectively. The group using propofol experienced a faster and deeper sedation. Just as importantly, the patients under propofol recovered sooner and were discharged earlier than those using midazolam/fentanyl40. Propofol for sedation is a popular choice due to its effectiveness and low risks under the care of appropriately trained anesthesiologists41. Anecdotal experience from one of the authors related to propofol sedation alone for colonoscopy showed no post procedure pain as would be expected since the colonoscope is simply maneuvered within the hollow viscus of the gut.

Patients can undergo two types of sedation procedures: patient-controlled sedation (PCS) with propofol and nurse-administered propofol sedation (NAPS). Studies reveal that both methods achieve the same levels of safety42,43,44. A 2003 randomized trial study compared PCS with propofol and alfentanil to a combination of physician-administered midazolam and pethidine. The study revealed that patients in the PCS group had significantly higher pain scores as well as recall than those in the midazolam and pethidine group. However, subjectively, both patient groups were satisfied with the sedation they received. On the other hand, PCS demonstrated significantly faster recovery times, an important factor in the outpatient setting45.

Music therapy has also been linked to sedation, and has been shown to reduce anxiety, heart rate, and blood pressure. The reduction in anxiety is not significant, but there is a trend showing that state anxiety is reduced with music therapy. Hence, potential exists for music to reduce pre-
procedural anxiety and potentially the need for sedation in patients undergoing colonoscopy. Recently, patient education regarding the procedure through videotape has been shown also to improve outcomes.

For children undergoing GI endoscopy, current literature asserts that ketamine is the sedation drug of choice. The sedative agent reduces complications while improving sedation. Different combinations of sedative agents were tested in 402 procedures. The combinations were the following: 1) midazolam and meperidine, 2) midazolam, meperidine, and ketamine, 3) midazolam and ketamine. The results showed that the highest level of efficacy and safety was achieved with the combination of midazolam and ketamine. Certainly more than adequate sedation could be accomplished by combining mask anesthesia with an inhalational agent in the pediatric population.

Preoperative Tests

To prepare for colonoscopy, patients are instructed to follow certain procedures the day before. One day before, patients take a clear liquid diet. Next, patients are required to begin drinking polyethylene glycol (PEG) 8 oz every 10 minutes for 3 hours starting in the afternoon of the day before the exam. The night before, patients undergo a fast. This regimen is used to clean and prepare the colon for a successful colonoscopy. A study consisting of 69 patients was performed to identify a correlation between the success of the exam and the hydrogen content of the fasting breath of the patient. The results indicate that people with poor colonic preparation have a higher fasting breath hydrogen level compared to those who have a well prepared colon. Hence, testing the hydrogen level may prove to be helpful to ensure that the colon is well cleansed and prepared for a successful examination and the patient has been compliant.

PEG is not the only option sodium phosphate tablets have been tested and are concluded to be just as effective and better tolerated. In a study of 845 patients comparing sodium phosphate tablets and PEG,
greater patient compliance and fewer GI side effects were associated with the tablet. Hence, it can be seen that sodium phosphate tablets are just as effective, more convenient for patients and have fewer side effects than the PEG regime\textsuperscript{50}.

The increase in popularity of propofol for colonoscopies prompted a study to determine if sodium phosphate tablets were compatible with its administration. A review of 97 outpatients concluded that colonic cleansing with the use of sodium phosphate tablets was safe for patients using propofol based sedation\textsuperscript{51}. Some patients, however, experienced intravascular volume contraction. This problem can be treated with carbohydrate-electrolyte rehydration, thereby allowing patients to cleanse the colon in a tolerable manner without hypovolemic variations caused by the tablets\textsuperscript{52}.

**Equipment**

Colonoscopy equipment has been revolutionized over the past two decades to make the procedure more safe, efficient, and provide easier visualization. There is no doubt that recent and future advancements in colonoscopy equipment will further modernize this useful procedure. The following summarizes the most common type of equipment used in colonoscopy today.

Colonoscopy begins with the video colonoscope\textsuperscript{53}. It has an outer polymer layer that gives it the right combination of flexibility and elasticity to be able to maneuver through tortuous bowel without twisting. Because different levels of stiffness are required depending on the conditions of the bowel, a variable stiffness colonoscope was produced\textsuperscript{54}. Thus the endoscopist can alter the stiffness of the colonoscope during the course of the procedure.

At the distal end of the colonoscope is a video lens the position of which is controlled by the endoscopist via simple finger controls at the proximal end of the scope. Located within the colonoscope itself is the machinery necessary for transmitting the internal image to an external
video source. The light which projects into the bowel comes from an external light source, connected to the colonoscope and projected to the lens through fiber optics. An automatically controlled lens aperture regulates the amount of light transmitted through this lens.

Implanted within the colonoscope are solid-state image sensors called “charge-coupled devices” (CCD). These photosensitive sensors capture the light reflected back from the bowel tissue and send integrated signals to a video screen on which the image is reconstructed. To produce colors images, special CCDs called “color chips” are used which contain a multicolored filter that resolves the image into its component primary colors.

In addition to finger controls that regulate the illumination system of the colonoscope, the user has access to controls that are used to operate the air, water, and suction systems. By manipulating a valve, which tonically releases air from the colonoscope, the endoscopist can insufflate the colon for better viewing. The colonoscope also contains a tube that can expel water from an external water source when a valve is depressed. Furthermore, the endoscopist can take advantage of a suction valve that is used to suction air or water from the lumen.

A recent innovation, which is used to accurately determine the position of the colonoscope during colonoscopy and to locate problematic loops of bowel, is the magnetic three-dimensional imaging system\textsuperscript{55}. This innovation was introduced in 1993 by two groups of British researchers\textsuperscript{56,57}. The colonoscope is equipped with internal sensor coils that detect low-frequency magnetic pulses from a special table upon which the patient is positioned. The pulses induce electrical signals within the coils that are transmitted to a computer. The computer is then able to decipher the signals to produce a 3-D display of the colonoscope onto a computer screen.

There are many accessories associated with the colonoscope that are used for specific functions such as polypectomy, biopsy, image enhancement, and ablation. These include polypectomy snares, which consist of a wire loop within a polymer sheath. The snare is passed
through an accessory channel in the colonoscope and is manipulated using a handle connected to the end. The polyp is released into a retrieval device that can be extruded from the patient along with the snare. Similarly, biopsy forceps can be used in the same manner to sample and retrieve tissue for further examination. Other accessories that can be passed through the colonoscope’s accessory channel include injection needles to inject the tissue with a desired solution, spray catheters which spray dyes onto the bowel tissue to enhance its visibility, and thermal devices which are used for tissue ablation.

**Basic Procedure**

Colonoscopy involves inserting an endoscope into the anal canal and navigating it through the bowel from the rectum to the ileocecal junction. The endoscope contains a camera lens so that the whole procedure can be visualized in detail on a television screen. Although specific techniques might vary depending on the standards of the institution or because of physician personal preference, there are some general principles that should be followed.

Once the patient is positioned either on the left side or in a supine position, the physician lubricates the anal canal and relaxes the anal sphincters. The distal 10 cm of the endoscope is also lubricated and inserted obliquely into the anus while the physician supports the bending section with his forefinger. Once inside the rectum, the physician rotates and angulates the endoscope to clearly visualize the lumen of the rectum. Furthermore, fluid and residue can be aspirated at this stage or any other stage of the procedure to clear out the lumen. Once the rectum has been clearly visualized, the physician slowly navigates the endoscope through the following sections: sigmoid colon, descending colon, transverse colon, ascending colon, and cecum. When necessary to improve vision, the physician can insufflate or aspirate the section of bowel using the controls at the end of the endoscope. Navigation should be slow and exact, and the physician may move the endoscope in a retrograde direction to review specific areas. Furthermore, caution needs to be
exercised when traversing the sigmoid-descending colon junction, splenic and hepatic flexures, and the ileocecal junction. After viewing the length of the colon, the endoscope is withdrawn, whereupon further inspection of the colon may be attained.

**Complications**

Being an invasive procedure, colonoscopy is associated with a variety of complications. However, in the care of expert physicians in a clinical setting, the frequency of any significant complications occurring is extremely low. Recent advancements in colonoscopy equipment and technique are some factors that can be attributed to such low rates. Recently it has been suggested that quality assurance programs, which highlight “core quality indicators” developed by the ASGE, can be implemented in endoscopy units to address the complications associated with colonoscopy.

Low mortality rates are attributed to colonoscopy and death results only when there are serious complications associated with the procedure. Local studies have put this rate at around 0.01%\(^{90,91}\). Careful selection of patients is critical to ensuring survival after the procedure. The physician must take into account the patient’s physical state and any contraindications. Several studies have been done yielding the complication rates associated with colonoscopy. These have been categorized based on whether procedures were diagnostic or therapeutic, with a significant increase in therapeutic procedures. Perforation rates for diagnostic procedures were low (0.029 percent to 0.61 percent) versus a higher 0.07 percent to 0.72 percent for perforations with therapeutic procedures. The side effect of bleeding was not reported enough to generate an estimate of its frequency with diagnostic procedures and occurred 0.2 percent to 2.67 percent with therapeutic procedures. Patient death occurred with a low frequency. The reported rates were from 1 in 30,000 to 1 in 3,000 with increased mortality rates in the older patient and more symptomatic patient groups. In terms of death occurring during the screening process, rates were even lower; one cost-effectiveness analysis
estimated it to be 1 per 20,000 patients.\textsuperscript{62}

Bowel perforation caused by endoscope puncture presents as one of the more obvious complications involved in colonoscopy. This complication is not considered to be serious in an otherwise healthy individual. Data from previous procedures have consistently put the incidence of perforation at between 0.1-0.3\%\textsuperscript{61,63,64}. However, the relative safety of diagnostic vs. therapeutic colonoscopy in regard to perforation is disputed\textsuperscript{63,64}.

Bleeding, another common problem, occurs with about the same frequency as perforation\textsuperscript{61}. It can result either because of tissue perforation or polypectomy. Medication must be taken into account when predicting the effects of bleeding on the patient. If the patient is on anticoagulant or antiplatelet therapy, decisions on whether to discontinue therapy and for how long must be made according to established guidelines before the procedure begins\textsuperscript{35}.

Complications from bacterial infection obtained during colonoscopy are not of tremendous concern. If instruments are properly disinfected before use, the occurrence of exogenous infection remains low\textsuperscript{32}. Additionally, endogenous contamination is quite infrequent and rarely results in any serious symptoms\textsuperscript{33}.

In a recent study in Germany, the effects of sedation on the cardiopulmonary system of patients undergoing colonoscopy were explored\textsuperscript{65}. The study showed that 2.4\% of sedated patients experienced adverse cardiopulmonary side effects. Specifically, 1\% experienced short bouts of oxygen desaturation and 0.9\% had vagovagal reactions, including low blood pressure and heart rate. Other studies indicate that sedation plays a role on the autonomic nervous system and this may be a factor leading to complications. For example, midazolam potentiates the sympathetic nervous system may accentuate cardiovascular incidents during colonoscopy\textsuperscript{66}. In another study consisting of 180 patients, midazolam lowered systolic and diastolic blood pressure resulting in hypotension (systolic blood pressure lower than 100 mmHg). Hence, sedation with midazolam can show a significant decrease in arterial
oxygen saturation and can increase the occurrence of hypotension. Although these complications may arise, colonoscopy with or without sedation is still considered safe\textsuperscript{67}. However, close observation relating to sedation during endoscopic procedures is warranted\textsuperscript{67}. A study of 53 patients showed that patients may still reach hazardous levels of sedation in the first 24 hours after the operation. Continued monitoring by family or friends in the outpatient setting is indicated.

Similarly, anxiety is seen as a more frequent complication of colonoscopy. A patient’s state-anxiety will usually go up during the procedure when assessed using the State-Trait anxiety index and compared to their score before the procedure\textsuperscript{68}. Recent studies indicate that having the patient listen to self-selected music either before or during the procedure is successful in significantly lowering anxiety\textsuperscript{69,70,71}.

Although colonoscopy has been effective for colorectal cancer screening, there can still be instances of missed lesions. Most of the lesions that are overlooked are less than 10 mm in diameter and are missed for a variety of reasons\textsuperscript{72,73}. Virtual colonoscopy, like fiber optic colonoscopy, has been shown to be capable of detecting lesions that are at least 10 mm in diameter\textsuperscript{74}. However, no evidence has been published comparing the efficacy of virtual colonoscopy with the traditional fiber optic approach.

**Discharge Criteria**

Currently, no standardized discharge criteria exist for health professionals dealing with colonoscopy candidates. It can be assumed, however, that each institution determines a minimum length of stay for patients who have just undergone a colonoscopy or has other criteria to determine when to discharge these patients\textsuperscript{74}. Only a 1996 study at Beth Israel Medical Center in New City\textsuperscript{75} asked the question of whether patient risk factors, intraoperative occurrences, and medications used during endoscopy could be used to predict a minimum stay after postconscious sedation. In a study of 405 adult patients who underwent an upper endoscopy or colonoscopy, preprocedural data (demographic and risk
factor data), intraprocedural data (medications and intraoperative occurrences), and postprocedural data (time of recovery and postprocedure occurrences) were obtained. The results concluded that “Age predicted length of time in recovery, but only 2% of the variation in recovery time was predicted by study variables”.

Furthermore, this study could not predict a better method for discharge than the ones already established at individual institutions.

Patient discharge can be affected by the type of anesthetics used during the colonoscopy. In a study comparing propofol versus midazolam/fentanyl, patients receiving propofol, recovered faster and were discharged about 10 minutes earlier than the patients using other sedation methods. In another study comparing remifentanil/propofol with intravenous anesthesia using fentanyl/midazolam/propofol, the remifentanil/propofol combination provided sufficient sedation and allowed patients to be discharged about 15 minutes after the procedure.

Another study compared total intravenous anesthesia versus inhalational anesthesia. A group of 69 patients underwent tests that used an intravenous fentanyl, midazolam, propofol combination or an inhalational combination of sevoflurane/nitrous oxide anesthetic. The inhalational anesthesia showed recovery of psychomotor abilities to be 30-90 minutes faster compared to the intravenous anesthesia. These types of studies show that certain types of sedation may be more suitable and should be examined to improve patient discharge times after colonoscopies.

Follow-up and Surveillance

Approximately 33% of patients initially treated by surgery with curative purpose will experience re-emergence of their cancer. Furthermore, many of these patients will die from a disseminated form of the disease. The goal of post-operative follow-up in these patients is to reduce these numbers. There is no consensus on the type of strategy to implement, however, any strategy is justifiable as long as it positively affects quality of life, the disease-free period, and overall global survival.
For non-cancer patients, the value of follow-up is controversial. Literature reveals that a more intensive and frequent follow-up leads to an increased number of reoperations and an overall more aggressive oncological approach in non-resectable cases. The benefits of this type of intensive follow-up, however, have not been determined; additionally, requiring that all patients undergo intensive surveillance is not cost-effective and is not evidence-based medicine.

The individual characteristics of each case must be taken into consideration before creating a follow-up plan. It has been suggested that physicians lean more toward intensive follow-up with patients at high risk of treatable recurrence and willingness to undergo reoperation. Along the same lines, low-risk cases could be followed with few tests such as referential colonoscopy, history and physical exams, carcinoembryonic antigen (CEA), and rectoscopy. Recent studies have shown that new diagnostic tests such as CT colonography may reduce the number of colonoscopies used for screening. In fact, Gluecker et al (2003) have shown that patients undergoing colorectal cancer screening prefer CT colonography to both double-contrast barium enema examination and colonoscopy.

Recent literature has shown, via meta-analyses, that survival rates can improve with intensive follow-up; however, there are still no large controlled studies that have proven any survival benefit with this strategy. Furthermore, studies are needed to examine the need and timing criteria for subsequent surveillance in order to contain costs associated with the procedure and to increase public awareness of the benefits that surveillance screening can and cannot provide.

**Conclusion**

There is no doubt that colonoscopy continues to be a valuable tool for the gastroenterologist to investigate diseases and malignancies of the GI tracts. The use of colonoscopy calls for a thorough examination of each case as an individual. Criteria such as risk factors, age, yield, potential complications, and the most effective sedation protocol must be
discussed among the anesthesiologist and gastroenterologist. Although much research has been conducted concerning general risks, benefits, and sedatives associated with the procedure, more studies must be conducted to determine proper guidelines for discharge criteria, surveillance, and anticoagulation. With the elderly population increasing in numbers and a greater willingness of younger patients at higher risk stratifications to have the test, frequency and prevalence colonoscopy will increase. Awareness and familiarity with the most recent developments concerning the procedure will help the anesthesiologist ensure that the patient receives the most successful course of action.
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PERIOPERATIVE USES OF DEXMEDETOMIDINE

VANDA G. YAZBEK-KARAM* AND MARIE M. AOUAD**

Dexmedetomidine is a new alpha2-agonist that received FDA approval in 1999 for use as a short-term (less than 24 h) sedative-analgesic in the intensive care unit. The use of alpha2-agonists as anesthetics is not new since many alpha2-agonists are used in veterinary medicine to induce anesthesia. Clonidine, the prototype of alpha2-agonists, has been synthesized in early 1970’s for its use as nasal decongestant and antihypertensive drug. Clonidine is widely used as an adjunct to anesthesia and pain medicine; however, it has been little used as sedative.

With dexmedetomidine, there are a number of reasons for the growing and renewed interest in the use of alpha2-adrenoceptors agonists as sedatives: Dexmedetomidine compared to Clonidine is a much more selective alpha2-adrenoceptor agonist, which might permit its application in relatively high doses for sedation and analgesia without the unwanted vascular effects from activation of alpha1-receptors. In addition, Dexmedetomidine is shorter-acting drug than clonidine and has a reversal drug for its sedative effect. Atipamezole. These properties render Dexmedetomidine suitable for sedation and analgesia during the whole perioperative period: as premedication, as an anesthetic adjunct for general and regional anesthesia, and as postoperative sedative and analgesic.

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Physiology of alpha2-adrenoceptors

Alpha2-receptors are found in many sites throughout the body. Alpha2-adrenoceptors are found in peripheral and central nervous systems, in effector organs such as the liver, kidney, pancreas, eye vascular smooth muscles and platelets. Physiologic responses mediated by alpha2-adrenoceptors vary with location and can account for the diversity of their effects.

The classification of alpha2-receptors based on anatomical location is complicated since these receptors are found in presynaptic, postsynaptic and extrasynaptic locations. Alpha2-adrenoceptors are divided into three subtypes; each subtype is responsible uniquely for some of the actions of alpha2-receptors. The subtype A, the predominant subtype in CNS, is responsible for the sedative, analgesic and sympatholytic effect; the subtype B, found mainly in the peripheral vasculature, is responsible for the short-term hypertensive response, and the subtype C, found in the CNS, is responsible for the anxiolytic effect.

There is no alpha2-subtype agonist and therefore the goal of producing a desirable alpha2-agonist effect such as sedation without the unwanted effect such as hypotension is elusive. All the subtypes produce cellular action by signaling through a G-protein which couples to effector mechanisms. This coupling appears to differ depending on the receptor subtype and location. The alpha2 A-adrenoceptor subtype seems to couple in an inhibitory fashion to the calcium channel in the Locus Ceruleus of the brainstem, whereas, in the vasculature, the alpha2 B-adrenoceptor subtype couple in an excitatory manner to the same effector mechanism.

Mechanism of action of Dexmedetomidine

The mechanism of action of dexmedetomidine is unique and differs from the currently used sedative drugs. Alpha2-adrenoceptors are found in many sites through the CNS, however, the highest densities of alpha2-receptors are found in the Locus Ceruleus, the predominant noradrenergic nuclei of the brainstem and an important modulator of vigilance. Presynaptic activation of the alpha2-A adrenoceptor in the Locus
Ceruleus inhibits the release of norepinephrine (NE) and results in the sedative and hypnotic effects\(^9\). In addition, the Locus Ceruleus is the site of origin for the descending medullospinal noradrenergic pathway, known to be an important modulator of nociceptive neurotransmission. Stimulation of the alpha2-adrenoceptors in this area terminates the propagation of pain signals leading to analgesia. Postsynaptic activation of alpha2-adrenoceptors in the CNS results in decrease in sympathetic activity leading to hypotension and bradycardia. Also, activation of the alpha2-adrenoceptors in the CNS results in an augmentation of cardiac-vagal activity. Combined, these effects can produce analgesia, sedation and anxiolysis.

At the spinal cord, stimulation of alpha2-receptors at the substantia gelatinosa of the dorsal horn leads to inhibition of the firing of nociceptive neurons and inhibition of the release of substance P\(^{10}\). Also, the alpha2-adrenoceptors located at the nerve endings have a possible role in the analgesic mechanisms of alpha2-agonists by preventing NE release. The spinal mechanism is the principal mechanism for the analgesic action of Dexmedetomidine even though there is a clear evidence for both a supraspinal and peripheral sites of action\(^{11}\).

Alpha2-receptors are located on blood vessels where they mediate vasoconstriction, and on sympathetic terminals, where they inhibit NE release. The responses of activation of alpha2-adrenoceptors in other areas include contraction of vascular and other smooth muscles; decreased salivation, decreased secretion, and decreased bowel motility in the gastrointestinal tract, inhibition of renin release, increased glomerular filtration, and increased secretion of sodium and water in the kidney; decreased insulin release from the pancreas, decreased intraocular pressure, decreased platelet aggregation and decreased shivering threshold by 2°C\(^4\).

**Pharmacodynamics of Dexmedetomidine**

Alpha-adrenoceptors agonists have different alpha2/alpha1 selectivity. Clonidine, the first developed and the most known alpha2-
agonist is considered as a partial alpha2-agonist since its alpha2/alpha1 selectivity = 200, while the alpha2/alpha1 selectivity of dexmedetomidine is 1620 and hence is 8 times more powerful alpha2-adrenoceptor than clonidine and is considered as a full alpha2 adrenoceptor agonist. The alpha2-adrenoceptor selectivity of dexmedetomidine is dose-dependent; at low to medium doses or at slow rates of infusion, high levels of alpha2-adrenoceptor selectivity are observed, while high doses or rapid infusions of low doses are associated with both alpha1 and alpha2 activities.

Dexmedetomidine-induced sedation qualitatively resembles normal sleep. The participation of nonrapid eye movement sleep pathways seems to explain why patients who appear to be “deeply asleep” from dexmedetomidine are relatively easily aroused in much the same way as occurs with natural sleep. This type of sedation is branded “cooperative” or “arousable”, to distinguish it from the sedation induced by drugs acting on the GABA system, such as midazolam or propofol, which produce a clouding of consciousness. Sedation induced by dexmedetomidine is dose-dependent; however, even low doses might be sufficient to produce sedation. Hall evaluated sedation, analgesia and cognition after infusion of small and moderate doses of dexmedetomidine (0.2 and 0.6 µg/kg/h) in seven healthy volunteers. He found that both doses produced significant sedation, analgesia and reduced performance on psychomotor tests. However, dexmedetomidine may lack amnestic properties: more patients who received dexmedetomidine for postoperative sedation were able to recall their ICU stay when compared to those receiving propofol for sedation.

Studies conducted on human volunteers to explore the analgesic properties of intravenous dexmedetomidine showed conflicting results. Ebert found that increasing concentrations of dexmedetomidine resulted in a dose-dependent sedation and analgesia based on VAS pain score in response to the cold pressor test. Jaakola found that a single IV dose used for human tourniquet pain resulted in analgesia with a ceiling effect at the dose of 0.5 µg/kg. Another study comparing the analgesic and mental effects of increasing plasma concentrations of dexmedetomidine and alfentanil concluded that systemic dexmedetomidine lacks analgesic
efficacy for heat and electrical pain at doses causing mild to severe sedation\textsuperscript{18}. However, clinical studies showed that systemic administration of the alpha2-adrenoceptor agonists dexmedetomidine and clonidine produce sedative and opioid-sparing effects in the perioperative setting, providing indirect evidence for some analgesic efficacy\textsuperscript{19,20,21}, although it is difficult in this special setting to distinguish between sedation and analgesia as a cause for this opioid-sparing effect. While the analgesic effect of systemic dexmedetomidine is still debatable, administration of an alpha2-agonist (clonidine) via the intrathecal or epidural route provides analgesic effects in postoperative pain and in neuropathic pain state without severe sedation\textsuperscript{3}. This effect is due to sparing of the supraspinal CNS sites from excessive drug exposure resulting in robust analgesia without heavy sedation.

Alpha2-adrenoceptors do not have an active role in the respiratory center, therefore, dexmedetomidine throughout a broad range of plasma concentration, has minimal effects on the respiratory system\textsuperscript{14}. However, doses of 2 µg/kg given as a bolus resulted in short episodes of apnea. Also, coadministration of dexmedetomidine with other sedatives, hypnotics or opioids is likely to cause additive effects\textsuperscript{22}.

Dexmedetomidine does not appear to have direct effects on the heart. In the coronary circulation, dexmedetomidine causes a dose-dependent increase in coronary vascular resistance and oxygen extraction, but the supply/demand ratio is unaltered\textsuperscript{23}. A biphasic cardiovascular response has been described after the administration of dexmedetomidine. A bolus of 1 µg/kg results in a transient increase in blood pressure (BP) and a reflex decrease in heart rate (HR), especially in the young healthy patients. This initial response is attributed to the direct effects of alpha2 B-adrenoceptor stimulation of vascular smooth muscle. This response can be attenuated by a slow infusion over 10 min, but even at slower infusion rates, the transient increase in mean BP and the decrease in HR over the first 10 min is shown. This initial response lasts for 5 to 10 min and is followed by a decrease in BP of 10-20% below baseline and by stabilization of the HR below baseline values. Both these effects are presumably caused by an inhibition of
central sympathetic outflow that overrides the direct effects of dexmedetomidine on the vasculature. Hypotension and bradycardia induced by dexmedetomidine are reversed by ephedrine and atropine respectively, but large doses are required\textsuperscript{24}.

Ebert\textsuperscript{16} studied the autonomic, cardiovascular, and sedative responses to increasing plasma concentrations of dexmedetomidine; he found that low plasma concentrations resulted in sedation, mild analgesia with preservation of recall and recognition. In addition, it resulted in a decrease in HR and BP, without changes in central venous pressure or pulmonary artery pressure and without respiratory changes. Subsequent higher doses resulted in increased sedation, analgesia and memory impairment, as well as an increase in BP, systemic and pulmonary vascular resistance. A significant decrease in HR and progressive decreases in cardiac output, and stroke volume is also noted. Even at higher doses, there was no respiratory compromise.

**Pharmacokinetics of Dexmedetomidine**

Dexmedetomidine, an imidazole compound, is the active d-isomer of medetomidine. Following intravenous administration, dexmedetomidine exhibits the following pharmacokinetic parameters: a rapid distribution phase with a distribution half-life (\( t_{1/2_d} \)) of 6 min, a terminal elimination half-life (\( t_{1/2_b} \)) of 2 hours, and a steady-state volume of distribution (\( V_{ss} \)) of 118 liters. Dexmedetomidine exhibits linear kinetics when infused in the dose range of 0.2-0.7 \( \mu \)g/kg/h for no more than 24 hours. Dexmedetomidine undergoes almost complete biotransformation through direct glucuronidation and cytochrome P450 metabolism. Metabolites of biotransformation are excreted in the urine (95%) and feces. It is unknown if they possess intrinsic activity.

The average protein binding of dexmedetomidine is 94%, with negligible protein binding displacement by fentanyl, digoxin, theophylline, lidocaine and ketorolac. There have been no sex or age-based differences in the pharmacokinetics of dexmedetomidine; however, it has not been studied in pediatric patients. The dose of dexmedetomidine should be decreased in
patients with hepatic or renal impairment. Dexmedetomidine do cross the
placenta and should be only used during pregnancy if the potential benefits
justify the potential risk to fetus.

Dexmedetomidine is a white powder that is freely soluble in water and
has a pka of 7.1. It is supplied as 100 μg/ml 2 ml vial which must be diluted
with 48 ml of 0.9% sodium chloride prior to administration. For adult
patient, dexmedetomidine is administered by a loading infusion of 0.5-1
μg/kg over 10 minutes, followed by a maintenance infusion of 0.2 to 0.7
μg/kg/h. The effect appears in 5-10 min, and is reduced in 30-60 min. The
maintenance infusion is adjusted to achieve the desired level of sedation.25

The most frequently observed adverse events in patients receiving
dexmedetomidine for ICU sedation include hypotension, hypertension,
nausea, bradycardia, atrial fibrillation and hypoxia.15 Most of these events
occur after or during the loading dose, therefore, reducing or omitting the
loading dose could result in decreasing the incidence and severity of these
adverse events.15

Appropriate patient selection for dexmedetomidine administration is
crucial; because it decreases sympathetic nervous activity, its effects may
be most pronounced in patients with decreased autonomic nervous system
control such as the elderly, diabetic patients, patients with chronic
hypertension or severe cardiac disease such as valve stenosis or
regurgitation, advanced heart block, severe coronary artery disease, or in
patients who are already hypotensive and/or hypovolemic.4

The tolerability of dexmedetomidine was noted in three cases of
overdose.26 In 2 cases, the dose administered was 0.5 mg/kg/h instead
of 0.5 μg/kg/h, and in one case, the dose 4 μg/kg/h instead of 0.4 μg/kg/h.
In the three cases, the overdose resulted in oversedation only. However,
first and second-degree heart block or even cardiac arrest following
administration of dexmedetomidine were reported.27

Dexmedetomidine do not affect the synthesis, storage or metabolism
of neurotransmitters and do not block the receptors, thus providing the
possibility of reversing the hemodynamic effects with vasoactive drugs or
the specific alpha2-antagonist: Atipamezol (Antisedan).28 Atipamezol acts
by increasing the central turnover of norepinephrine. Its duration of action is 2 hours\(^{29}\).

**Perioperative uses of dexmedetomidine**

I – Premedication

Dexmedetomidine possesses anxiolytic, sedative, analgesic, antiallogogue and sympatholytic properties, which render it suitable as a premedication agent. Dexmedetomidine potentiates the anesthetic effects of all intraoperative anesthetics\(^{30,31,32}\) (intravenous, volatile or regional block). Bohrer\(^{33}\) showed that preoperative administration of intravenous or intramuscular dexmedetomidine resulted in a decrease in induction dose of thiopentone by up to 30%. The administration of intramuscular dexmedetomidine at a dose of 1 µg/kg for premedication in outpatient cataract surgery resulted in sedation, and decrease in intraocular pressure without significant hypotension or bradycardia\(^{34,35}\). Also, the administration of dexmedetomidine for premedication decreases oxygen consumption intraoperatively by 8% and postoperatively by 17%\(^{36}\). Indications to the use of dexmedetomidine as premedication include patients susceptible to preoperative and perioperative stress, drug addicts and alcoholics, chronic opioid users and hypertensive patients.

II – Intraoperative uses of dexmedetomidine

Intraoperative uses of dexmedetomidine include its use as adjunct to general anesthesia, as adjunct to regional anesthesia, in monitored anesthesia care (MAC), or as a sole agent for total intravenous anesthesia (TIVA).

I – Use of dexmedetomidine as adjunct to general anesthesia

The use intraoperative dexmedetomidine may increase hemodynamic stability because of attenuation of the stress-induced sympathoadrenal responses to intubation, during surgery and during emergence from anesthesia\(^{37}\). Talke\(^{38}\) evaluated the effects of varying plasma concentrations
of dexmedetomidine on HR, BP and catecholamines concentrations during emergence from anesthesia in the setting of vascular surgery. This study demonstrated that dexmedetomidine attenuates the increases in heart rate and plasma norepinephrine levels observed during the emergence from anesthesia.

Administration of intravenous dexmedetomidine produces an anesthetic-sparing effect. Aho showed 25% reduction of maintenance concentrations of isoflurane in patients undergoing hysterectomy. Khan found 35%-50% reduction in isoflurane concentrations with either low or high doses of dexmedetomidine. Fragen noted 17% reduction in sevoflurane requirements for maintenance of anesthesia in elderly patients. In addition, the use of dexmedetomidine produces intraoperative and postoperative opioid-sparing effect. Aho administered dexmedetomidine at dose of 0.4 μg/kg in patients undergoing laparoscopic tubal ligation and found a 33% decrease in morphine use postoperatively.

Talke investigated the muscle relaxant effects of dexmedetomidine on the neuromuscular junction and found no clinically relevant effects. Dexmedetomidine reduces the vasoconstriction threshold and the shivering threshold and is associated with a lower incidence of shivering.

2 – Use of dexmedetomidine for regional anesthesia

The use of dexmedetomidine as adjuvant in regional anesthesia is still not validated. Maarouf explored the effect of epidural dexmedetomidine on the incidence of postoperative shivering in 60 patients undergoing orthopedic surgery. He found that patients who received dexmedetomidine at a dose of 100 μg added to 20 ml 0.5% bupivacaine showed lower incidence in postoperative shivering when compared to patients who received epidural bupivacaine alone (10% vs. 36%). Memis noted that the addition of 0.5 μg/kg dexmedetomidine to lidocaine for intravenous regional anesthesia improves the quality of anesthesia and perioperative analgesia without causing side effects. Kanazi et al. investigated the effect of adding a small dose of 3 μg of
intrathecal dexmedetomidine to 12 mg bupivacaine. They found a significant prolongation of sensory and motor block as compared to bupivacaine alone. In this study, the effect of 3 μg intrathecal dexmedetomidine was similar to that produced by the addition of 30 μg of intrathecal clonidine.

3 – Use of dexmedetomidine in monitored anesthesia care

Dexmedetomidine confers arousable sedation with ease of orientation, anxiolysis, mild analgesia, lack of respiratory depression and hemodynamic stability at moderate doses. These properties allow dexmedetomidine to be an almost ideal agent for MAC despite its lack of amnesia and poor controllability because of its slow onset and offset. The efficacy, side effects, and recovery characteristics of dexmedetomidine were compared to propofol when used for MAC19. This study showed that dexmedetomidine achieved similar levels of sedation to propofol, albeit with a slower onset and offset of sedation. Neither dexmedetomidine nor propofol influenced respiratory rate, but propofol resulted in lower mean arterial pressure during the intraoperative period. In the recovery room, dexmedetomidine was associated with an analgesia-sparing effect, slightly increased sedation, but no compromise of respiratory function or psychomotor responses. Dexmedetomidine in MAC was used successfully in many situations: when patient arousability needed to be preserved, as for awake craniotomy46-47, for awake carotid endarterectomy48 and for vitreoretinal surgery49. In addition, dexmedetomidine was used for sedation in difficult airway patients; during fiberoptic intubation50,51, and for sedation of a patient with difficult airway undergoing lumbar laminectomy surgery in the prone-chest position under spinal anesthesia52.

4 – Use of dexmedetomidine as a sole anesthetic agent

Ramsay53 has used dexmedetomidine as a sole anesthetic agent. The report describes three patients who presented for surgery with potential
airway management challenges. Dexmedetomidine was infused in increasing doses (up to 10 µg/kg/h) until general anesthesia was attained. No respiratory depression was noted, only one patient required chin lift. Also no hypotension or severe bradycardia were noted. The rationale for this new, off-label use of dexmedetomidine is based on its known properties to provide sedation, analgesia while avoiding respiratory depression at low doses. These effects were maintained at higher doses without hemodynamic instability.

III – Use of dexmedetomidine in the postoperative period

Dexmedetomidine special properties favor its use in recovery room. In addition to its sympatholytic effects, analgesic effects and decreased rate of shivering, the preservation of respiratory function allows the continuation of the dexmedetomidine infusion in the extubated, spontaneously breathing patient. The possibility of ongoing sedation and sympathetic block could be beneficial in reducing high rates of early postoperative ischemic events in high-risk patients undergoing non-cardiac surgery [5]. In a study conducted by Talke [8], high-risk patients who received dexmedetomidine from 1 h before until 48 h after vascular surgery experienced significantly fewer ischemic episodes than did patients in the placebo group (8% vs 29%). During emergence from anesthesia, NE levels in the placebo group were 2 to 3 times higher than those in the dexmedetomidine group. However, patients who received intraoperative dexmedetomidine needed more fluids to avoid hypotension, a side effect that may be unfavorable in volume-sensitive patients with reduced left ventricular function. In addition, care should be taken in patients who depend on a high level of sympathetic tone or in patients with reduced myocardial function who cannot tolerate the decrease in sympathetic tone [4]. Perioperative administration of dexmedetomidine could be beneficial in chronic opioid users and alcoholics, in high-risk patients as well as in cardiac patients with good to moderately decreased left ventricular function.
IV – Use of Dexmedetomidine in the pediatric-age group

Only few cases about the use of dexmedetomidine in the pediatric-age group are found in the literature\textsuperscript{55,56}. Tobias used dexmedetomidine for ICU sedation in a 10-week old infant requiring mechanical ventilation and in a 14-y old patient after posterior spinal fusion for scoliosis. The use of dexmedetomidine at a dose of 0.25 µg/kg/h for 24 h in these two cases resulted in acceptable sedation without significant hemodynamic changes. Dexmedetomidine was also used for sedation and anesthesia in an 11-y old patient undergoing gastroscopy; however, it resulted in insufficient sedation. Another study conducted in pediatric-age group explored the use of intraoperative dexmedetomidine at different doses with the goal of reducing the post sevofoflurane agitation in children aged 1-10 y. The optimal dose of dexmedetomidine was 0.3 µg/kg and its use did not result in adverse effects\textsuperscript{57}.

Conclusions

In summary, dexmedetomidine is a short-acting alpha2-adrenoceptor agonist with many desirable clinical benefits that encourage its use in the perioperative period.

Dexmedetomidine provides a sedated patient in the preoperative period. Intraoperatively, in addition to its anesthesia-sparing effects, it provides a stable hemodynamic profile by attenuating the stress response during tracheal intubation, during surgery and emergence from anesthesia. Dexmedetomidine offers the possibility of continuing sedation throughout the extubation process and in the recovery room without significant respiratory impairment, and with lower analgesic requirements. In addition, it may offer protection from ischemia due to attenuated neuroendocrine response in the perioperative period. Dexmedetomidine offers a special type of sedation in which patients are readily arousable with preservation of respiratory function; therefore, it could be useful for surgery performed under MAC, especially in patients with compromised airway, and whenever patients’ arousability is needed to be present as during awake craniotomy.
carotid endarterectomy and vitreoretinal surgery.

Because of its sympatholytic and vagomimetic actions, dexmedetomidine is approved with a warning about hypotension, bradycardia, and sinus arrest, and therefore, appropriate patient selection is crucial. In addition, we should be mindful that many of the perioperative applications of dexmedetomidine remain “off-label”\textsuperscript{58}.

Fundamentally, whether or not dexmedetomidine turns out to be just another sedative agent depends on how we benefit from the new opportunities it provide.
References


THE EFFECT OF POSITIVE PRESSURE VENTILATORY PATTERNS ON POST-BYPASS LUNG FUNCTIONS

MOHAMED ESSAM A-MEGUID*, EMAD EL-DIN MANSOUR* AND KHALED M. ABDULLAH**

Abstract

Background: This study aimed at evaluating the effect of application of different patterns of positive ventilatory pressure either during or after cardiopulmonary bypass (CPB), on lung functions.

Methods: 30 patients undergoing coronary artery revascularisation under the management of CPB were randomly allocated into 3 groups. Group 1 (VCM) 10 patients were subjected to manual vital capacity manoeuvre (VCM) before weaning off the CPB. Group II (CPAP) 10 patients were subjected to continuous positive airway pressure (CPAP) of 10 cmH₂O during CPB. Group III (PEEP) 10 patients were subjected to positive end expiratory pressure (PEEP) of 7 cmH₂O after weaning off the CPB. Measurements included the PO₂, PCO₂, together with derived calculated parameters as the alveolar-arterial oxygen difference [P (A-a) DO₂] and shunt fraction, as well as the dynamic lung compliance being recorded directly from the anesthetic and ventilatory equipments. All readings were taken on closed chest and on FiO₂ of 0.5. Intraoperative anesthetic and surgical data as well as postoperative extubation time and length of ICU stay were also evaluated.

Results: Statistical analysis of ventilatory parameters showed no
significant differences for both $\text{PO}_2$ and $\text{PCO}_2$ in between the studied
groups. Alveolar-Arterial oxygen difference mean values were
comparable in the 3 studied groups. The mean values of intrapulmonary
shunt fraction showed a significant difference in relation to the baseline
values in Group I (VCM) and Group III (PEEP) at 30 minutes after ICU
admission and 4 hours post CPB with estimated $P$ value <0.01 and <0.05
respectively, while in Group II (CPAP) mean values started to be
significant after chest closure with a $P$ value <0.05, but there was no
significant intergroup differences with a $P$ value >0.01. Dynamic lung
compliance mean values showed no intergroup statistical significance.

Conclusion: Maintenance of ventilatory parameters was achieved in
all the positive pressure ventilatory methods applied, either being applied
during or after CPB.

Key words: Cardiopulmonary bypass; Vital capacity manoeuvre;
CPAP; PEEP.

Introduction

Pulmonary dysfunction after cardiopulmonary bypass (CPB) is
considered one of the major consequences in cardiac surgery that results
either from increased lung water content or development of postoperative
atelectasis. Both will result in decreased lung compliance and in return
result in deficient gas exchange as a result of increased shunt fraction\(^1\).
The main clinical manifestation of post-pump lung syndrome is defective
oxygenation that may result in a spectrum of consequences resulting in
prolonged postoperative mechanical ventilation and failure of fast
tracking concept in cardiac surgery. Atelectasis and decreased lung
compliance is the main feature of post-pump lung syndrome\(^2\), thus with
prevention of those consequences proper oxygenation could be achieved
and hence shortening of intubation time postoperatively as well as
shortening of length of ICU stay. Application of positive ventilatory
pressure using continuous positive airway pressure (CPAP) during CPB
was proved to have beneficial effects on maintenance of oxygenation
parameters\(^2,3\). Manual application of positive ventilatory pressure on the
conclusion of CPB using the vital capcity manoeuvre (VCM) showed significant improvement in ventilatory parameters when compared to deflated lungs throughout the CPB interval\(^4\).

In the present study comparison was made between different patterns of positive ventilatory pressure applied either during or after CPB, including the application of positive end expiratory pressure (PEEP) after weaning off CPB. This was not studied before on humans.

**Patients and Methods**

After obtaining our Hospital Research Review Board approval, the study was performed between November 2003 and May 2004. An informed patient consent was taken from eligible patients before being enrolled to the study.

In a randomised prospective observational study, 30 patients scheduled for elective cardiac revascularisation procedure that was previously determined to be under the management of cardiopulmonary bypass (CPB) whether by the tepid CPB method or by the on pump beating heart technique, were enrolled to the study. Randomisation of patients was taken through sealed envelopes. Exclusion criteria included pre-existing pulmonary disease, poor LV function with EF <30\%, morbid obese patients with a BMI >30, lengthy CPB time >120 min, severe hemodynamic instability necessitating either a high inotropic support or application of a ventricular assist device as intra-aortic balloon pump (IABP), or prolonged ventilatory support due to any other reason rather than ventilatory derangements.

Patients were randomly allocated into 3 groups. **Group I (VCM)** 10 patients were subjected to manual ventilation using the vital capacity manoeuvre (VCM) just before weaning off the CPB and before resuming mechanical ventilation while lungs being deflated all through the CPB interval. VCM was achieved by manually ventilating lungs to an airway pressure of 40 cmH\(_2\)O for 15 seconds. In **group II (CPAP)** 10 patients were subjected to a CPAP of 10 cmH\(_2\)O all through CPB interval, then to resume mechanical ventilation directly without applying VCM. In **group**
III (PEEP) 10 patients were subjected to a PEEP of 7 cmH2O on resuming mechanical ventilation provided that hemodynamic parameters permit the application of such pressure. PEEP was continued throughout the postoperative period till weaning from mechanical ventilation down to 5 cmH2O before extubation.

Data collection of ventilatory parameters involved PO2 and PCO2, alveolar-arterial oxygen difference [P (A-a) DO2], shunt fraction and dynamic lung compliance (DLC). Shunt fraction was calculated based on the three-compartment model proposed by Riley and colleagues. Dynamic lung compliance (DLC) in ml/cmH2O was directly recorded from the anesthetic and ventilatory equipments. Data were collected at the following specified time points:

- Baseline reading after induction of anesthesia and before sternotomy.
- After chest closure
- 30 min after admission to ICU
- 4 hours post CPB
- 1 hour post-extubation

Times from ICU admission to extubation as well as the length of ICU stay were also recorded.

All patients received premedication in the form of lorazepam 2 mg orally at night of the operation in addition to intramuscular morphine sulphate 0.1 mg/kg 1 h prior to transfer to the operating room (OR). On receiving patient in OR, standard monitoring connected and a large bore peripheral venous as well as 20-gauge radial arterial cannulae were inserted. Induction followed with Sufentanil 1-1.5 μg/kg, Midazolam 0.05-0.1 mg/kg and Rocuronium 0.9 mg/kg. Patients were anesthetically maintained on total intravenous infusion of same inducing agents supplemented with Sevoflurane guided by the Bispectral index (Aspect industries, USA) monitoring in a range of reading 40-60. The lungs were mechanically ventilated with controlled mode delivering a tidal volume of 8 ml/kg while the respiratory rate was adjusted to keep end tidal CO2 of 32-36 mmHg. Ventilatory parameters were recorded through the
anesthesia machine ventilatory monitoring system (Datex-Ohmeda, Type). All ventilatory and oxygenation data were recorded on FiO2 of 0.5 and in closed chest to provide proper standardization.

Anticoagulation was induced with 300 units/kg of unfractionated heparin IV push before cannulation of the aorta where a celite-activated coagulation time of >400 sec must be achieved. The CPB circuit consisted of a membrane oxygenator (Medtronic cardiovascular, Brooklyn Park, MN), non-occlusive roller pump and arterial filter. The oxygenator was primed with 2000 ml of crystalloid solution, 100 ml mannitol 20%, NaHCO3 50 mEq, unfractionated heparin and solu-medrol 500 mg. Tepid technique was used while maintaining temperature at 32-33 C° with a pump flow rates of 2.4-2.8 L/min/m² to maintain a mean arterial pressure of 60-80 mmHg. Myocardial preservation was achieved through warm blood cardioplegia, the tepid CPB technique, while in other cases normothermic on pump beating heart technique was used for revascularisation.

During CPB, the lungs were deflated in group I (VCM) and group III (PEEP), while in group II (CPAP) a CPAP was adjusted to 10 cmH2O using the pop-off valve. On going weaning off the CPB, patients in group I resumed mechanical ventilation after application of VCM, patients in group II resumed mechanical ventilation directly without application of VCM, while patients in group III resumed mechanical ventilation with application of PEEP of 7 cmH2O. Ventilation was adjusted as pre-bypass parameters to be continued in the ICU until fulfilling the criteria for weaning from mechanical ventilation. That included appropriate sensorium, hemodynamic stability with CI of 2.1 L/min/m², minimal chest tube output, urine output >0.5 ml/kg/hr, temperature >35.5° C and stable ventilatory parameters with PO2 >60 mmHg, PCO2 <40 mmHg, pH 7.36-7.4 and SpO2 >93%. All this while maintained on pressure support ventilation for at least 15 min and maintaining stability.

Statistical Analysis

Data were analysed using a statistical software package (GraphPad InStat® version 3.00 for Windows, GraphPad Software Inc., San Diego,
California, USA). Data was expressed as mean (SD) unless otherwise indicated. One way analysis of variance (ANOVA) was used to compare the mean values between the studied groups. For significant finding a post-ANOVA pair wise comparisons of means was conducted. Chi-square test and student’s t-test were applied when appropriate. P values <0.05 were considered significant.

Results

Results showed that the three groups were comparable with regard to patient demography (Table 1), anesthetic requirements, and surgical management (Number of grafts and Total CPB time) (Table 2).

Table 1

<table>
<thead>
<tr>
<th>Patient Demography [mean (SD) or ratio]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Gender (Male/Female)</td>
</tr>
<tr>
<td>BW (Kg)</td>
</tr>
<tr>
<td>BSA (m²)</td>
</tr>
</tbody>
</table>

VCM = vital capacity manoeuvre; CPAP = continuous positive airway pressure; PEEP = positive end-expiratory pressure; n = number; P value ≤ 0.05 considered significant

Table 2

<table>
<thead>
<tr>
<th>Intraoperative Data [mean (SD)]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Total Anesthetic Doses</td>
</tr>
<tr>
<td>Midazolam (mg)</td>
</tr>
<tr>
<td>Sufentanil (µg)</td>
</tr>
<tr>
<td>Rocuronium (mg)</td>
</tr>
<tr>
<td>CPB Total Time (minutes)</td>
</tr>
<tr>
<td>Surgical Number of Grafts</td>
</tr>
</tbody>
</table>

VCM = vital capacity manoeuvre; CPAP = continuous positive airway pressure; PEEP = positive end-expiratory pressure; n = number; P value ≤ 0.05 considered significant
Regarding the mean values of PO₂ and PCO₂, results showed no statistical significance to the baseline values of intergroup differences at any time of recording (Table 3).

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Group I (VCM group) n = 10</th>
<th>Group II (CPAP group) n = 10</th>
<th>Group III (PEEP group) n = 10</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>224 (73)</td>
<td>231 (92)</td>
<td>236 (87)</td>
<td>0.950</td>
</tr>
<tr>
<td>2</td>
<td>212 (71)</td>
<td>216 (67)</td>
<td>227 (88)</td>
<td>0.900</td>
</tr>
<tr>
<td>3</td>
<td>196 (66)</td>
<td>235 (57)</td>
<td>219 (56)</td>
<td>0.356</td>
</tr>
<tr>
<td>4</td>
<td>217 (82)</td>
<td>202 (49)</td>
<td>234 (67)</td>
<td>0.575</td>
</tr>
<tr>
<td>5</td>
<td>186 (45)</td>
<td>197 (59)</td>
<td>182 (45)</td>
<td>0.788</td>
</tr>
<tr>
<td>PCO₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>34 (4.3)</td>
<td>36 (5.3)</td>
<td>38 (4.5)</td>
<td>0.185</td>
</tr>
<tr>
<td>2</td>
<td>39 (6.7)</td>
<td>41 (7.2)</td>
<td>41 (5.8)</td>
<td>0.738</td>
</tr>
<tr>
<td>3</td>
<td>41 (7.3)</td>
<td>38 (6.7)</td>
<td>39 (4.2)</td>
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</tr>
<tr>
<td>4</td>
<td>37 (6.2)</td>
<td>39 (6.6)</td>
<td>42 (5.5)</td>
<td>0.203</td>
</tr>
<tr>
<td>5</td>
<td>42 (5.4)</td>
<td>38 (4.3)</td>
<td>41 (5.1)</td>
<td>0.190</td>
</tr>
<tr>
<td>P (A-a) DO₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>228 (34)</td>
<td>231 (39)</td>
<td>224 (54)</td>
<td>0.936</td>
</tr>
<tr>
<td>2</td>
<td>248 (33)</td>
<td>239 (45)</td>
<td>231 (58)</td>
<td>0.718</td>
</tr>
<tr>
<td>3</td>
<td>253 (49)</td>
<td>228 (57)</td>
<td>229 (55)</td>
<td>0.509</td>
</tr>
<tr>
<td>4</td>
<td>251 (50)</td>
<td>241 (58)</td>
<td>206 (49)</td>
<td>0.151</td>
</tr>
<tr>
<td>5</td>
<td>245 (48)</td>
<td>223 (64)</td>
<td>228 (56)</td>
<td>0.662</td>
</tr>
<tr>
<td>Shunt %</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>3.4 (0.6)</td>
<td>3.1 (0.5)</td>
<td>2.9 (0.6)</td>
<td>0.161</td>
</tr>
<tr>
<td>2</td>
<td>4.1 (1.1)</td>
<td>3.9 (0.8)</td>
<td>3.2 (0.7)</td>
<td>0.074</td>
</tr>
<tr>
<td>3</td>
<td>4.7 (0.9)**</td>
<td>4.1 (1.0)***</td>
<td>3.7 (0.8)</td>
<td>0.061</td>
</tr>
<tr>
<td>4</td>
<td>4.5 (1.0)**</td>
<td>4.4 (0.9)****</td>
<td>3.8 (1.0)</td>
<td>0.235</td>
</tr>
<tr>
<td>5</td>
<td>---</td>
<td>---</td>
<td>---</td>
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</tr>
<tr>
<td>DLC</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>54 (7.9)</td>
<td>49 (8.1)</td>
<td>51 (7.3)</td>
<td>0.364</td>
</tr>
<tr>
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<td>51 (6.4)</td>
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<td>0.411</td>
</tr>
<tr>
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<td>46 (7.9)</td>
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<td>0.449</td>
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<td>50 (5.8)</td>
<td>46 (6.9)</td>
<td>47 (6.4)</td>
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</tr>
<tr>
<td>5</td>
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</tr>
</tbody>
</table>

VCM = vital capacity manoeuvre; CPAP = continuous positive airway pressure; PEEP = positive end-expiratory pressure; n = number; 1 = Baseline (after induction and before sternotomy); 2 = After Chest closure; 3 = 30 minutes after ICU Admission; 4 = 4 hours Post-bypass; 5 = 1 hour post-extubation; P (A-a) DO₂ = alveolo-arterial oxygen tension difference; DLC = Dynamic Lung Compliance; P value < 0.05 considered significant

* = P value < 0.05 compared with the baseline (unpaired t-test)

** = P value < 0.01 compared with the baseline (unpaired t-test)
The mean alveolar-arterial oxygen difference [P (A-a) DO₂], results revealed insignificant intergroup differences at any time point of assessment or to the baseline values (Table 3).

The calculated intrapulmonary shunt fraction, was significantly high in group I (VCM) and group 111 (PEEP) 30 minutes after ICU admission and at 4 hours post-bypass when compared to the baseline values (P <0.01, <0.05 respectively). In group II (CPAP) the mean shunt fraction increased significantly after chest closure compared with the baseline value (P <0.05). There was no significant intergroup difference at any time point of recording (P >0.05) (Table 3).

Regarding the DLC, the 3 studied groups showed insignificant differences whether to baseline values or with intergroup comparison at any definite point of recording (Table 3).

The postoperative parameters were comparable in the three studied groups with no significant statistical differences (Figure 1).

Fig. 1
Time to Extubation and Length of ICU stay (Hours)
Discussion

There is good evidence that early extubation is safe and well tolerated after cardiac surgery, while it requires identifying eligible patients and adapting both surgical and anesthetic management to serve this process\textsuperscript{7}. Ventilatory management providing optimum gas exchange parameters is crucial to achieve early extubation, especially when it was proved that impaired pulmonary gas exchange was found to be a major consequence after cardiac surgical procedures performed under the management of CPB\textsuperscript{1}.

Positive ventilatory pressure had been proposed to play a role in the improvement of gas exchange and explained by the reduction in lung water which in return provides a more compliant interstitial space allowing better gas exchange\textsuperscript{1}. This was supported by many clinical trials. One of which studied 14 patients, 7 subjected to CPAP during CPB, while the other control 7 patients, the lungs were kept deflated all through the CPB time. They demonstrated that application of CPAP 10 cmH\textsubscript{2}O during CPB provides better oxygenation and less shunt fraction than their control group\textsuperscript{3}. On the other hand, other trials failed to prove such effect of CPAP application during CPB. In one of the clinical studies they failed to demonstrate positive results with application of CPAP of 5 cmH\textsubscript{2}O during CPB\textsuperscript{8}. Also others found that low levels of CPAP applied during CPB did not improve the oxygenation or the mechanical ventilatory parameters\textsuperscript{9}.

While considering that the VCM which was proved to have a beneficial role in gas exchange and improvement in lung compliance, in an experimental study done on pigs models, demonstrated that VCM effectively prevents post-CPB atelectasis\textsuperscript{10,11}. Also in another clinical trial on humans undergoing cardiac surgical procedure comparing the VCM to a control group where no re-expansion manoeuvre was used, their results showed a significant difference in ventilatory parameters specially in shunt fraction\textsuperscript{4}.

In the present study, comparison was made between the application of both VCM and CPAP, and our results showed no statistical significant
differences in the ventilatory parameters between the two positive pressure ventilatory methods applied, apart from the increase in the shunt fraction which was significantly higher than the baseline in both groups, yet it was within the normal physiological range (2-5%)\(^1\) thus with no clinical significance.

The influence of the application of PEEP after CPB has not been previously studied in humans undergoing cardiac surgery, probably due to the fear of its deleterious hemodynamic effects in such a critical period. That was the objective in the present study of applying a minimal pressure of 7 cmH\(_2\)O in a trial to fasten the slow re-expansion of alveoli in the post-bypass period and to compare its ventilatory effects with other ventilatory patterns being applied. PEEP when applied was readily tolerated by the patients and showed a comparable effects on the ventilatory parameters as compared to the other two studied groups.

Considering the postoperative parameters recorded, the studied groups were comparable regarding the extubation time and length of ICU stay. From the ventilatory point of view, their parameters were maintained all through the postoperative period, thus fulfilling the criteria for extubation and weaning from mechanical ventilation was conducted.

The present study showed that different ventilatory patterns could be applied to maintain lung functions all through the perioperative period. Comparison was done to the VCM as a ventilatory pattern being now the standard technique applied in patients ongoing weaning off CPB and before resuming mechanical ventilation.

Based on clinical evidence, a CPAP when applied all through, CPB time will eventually prohibit the conventional endotracheal suctioning before ongoing weaning off the CPB and thus may have a prophylactic role in preventing mechanical lobular and even lobar lung collapse. This suctioning manoeuvre when applied will alleviate all the beneficial effect of CPAP during CPB. On the other hand, application of PEEP in the post-bypass period may have undesirable hemodynamic effects in the immediate post-bypass period with its well known criticality from the hemodynamic point of view. Here, the VCM could be considered a safe
and practical positive pressure ventilatory method if being applied cautiously so that over inflation of the lungs do not interrupt the course of the left internal mammary artery (LIMA) after being harvested and anastomosed to the native coronary vessel.

In conclusion, this study has shown that application of VCM at the end of CPB and before resuming mechanical ventilation gives comparable ventilatory parameters to the positive ventilatory pressure whether applied during (CPAP) or after (PEEP). Thus, the application of such manoeuvre will provide safe and reliable maintenance in gas exchange parameters of patients being subjected to CPB. The application of minimal PEEP in the post-bypass period in an attempt to help in alveolar recruitment and prevention of atelectasis still needs further clinical investigations.
References

MANAGEMENT OF PATIENTS WITH REPAIRED CONGENITAL HEART DISEASE

JOYCE JABIB

The population of children and adults who have undergone repair or palliation of congenital heart disease (CHD) is on the rise\(^1\). The advances in echocardiography, anesthesia, intensive care, and perhaps more importantly early and more definitive surgical intervention and improved surgical techniques, have increased the survival of babies born with complex cardiac anomalies into adulthood\(^2\).

In the year 2000, there were about 785,000 adult patients with congenital heart disease living in the U.S, the majority of them having undergone reparative cardiac surgery in infancy or childhood\(^3\). This population is likely to increase tremendously over the next few years as estimates predict and an annual addition of the 10,000 to 30,000 patients/year with doubling of survival rate in patients with complex physiology\(^4\).

As life expectancy of adults with CHD has dramatically improved, noncardiac medical and surgical issues typical of any adult population have become more prominent\(^5\). Over the next few years, more and more patients with repaired/palliated CHD are likely to be scheduled for noncardiac surgery. The anesthesiologist caring for these patients faces the challenge of dealing with the complications that may arise intra- or postoperatively.

McGowan emphasizes the importance of addressing the outcome and problems associated with specific CHD lesions as well as their repair in order to formulate rational perioperative management strategies. According to him, “the anesthesiologist caring for patients with

repaired/palliated CHD undergoing noncardiac surgery needs to have a complete understanding of the physiology of the lesion, the type and natural history of repair, and the likely interactions of all of these with the planned procedure.1

What is the outcome of repaired CHD?

Stark defines corrective surgery for CHD as that which achieves and maintains a normal cardiac function, results in normal life expectancy and requires no subsequent surgical or medical therapy4. Based on this, very few types of repairs are truly curative. These would include PDA ligation, early repair of isolated ASD or VSD1,5. All other forms of repair have the potential for residua and sequelae that can become progressive as patients grow older1.

Overview of common types of CHD

Congenital heart disease occurs in 6 to 8 out of every 1000 births5. Grossly, common defects discussed in this review include VSD, PDA, ASD, TOF, TGA, coarctation of the aorta and “single ventricle” defects (e.g. tricuspid atresia, hypoplastic left heart syndrome etc.).

Three physiological factors are important in determining the type of defect and the timing of surgical intervention for CHD6. Defects are classified according to the amount of oxygenated blood delivered to the systemic circulation (cyanotic vs. acyanotic), the amount of pulmonary blood flow (increased, normal or decreased), and the presence or absence of obstructive lesions6.

As such, acyanotic CHD can be further classified into two categories:

1) acyanotic disease with increased pulmonary blood flow (PBF) (namely left-to-right shunts such as ASD, VSD, PDA).

2) acyanotic CHD disease with normal blood flow (mainly obstructive lesions such coarctation of the aorta).

On the other hand, cyanotic CHD is also divided into defects with increased pulmonary blood flow (e.g. TGA, truncus arteriosus) vs. defects with decreased pulmonary blood flow (TOF, tricuspid atresia).
The significance of such a classification is to emphasize the hemodynamic abnormalities associated with each type of lesions and to understand the rationale of surgical repair\(^6\).

**Acyanotic CHD with increased PBF (left-to-right shunt)**

Shunt lesions whether intracardiac (ASD, VSD) or extracardiac (PDA) operate by the same principle. Blood flow through the shunt depends on the size of the shunt and the relative resistances on either side of the shunt\(^7\). Grossly, if defect is large enough not to impede blood flow (i.e. non-restrictive defect), then the main determinant of the degree of shunting across this defect is the resistance on both sides of the shunt\(^8\). If the defect opening is small (i.e. restrictive defect), then the degree of shunting will depend more on the size of the defect and less on the resistance across the defect\(^8\). The drop in PVR occurring shortly after birth creates the driving force for the left-to-right shunting of blood across the defect.

1 - **Ventricular Septal Defect (VSD)**

Whether located in muscular or membranous portion of the septum, the hemodynamics associated with VSD depend mostly on the size of the defect. Small defects account for about 85% of all VSDs\(^9\). The extent of shunting is limited by the size of the defect therefore the blood flow across the defect is minimal and decreases with time. Most of these defects close spontaneously (90% close by the age of 6 years)\(^9\) with those in the muscular portion of the interventricular septum closing sooner than those in the membranous part\(^6\). Children with small defects are usually followed up with echocardiography until the defect closes.

Larger non-restrictive VSDs become more problematic as there is more blood shunted across the defect. The physiology of the shunting results in volume overload of the RV, RA and the pulmonary circulation that is transmitted to the left side of the heart as well\(^8\). Initially, the increased blood volume returning to the LV increases the stroke volume (Frank-Starling mechanism), however with time the volume overload can
lead to LV dilatation, systolic dysfunction and symptoms of left-sided heart failure as early as 2-3 months of age (failure to thrive, tachypnea, lower respiratory tract infections)\textsuperscript{3,6}.

The volume overload of the pulmonary vasculature leads to increased PAP and pulmonary arteriolar hypertrophy with time with PHTN setting in as early as the age of 2\textsuperscript{3}. The initial medial hypertrophy of the pulmonary arterioles, intimal proliferation and fibrosis, and occlusion of capillaries and small arterioles are potentially reversible. As the disease progresses, the more advanced morphologic changes (necrotizing arteritis and plexiform lesions) are irreversible; resulting in obliteration of the pulmonary vascular bed, leading to increased pulmonary vascular resistance\textsuperscript{6}. The flow across the VSD decreases as PVR increases; once the PVR exceeds the SVR, reversal of flow occurs (Eisenmenger syndrome)\textsuperscript{34}. When the shunt reverses (that is, when right-to-left shunting occurs), cyanosis and erythrocytosis develop.

Eventually, most patients with the Eisenmenger syndrome have one or more of the following:

1) symptoms of a low cardiac output (such as dyspnea on exertion, fatigue, or syncope).

2) subtle neurologic abnormalities (such as headache, dizziness, or visual disturbances) due to erythrocytosis and hyperviscosity.

3) symptoms of congestive heart failure\textsuperscript{11}.

In addition, arrhythmias (atrial fibrillation/flutter, ventricular tachycardia) and hemoptysis (secondary to bleeding bronchial vessels or pulmonary infarction) are common\textsuperscript{3,11}. Both arrhythmias and massive hemoptysis account for most of the sudden death in patients with Eisenmenger syndrome\textsuperscript{31}. Cerebrovascular accidents frequently occur mainly because of hyperviscosity but they can also be the result of paradoxical emboli\textsuperscript{13}. Renal dysfunction is also a common problem; more than one third of adult patients with cyanotic congenital heart disease have evidence of glomerulopathy (proteinuria; elevated serum creatinine concentration; or abnormal urinalysis results with hematuria, sterile pyuria, or casts)\textsuperscript{12}. Renal dysfunction is mainly the result of diminished
renal blood flow secondary to erythrocytosis and as such the incidence of renal abnormalities increases with the degree and duration of cyanosis and accompanying erythrocytosis11.

**Surgical repair of VSD**

Surgical repair of VSD is usually done electively between 3-9 months of age3. Surgery is performed before 2 because of increased risk of irreversible PHTN after this age3. Surgical repair of isolated VSD is done using CPB to close the defect by direct sutures or patching3. The closure is usually performed through the right atrium or pulmonary valve to avoid a ventriculotomy6. Transcatheter closure of VSD is less commonly used3.

**Postoperative sequelae**

**Early repair:** Most patients who undergo repair do well8. For patients with good left ventricular function prior to surgery, life expectancy after surgical correction is close to normal9. Problems that may arise after early repair may be due to any residual defect (especially with multiple VSDs), aortic regurgitation after repair of perimembranous VSD, LVOT or RVOT obstruction secondary to patching, heart block requiring temporary or long term pacemaker support5.

**Late repair:** Patients who had late repair of VSD deserve special consideration as they are at increased risk of LV dysfunction and decreased EF long after repair15. Residual hemodynamic problems occur when repair is delayed to late childhood because by then the change in PVR has become irreversible. After closure of VSD, the RV is forced to pump against an increased PVR. It must suddenly change from pumping against a volume load to support a pressure load5. Similarly, the LV must pump a smaller volume load against SVR without having the advantage of pumping any extra volume through the VSD and into the lower pressure right-sided circulation8. The LV function may be further compromised if the RV is significantly dilated with the interventricular septum shifting into the LV8. The altered LV geometry further impairs LV ejection and thus decreases CO. It is therefore important for any patient with known late repair to be evaluated before any major procedure to assess LV
function and EF.

Patients with Eisenmenger syndrome: These patients are particularly vulnerable to the alterations in hemodynamics associated with surgery or anesthesia. Any minor decrease in SVR can increase right-to-left shunting and can therefore precipitate cardiovascular collapse.

Because noncardiac surgery in patients with the Eisenmenger syndrome is associated with a high perioperative mortality rate it should be avoided, if possible. When surgery is necessary, a number of peri, intra and postoperative considerations should be followed. Prolonged fasting should be avoided perioperatively. The use of antibiotic prophylaxis of endocarditis is recommended depending on the type of surgery.

The choice of general or epidural-spinal anesthesia is controversial. The latter technique causes sympathetic blockade resulting in systemic arterial vasodilation and hypotension. On the other hand, many of the agents used for induction and maintenance of general anesthesia depress myocardial function and reduce systemic vascular resistance.

Intraoperative monitoring of BP is critical. Systemic arterial hypotension should be treated aggressively (with methoxamine or phenylephrine for example) or intravenous volume replacement if the patient is hypovolemic. Blood loss should be minimized and excessive bleeding should be promptly treated with blood products. In addition all IV lines used intraoperatively should be equipped with air filters to prevent the occurrence of paradoxical air embolism.

Patients with Eisenmenger syndrome are at increased risk for postoperative arrhythmias and DVT. It is preferable to closely observe postoperative patients in an intensive care unit setting. Early ambulation should be encouraged to prevent thromboembolism and subcutaneous heparin should be considered when prolonged immobilization is anticipated.

2 - Atrial Septal Defect (ASD)

The physiology of ASD is that of left-to-right shunting with volume
overload of the RA and RV. The extent of shunting is not as significant as compared to shunting across VSD mainly because the atrial system is a lower pressure system. In ASD, signs of congestive heart failure are late manifestations therefore patients may go undetected until later in childhood or even adulthood.

Surgical repair for ASD is electively done between 2-5 years of age as a prophylaxis for late pulmonary HTN, paradoxic emboli and arrhythmias.8

Device closure of secundum ASD can be performed percutaneously under fluoroscopy and TEE or with intracardiac echo guidance15. Other types of ASDs have to be closed by patching or surgical suturing using CPB (via a median sternotomy or right anterior thoracotomy)6.

Postoperative sequelae

In one of the earliest long-term follow-up studies on patients with repaired ASD, Murphy et al. found that patients with ASDs repaired at ages less than 25 had similar survival rates compared to age-matched control subjects16.

However patients who underwent repair when they were older than 25 years old had decreased long-term survival compared to control subjects16. Decreased survival is probably related to the long-standing deleterious effects of volume overload on the right-sided cardiac chambers and the pulmonary vasculature including development of PHTN, atrial enlargement predisposing patients to atrial arrhythmias (atrial flutter and atrial fibrillation) and stroke secondary to atrial thrombosis6.

Acyanotic Congenital Heart Disease with Normal PBF

Coarctation of the aorta

The physiology of coarctation of the aorta consists of a pressure overload on the LV (secondary to increased afterload) leading to compensatory LV hypertrophy to sustain CO. Another type of
compensatory mechanism is the formation of collateral blood vessels in the intercostals arteries to supply blood to the descending aorta therefore bypassing the coarct site. The presence of such collaterals should be kept in mind when performing procedures such as epidural anesthesia in patients with a history of coarctation.

Another important consideration is that this type of CHD is associated with other defects such as bicuspid aortic valve and cerebral aneurysms in respectively 50% and 10% of patients.

*Surgical repair*

Repair for coarctation of the aorta is usually performed electively at 2 to 3 years of age. Timing of surgery is controversial because of the high recurrence rate in infants (up to 25%). After the age of 3, the risk of recurrence becomes theoretically less than 2%. Repair is done by either subclavian flap arterioplasty or coarctation segment resection with end-to-end anastomosis with prophylaxis needed for prevention of endarteritis.

*Postoperative sequelae*

Long-term follow-up of patients after surgical correction reveals an increased incidence of premature cardiovascular disease and death.

Patients with repaired coarctation can demonstrate recoarctation, aneurysms at the coarctation site, residual hypertension, stroke secondary to either cerebral aneurysm or bacterial endocarditis.

The prevalence of recoarctation reported in the literature varies from 7 to 60% depending on the definition of recoarctation, the length of follow-up and the age at surgery. For example, recoarctation was found to be more common with end-to-end anastomosis repair as compared to subclavian flap angioplasty.

Recoarctation is usually addressed with balloon dilatation if the obstruction is relatively localized. In the presence of a long-segment narrowing, surgical intervention may be necessary.

Aneurysm formation is also one of the recognized sequelae of coarct repair with a reported incidence of 2 to 27%. Aneurysms are particularly common after Dacron patch aortoplasty and usually occur in the segment
of the aorta opposite to the patch. Parikh et al. demonstrated aneurysmal formation in 5% of patients after Dacron patch repair but not after subclavian flap angioplasty or end-to-end anastomosis. It is very important that these higher risk patients get followed up after repair with Doppler ultrasound or MRI for aneurysmal formation or recoarctation.

Another possible complication of reparative surgery for coarctation is systemic hypertension in the absence of residual coarctation. The pathophysiologic mechanism underlying residual hypertension is not very well understood but is thought to be due to residual abnormal vascular reactivity in the arterial system. Some studies suggested increased risk of residual hypertension when reparative surgery is done at an older age, but more recent studies suggest that residual hemodynamic abnormalities are common even after early repair.

Patients with normal BP at rest can demonstrate systolic hypertension in response to physical exercise. The significance of exercise induced systolic hypertension is still unknown but is thought to contribute to the increased LV mass frequently seen in patients after surgery. In long-term follow-up studies, LV hypertrophy is seen in 25-33% of repaired coarct patients. It is by itself a predictor of future cardiovascular complications.

Other problems that might occur postoperatively include endarteritis at the coarct site with embolic manifestation usually restricted to the lower extremities. Any co-existent bicuspid aortic valve may become stenotic or regurgitant as patients grow older so periodic assessment of possible aortic valve disease is warranted even after successful reparative surgery.

### Cyanotic Congenital Heart Disease

#### 1 - Tetralogy of Fallot

Tetralogy of Fallot (TOF) is one of the most common cyanotic lesions in infancy. The functional problems in TOF are the presence of VSD, RV outflow tract obstruction (at valvular, infundibular or
pulmonary arterial level) and right-to-left shunting resulting in decreased PBF. The extent of right-to-left shunting depends mainly on the magnitude of the RV outflow tract obstruction as well as the SVR.

Surgical repair

Treatment of TOF has shifted from palliation with subsequent repair to early total repair. Symptomatic children are now repaired at any age, and elective surgical repair in asymptomatic infants is usually done during the first 6 months of life. Currently, earlier corrective surgery has allowed more than 85% of children with TOF to survive to adulthood.

Repair of TOF consists of right ventriculotomy, patch closure of VSD, resection of infundibular stenosis and patch augmentation of RVOT. If the pulmonary valve is too small, then the RV incision is extended across the pulmonary valve annulus and onto the pulmonary artery. Because of the common finding of a small annulus (especially in younger infants), repair often involves the placement of a transannular patch. Although the patch is effective in relieving obstruction, it distorts the pulmonary valve apparatus and pulmonary regurgitation inevitably occurs with time.

Thus, earlier repair has minimized the deleterious consequences of long-standing cyanosis but this is often at the expense of transannular patch enlargement of the RVOT, which may predispose patients for later complications due to pulmonary regurgitation.

Anatomical variants in coronary artery anatomy alter the surgical approach in patients with TOF. When an anomalous coronary artery crosses the RVOT making transection not feasible, an extracardiac conduit can be placed between the RV and PA bypassing the RVOT obstruction.

Postoperative sequelae

Most of the complications relate to abnormal RV loading and to problems associated with RVOT reconstruction. Progressive RV dysfunction, arrhythmias and sudden cardiac death are major problems after repair.
Progressive RV systolic dysfunction may be the result of many interplaying factors but in most cases it is the result of long-term volume overload secondary to pulmonary regurgitation (especially after transannular patch repair). Patients with RV dysfunction may be completely asymptomatic or can manifest with decreased exercise tolerance or even signs of right-sided heart failure.

Since RV dysfunction predisposes patients to increased cardiac morbidity and mortality (by increasing the risk of arrhythmias and sudden cardiac death), cardiac imaging namely echocardiography and MRI should be used before any major procedure to quantify the degree of RV dysfunction. Cardiac MRI has become particularly useful because it allows to assess RV function as well as pulmonary regurgitation and to image potential sites for RVOT obstruction. The value of MRI over echocardiography in the evaluation of the RV is becoming increasingly appreciated in complex CHD lesions (such as TOF, TGA) where the CO is greatly dependent on RV function.

Atrial and ventricular arrhythmias are common sequelae after TOF repair. Atrial arrhythmias may be present in up to one-third of patients after repair and are a major source of morbidity. Ventricular arrhythmias may occur early or years after repair. Factors such as chronic pulmonary regurgitation, RV dysfunction, RV scarring at the surgical incision site can lead to the development of arrhythmias. The incidence of ventricular arrhythmias (RBBB, complete heart block, PVBs) and non-sustained ventricular tachycardia on ambulatory Holter or exercise testing is considerable and increases with age. These types of arrhythmias do not predispose patients to develop sustained ventricular tachycardia. Sustained ventricular tachycardia are less prevalent than other types of arrhythmias but they are believed to be responsible for incidence of SCD in patients after repair.

There is little information in the medical literature concerning peroperative considerations for patients with repaired TOF. Because of the complexity of problems arising after repair, it is impossible to design an algorithm that fits all patients.
However in light of the physiology of the repair and its sequelae, some issues are important to address before any major procedure.

First, the degree of RV dysfunction needs to be assessed with consideration given to interventional catheterization for lesions amenable to improvement (e.g. RVOT or PA obstruction, residual VSD, ventricular arrhythmias).1

Second, the potential for positive-pressure ventilation to compromise CO (especially in patients with significant pulmonary regurgitation and RV dysfunction) should be recognized.2 By increasing intrathoracic pressure, positive-pressure ventilation increases RV afterload and therefore decreases RV filling leading to underfilling of the LV as well and decreased CO.1

Third, any increase in PVR especially in the setting of pulmonary regurgitation and RV dilation can compromise RV filling.1

For patients with repaired TOF undergoing surgery, it is very important to 1) maintain adequate contractility and filling volume of RV and 2) avoid fluctuations in HR, BP as the combination of tachycardia, hypotension, acidosis is particularly detrimental in these patients.1

2 - Transposition of the great arteries (TGA)

This defect, characterized by atrial-ventricular concordance with ventricular-arterial discordance, is one of the most common cyanotic lesions encountered in the newborn period.26 Because of the existence of two parallel circulations instead of the normal in series circulation, survival depends on intracardiac or extracardiac mixing of the two circulations.6

Surgical repair of TGA

Reparative surgery is usually done either in the neonatal period or during the first 6 months of life.5 Palliation with balloon atrial septostomy can be used to stabilize hemodynamically compromised infants before corrective surgery can be performed.3 Two reparative procedures exist: the atrial switch operation (Mustard or Senning) developed in the 1950’s and 1960’s replaced nowadays by the arterial switch repair adopted in the
1980's. However in the current adult population with repaired TGA, the atrial switch is still the most encountered type of procedure.

A) Atrial switch repair:

The atrial switch repair is an example of physiologic repair whereby the parallel circulation is transformed into a circulation in series. Blood is redirected at the atrial level using either baffles made of Dacron or pericardium (Mustard procedure) or atrial flaps (Senning procedure). As a result, systemic venous return is diverted through the mitral valve to the LV and out to the PA whereas the pulmonary venous return is diverted through the tricuspid valve into the RV and then into the aorta.

By virtue of this repair, the RV and tricuspid valve are left in series with the aorta and therefore the RV functions as the systemic ventricle supporting the systemic circulation.

Functional outcome of atrial switch repair

Patients with atrial switch repair have shortened life expectancy compared to the normal population (70-80% survival rate at 20 to 30 years' follow-up in one series of patients with Mustard repair).

The long-term prognosis for cardiac function is not good. The RV has a limited capacity to function as the systemic ventricle, therefore progressive deterioration of the RV function occurs with time often with concomitant tricuspid regurgitation (echocardiographic evidence of moderate to severe systemic RV dysfunction in up to 40% of patients on long-term follow-up). Progressive RV dysfunction along with tricuspid regurgitation lead to the development of signs and symptoms of right-sided heart failure. Even asymptomatic patients with Mustard repair were found to have decreased exercise tolerance (less increase in HR and blunted increase in SV with exercise as compared to control subjects). The importance of exercise challenge probably lies in demonstrating abnormal ongoing RV physiology in otherwise asymptomatic patients.

Arrhythmias also complicate the course of atrial switch repair for TGA. Sinus rhythm is found in only 35% of patients 10 years after surgery. Arrhythmias can be the result of the reparative surgery itself.
(septectomy/septostomy of the atrial septum with excision of one or more intermodal pathways)\(^5\) or can result from the progressive RV dysfunction resulting in atrial enlargement\(^1,5\). Significant arrhythmias include atrial flutter (occurring in 20% of patients by 20 years of age\(^3\)) and sinus node dysfunction mainly sick sinus node syndrome warranting occasionally pacemaker insertion\(^1\). Sudden cardiac death occurs in 10% of patients 8 to 10 years after atrial repair of TGA, possible because of arrhythmias and hemodynamic complications (mainly RV dysfunction)\(^27\).

Other problems associated with atrial repair include baffle obstruction with obstruction of the SVC return being the more common than either IVC obstruction or pulmonary venous obstruction\(^8\). Pulmonary venous return obstruction can lead to pulmonary edema acutely or pulmonary hypertension chronically\(^8\).

**B) Arterial switch repair:**

In contrast to the atrial switch, the arterial switch procedure is an anatomic reparative surgery whereby the arterial trunks (aorta and PA) are transected and reanastomosed with the contralateral root and the coronary arteries are excised and reimplanted into the proximal neoaorta\(^1,3\). The major advantages of this type of repair are the restoration of the LV as the systemic pump and the long-term maintenance of sinus rhythm mainly because there is no manipulation of the atrial septum\(^3\).

**Functional outcome of arterial switch repair**

Long-term follow-up on patients with arterial switch repair is lacking because most of these patients have not yet reached adulthood\(^3\). The currently available studies have so far shown good LV function and normal exercise capacity in patients with this type of repair\(^26,29\).

Recognized sequelae of arterial switch repair include supravalvular pulmonary or aortic stenosis at the anastomotic sites (which can be addressed by balloon angioplasty), neoaortic regurgitation as well as coronary occlusion\(^3\). So far, a 25-30% incidence of neoaortic regurgitation, usually trivial to mild, has been reported\(^1\). The development of severe regurgitation has been rare\(^1\). In addition, the significance of coronary ostial lesions found in 3-5% of patients on coronary
angiography is still unclear. Myocardial ischemia secondary to stenosis at the aortocoronary anastomosis has been identified by angiography or wall motion abnormalities on echocardiography. However no myocardial infarct has been reported yet. It remains to be determined by future studies whether neoaortic regurgitation or coronary ostial lesions will predispose patients to significant morbidity or mortality on long-term follow-up.

"Single Ventricle" CHD: the Fontan Physiology

The Fontan procedure is a palliative surgical procedure that directs systemic venous return to the pulmonary arteries without passing through a subpulmonary ventricle. It is usually performed in patients with a "functional single" ventricle such as patients with tricuspid atresia or hypoplastic left heart syndrome.

The initial Fontan procedure consisted of an anastomosis between the right atrial appendage and the pulmonary arteries. This type of repair was associated with right atrial dilatation with secondary arrhythmias and thrombosis. Nowadays, several modifications of this procedure exist. These include the modified Fontan procedure, fenestrated Fontan and cavopulmonary anastomosis (a.k.a. “partial Fontan procedures”)

1) Modified Fontan

When the total systemic return (of both SVC and IVC) is directed to the pulmonary arteries, the procedure is called modified Fontan procedure. In the modified Fontan, IVC blood flow is directed to the pulmonary arteries via either a lateral tunnel or an extracardiac conduit. The SVC itself is directly connected to the right and left pulmonary arteries. This surgical arrangement allows all the systemic venous return to passively enter the pulmonary circulation. With such a circuit, cardiac output becomes preload limited. Blood returning to the single ventricle depends on maintaining a pressure gradient between the systemic venous return, the pulmonary vasculature and the single ventricle. Patients with a modified Fontan circuit have higher than
normal RA pressure and systemic venous pressure both having an adverse effect on CO\(^9\).

Both the lateral tunnel circuit and the extracardiac conduit have been used to achieve a modified Fontan circuit. The lateral tunnel circuit was introduced in the mid 80’s and consists of connecting the IVC to the PA using a prosthetic baffle and a portion of the lateral atrial wall\(^9\). The main advantage of this circuit is that it has the potential to grow with the child therefore it can be created in children as young as 1 year\(^9\). Another important improvement compared to the classic Fontan is that this connection allows minimal amount of atrial tissue exposed to high pressure therefore decreasing the risk of future arrhythmias\(^8,20\).

The extracardiac conduit was introduced in the 1990’s and consists of a tube graft connecting the IVC to the PA. This circuit allows minimal suturing of the atrium and leaves the atrium at low pressure minimizing the risk of arrhythmias. The disadvantage of this circuit is that it does not have the potential to grow so it can only be offered in older patients\(^9\).

2) *Fenestrated Fontan*

The fenestrated Fontan consists of the same design as the modified Fontan, however a punch hole is placed in the tube graft connecting the IVC and SVC. The punch hole is supposed to create a right-to-left shunt allowing approximately 20% of the venous return to cross from the RA to the LA thereby increasing CO\(^8\).

3) *“Partial” Fontan (cavopulmonary anastomosis)*

In the “partial Fontan” technique, the SVC alone is anastomosed to the pulmonary arteries while the blood flow from the IVC enters the physiologic LA and mixes with pulmonary venous blood (thus creating a physiologic left-to-right shunt)\(^9\). The classic Glenn shunt is a cavopulmonary anastomosis connecting the SVC to the right PA\(^8\). The left PA is left separated from the right PA and from the SVC, therefore systemic venous return is directly only to the right lung\(^3,8\). A more preferred form of cavopulmonary anastomosis is the bidirectional Glenn shunt whereby the SVC is connected to both right and left PA’s\(^3,8\).
In both fenestrated Fontan and classic/bidirectional Glenn shunt, cardiac output is increased (secondary to left-to-right shunting) at the expense decreasing systemic oxygen saturation. By allowing part of the systemic venous return to bypass the pulmonary circulation both of these circuits result in lower levels of venous congestion. The advantages of the bidirectional Glenn shunt over the fenestrated Fontan consist in achieving lower IVC pressure (because the entire IVC blood return is dumped into the LA) with a larger increase in CO. This is usually at the expense of a greater degree of arterial desaturation and cyanosis.

In any type of “single ventricle” defect, performing a Fontan circulation at birth is not feasible. This is because the pulmonary vascular resistance is still increased for several weeks after birth. Furthermore caval veins and pulmonary arteries are usually too small for cavopulmonary anastomosis. Therefore, a staged approach is usually undertaken allowing the body to adapt progressively to the altered hemodynamic loads. Initially in the neonatal period, management is mainly focused on providing both adequate CO and well balanced yet limited blood flow to the pulmonary vasculature (via PA banding, BT shunt etc.). Once the pulmonary vasculature is reasonable developed (usually after age of 3 months), the cavopulmonary connection (mainly bidirectional Glenn shunt) is introduced. Because of the deleterious effects of long-term arterial desaturation and secondary cyanosis, the cavopulmonary anastomosis is converted at around 1 year of age to a modified Fontan circuit. A fenestrated Fontan can be performed as an intermediate stage before achieving a modified Fontan circuit.

**Physiology of Fontan circulation**

In all of its forms, the Fontan circulation operates by passive flow of the systemic venous return to the pulmonary vasculature and then to the single ventricle. As such, PBF and CO are the result of the pressure differential existing between the “upstream” component of the circuit (consisting of the caval veins and the PA) and the “downstream” component (the pulmonary veins/atrium/single ventricle system). The systemic venous pressure of an ideal Fontan circulation is approximately
10-15 mmHg and the pulmonary venous atrial (functional left atrium) pressure is approximately 5-10 mmHg; this allows a transpulmonary gradient driving pressure of 5-8 mmHg. Anything that affects this gradient might compromise the single ventricle filling and subsequently the CO.

Adequate flow in the upstream component of the circuit depends on 1) an unobstructed venous return from IVC and SVC, 2) adequate systemic venous return (i.e. preload), 3) patent anastomotic connections between the caval veins and pulmonary arteries, 4) low intrathoracic pressure.

At the level of the lungs and pulmonary circulation, Fontan physiology requires low PAP (<15-20 mmHg), low PVR, unobstructed pulmonary arterial/pulmonary venous flow and normal lung parenchyma. At the level of the single ventricle, CO is maintained by adequate ventricular filling, normal AV valve, adequate diastolic and systolic function and normal sinus rhythm. Small alterations in ventricular function (particularly diastolic function), circuit efficiency (e.g. increased PVR secondary to pneumonia) or the onset of arrhythmias can lead to decreased CO and symptomatic deterioration.

Functional outcome of the Fontan circulation

Arrhythmias: Arrhythmias (atrial flutter/fibrillation, sick sinus syndrome, sinus bradycardia) and heart block occur in more than 20% of patients by 10 years after surgery. Arrhythmias are more common in patients with older versions of the Fontan procedure whereby part of the atrial wall is incorporated into the circuit leading to progressive atrial dilatation and hypertrophy. Another possible cause could be the damage to the sinus node (or its arterial supply) associated with extensive atrial manipulation in older versions of the Fontan procedure. Recent data show a lower incidence of arrhythmias in patients with cavopulmonary anastomosis or modified Fontan procedure; however this may be partly due to the shorter length of follow-up.

Atrial flutter/fibrillation carries a significant morbidity and require medical therapy, ablation or at times conversion of the old Fontan circuit.
to an extracardiac cavopulmonary anastomosis\textsuperscript{1,3,30}. Sinus node dysfunction and complete heart block may require pacemaker insertion\textsuperscript{3}.

**Thromboembolic events**: The incidence of thromboembolic complications in the Fontan circuit varies from 6 to 25\%\textsuperscript{3}. Thrombus formation can be the result of atrial dilatation, supraventricular arrhythmias, systemic venous dilatation with blood stasis, the presence of prosthetic material in the circuit etc.\textsuperscript{3,30}. Patients with a Fontan physiology suffer from increased systemic venous pressure with secondary hepatic congestion. As such, they develop coagulation factor abnormalities seen in other types of chronic hepatic congestion namely protein C, protein S and antithrombin III deficiency\textsuperscript{30}. Other coagulation factor abnormalities have also been reported less consistently in the medical literature. The result is a “hypercoagulable” state that contributes to the increased incidence of thromboembolic events in Fontan patients (stroke, pulmonary emboli etc.) A particularly detrimental complication would be the development of multiple pulmonary microemboli leading to the progressive onset of obstructive pulmonary vascular disease with subsequent increase in PVR\textsuperscript{32}. There are no guidelines concerning how to use anticoagulation in Fontan patients. Patients with a history of arrhythmias, previous thromboembolic events can particularly benefit from anticoagulation\textsuperscript{3}.

**Protein-losing enteropathy**: Protein-losing enteropathy (PLE), characterized by loss of serum proteins into the gut, occurs in 4 to 13\% of patients after a Fontan procedure\textsuperscript{3}. PLE is thought to be the result of chronic state of venous congestion leading to the development of lymphatic telangiectasia with leakage of albumin, immunoglobulins, lymphocytes, chylomicrons into the gut\textsuperscript{3,30}. The clinical manifestations of PLE include generalized edema, pleural effusion, immunodeficiency, chronic diarrhea etc. The diagnosis of PLE is confirmed by finding an elevated alpha-1 antitrypsin stool clearance\textsuperscript{3}. The diagnosis of PLE is a poor prognostic factor in Fontan patients\textsuperscript{30}. The 5-year survival rate after diagnosis is approximately 46 to 59\%\textsuperscript{31,32}. Conservative therapy for PLE (high-protein, low-fat diet, albumin infusions, diuretics, afterload reducing agents) has a high failure rate\textsuperscript{330}. The majority of patients will
require modification of the Fontan circulation (e.g. creation of an atrial fenestration to decrease venous congestion); some patients may even require cardiac transplanatation\(^9\).

**Peri- intra- and postoperative considerations in Fontan patients**

For patients with a Fontan circulation undergoing noncardiac surgery, certain perioperative considerations should be kept in mind. First, assessment of the functional level of the cardiovascular system cannot be overemphasized. Echocardiography should be used to assess both ventricular function and the patency of circulation\(^1\). Some patients may even require a more invasive approach (catheterization, radiofrequency ablation)\(^1\).

The use of invasive monitoring depends on the individual patient and the type of surgery to be performed. Central venous cannulation offers the advantage of monitoring venous filling and PAP however it carries an increased risk of venous return impairment and the possibility for thromboembolic complications.

Intraoperatively, the main target would be to focus on maintaining adequate CO. Patients with a Fontan circulation have decreased compensatory mechanisms and even a slight compromise in CO can be disastrous. Effort should be made to ensure adequate preload, good ventricular filling and contractility while avoiding an increase in afterload\(^1\). Because of the passive nature of blood flow from the systemic veins to the pulmonary circulation, any increase in PVR can compromise ventricular filling and CO.

Therefore, it is very important to avoid any increase in PVR that might be precipitated by hypoxia, hypercarbia, acidosis, excessive mean airway pressure, compression of the lung by pleural effusion etc\(^8\). Positive-pressure ventilation at relatively high lung volume can increase PVR. Positive-pressure ventilation can compromise the pulmonary blood flow by increasing PA pressure mainly by transmission of increased intrathoracic pressure but also by compression of pulmonary vasculature secondary to alveolar distention\(^7\).

A postoperative complication of surgery, usually occurring in older
Fontan patients, is end-organ dysfunction (namely liver and kidneys)\textsuperscript{1}. Organ perfusion, already compromised because of limited CO, can further deteriorate after surgery (possibly secondary to anesthetics or intraoperative blood loss)\textsuperscript{1}. The risk of thromboembolic complication after surgery can be decreased by using subcutaneous heparin or low molecular weight heparin along with adequate hydration and early ambulation\textsuperscript{1}.

**Conclusion**

The increase in the population of adults with repaired congenital heart disease over the past years has put forth new issues pertaining to the problems and complications ongoing after reparative surgery. This review, although by no means comprehensive, deals with some of the common ongoing problems in these patients that need to be addressed before any type of major elective surgery.

**Acknowledgement:** I would like to thank Dr. Anis Banaka for his support patience and mostly for allowing me to do this article.

**Abbreviations and acronyms**

- PDA: Patent ductus arteriosus
- ASD: Atrial septal defect
- VSD: Ventricular septal defect
- TOF: Tetralogy of Fallot
- TGA: Transposition of the great arteries
- PVR: Pulmonary vascular resistance
- SVR: Systemic vascular resistance
- RA: Right atrium/atrial
- RV: Right ventricle/ventricular
- LA: Left atrium/atrial
- LV: Left ventricle/ventricular
- AV: Atrioventricular
PBF: Pulmonary blood flow
HTN: Hypertension
PHTN: Pulmonary hypertension
PA: Pulmonary artery/arterial
PV: Pulmonary vein/venous
PAP: Pulmonary artery pressure
CBP: Cardiopulmonary bypass
LVOT/RVOT: Left/right ventricular outflow tract
BP: Blood pressure
TEE: Transesophageal echocardiography
SVC: Superior vena cava
IVC: Inferior vena cava
References

PULMONARY HYPERTENSION AND ANESTHESIA

ROLAND N. KADDOUM*, KAMAL MUBARAK **
AND ELIE JOSEPH CHIDIAC***

Introduction

Pulmonary circulation is a high flow, low resistance circuit capable of accommodating the entire right ventricular output at one-fifth the pressure of the systemic circulation. This is due to the higher compliance of the pulmonary circulation compared to the systemic circulation. Normal pulmonary arterial pressure (PAP) is 18-30/4-14 mmHg, and normal mean pulmonary arterial pressure (mPAP) is 12-16 mmHg.

Pulmonary hypertension can be defined by echocardiography or by cardiac catheterization. Pulmonary hypertension is suspected when systolic pulmonary arterial pressure is >40 mmHg by echocardiography (2-58). It is confirmed by cardiac catheterization when mPAP > 25 mmHg at rest or >30 mmHg with exercise^1. Pulmonary arterial hypertension (PAH) is defined as:

1 – Pulmonary hypertension.
2 – Pulmonary capillary wedge pressure PCWP < 15 mmHg.
3 – Pulmonary vascular resistance PVR > 3 woods units (240 dynes. sec. cm⁻⁵).

Since the diagnosis requires measurement of PCWP and PVR, a cardiac catheterization is required to make the diagnosis.

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Pulmonary arterial hypertension is a very serious disease. Survival in untreated PAH is 2-3 years.

Traditionally, pulmonary hypertension had been classified as primary or secondary. The classification proposed by the World Health Organization symposium in 1998 was replaced by the 2003 Venice Clinical Classification of Pulmonary Hypertension\(^2\). (Table 1)

*Classification does not include pulmonary hypertension due to end-stage renal disease.*
While the prevalence of IPAH is 1-2 cases per million per year, it is 25 to 50 per million per year among anorexigen users, such as fenfluramine, 6 to 60% in scleroderma, 4 to 14% in lupus, 21% in rheumatoid arthritis, 20-40% in sickle cell disease, and 0.5% in HIV patients. Pulmonary hypertension is found surprisingly in 40% of hemodialysed patients.

Fig. 1  

Clinical Manifestations of Pulmonary Hypertension

Symptoms
- Progressive onset of exertional dyspnea (60%)
- Fatigue (19%)
- Chest pain or discomfort (17%)
- Dizziness and light-headedness. There may be a history of near-syncope or syncope (13%)
- Raynaud’s phenomenon (10%)
- Palpitation (5%)
- Ortner’s syndrome: hoarseness from compression of the left recurrent laryngeal nerve by an enlarged pulmonary artery (<1%)

Signs
- Loud P2 (93%)
- Tricuspid regurgitation murmur (40%)
- Right ventricular heave
- Jugular venous distension with prominent “a” wave
- Graham Steell’s murmur: diastolic pulmonary regurgitation murmur best heard at the left upper sternal border (13%)
- Signs of right heart failure including S3 gallop, “v” wave in central venous pressure tracing, hepatojugular reflux, peripheral edema, and ascites.
- Cutaneous telangiectasia

**Occurrence of pulmonary hypertension during anesthesia**

- Thromboembolism – Thrombectomy of deep veins, pregnancy, childbirth
- CO₂ embolism – Laparoscopy
- Air embolism – Surgery with patient in sitting position (e.g., neurosurgery)
- Bone cement – Orthopedics
- Protamine – Cardiac surgery
- Extracorporeal circulation – Cardiac surgery
- Ischemia – reperfusion syndrome – Clamping/declamping of the abdominal aorta (e.g., liver transplantation)
- Loss of lung vessels – Pneumonectomy

**Recommended tests before anesthesia in patients with pulmonary hypertension**

1. Electrocardiography: showing tall P wave in lead II, right axis deviation.
2. Chest radiograph: showing prominent pulmonary artery. (Fig. 2)
4. Echocardiography: information obtained includes size of right heart (dilation or hypertrophy), tricuspid regurgitation, myocardial function, shift of intravenous septum, patency of foramen ovale, estimation of pulmonary pressure, left heart function.
5. Cardiac catheterization: information obtained includes pulmonary pressure, cardiac output, response to vasodilators, patency of foramen ovale, status of coronary circulation.
Challenge to the anesthesiologist

Limitations of the gold standard test: echocardiography

Echocardiography estimates systolic pulmonary artery pressure from the velocity of tricuspid regurgitation found during the test, using the modified Bernoulli equation:

\[ \text{SPAP} = (4 \times \text{TR}^2) + \text{RAP} \]

Where SPAP = systolic pulmonary artery pressure; TR = tricuspid regurgitation jet velocity; RAP = right atrial pressure.

If tricuspid regurgitation is not detected during the test, the systolic pulmonary artery pressure cannot be estimated. Echocardiography
identifies TR in 80% of patients when systolic PAP > 35 mmHg by catheterization, and in 95% of patients when systolic PAP > 50 mmHg by catheterization. Thus, only a small number of patients with pulmonary hypertension can be missed by echocardiography. This makes echocardiography a very useful screening tool. The mean PAP can be calculated from systolic PAP by using the formula: $MPAP = 0.61 \times SPAP + 2 \times mmHg$.

Another issue is that the correlation of mean pulmonary arterial pressure to disease severity is not straightforward. Lower pulmonary artery pressure does not necessarily indicate improvement of the pulmonary hypertension, on the contrary, lower PAP may reflect worsening of the disease (Figure 3). This could be explained by the following:

$$PVR = (MPAP - PCWP)/CO, \text{ thus } MPAP - PCWP = PVR \times CO$$

Fig 3
Effects of Progression of Pulmonary Hypertension

With progression of the disease, the PVR increases and CO decreases by a larger amount. The net product (CO X PVR) may be decreased, resulting in lower PAP. For this reason, the severity of pulmonary arterial hypertension is better determined by functional assessment. The New York Heart Association (NYHA) classification of dyspnea has been
modified by the World Health Organization (WHO) to categorize PH by the severity of symptoms, which, unlike pulmonary arterial pressure, correlates well with survival. Even with epoprostenol treatment, functional class III patients have a survival of 60% at 7 years compared with less than 20% for class IV patients.

**WHO Classification of Pulmonary Hypertension Correlated with Symptoms**

Class I: Patients with pulmonary hypertension but without limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.

Class II: Patients with pulmonary hypertension resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.

Class III: Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.

Class IV: Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea or fatigue may be present even at rest. Discomfort increases with any physical activity.

**Anesthetic Considerations**

*Preoperative Medications*

Maintain all pulmonary vasodilators, such as intravenous or inhaled prostacyclin, calcium channel blockers, phosphodiesterase-5 inhibitors (sildenafil, dipyridamole), endothelin receptor antagonists (bosentan), and oxygen.

If pulmonary hypertension has been discovered in the immediate
preoperative period and if the surgery cannot be delayed, a treatment with sildenafil (20-25 mg 3 times daily) and should be started as soon as possible.

Short acting anticoagulant like heparin should replace indirect anticoagulant until the surgical procedure.

Premedication

Slight sedation (midazolam) is allowed as long as respiratory acidosis is not induced.

Induction

Opioids, such as fentanyl, alfentanil, sufentanil, and remifentanil, should be used at a dose to block the cardiorespiratory response of intubation. They have no direct vascular effect on pulmonary vessels.

Lidocaine, 1 mg/kg, can also suppress the response to intubation.

Propofol, 1-2 mg/kg; pentothal, 1-2 mg/kg; or etomidate, 0.2-0.4 mg/kg, may be used.

Depolarizing or nondepolarizing muscle relaxants can be used.

Maintenance

Volatile anesthetics, such as isoflurane, desflurane, or sevoflurane, can be administered (isoflurane has been the most commonly used).

Opioids should be maintained at a surgical analgesic level.

Muscle relaxation should be maintained.

Monitoring

Arterial line and CVP should be placed for every patient with pulmonary hypertension. Swan Ganz and/or TEE recommended in low cardiac output states.
Postoperative treatment

Hospitalization in an intensive care unit. Optimal analgesia with continuous epidural, regional block, or parenteral opioids.

CVP _central venous pressure; TEE _transesophageal echocardiography.

Maintenance of Cardiac Output

The main challenge to the anesthesiologist is to maintain good cardiac output and oxygenation in patients with known pulmonary hypertension. Acute increase in mean PAP above approximately 40 mmHg results in a significant decrease in RVEF even in the presence of a normal RV contractility. In the presence of deceased RV contractility, the RV is even more susceptible to acute increases in afterload. In chronic pulmonary hypertension, increases in PVR gradually worsens right ventricular failure. The ejection fraction of the right ventricle is also gradually reduced, thus, the volume available for left ventricular filling is decreased. A dilating RV leads to left ventricular septal bowing and reduces left ventricular volume in early diastole and impair left ventricular filling in the most important phase of rapid filling. A dilated right atrium can shift the interatrial septum and compress the left atrium, reducing LV and diastolic volume.

The RV normally receives coronary blood flow in both systole and diastole. The continuous pressure gradient between the aorta and the RV (coronary perfusion pressure) is responsible for the coronary blood flow to the RV free wall during systole and diastole. Systemic hypotension or increased RV pressure results in a decreased RV coronary perfusion pressure, which leads to ischemia and decreased performance of the RV.

Vlahakes et al showed that the right heart performance is directly related to systemic pressure during pulmonary hypertension, and concluded that two important principles emerged in the management of right heart failure: First, RV afterload must be reduced and second, systemic pressure must be maintained or increased.
The anesthesiologist should then keep in mind that maintaining blood pressure alone is not enough for hemodynamic stability. While adequate BP may insure coronary and cerebral perfusion (autoregulation), it does not insure renal and mesenteric perfusion. Renal and mesenteric perfusion is pressure as well as CO dependent. So raising BP with pressors will increase vascular resistance rather than CO and may impair gut and renal perfusion.\(^17\)

\[
\text{MAP} = (\text{SVR} \times \text{CO}) + \text{CVP}
\]

Because invasive monitoring of BP is more common than CO monitoring, this probably explains why hemodynamic instability is most often recognized as hypotension, rather than low CO. Clinical recognition of low CO in the absence of hypotension can be difficult. Urine output, long regarded as an indicator of adequate organ perfusion, is actually not a very reliable indicator in patients who may have SIADH, or who received diuretics. Toe temperature may be more useful, and studies suggested that patients cannot be in cardiogenic shock if they have warm toes.\(^18,19\) Acid-base status can be misleading given the numerous causes of metabolic acidosis. Direct measurement of lactate is useful\(^20\). Normal lactate is fairly specific for adequate perfusion. High lactate can be due to hypoperfusion, sepsis, hypermetabolic states or hepatic dysfunction.

Because hypotension could be detrimental during anesthesia, it is the anesthesiologist priority to stay vigilant and correct hypotension when it presents.

\[
\text{SVR} = (\text{MAP} - \text{CVP})/\text{CO}
\]

\[
\text{MAP} = (\text{SVR} \times \text{CO}) + \text{CVP}
\]

This formula suggests three etiologies leading to hypotension:

1. Hypotension due to vasodilation (decreased SVR).
2. Hypotension due to low CO.
3. Hypotension due to hypovolemia (low CVP).

However, blood pressure could be normal (normal MAP) in the presence of low CO and increased SVR. This possibility can be seen in patients with pulmonary hypertension and is difficult to detect, unless
measurement of CO throughout the surgery is performed. Knowing that normal blood pressure does not guarantee normal CO, every effort should be directed at maintaining normal values of both parameters, especially in patients with known or suspected pulmonary hypertension. In these patients, arterial blood monitoring is advised, with the use of swan Ganz, or TEE.

Recently, another monitor was introduced to the operating room. The non invasive cardiac output monitor (NICO) uses the modified Fick equation to monitor cardiac output. Continuous blood pressure monitoring can be monitored noninvasively by connecting the loop of the NICO monitor to the ETT.

**Treatment of Low CO**

\[
PVR = \frac{(MPAP - PCWP)}{CO} \Rightarrow CO = \frac{(MPAP - PCWP)}{PVR}
\]

Once cause of low CO in pulmonary hypertension is increased PVR. Decreasing PVR in this population will help in maintaining good hemodynamic stability.

- Avoid hyper and hypoinflation: the U shape of the curve (Figure 4) relating lung volumes and PVR, is the contribution of intra and extralveolar vessels. PVR is minimal at functional residual capacity and increased with hyper and hypoinflation.
- Hyperoxgenation: in contrast to the systemic arteries, pulmonary vessels constrict with hypoxia and relax with hyperoxia.
- Hyperventilation: hypcapnia decreases PVR (PaCO₂ 30-35 mmHg).
- Correction of metabolic acidosis (PH > 7.4).
Fig. 4
Relationship between lung volume and pulmonary vascular resistance.

PVR = pulmonary vascular resistance. RV = residual volume. FRC = functional residual capacity.
TLC = total lung capacity.

Drugs used by anesthesiologists

Drugs that increase the formation of camp or cGMP produce vasodilation. Drugs that increase camp or cGMP are: nitric oxide, nitroglycerine, nitroprusside, PGE1, PG12 and beta2 agonists. Drugs that inhibit camp and cGMP degradation also produce vasodilation. Phosphodiesterase is the enzyme responsible of camp and cGMP breakdown. Drugs that inhibit this enzyme produce vasodilation. Phosphodiesterase inhibitors are: amrinone, milrinone, Sildenafil (Viagra).

Treatment of Pulmonary Hypertension during Surgery

1. Inhaled nitric oxide (NO): 20-40 ppm. Potent, rapidly acting and selective pulmonary vasodilator. it activates the enzyme guanylate
cyclase, which results in increased levels of cGMP in smooth muscle and decreases PVR and pulmonary pressure without affecting systemic vascular resistance. Nitric oxide is quickly inactivated by hemoglobin, forming methemoglobin, nitrate and nitrite ions. An important advantage of inhaled nitric oxide is that it reduces ventilation/perfusion (V/Q) mismatch (figure 5). Inhalation anesthetics inhibit hypoxic pulmonary vasoconstriction, thus blood is not shifted away from the nonfunctional alveolus, and V/Q mismatch is high. The use of nitric oxide will shift blood from the nonfunctional alveolus to the functional one, reducing shunting of blood.

2 - Milrinone/Amrinone (phosphodiesterase III inhibitor)\textsuperscript{26,27}: 50 mcg/kg bolus of milrinone followed by a perfusion of 0.5-0.75 mcg/kg/min. It is a phosphodiesterase III inhibitor (enzyme responsible of breakdown of camp/cGMP), avoids stimulation of downregulated or desensitized beta-receptors, which may be commonly seen in heart failure patients managed with long term dobutamine therapy. Beta agonist can be combined with phosphodiesterase inhibitor to produce synergistic effect via two separate mechanisms.

3 - Dipyridamole\textsuperscript{28}: 0.2-0.6 mg/kg intravenously over 15 min; to be repeated every 12 hours. 228-232 is used to treat pulmonary hypertension. It inhibits phosphodiesterase V and cGMP degradation. It also blocks adenosine cellular reuptake, leading to adenosine accumulation which results in dilation of coronary, systemic and pulmonary arteries.

4 - Inhaled prostacyclin or iloprost\textsuperscript{29}: Two modalities of application 1. Intermittent administration: 50 mcg is diluted in 50 ml saline and nebulized in 15 min, which aerosolizes a dose between 14 and 17 mcg. This treatment must be repeated every hour. 2 Continuous administration at a concentration of 50 ng/kg/min.

5 - Prostaglandin E1 (alprostadyl) and prostacyclin (PGI2)\textsuperscript{30}: potent pulmonary vasodilators. They activate adenylate cyclase to increase camp. After IV infusion, prostaglandin E1 is almost completely cleared from the circulation during the first pass through the lungs. Prostacyclin also has a short half life, but is metabolized in the liver.
Prostacyclin, 1.5 mg, can be dissolved in 100 ml sterile glycine buffer (final concentration, 15 mcg/ml); the drug is administered by means of an inline nebulizer connected to the inspiratory line. If no nebulizing device is available, prostacyclin can be infused intravenously at a dose between 2 and 10 ng/kg/min.

These medications should be weaned slowly after the pulmonary hemodynamic response in the postoperative period.

Epinephrine and norepinephrine\(^3\) have been used to treat persistent systemic hypertension; norepinephrine has the advantages of being both a vasoconstrictor and a positive inotropic agent. This medication should be titrated according to the clinical response.

**6 - Nitroglycerine**\(^3\): is a nitric oxide (NO) donor that has the same mechanism of action as inhaled NO via the cGMP pathway.

**7 - Dobutamine**\(^3\): is a beta agonist. It stimulates cyclic adenosine monophosphate (cAMP). It may induce arrhythmias and increase oxygen demand.

**8 - Isoproterenol**\(^3\): nonselective beta agonist that causes pulmonary and peripheral vasodilatation. It should be gradually reduced because PVR may return quickly to elevated baseline levels after discontinuation of this drug.

---

**Fig 5**

*Inhaled nitric oxide shifting blood from the nonfunctional alveolus (left) to the functional alveolus (right), thus decreasing shunting of blood.*
Postoperative Treatment of Pulmonary Hypertension

1 – **Viagra (sildenafil)**: inhibit phosphodiesterase type 5 which is responsible for degradation of cGMP.

2 – **Bosentan**: Blocks the binding of endothelin-1 at both endothelin receptor. The usual dose is to start at 62.5 mg po bid for 4 weeks and increase to 125 mg bid for maintenance.

   CVP _central venous pressure; ppm _parts per million.
References

PARENTAL SATISFACTION WITH PEDIATRIC DAY CASE SURGERY

I. AYDIN ERDEN, A. GULSUN PAMUK, TURGAY OCAL and ULKU AYPAR

Abstract

Background and aims: Children make excellent candidates for day case surgery. Satisfaction is an important measure of the outcome. The aim of this study was to establish the degree of parental satisfaction with day-case surgery for their children.

Materials and Methods: Parents of one hundred children were questioned. They were asked to answer questions on their level of satisfaction in several areas; communication with doctors (surgeon and anaesthesiologist), physical conditions, staff’s care, patients’ problems and 2 open ended questions.

Results: Parents were most satisfied with nursing care and most dissatisfied with physical conditions. Ninetyseven per-cent of parents stated that, if given a choice they would opt for day case surgery for their child again.

Conclusions: There is a high rate of satisfaction with day case surgery, however, considerable effort is needed to prepare better physical conditions, better time schedule organizations, more anesthesia outpatient clinic consultations.

Keywords: Day-case surgery, parental satisfaction.

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Introduction

In recent years there has been an inclination towards performing increasing amounts of surgery on children on a day stay (ambulatory or outpatient) basis. Children make excellent candidates for day case surgery as they are usually healthy, free of systemic disease and typically require straight-forward, minor or intermediate surgical procedures. More than 60% of pediatric surgery in the USA is performed on an ambulatory basis.

There is evidence that satisfaction is an important measure of the outcome, both because it is related to improvement in health status and because it is useful in assessing patterns of communication. The latter is particularly important in pediatric care, because the quality of care has to satisfy both the children and their accompanying parents. Additionally, because the aim of outpatient surgery is to maximize surgical capacity, it is important to ensure that increased efficiency is not obtained at the expense of the overall quality of the treatment.

Evaluation of quality of health care remains complex and challenging; a process which we nowadays cannot ignore. A total quality management used in many health care organizations emphasizes the use of outcome indicators as measures of quality. Satisfaction only occurs when services meet or exceed the customer’s expectations or perceptions. For continued quality improvement, it is therefore imperative that health care providers know the customers’ perceptions and expectations. This is especially true for day-case surgery. Data on this subject is very rare in the current literature.

Although we know much about patient satisfaction in general, surgery in children differs in many ways from that in general population. First, there is external pressure from health authorities in the form of increasing demands for cost effectiveness and maximisation of surgical capacity. In addition, the tight schedule in outpatient surgery may reduce the staff’s ability to satisfy patients’ needs. Furthermore, children do not have the same ability to express their needs as adults; thus, measures of treatment satisfaction in childhood surgery must consider both the
parents’ and the children’s experiences of surgery and care\textsuperscript{24}.

The aim of this study was to establish the degree of parental satisfaction with day-case surgery for their children.

**Patients and Methods**

The parents of the 100 children who were admitted for elective day-case surgery over a two-month period (April and May 2003) at Hacettepe University Hospital Ankara, Turkey, were prospectively studied. A prestudy was applied on 10 parents and questions were standardized. These were not included in the study.

Parents who refused to fill the questionnaire, were illiterate and whose children had to be admitted for overnight stay were excluded.

Before discharge parents were given a self-completion questionnaire. They had been informed that their answers would not effect the care given to their children. Parents were asked to answer questions regarding their level of satisfaction in several areas; communication with doctors (surgeon and anesthesiologist), physical conditions, staff’s care, patients’ problems and 2 open ended questions. Questions could be answered; very satisfied, satisfied, not sure, dissatisfied and extremely dissatisfied. But because of statistical problems questions were evaluated as satisfied (very satisfied, satisfied) or non satisfied (not sure, dissatisfied and extremely dissatisfied).

Responses from questionnaires were entered into statistical software for analysis. Standardized methods for exploration of ordinal variables were used. Inferences were examined by cross-table analysis (pearson $\chi^2$, likelihood, continuity correction and fishers exact tests). Differences were considered significant at a probability level of $p<0.05$.

**Results**

One hundred children were included in the study. Children aged between 0-18 (Mean 5.52). Types of surgery were: ENT (57%), pediatric
surgery (27%), ophthalmic (7%), orthopedics (4%), plastic surgery (2%),
urology (2%) and dental procedures (1%) (Table I).

Table I
Type of surgery

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<td>ENT</td>
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<tr>
<td>Orthopedics</td>
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<tr>
<td>Plastic surgery</td>
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<td>Urology</td>
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<tr>
<td>Dental procedures</td>
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The parental education levels were as follows; Primary school 16%,
high school 47% and university 37%. Thirty-six percent of children had
previous surgery before this procedure (Table II).

Table II
Demographic data

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<td><strong>Children</strong></td>
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<tr>
<td>Age (mean)</td>
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<td>Female / male</td>
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<tr>
<td><strong>Parents</strong></td>
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<td>Age (mean)</td>
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<tr>
<td>University</td>
<td>37</td>
</tr>
<tr>
<td><strong>Previous surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Yes / No</td>
<td>36 / 64</td>
</tr>
</tbody>
</table>

In the Questionnaire. The first group of questions, parents were
asked about communication with doctors. 88% of parents were satisfied
with obtaining information from their surgeon. 64% of parents were
visited by their anesthetist. When we asked these 64% of parents,
satisfaction from their anesthetist, 64% were satisfied.
Questionnaire

You don’t need to write your name. Your answers does not effect the patient care. Your opinions will help to improve our quality. After you finish the questionnaire please give it back to the nurse who handed it to you. Thank you.

Type of surgery: Parent’s age:
Procedure: Parent’s education:
Child’s age: Child’s sex:
Child’s previous operation:
Please choose the best answer:

1. Obtaining information from your surgeon before the operation
   a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

2. Did you meet with your anaesthetist
   a) Yes  b) No

3. Meeting your anaesthetist before the operation
   a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

4. Finding the location of day-care surgery unit
   a) very easily  b) easily  c) not sure  d) difficult  e) very difficult

5. Waiting time before surgery
   a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

6. Fasting period of your child
   a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

7. Waiting room’s cleanliness
   a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

8. Waiting room’s comfort
   a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

9. Playing area for children
   a) very needed  b) needed  c) not sure  d) needless  e) extremely needless

10. Quality of patient care
    a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

11. Waiting area used by pre and postoperative patients in the same time
    a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

12. Nursing care
    a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

13. Privacy
    a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

14. Receiving information about procedures
    a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

15. Receiving satisfactory answers to your questions
    a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

16. Adequate control of pain after the operation
    a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

17. Adequate control of nausea-vomiting after the operation
    a) very satisfied  b) satisfied  c) not sure  d) dissatisfied  e) extremely dissatisfied

18. Would you opt for day case surgery unit for your child again
    a) Yes  b) No

1. For improving our quality of care what would you prefer us to do/adv?
2. What member/members of our staff were you most satisfied with?
The second group of questions were about physical conditions of day-case surgery unit. Ninety-eight per-cent of parents found the place of day-case surgery unit easily. Parents were satisfied with cleanliness (88%) and comfort (83%). Ninety-two per-cent of parents wanted playing area for their children. 74% of parents were dissatisfied with the fact that the waiting area was used by both preoperative and postoperative patients.

Third group of questions were about staff care. Satisfaction about quality of patient care was 91%, about nursing care was 100%, about receiving information about procedures was 70%, about their questions being answered satisfactorily was 80%.

The fourth group of questions was about patients’ problems. Satisfaction with waiting times before surgery was 68%, adequate control of pain 83% and nausea-vomiting 84%, fasting period 58%. However, parents of children aged between 0-12 months were more dissatisfied (63.6%) with fasting period.

Ninetyseven per-cent of parents stated that, if given a choice they would opt for day surgery for their child again.

In the open ended questions parents emphasized that they wanted more information from doctors and better physical conditions.

In families with low maternal education levels, the degree of satisfaction with the preoperative information given by the surgeon and waiting area arrangements was higher than the families with high parental education levels (p<0.05).

Discussion

Increasing numbers of day surgery cases are being scheduled in most countries. Expansion of day surgery is now widely recommended and supported by healthcare professionals. Any further growth of day surgery, however, will be strongly influenced by consumer attitudes; this is an important outcome measure and the views of patients are increasingly sought on it6.
Day case surgery is generally regarded positively by parents, children and the doctors involved, and is therefore indispensable for the daily routine in the hospital. A further advantage of day case surgery is the supposition that these children will not display behavioral disturbances, in contrast to those children who are hospitalized longer. Significantly less psychological disturbance is reported in children undergoing day-case surgery compared with children admitted on the day before and discharged on the day after surgery. Overnight stay in hospital may frequently be associated with separation of children from parents which is distressing and disturbing to both.

Only 64% of parents were visited by an anesthetist before the operation. 64% of the parents who met their anesthetist were satisfied while satisfaction with their surgeon was 88%.

The physical premises are very important in day-case surgery units. Ideally, separate secretarial services, a waiting room, operating rooms, and a recovery area are desirable. To make the entire process function smoothly, personnel and facilities should be designated solely for outpatients. Secretaries, clerks, nurses, and physicians who have an understanding of the special needs of the outpatient tend to provide unique care that is frequently not possible when outpatients are mixed with inpatients. Playrooms for both preoperative pediatric patients and those recovering after surgery make the environment more comfortable. Facilities for progressive care and feeding should also be available.

We have shortcomings in our premises where parents were most dissatisfied. In our day-case surgery unit we have a separate secretarial service, a waiting room, recovery area which is also used as a premedication area, where pre and postoperative patients meet. We need a playroom and separate areas for preoperative and postoperative patients.

Parents were most satisfied with nursing care. The fact that the questionnaire was given to parents by nurses might have contributed to this.

With many parents, complaints arose due to the long waiting and fasting periods between admission in the morning and commencement of

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surgery. In order to reduce the unnecessarily long waiting and fasting periods and to guarantee the sequence of day case surgical procedures, demands considerable organizational effort. Children should be operated at scheduled times as late as possible before surgery would begin. In our institution a common starvation regimen is used as; 6-8h for formula or solids, 2-3h for clear fluids (includes water, carbonated drinks, black tea). But sometimes because organization problems waiting and fasting times are prolonged.

It has been claimed that parents' satisfaction is based firmly on their expectations and that those expectations vary substantially as a function of background and demographic factors. Variability in parental expectations may explain higher satisfaction among those with low parental education levels. Lower parental education levels offering lower expectations, is a subject of another study.

In our study, parents were highly satisfied with overall care. Ninetyseven per-cent of parents stated that, if given a choice they would opt for day surgery for their children again. This finding supports other studies; in Tönz et al, 98%, Hicklin et al, 87%, Callanon et al, 70%.

In summary, there is a high rate of satisfaction with day case surgery. However, considerable effort is needed to prepare better physical conditions, better time schedule organizations, more anesthesia outpatient clinic consultations. Improvements in these areas should result in further enhancement of parental satisfaction.
References


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AYDIN ERDEN
POSTOPERATIVE COGNITIVE DYSFUNCTION
IN ADULT AND ELDERLY PATIENTS

- General Anesthesia vs Subarachnoid or Epidural Analgesia

HISHAM MF ANWER*, SHAFIK E. swelem **, ADEL EL-SHESHAI*** AND AYMAN A. MOUSTAFA*

Abstract

This study compared the effect of general anesthesia or regional vertebral analgesia (subarachnoid or epidural) on postoperative cognitive function in 60 young adult (group A) and 60 elderly (group E) patients undergoing orthopedic and urologic surgery. Wechsler Adult Intelligence Scale-Revised for cognitive functions assessment was done preoperatively, and postoperatively; one day and three days after surgery. Variations in heart rate, blood pressure, arterial oxygen and carbon dioxide tensions, and pH as well as serum bicarbonate, sodium and potassium levels, were assessed at the same time intervals. They did not show any significant change from the preoperative levels. Cognitive functions, one and three days after surgery, did not change significantly in young adult patients after either general or regional vertebral nor in elderly patients who received regional vertebral, as compared with the preoperative levels. Only elderly patients who received general anesthesia had significant decline in cognitive function one day after surgery. It significantly improved on the third postoperative day but still was significantly less than the preoperative level. Moreover, significantly better WAIS-R Scores were found in the elderly group one and three days after spinal analgesia than after general anesthesia. The results indicate

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that general anesthesia poses a significant risk for the occurrence of early postoperative cognitive dysfunction in elderly patients that can persist for 3 day after surgery. Regional vertebral analgesia is advantageous over general anesthesia for elderly patients in terms of a better postoperative neuropsychological functioning.

Introduction

Elderly surgical patients present some specific challenges to anesthetists. Their number is increasing and they suffer more frequent major morbidity and mortality than younger counterparts undergoing comparable surgeries.

In recent years, attention has focused on the cognitive dysfunction that affects elderly patients after anesthesia and surgery. This condition may occur following surgeries that were considered uncomplicated, or even after minor procedures. This even may not be apparent until the patient is discharged from hospital and tries to resume normal activities. The patient may then discover problems with recalling recent events and may tend to forget appointments, phone numbers, and names. For those who have not retired yet this deterioration can have serious consequences on their ability to work.

This condition is called Postoperative Cognitive Dysfunction (POCD). Unlike delirium, it is not associated with changes in level of consciousness and it does not fluctuate over the course of the day. Due to the subtle nature of POCD, the problem may be recognized only by the patient’s relatives and a neuropsychological testing is necessary for its detection. It covers a large range of neuropsychological modifications ranging from concentration impairment to delirium, and affecting the full range of cognitive functions, including visual and auditory attention, primary and secondary memory, implicit memory and visiospatial functioning.

It has been recognized that there is no postoperative complication more frequent and of longer duration than postoperative cognitive dysfunction (POCD) in the elderly. It can result in increased morbidity,
delayed functional recovery, prolonged hospital stay, delay in rehabilitation, adverse social consequences with reduced quality of life and a concern of inducing some elderly patients prematurely into dependency. Indeed, the recognition of this situation must be incorporated into service provision.

Too many mechanisms and predisposing factors have been incriminated in the occurrence of POCD. Increasing age, duration of anesthesia, episodes of hypoxemia, lack of education, a second operation, postoperative infections and respiratory complications, were identified as risk factors. Correlation with these factors however, has been inconsistent. Is the problem related to anesthesia, the impact of hospitalization, drugs unrelated to anesthesia, disease processes or is a consequence of the surgical problem? These are still unanswered questions. Attempts to reduce the severity of POCD have been hampered by lack of a definite etiology.

This study was undertaken to evaluate the influence of age and the type of anesthesia (general or regional vertebral) on the incidence of POCD following anesthesia and surgery.

Patients and Methods

The University of Alexandria Medical Institutional Review Board approved the study protocol. Following a written informed consent, 120 ASA I & II patients admitted for elective surgery in the orthopedic and in the urology surgical departments in Alexandria University Hospitals, were recruited to the study. Patients were selected of nearly matched ages; half of them over 60 years (elderly or group E), and the other 60 patients aged between 20 and 30 years (younger adults or group A). Patients in each group were randomly allocated to receive either standard general anesthetic (subgroups E_G and A_G) or regional vertebral (subarachnoid or epidural) analgesia (subgroups E_S and A_S). Patients were excluded if they had a history of any psychiatric or neurologic problems, or if they were subjected to gross hemodynamic or ventilatory fluctuations during the operation.
Patients who received general anesthesia (30 patients in group E and 30 patients in group A) had midazolam 0.1 mg/kg I.M. as a premedication 30 min before the operation. Anesthesia was induced with thiopentone 4-6 mg/kg and maintained with halothane 1-2% in 60% nitrous oxide in oxygen. Atracurium 0.5 mg/kg was used to facilitate tracheal intubation and to achieve muscular relaxation. At the end of the procedure, neuromuscular blockade was reversed with 2.5 mg neostigmine and 1 mg atropine.

Patients who received regional vertebral analgesia consisted of 30 patients of group E (17 subarachnoid and 13 epidural), and 30 patients of group A (11 subarachnoid and 19 epidural anesthesia). Heavy bupivacaine 0.5% (2-4 ml) was used for subarachnoid analgesia, and plain lidocaine 1.5% (15-20 ml) was used for lumbar epidural analgesia. Patients breathed oxygen-enriched air through nasal prongs. Midazolam 0.1 mg/kg I.V. was used for sedation during the operation with a 10% decrease in the dose for each 10 years over the age of 50. Crystalloids were used for I.V. infusion and blood loss of ≥15% of estimated blood volume was replaced with packed cells. Postoperative care was administered according to the usual routine in the recovery area and later on in the ward.

One day before surgery, all patients were examined and base line data were obtained; pulse rate mean arterial blood pressure using the pace-tec multichannel monitor, arterial blood gas analysis for arterial oxygen and carbon dioxide tensions, blood pH and serum bicarbonate levels using ABL II apparatus, and serum sodium and potassium levels using CIBA CORNING 614 apparatus. Also, the preoperative cognitive function was evaluated using Wechsler Adult Intelligence Scale-Revised (WAIS-R)©. This is an individually administered series of standardized test used to evaluate cognitive abilities and intellectual functions. It consists of 11 subsets; 6 verbal and 5 nonverbal performance tests and includes information, digit span, vocabulary, arithmetic, comprehension, similarities, picture completion, picture arrangement, block design, object assembly, and digit symbol. The scales have a mean, or average, standard score of 100 and a standard deviation of 10 (Table 1). It measures a broad
spectrum of mental abilities with a very high degree of reliability. All the previously mentioned data were re-measured 1 and 3 days after recovery.

Table 1
Mental ability scoring by the WAIS-R [From the Diagnostic and Statistical Manual of Mental Disorders, version IV (DSM-IV)].

<table>
<thead>
<tr>
<th>Classification</th>
<th>Scale range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Profound mental retardation</td>
<td>&lt; 25</td>
</tr>
<tr>
<td>Severe mental retardation</td>
<td>25-40</td>
</tr>
<tr>
<td>Moderate mental retardation</td>
<td>40-55</td>
</tr>
<tr>
<td>Mild mental retardation</td>
<td>55-70</td>
</tr>
<tr>
<td>Border line</td>
<td>70-80</td>
</tr>
<tr>
<td>Dull normal</td>
<td>80-90</td>
</tr>
<tr>
<td>Normal</td>
<td>90-110</td>
</tr>
<tr>
<td>Bright normal</td>
<td>110-120</td>
</tr>
<tr>
<td>Superior</td>
<td>120-130</td>
</tr>
<tr>
<td>Very superior</td>
<td>&gt;130</td>
</tr>
</tbody>
</table>

Variables were identified as nonparametric when analyzed by Kolmogorov-Smirnov and Shapiro-Wilk tests for normality. Statistical analysis of Inter-subgroup differences in demographics consisted of Chi-square test for sex distribution, Kruskal-Wallis test for the duration of surgery and Man-Whitney U test for age differences between the two subgroups within each group. Repeated-measures analysis of variance on ranks (Friedman’s test) was used for analyzing changes within each subgroup. Significant results were further analyzed with Wilcoxon Signed Ranks test to identify the area of significance. Between subgroups the differences were tested with Mann-Whitney U test. Statistical significance was defined as a two-sided p-value of less than 0.05 and the results are presented as medians with 25th and 75th percentiles.
Results

Of the 120 patients included in our study, 102 underwent orthopedic surgery and 18 underwent urosurgical procedures, all were classified as moderate to major surgery, with a duration ranging from 30-110 minutes with a mean of 59.99 ± 23.51 (62.82 ± 26.2 in group E, and 57.17 ± 19.45 in group A). Patients were allocated into four subgroups (E₂, E₃, A₂ and A₃), 30 patients each, according to age and to the type of anesthesia used.

The four subgroups were comparable as regards; sex (P=0.24) and duration of surgery (P=0.29), and each of the groups had its two subgroups comparable as regards the age of the patients (P=0.26 and P=0.08 for groups E and A respectively) (Table II).

<table>
<thead>
<tr>
<th></th>
<th>Group E</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>General</td>
<td>Reg. vertebral</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>19/11</td>
<td>17/13</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>62.0</td>
<td>61.0</td>
</tr>
<tr>
<td></td>
<td>(61.0-64.3)</td>
<td>(60.0-63.3)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>67.5</td>
<td>57.5</td>
</tr>
<tr>
<td></td>
<td>(35.0-91.3)</td>
<td>(40.0-80.0)</td>
</tr>
</tbody>
</table>

No significant changes were found in the mean arterial pressure, heart rate and blood pH, nor in the serum levels of sodium, potassium and bicarbonate in the four subgroups, one and three days after the operation as compared to the preoperative values (Table III).
Table III

Hemodynamic (B.P. and H.R.) Arterial blood gas tensions (PaO₂ and PaCO₂), blood pH and Serum bicarbonate, Sodium and Potassium levels in the four subgroups preoperatively, one day and three days after the operation.

The values expressed are medians with 25th and 75th percentiles.

<table>
<thead>
<tr>
<th>Group E</th>
<th>Group A</th>
<th>Group E</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>General</td>
<td>Reg. vertebral</td>
<td>Reg. vertebral</td>
</tr>
<tr>
<td>B.P.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>96.5</td>
<td>96.5</td>
<td>99.5</td>
<td>98.5</td>
</tr>
<tr>
<td>(90.0-)</td>
<td>(92.0-)</td>
<td>(93.0-)</td>
<td>(95.0-)</td>
</tr>
<tr>
<td>(100.3)</td>
<td>(100.3)</td>
<td>(102.5)</td>
<td>(101.3)</td>
</tr>
<tr>
<td>P</td>
<td>0.063</td>
<td>0.389</td>
<td>0.305</td>
</tr>
<tr>
<td>H.R.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>72.0</td>
<td>71.5</td>
<td>85.0</td>
<td>85.5</td>
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<tr>
<td>(70.0-)</td>
<td>(70.0-)</td>
<td>(82.0-)</td>
<td>(81.0-)</td>
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<tr>
<td>(74.0-)</td>
<td>(69.0-)</td>
<td>(89.0-)</td>
<td>(89.0-)</td>
</tr>
<tr>
<td>P</td>
<td>0.436</td>
<td>0.885</td>
<td>0.097</td>
</tr>
<tr>
<td>P.O₂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>96.0</td>
<td>95.0</td>
<td>95.0</td>
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<td>(94.0-)</td>
<td>(94.0-)</td>
<td>(93.0-)</td>
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<tr>
<td>(97.0)</td>
<td>(96.5)</td>
<td>(96.0)</td>
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<tr>
<td>P</td>
<td>0.744</td>
<td>0.102</td>
<td>0.736</td>
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<tr>
<td>P.CO₂</td>
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</tr>
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<td>41.0</td>
<td>41.0</td>
<td>41.0</td>
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<tr>
<td>(40.0-)</td>
<td>(40.0-)</td>
<td>(40.0-)</td>
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<tr>
<td>(43.0-)</td>
<td>(42.0-)</td>
<td>(43.0-)</td>
<td>(45.0-)</td>
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<tr>
<td>P</td>
<td>0.881</td>
<td>0.098</td>
<td>0.575</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>22.0</td>
<td>22.0</td>
<td>22.0</td>
<td>22.0</td>
</tr>
<tr>
<td>(21.0-)</td>
<td>(20.8-)</td>
<td>(22.5-)</td>
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<td>(24.0-)</td>
<td>(24.0-)</td>
<td>(24.0-)</td>
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<tr>
<td>P</td>
<td>0.388</td>
<td>0.498</td>
<td>0.424</td>
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<td>PH</td>
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<tr>
<td>(7.35-)</td>
<td>(7.32-)</td>
<td>(7.32-)</td>
<td>(7.32-)</td>
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<tr>
<td>(7.40-)</td>
<td>(7.40-)</td>
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<tr>
<td>P</td>
<td>0.648</td>
<td>0.085</td>
<td>0.816</td>
</tr>
<tr>
<td>S. Na</td>
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<td></td>
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</tr>
<tr>
<td>139.0</td>
<td>139.0</td>
<td>140.0</td>
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<tr>
<td>(137.0-)</td>
<td>(136.0-)</td>
<td>(136.0-)</td>
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<td>(143.0-)</td>
<td>(140.0-)</td>
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<tr>
<td>P</td>
<td>0.340</td>
<td>0.337</td>
<td>0.101</td>
</tr>
<tr>
<td>S. K</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.50</td>
<td>4.60</td>
<td>4.40</td>
<td>4.30</td>
</tr>
<tr>
<td>(4.30-)</td>
<td>(4.28-)</td>
<td>(4.18-)</td>
<td>(4.00-)</td>
</tr>
<tr>
<td>(4.90-)</td>
<td>(4.73-)</td>
<td>(4.73-)</td>
<td>(4.80-)</td>
</tr>
<tr>
<td>P</td>
<td>0.580</td>
<td>0.426</td>
<td>0.168</td>
</tr>
</tbody>
</table>
The preoperative WAIS-R scores were in the normal category (90-110) in all the tested subgroups. The scores however, decreased significantly in the elderly subgroup who received general anesthesia (subgroup E_G), when measured one day after surgery to the borderline level (70-80). Three days after surgery, the measured scores in this subgroup were significantly improved to $85.17 \pm 5.3$ (null normal level) but were still significantly lower than the preoperative value. Also, the scores one and three days after surgery were significantly better in elderly patients who received regional vertebral than general anesthesia. There was no significant deterioration in the measured WAIS scores in the rest of the tested subgroups (E_S, A_G and A_S), neither at one day nor at three days after the operation as compared to the preoperative levels (Table IV, Fig. 1).

**Table IV**

Wechsler Adult Intelligence Scores-Revised (WAIS-R) for the four subgroups, preoperatively, one day and three days after the operation. Medians with 25th and 75th percentiles are shown.

| Patient group | Group E | | | Group A | | |
|---------------|---------|--|----|----|----|
| | General | Reg. vertebral | p* | General | Reg. vertebral | p* |
| WAIS-R Score  | Preop | 90.0 | 93.5 | 0.079 | 100.0 | 103.5 | 0.623 |
| | (87.8-94.0) | (89.0-96.0) | | | (95.0-107.3) | (97.0-110.0) | |
| 1 day | 73.0* | 93.0 | <0.001 | 100.0 | 103.5 | 0.552 |
| | (70.0-74.0) | (88.8-95.0) | | | (94.8-107.3) | (96.5-110.0) | |
| 3 days | 87.0* | 93.0 | <0.001 | 102.5 | 103.5 | 0.504 |
| | (80.0-90.0) | (90.0-95.3) | | | (94.0-106.3) | (96.5-110.0) | |
| p* | <0.0001 | 0.094 | 0.445 | 0.068 |

*: Significant difference with preoperative value (P<0.001). (Wilcoxon Signed Rank test).

†*: Significant difference with one-day value (P<0.001). (Wilcoxon Signed Rank test).

Φ: Mann-Whitney test.

Ω: Friedman test.
Discussion

Our study confirmed the occurrence of short-term postoperative cognitive deficit in a significant number of elderly patients after non-cardiac surgery performed under general anesthesia. Although there is consensus on its existence, attempts to reduce its severity have been hampered by lack of a definite etiology, which is likely to be multifactorial.

In this study we investigated the influence of age and the type of anesthesia (general or regional vertebral), on the occurrence of POCD. While avoiding a number of potential confounding factors, this excludes the possibility of examining interaction effects. For example a history of preoperative neurologic disease has been demonstrated to increase the rate of POCD. Therefore, we had excluded patients with pre-existing cognitive, psychiatric or central nervous system disorders. In addition, the effects of other factors such as blood loss, hypoxemia and hypercarbia had been minimized by excluding patients who were subjected to gross hemodynamic or ventilatory fluctuations during the operation. Also, all the hemodynamic, ventilatory and the metabolic parameters that could be impeached in the occurrence of POCD were carefully monitored during the whole study and did not show any significant change from the preoperative levels. Ultimately, the impact of age and anesthetic technique on the occurrence of POCD had been focused.
Age frequently has been reported as a risk factor for cognitive alteration after anesthesia\textsuperscript{2,3}. This was quite evident in our results and is probably related to the important changes in both physiology and pharmacokinetics occurring with ageing and the possible interaction of anesthetic drugs with current medication in the elderly\textsuperscript{10,11}.

Actually, little is known about the effects of anesthetics on the aged brain. The age-associated structural and functional changes in the CNS have reduced functional reserve and the current assumption is that this makes the elderly more vulnerable to the development of POCD\textsuperscript{11}. The mechanism is unknown but one hypothesis is that it may be related to further decreases in already low levels of neurotransmitters such as acetylcholine\textsuperscript{12}. Drugs used as a part of general anesthesia interact with central cholinergic receptors and may modulate cognitive functions\textsuperscript{10,13}. Propofol at high doses and volatile anesthetics are potent inhibitors of nicotinic acetylcholine receptors while atracurium and its metabolite laudanosine activate them, and some other anesthetics may cause block of the central muscarinic acetylcholine receptors. The effects of these drugs and their multiple interaction sites with different affinities could explain POCD\textsuperscript{11}. However, several old studies\textsuperscript{14,15,16} failed to validate this relationship. This had been attributed to the rough psychological evaluation used in these studies that could not detect more subtle defects\textsuperscript{3,16}. We chose the Wechsler Adult Intelligence Scale-Revised for its applicability to wide differences in level of functioning, sensitivity to small changes in function and extensive psychometric data documenting the instrument's reliability and validity\textsuperscript{17}. Also, to guarantee more accuracy and validity the test was performed by the researcher and by a specialized psychiatric technician, well trained in performing and interpreting the test results. Most recent studies\textsuperscript{2,4,18,19} agreed with our results in approving old age as a major risk factor in the occurrence of POCD.

The evidence to date suggests that although cognitive deficits may occur postoperatively, no particular anesthetic technique appears to be implicated\textsuperscript{20}. There is presently no scientific basis for recommending (or avoiding) a specific anesthetic agent or technique for anesthesia in this
regard. Although still in controversy, recent studies did not show that anticholinergic drugs, barbiturate premedication or benzodiazepines are implicated in the development of postoperative delirium. The anesthetic technique used in our study was standardized to the customary work in our operating room because the objective of this study was to detect alterations in cognitive function that could be found after either general or neuroaxial regional anesthesia under conditions generalisable to the real-life situation of a busy operating room, rather than to compare the effects of different anesthetic agents. The choice between subarachnoid and epidural blocks in the regional anesthesia group was left to the anesthesiologist responsible for the patient because the physiologic effects of both techniques are almost the same and there is no reason to expect different behavioral sequelae. All the patients receiving regional vertebral analgesia received midazolam sedation. This may have served to negate any differences between the groups.

Our data support the recent trends towards increased use of neuroaxial blockade to reduce major complications in the elderly. POCD significantly occurred in elderly patients who received general anesthesia but did not in those who received regional vertebral analgesia with sedation. This demonstrates that exposure to general anesthesia also should constitute a major risk factor that can lead to POCD in the elderly. Several studies have looked at general versus regional anesthesia, since general anesthesia may lead to changes in cerebral blood flow and cerebral metabolic oxygen consumption. It also could provoke persistent alterations in specific cognitive domains in the elderly where age-related neuronal changes may exacerbate pharmacotoxic effects. Neuraxial blockade on the other hand has several physiological effects that provide a rationale for expecting to improve outcome. In addition to avoidance of adverse effects of general anesthesia and minimizing the number of medications used, its use may carry the benefit of reducing several major postoperative complications in a wide range of elderly patients. Neuraxial blockade with epidural or subarachnoid analgesia reduces the incidence of deep vein thrombosis, pulmonary embolism, transfusion requirements, pneumonia, respiratory depression, myocardial
infarction, and renal failure\textsuperscript{24}. All these complications can predispose to the development of POCD\textsuperscript{8,9,20}. Furthermore, the induced surgical stress response that could also contribute to the occurrence of POCD is substantially altered by neuraxial blockade but not by general anesthesia\textsuperscript{8,20,24}.

Nevertheless, the issue of whether neuraxial analgesia offers advantages over general anesthesia for elderly patients in terms of neurophysiological functioning and the ability to perform activities of daily living, had remained controversial. Riis\textsuperscript{25}, Berggren\textsuperscript{26}, Ghoneim\textsuperscript{27} and Williams-Russo\textsuperscript{27} could not find differences in the postoperative mental abilities between patients who received general and regional vertebral anesthesia. On the other hand, significant cognitive impairment in elderly patients after general anesthesia and not after subarachnoid or epidural analgesia, had been detected by Hole\textsuperscript{28} and by Chung\textsuperscript{29} during the early postoperative days. Rasmussen\textsuperscript{30} also found that the incidence of POCD was significantly greater one week after general anesthesia than after regional analgesia and Campbell\textsuperscript{31} noted that his elderly patients who received general anesthesia tended to perform less well in some aspects of cognitive function than those who received local analgesia at 24 hours after cataract surgery. Finally, Tzabar\textsuperscript{32} reported a highly significant greater incidence of cognitive failures after general anesthesia compared with local analgesia for 3 days after day case surgery, and Bigler\textsuperscript{35} noted a shorter time of ambulation as an advantage for subarachnoid analgesia over general anesthesia for acute hip surgery in elderly patients despite his observation of the absence of persistent mental function impairment after either of the techniques.

The variability of the results of various studies could largely be attributed to the absence of a standard POCD definition, the heterogeneity of procedures to measure cognitive deficits and the methods used for statistical analysis, but could also be related to the disparity in targeted population\textsuperscript{3,33}. In addition, the complex interaction of diverse etiological factors can make it difficult to isolate the influence of anesthesia itself\textsuperscript{33,34}. 
Looking for changes in mental status is an important part in the postoperative care in the geriatric patient. The condition can be silent, and unnoticed, or misdiagnosed as depression. However, the effects are evident in increased morbidity, delayed functional recovery, prolonged hospital stay, delay in rehabilitation and may jeopardize return to independence.\textsuperscript{4,20,35} Substantial additional costs accrue after discharge from the hospital, because of the increased need for institutionalization, rehabilitation, and home care. In order to avoid delays in the postanesthesia care unit (PACU) and in the time to discharge after outpatient anesthesia, fast and predictable recovery of cognitive function is of major importance. Nevertheless, the importance of perioperative cognitive decline has long been debated.\textsuperscript{35} Descriptions such as “subtle”, “transient”, and “subclinical” have been used to minimize the importance of these changes to clinicians, patients, and their families. Fortunately, POCD is a reversible condition in the majority of elderly surgical patients. However, a significant correlation between perioperative cognitive decline and long-term cognitive dysfunction had recently been demonstrated.\textsuperscript{36} This linkage between perioperative injury and long-term cognitive function suggests that perioperative dysfunction may serve either as a marker of brain injury, increased susceptibility to brain injury, decreased reserve capacity, or inability to recover or tolerate similar injury (plasticity).\textsuperscript{35} The clinical importance of cognitive dysfunction further emphasize the need for aggressive strategies to monitor and improve both the neurocognitive function in elderly surgical patients.

Understanding the risk factors and etiologic mechanisms and trying to eliminate or reduce them in addition to better psychologic care preoperatively and postoperatively when indicated must have contributed to better outcome.\textsuperscript{37} This can improve our understanding of the problems affecting older patients and lead to development of improved strategies for diagnosis, care, research, and medical education in this area. Concern that the elderly brain “takes a hit” during general anesthesia and surgery is better justified and guidelines for the anesthesiological management of at risk patients are mandatory.
References


MANAGEMENT OF SICKLE CELL DISEASE DURING CABG SURGERY

- A Case Report -

MADAN MOHAN MADDALI*, MUTHUKKUMAR CHETTIAR RAJAKUMAR**, PRASAD PANDURANGA VISHNU*** AND JOHN VALLIATTU****

Abstract

Elective Coronary Artery Bypass Graft (CABG) surgery using cardiopulmonary bypass techniques following preoperative transfusions to increase the hemoglobin A levels to above 60%, in a male patient with sickle cell disease [SCD] is described. Avoidance of hypoxia and acidosis lead to an uneventful perioperative period. Our institutional protocol for preoperative transfusions is highlighted.


Introduction

Sickle cell hemoglobinopathies are inherited disorders ranging from the usually benign sickle cell trait [SCT] to the potentially fatal sickle cell anemia. Sickle cell disease [SCD] is a homozygous genotype [HbSS], with the fractional concentration of HbS varying from 70-98%.

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SCD in patients undergoing open-heart procedures presents a multitude of challenges to the treating medical staff. A major concern in these patients is the development of an intraoperative sickle cell crisis. Cardiopulmonary bypass [CPB] techniques, which can possibly lead to hypoxia and acidosis can trigger off the sickling process.

**Case Report**

We report the case of a 40-year-old man with SCD who required elective Coronary Artery Bypass Graft [CABG] surgery. He had history of chronic stable angina [NYHA class II] of one-year duration. The coronary angiogram revealed critical lesions of LAD, OM2 & RCA, and was advised CABG surgery. His preoperative complete blood counts [CBC] revealed hemoglobin levels of 10.7 g/dl [normal: 14-18.1], hematocrit of 31.4% [normal: 35-53], with normal platelets and WBC counts. He tested positive for sickling and SCD was diagnosed on subsequent hemoglobinopathy screening (Table-1).

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Preoperative [After transfusions]</th>
<th>1st P.O.D</th>
<th>2nd P.O.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin [Normal: 14-18.1 g/dl]</td>
<td>10.7</td>
<td>12</td>
<td>11.2 g/dl</td>
<td>10.9 g/dl</td>
</tr>
<tr>
<td>Hemoglobin A (Adult)</td>
<td>21.9%</td>
<td>70%</td>
<td>74.1%</td>
<td>78.5%</td>
</tr>
<tr>
<td>Hb A2</td>
<td>5.6%</td>
<td>3%</td>
<td>3.2%</td>
<td>3.4%</td>
</tr>
<tr>
<td>Hb F</td>
<td>3.6%</td>
<td>1%</td>
<td>1.1%</td>
<td>2%</td>
</tr>
<tr>
<td>Hb S</td>
<td>68.9%</td>
<td>26%</td>
<td>21.6%</td>
<td>16.1%</td>
</tr>
<tr>
<td>Other variant of hemoglobin</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

4 units of blood were transfused preoperatively to raise the Hb A level to >60% 48 hrs prior to surgery as per our institutional protocol [Table-1].

Anesthesia was induced with fentanyl, midazolam, thiopentone, and
pancuronium and maintained with fentanyl, isoflurane and propofol infusion throughout the surgical procedure. Propofol and fentanyl infusions were continued postoperatively for sedation and analgesia.

Monitoring techniques were standard: ECG with ST segments analysis, SpO₂, EtCO₂, nasal/skin temperature, invasive arterial and central venous pressure and urine output. CPB parameters for good tissue perfusion like arterial inflow line pressure, cardiac index, and temperature gradients were monitored, as well as arterial and venous blood gas status. Venous oxygen saturation was kept above 75% and perfusion pressures equal to or >60 mmHg were maintained at all times. All residual pump blood was discarded.

During CPB the patient received vasodilators as needed (Inj Nitroglycerine or Inj. Phentolamine) to improve peripheral perfusion and to reduce stasis.

The patient received 4 grafts [left internal mammary artery to LAD and 3 saphenous venous grafts to OM₂, D₂ and distal RCA] on CPB with cold anterograde cardioplegia [St. Thomas solution] and moderate hypothermia. The total CPB time was 75 mins and with an aortic cross clamp time of 57 mins. A blood prime was used and 3 units of blood were transfused perioperatively.

After an uneventful postoperative course, the patient was extubated after 8 hrs of artificial ventilation. The hemoglobin screening on the 1st and 2nd postoperative days showed Hb A levels above 70% [Table-1]. Early anticoagulation was initiated with IV heparin 6 hrs after surgery, which was overlapped with oral warfarin on the third day. Heparin was withdrawn on the 6th postoperative day.

A 12 lead ECG was recorded immediately on reaching the PSCU, and every day thereafter until discharge from PCSU, for early identification of myocardial ischemia.

Discussion

Hypoxia or acidosis initiates the sickling phenomenon, which is
initially reversible but then becomes irreversible. The danger of sickling provoked by CPB has been emphasized\textsuperscript{16}. CPB by causing hypoxia or acidosis or both can initiate a vicious cycle leading to increased viscosity resulting in capillary stasis, thrombosis, ischemia and necrosis. Sickle cells are mechanically more fragile and are prone for hemolysis\textsuperscript{26}. In addition, hypothermia used during CPB augments sickling\textsuperscript{26}.

The possible dangers of CPB in sickle cell hemoglobin states led to many recommendations:

Sickling may occur in the heterozygous state at a PO\textsubscript{2} of 20-25 mmHg, whereas in the homozygous form it occurs at a higher PO\textsubscript{2} of 40 mmHg\textsuperscript{4}. Hence optimal oxygenation with avoidance of acidosis through out is an important measure during cardiac operations to avoid sickling.

To decrease the risk of sickling reduction of HbS% by preoperative transfusions\textsuperscript{4} or by partial exchange transfusion immediately before bypass, has been suggested\textsuperscript{16,7}. This might necessitate the use of blood in the priming solution\textsuperscript{16,23,46}, which alone would be sufficient to decrease the percentage of HbS%\textsuperscript{2}.

Systemic hypothermia has not been recommended on theoretical basis since it can lead to sickling\textsuperscript{24}. Contrary to this, there is experimental evidence that hypothermia may actually be beneficial, as it slows the polymerization of HbS and delays the onset of sickling. Maintenance of peripheral perfusion during cooling by hemodilution decreases capillary transit time below that required for deoxygenation and sickling, and hence hypothermia is safe in these patients\textsuperscript{9}. From the formation of deoxygenated Hb to the onset of aggregation of the deoxygenated Hb into a gel, there is a delay time, which is inversely proportional to the temperature. The presence of significant amounts of polymerized HbS does not invariably produce a sickle cell. As the cell returns to less hypoxic environment, there is reversal of the polymerization\textsuperscript{9}. It has been postulated\textsuperscript{10} that sickling occurs if the capillary transit time is lengthened to exceed delay time.

This would suggest that hypothermia, hemodilution and vasodilation should to some extent have a protective effect in preventing sickling as
the red cells pass through an hypoxic environment. The proviso being a capillary transit time of the shortest possible duration. This would involve administration of vasodilator drugs, control of packed cell volume [hemodilution], and optimization of oxygenation.

Aortic cross clamping and topical hypothermia have been used successfully recently\(^7,10\) though they were not recommended initially for the fear of precipitating in situ sickling\(^24\).

In our part of the world, the prevalence of SCT is 6% and SCD is about 0.2%\(^11\). Since Middle Eastern countries are known for the increased incidence of SCD, every patient undergoing open-heart surgery is routinely screened for sickle cell and other hemoglobinopathies, if not known already.

The following is the protocol followed in our institution for simple and exchange transfusion in SCD patients: This applies to HbSS, HbS beta thalasimia, HbSC-disease and HbS with high Hb F. The algorithm expresses goals based on Hb A levels.

- For urgent surgery, 4 units of compatible, packed RBCs are administered as soon as possible with the intent to complete the last transfusion at least 48-72 hrs prior to any surgery. CBC & HPLC are repeated to see the effect of transfusions. If the post transfusion Hb is less than 12 gms% or the Hb A is less than 40%, 1 unit of packed RBCs is transfused for each gram of Hb less than 12 gms%. CBC and HPLC are repeated to see the effect of the transfusions. If the final Hb A does not meet the transfusion goals, exchange transfusion may be indicated.

- For elective surgery (>3 weeks before elective surgery), 10-15 ml/kg of compatible blood is transfused each week. The procedure is repeated for a total of three times. CBC and HPLC are checked to see the effect of the transfusions. If the final Hb A does not meet the transfusion goals [i.e.] Hb A <40%, exchange transfusion is considered.

We consider preoperative transfusion if the Hb A is <40% for minor surgical procedures and if Hb A is <50% for major surgeries.

There have been several reports of vaso-occlusive events and sudden death in subjects with sickle cell trait. However, the precise mechanism
underlying these episodes remains unclear. Sickle cell disorders, such as Hb SS and Hb SC, are associated with a hypercoagulable state that may contribute to the vaso-occlusive episodes observed in the disorders. Westerman et al reported that the d-dimers, TAT, F1.2, and monocyte count showed significant increasing trends through groups of increasing severity (Hb AA, Hb AS, Hb SC, and Hb SS). The measures of coagulation activity in SCT were lower than in patients with Hb SC and SCD\textsuperscript{12} suggesting that patients with SCD may be at risk for developing catastrophic vaso-occlusive complications such as pulmonary infarction or stroke. Keeping in view the possibility of a hypercoagulable state in SCD patients, we commenced anticoagulation quite early in the postoperative period. There was no ischemia detected in the ECG recordings.

In our patient, standard CPB using moderate hypothermia, aortic cross clamping and topical hypothermia was used. The patient had an uneventful recovery and was discharged home on 6\textsuperscript{th} postoperative day.

In conclusion, though theoretically CPB has been feared in sickle disease patients, increasing Hb A and reducing the HbS\% to acceptable levels by perioperative blood transfusions, makes CPB associated procedures like aortic cross clamping and hypothermia safe.
References

THE IMPACT OF OPERATIVE FLUIDS
ON THE PREVENTION OF POSTOPERATIVE
ANESTHETIC COMPLICATIONS IN
AMBULATORY SURGERY

- High Dose vs Low Dose -

ABDUL-HAMEED CHOHELDRI*, MASOOD MATIN
AND ABBAS KHOSRAVI

Abstract

Background/Aim: Adequate control of postoperative (postop.)
nausea, vomiting, dizziness and thirst, and early return to normal activity
are important anesthetic goals in the context of ambulatory surgery. This
study, investigated the impact of different preoperative fluid therapies or
regimens on preventing postop. nausea, vomiting, dizziness and thirst.

Materials and Methods: In a prospective randomized double-blind
study, from June 2002 to November 2003, two hundred ASA grade I-II
ambulatory surgical patients received 20 ml/kg of intravenous isotonic
electrolyte solution (0.9% sodium chloride) (group A) or 2 ml/kg of same
(group B) (n = 100 in each group), over 30 minutes before induction of
anesthesia. A standard general anesthetic technique and postop. analgesia
were used throughout the operation. Adverse postop. outcomes (nausea,
vomiting, dizziness, and thirst) were assessed at 30 and 60 minutes
postop. and at discharge.

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Results: The incidence of postop. vomiting and thirst significantly decreased in group A compared to group B ($p = 0.014$ and $p = 0.029$, respectively). There was no difference in the incidence of nausea and dizziness between the two groups.

Conclusion: We conclude that preoperative high dose hydration (20 ml/kg bolus) can efficiently decrease the incidence of postop. thirst and vomiting within the first 60 minutes, it was superior to low dose hydration and therefore, we recommend it in ambulatory surgeries.

Key words: Ambulatory surgery, vomiting, nausea, thirst, dizziness, preoperative hydration, postoperative anesthetic complications, antiemetic.

Introduction

In the past decade dramatic increase in ambulatory surgery has been observed. In recent years, up to 80% of patients in the United States are being admitted on the day of surgery. Ambulatory surgery and anesthesia can offer a large number of advantages to patients, health care providers and hospitals. However, it is unfortunately associated with a number of unpleasant postoperative experiences such as pain, nausea, vomiting, dizziness and thirst. Short acting anesthetic agents have provided major advantages in the field of acute pain. However, despite the availability of new antiemetic agents, the incidence of other postoperative adverse effects, especially nausea and vomiting, has remained significantly unchanged.

Nausea and vomiting are the most common and distressing symptoms associated with surgery and one of the most common reasons for poor patient satisfaction-rating, in the postoperative period. Currently, the overall incidence of postoperative nausea and vomiting for all surgeries and patients is estimated to be 25-30%. Postoperative nausea and vomiting may be associated with serious complications such as dehydration, electrolyte disturbances, wound dehiscence, pulmonary aspiration and esophageal rupture leading to a delay in post-anesthesia recovery room discharge and thereby increasing medical costs.
Recent studies have demonstrated that preoperative hydration of patients undergoing in-patient and out-patient surgeries can decrease the incidence of postoperative adverse outcomes\(^{46-8}\). However, the isotonic solution used in those studies are not easily accessible to our patients and in our setting.

The aim of this study was to investigate the efficacy of preoperative hydration with 0.9% sodium chloride (an easily available fluid in our setting) in decreasing and preventing postoperative nausea, vomiting, thirst and dizziness.

**Materials and Methods**

In a prospective randomized double-blind clinical trial, from June 2002 to November 2003, two hundred ASA grade I-II ambulatory surgical patients, who had been referred for surgery to the educational hospitals of Shiraz University of Medical Sciences, were studied. A written informed consent was obtained from each patient and the Shiraz University of Medical Sciences Research Committee had approved the study.

Patients’ age ranged from 17 to 60 years and they were scheduled for general, orthopedic and gynecologic surgeries. Patients who gave positive history of cardiovascular diseases, diabetes, preoperative history of nausea, vomiting or dizziness and motion sickness, were excluded from the study. Demographic characteristics, type of surgery and history of drug consumptions, were recorded.

Two hundred patients (77 males, 123 females) were randomly allocated to two equal groups of 100 each. The first group (group A) received 20 ml/kg of intravenous 0.9% sodium chloride (sodium chloride, 154 mEq/L). The second group (group B) received 2 ml/kg of the solution. The fluid was given as bolus over 30 minutes before induction of anesthesia.

A standard general anesthetic technique and postoperative analgesia were used throughout the operations. Induction was done with dazepam (0.1 mg/kg) and morphine (0.15 mg/kg). Endotracheal intubation was...
accomplished with 1.5 mg/kg of succinylcholine and 4 mg/kg Pentothal. Anesthesia was maintained with a mixture of oxygen (50%) and nitrous oxide (50%) with end-tidal halothane (0.5 MAC) in a semi closed circle system. Atracurium (0.3 mg/kg IV) was used for muscle relaxation. Neuromuscular block was reversed with neostigmine (50 μg/kg) and atropine (25 μg/kg). All patients received maintenance IV fluid therapy of isotonic saline, 1 ml/kg/hour, throughout the surgery and during the postoperative period. If more fluid was needed, due to hypotension or bleeding, the patient was excluded from the study.

Blood pressure, heart rate, oxygen saturation, electrocardiogram, tidal volume, end-tidal CO2, end-tidal concentration of the inhaled anesthetic, airway pressure, and minute volume, all were monitored.

Adverse postoperative outcomes (nausea, vomiting, dizziness, and thirst) were assessed by an anesthesiologist, at 30 and 60 minutes postoperatively and at discharge. Nausea was defined as subjective complain of nausea with increase in salivary secretion; vomiting, as active retching and active vomiting of gastric content; dizziness as subjective complain of faintness and inability to sit in bed or walk without support; and thirst, as a desire to drink and dry mucosa of the mouth. The anesthesiologist assessing the adverse outcomes, the attending anesthesiologist, and recovery room nurses were all blind to the patients’ allocation group and the amount of preoperative fluid therapy they had received.

All data were analyzed and computed by SPSS (Chicago, IL) software, version 10.0, and Microsoft EXCEL (Microsoft, Redmond, WA) software. Data are expressed as mean ± standard deviation (SD) and 95% confidence interval (CI) are also given when essential. The association between variables was assessed with Student’s t-test; Fisher’s exact, χ² test and Mann Whitney U-test. p values less than 0.05 were considered statistically significant.

Results

Among the two hundred patients (77 males, 123 females) enrolled in
the study, 66 patients had gynecological operations (vaginal cyst removal, IUD removal, and cervical polyp excision), 67 orthopedic (bone biopsy, pin removal, removal of bone exostosis, and treatment of carpal tunnel syndrome), and 67 general surgical operations (inguinal herniorrhaphy, breast mass biopsy, epigastric hernia repair, lateral sphincterectomy and hemorrhoidectomy).

Demographic characteristics, type of operation, and duration of operation are shown in Table 1. There was no significant difference between the two groups in demographic characteristics (age, weight and sex), type of operation, or ASA classification. Additionally, there was no significant difference between them in the amount of anesthesia given and the duration of anesthesia. Total amount of fluid infused in group A (High dose fluid therapy) was 1197 ± 25 ml and in group B (low dose fluid therapy) 171 ± 22 ml.

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p value</th>
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<tbody>
<tr>
<td></td>
<td>High dose fluid therapy</td>
<td>Low dose fluid therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n = 100)</td>
<td>(n = 100)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>34.58 ± 12</td>
<td>34.8 ± 11.1</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>57.52 ± 7.9</td>
<td>56.9 ± 8.3</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>39/61</td>
<td>38/62</td>
<td>NS</td>
</tr>
<tr>
<td>Type of operation</td>
<td>Gynecology operation</td>
<td>Orthopedic procedures</td>
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<td>33</td>
<td>33</td>
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</tr>
<tr>
<td></td>
<td>32</td>
<td>35</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of operation (min)</td>
<td>63.55 ± 19</td>
<td>64 ± 18.29</td>
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</tr>
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<td>ASA grade I/II</td>
<td>80/20</td>
<td>76/24</td>
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</tr>
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NS: not significant; p >0.05.

The incidence of postoperative thirst significantly decreased at both 30 and 60 minutes postoperative in group A when compared to group B (p = 0.029) (Figure 1).
Fig. 1
The incidence of postoperative thirst. Group A. High dose fluid therapy; Group B. Low dose fluid therapy; 30M = 30 min postop; 60M = 60 min postop; p < 0.05 for 30M and 60M for the two groups using χ² test.

The incidence of vomiting also was lower at all times; however only in the first 60 minutes it was statistically significant (Figure 2).

Fig. 2
The incidence of postoperative vomiting. Group A. High dose fluid therapy; Group B. Low dose fluid therapy; 30M = 30 min postop; 60M = 60 min postop; p > 0.05 for 30M; however for 60M p value not significant; using χ² analysis.

The incidence of nausea and dizziness was lower in group A, but the difference was not significant (p > 0.05; Figures 3 and 4, respectively). There was no statistically significant difference in the incidence of adverse effects and the type of operation (p > 0.05).
Fig. 3
The incidence of postoperative nausea. Group A, High dose fluid therapy; Group B, Low dose fluid therapy; 30M – 30 min postop; 60M – 60 min postop p value not significant (p > 0.05) for both 30M and 60M for the two groups using $\chi^2$ test.

Fig. 4
The incidence of postoperative dizziness. Group A, High dose fluid therapy; Group B, Low dose fluid therapy; 30M – 30 min postop; 60M – 60 min postop p value not significant (p > 0.05) for both 30M and 60M for the two groups using $\chi^2$ test.

Discussion
The incidence of postoperative adverse outcomes, such as thirst, nausea, vomiting, and dizziness depends on multiple factors; surgical procedure, anesthetic technique and the fluid status. Several studies
have been done on the prevention of nausea and vomiting and different regimens have been suggested\(^{2,4-11}\). However, only limited work had been done to determine the correlation between preoperative fluid therapy and the well being of patients in the postoperative period. Cook et al. reported decrease in the incidence of postoperative adverse effects with fluid administration, especially when sugar was added to the regimen\(^8\). However the study was not double-blinded. In a prospective double-blinded randomized study done by Yogendran et al, high-infusion fluid therapy was compared with low-infusion\(^8\). They demonstrated that the incidence of adverse outcomes, such as thirst, dizziness and drowsiness, was significantly lower in the high-infusion than in the low-infusion group at 30 min and 60 min after surgery, at discharge and on the first postop. day\(^8\). Our prospective double-blinded randomized study also demonstrated that high dose preoperative fluid therapy (20 ml/kg) could significantly decrease the incidence of thirst and vomiting at 30 and 60 minutes postop.

Postoperative adverse effects are potentially dangerous and disturbing for patients. They delay early discharge, home readiness and increase the workload of the nursing staff. Hydration was advantageous in reducing the incidence of adverse postoperative effects and therefore, achieving a higher rate of patients’ satisfaction.

Different intraoperative fluid therapy regimens have been suggested. These different methods have been proposed depending on the type of surgery. Most studies have suggested administering fluid in order to obtain a urine output of 1 ml/kg/hour\(^12\). However, there has been no standardized fluid regimen therapy for patients scheduled for ambulatory surgery.

Yogendran et al had suggested 20 ml/kg based on the daily water requirement of approximately 30 ml/kg per day\(^8\) confirming our finding that this amount of hydration had significant effects in decreasing postoperative side effects. This amount of hydration was especially useful in our patients, as in our setting, ambulatory surgeries are mostly done in the afternoon and elective operation are done in the morning. Therefore, our patients had been fasting for more than 12 hours (from 12 midnight
until 1 PM of the next day) and so patients were in a dehydrated condition.

Our study reveals that alleviating dehydration with adequate fluid therapy reduced the incidence of postop. thirst and vomiting, within the first 60 minutes. It is therefore concluded that preoperative hydration (20 ml/kg) for patients who are undergoing general anesthesia in short ambulatory surgery, is recommended.
References

MALPOSITION OF CENTRAL VENOUS CATHETER IN THE LEFT INTERNAL JUGULAR VEIN

- A Case Report-

MOHAMMAD REZA KHAJAVI*

AND MASSOUD SEDIGHI**

Abstract

Malposition of central venous catheter is a complication of central venous catheterization. A case of left internal jugular catheterization via left external jugular vein is reported. Details of the procedure are described and the literature is reviewed for similar malpositions.

Key Words

Central venous catheterization; Internal jugular vein; External jugular vein, Malposition.

Case Report:

A 14-yr-old girl with a 3-month history of seizure was admitted to intensive care unit for management of intractable seizure. On the forth day of her admission, a decision was made to start parenteral feeding. A 16 gauge single lumen 20 cm catheter-venoseld-was placed into the left...
external jugular vein. The entry point was midway from a line drawn between the suprasternal notch and the mastoid process. The patients ipsilateral arm was placed at the side and an assistant applied mild traction on the shoulder to straighten the course of the external jugular vein while the guide wire was advanced. By using guidewire the No. 16 catheter was inserted into the external jugular vein. The anteroposterior chest X-ray showed the tip of the catheter, in the left internal jugular vein (Fig. 1).

![Fig. 1](image)

*Fig. 1*

*Malposition of central venous catheter in the left internal jugular vein*

**Discussion**

Exact placement is an essential prerequisite for long-term use of a central venous catheter. Catheter malposition is a known complication of central venous catheterization. Reported data show an extremely wide range of catheter misplacements: from less than 1% to more than 60%. Malatinsky et al reported 5.3% occurrence of faulty positioning and coiling, while external jugular incidence was 30%. Paw stated that
catheterization via the left internal jugular vein results in more malposition and vascular perforation than catheter placed from the right internal jugular vein. According to Muhm et al. study the frequency of malpositioning was related to the anatomic approach and the catheter type used, but not to the physicians experience. Their reported respective incidences were 4.12% for the left internal jugular access, but were lower for the right internal jugular (1.1%); Misplacement was more frequent with soft silicone catheters (2.53%) than with semi-rigid catheters (0.79%).

External jugular vein traverses the deep fascia of subclavian triangle and ends in the subclavian vein, lateral or anterior to scalenus anterior (Fig.2). It has valves at its entrance in to the subclavian vein and about 4 cm above the clavicle.

Fig. 2
Communication between internal jugular vein and external jugular vein via brachiocephalic vein

MOHAMMAD REZA KHAJAVI
According to the described anatomy, the probability of left internal jugular catheterization via left external jugular vein is very low. There is no any reported case in the literature about such a misplacement. Our reported case has two factors that may be implicated in malpositioning. First, the size of chosen catheter is relatively large and not appropriate for the patients age. Second, the curved tip of guidewire led to its bending and entrance in to the internal jugular vein.

References
CARDIAC TEMPOANDE FOLLOWING
LEFT INTERNAL JUGULAR VENOUS
CATHETERIZATION
- A Case Report -
O. AL-AZAWI*, R. SHEHAB** AND M.O. ABABNEH***

Central venous catheterization is a routine procedure performed by
anesthetists. Various complications, have however, been reported during
this procedure. Cardiac temponade, for one, is a rare but serious life
threatening complication. Although percutaneous catheterization of
central veins is a routine procedure requiring advanced operating skills,
yet the monitoring, early detection and management of cardiac temponade
is vitally important.

We report a case of cardiac temponade following central venous
catheterization in a patient who underwent a living related liver
transplant, where the diagnosis of cardiac temponade, initially missed,
was later diagnosed and successfully managed.

Case Report

A 46 year old man, underwent a living related liver transplant
(LRLT). The patient was a known case of chronic B hepatitis with liver
cirrhosis and end stage hepatic failure. He was jaundiced, slightly
tachypneic with large abdominal distension due to ascitis. The liver
function tests were impaired, platelet count $81 \times 10^3/L$, prothrombin time
(PT) 37.7 sec., partial thromboplastin time (PTT) 69.7 sec., international
normalized ration (INR) 3.95 and impaired renal function with urea 117
mg/dl and creatinine 1.6 mg/dl. Otherwise normal electrolytes. 
Echocardiography showed no evidence of pericardial effusion and an

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ejection fraction (EF) of 70%.

After intravenous and left radial arterial cannulation, the patient was induced and the standard monitoring for the procedure was applied. A triple-lumen central venous catheter (Arrow-Howes, multi-lumen central venous, catheterization set with blue flextip Catheter) was introduced through the left internal jugular vein using Seldinger's technique. The procedure was performed by a senior anesthetist, a traumatically, from first attempt. A slight hematoma occurred at the site of the puncture with continuous blood ooze that necessitated firm pressure for nearly an hour.

Surgery progressed uneventfully for 2 hours: Patients vital signs were stable with systolic blood pressure ranging from 95-110 mmHg, diastolic blood pressure 55-70 mmHg, H.R. 90-110 beats/min with initially high central venous pressure (CVP) 11 mmHg which dropped to 3 mmHg after opening the peritoneum and draining the ascitis (7 liters).

Vigorous infusion of the patient with crystalloids, albumin 5% and fresh frozen plasma to keep the CVP 4-6 mmHg. But the patients blood pressure and pulse pressure started to decrease, and the CVP to increase. Epinephrine infusion was started with slight improvement. Later on it was not possible to keep the systolic blood pressure above 60 mmHg, and the CVP increased to reach 25 mmHg. Epinephrine boluses were given just to keep the blood pressure 40/30 mmHg and a further increase in CVO to 28 mmHg, and a heart rate of 140 beat/min.

At this stage the surgeon noticed bulging of the pericardium into the diaphragm, and in view of patient's condition, it was decided to open a pericardial window. A 700 ml of fresh blood was evacuated from the pericardial cavity. Immediately patient's vital signs improved, with arterial blood pressure measuring 120/80 mmHg, CVP decreased to 6 mmHg and the pulse rate to 100 beat/min. Patient remained stable and no further blood loss through the pericardial cavity was noticed, and the operation went uneventfully.

Discussion

Complications from central venous catheters are numerous. Cardiac
Cardiac tamponade is a rare but well documented complication that is often fatal\(^1\). The incidence is not clear as reports are extremely variable ranging from 0.0001% to 1.4% of all catheter insertions with no distinction in the causes, and under reporting of the condition is likely\(^2\). Mortality rate, ranges from 100% to 47%\(^3\). Cardiac tamponade can manifest itself within minutes of insertion of a central venous catheter to several months later\(^4\).

The variation in report incidence and time to presentation is partly related to the many risk factors associated with this complication. Direct trauma at insertion predispose to vascular or endocardial damage and perforation. The site of insertion and position of the catheter tip are important factors.

Cardiac tamponade is more frequent when catheters are inserted via peripheral rather than central veins\(^5\).

The angle that the catheter tip forms with the wall of a vein or cardiac chamber is thought to be an important factor responsible in vessel trauma. When the tip lies at a more perpendicular angle to the wall there is an increased chance of direct trauma and erosion\(^6\). This is relevant when considering catheters inserted via the subclavian veins or left internal jugular vein, as their more tortuous anatomical course.

In the case presented it was initially difficult to suspect cardiac tamponade, as the procedure was straightforward with no difficulties encountered even during the manipulation of excessive traction in the abdomen and the chest wall to facilitate hepatectomy and the presence of ascitic fluid loss. However, in retrospect we had signs and symptoms of cardiac tamponade. Our patient started to develop hypotension, raised central venous pressure, narrow pulse pressure and tachycardia, and unfortunately the diagnosis was missed considering that the patient had an end stage liver disease with abnormal bleeding profile and excessive manipulation and traction in the area.

Early recognition and treatment of cardiac tamponade is therefore essential if mortality to be avoided, as misdiagnosis of cardiac tamponade can lead to catastrophic outcome.

Percutaneous insertions of central venous catheters are usually done
by using surface anatomical landmarks (palpable or visible structures) with known relationships to the desired vein.

Catheterization via the internal jugular vein may result in fewer malpositions than catheterization via the subclavian vein. Generally, catheterization via left internal jugular vein results in more malposition and vascular perforation than a catheter placed from the right internal jugular vein. This is because the right internal jugular vein runs into the right brachiocephalic vein in a fairly straight course, whereas the left internal jugular vein forms a greater bend when it becomes the left brachiocephalic vein, and more perpendicular angle with which the tip may lie compared with the vessel wall. The left internal jugular vein was chosen in this case because there was a previous scar and a more dilated external jugular and subcutaneous veins on the right side.

In summary this case, illustrates the need to maintain a high level of awareness about the complications of central venous catheterization, even when preventive practices suggest it is sited correctly. Cardiac tamponade must be considered in any patient with an indwelling central venous catheter who shows evidence of clinical deterioration.

Reference

CERVICAL PLEXUS BLOCK FOR CAROTID ENDARTERECTOMY FOLLOWED BY GENERAL ANESTHESIA FOR ABDOMINAL AORTIC SURGERY

- A Case Report -
ALEXANDRE YAZIGI*, FADIA HADDAD*, SAMIA MADI-JEBARA*, GEMMA HAYECK* AND VICTOR JEBARA*

Abstract

The aim of this clinical report is to describe the use of sequential regional and general anesthesia for concomitant carotid and abdominal aortic surgery. We performed, in a 70-year-old man, a cervical plexus block for carotid endarterectomy (CEA) followed immediately by general anesthesia for resection of an abdominal aortic aneurysm. This anesthetic approach provided adequate surgical conditions. Intraoperative neurological status and cardiovascular parameters were stable and postoperative course was uneventful.

Sequential regional and general anesthesia may be an alternative to general anesthesia for concomitant carotid and abdominal aortic surgery. This approach offers an adequate neurological monitoring during the CEA phase of the combined surgery and the opportunity to postpone the aortic surgery should the CEA be associated with a non-reversible neurological deficit.

Key words: Cervical plexus block; carotid endarterectomy; abdominal aortic aneurysm; combined carotid and aortic surgery.

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Introduction

Combined carotid endarterectomy (CEA) and abdominal aortic surgery under general anesthesia has been reported in patients with coexisting severe carotid and aortic diseases\textsuperscript{1,2,3}. However, CEA may be complicated by decreased brain perfusion during carotid clamping and by cerebral emboli related to plaque dislodgement\textsuperscript{4}. These events could be undetected in patients under general anesthesia and aggravated when CEA is immediately followed by an abdominal aortic surgery.

Cervical plexus block is a regional anesthesia technique currently used for isolated CEA\textsuperscript{5,6}. The advantages of regional anesthesia in carotid surgery are efficient neurological monitoring in awake patient and avoidance of the routine use of an intra-luminal shunt. In an attempt to improve neurological monitoring in a patient undergoing combined CEA and resection of an abdominal aortic aneurysm, we report the use of a cervical plexus block for carotid surgery followed by general anesthesia for aortic surgery.

Case Report

A 70 year-old man weighing 100 kg with a history of diabetes, arterial hypertension and repeated transient ischemic attacks was admitted to Hotel Dieu de France hospital for further evaluation.

Detailed angiographic studies showed a 90% left internal carotid stenosis and an infrarenal aortic aneurysm with a diameter of 6 cm. Cardiac catheterization revealed no surgical coronary lesions and normal left ventricular wall motion with an ejection fraction of 50%. The patient was scheduled for combined left CEA and abdominal aortic aneurysm resection. The “combined” surgical approach was chosen by the medical team because of its feasibility and safety\textsuperscript{1,2,3}, and because it offers a single-stage treatment to the patient.

Regular medication, including atenolol and insulin, was continued up to the morning of surgery. Hydroxyzine 1 mg/kg was given as premedication. Baseline heart rate and blood pressure were 65 beats/min
and 140/70 mmHg.

In the operating room, a 16-gauge peripheral venous line and a 20-gauge right radial arterial line were inserted under local anesthesia. Monitoring was completed with pulse oxymetry and continuous electrocardiography with a multi-lead dual-channel oscilloscope and computerized ST-segment analysis.

A left deep and superficial cervical plexus block was performed by using a total of 30 mL of 1.5% lidocaine. To perform the deep cervical plexus block, the transverse processes of C2, C3 and C4 were located by drawing a line from the mastoid to the tubercle of Chassaignac and moving down the line 2 cm for each transverse process. Two-inch needles were placed at these processes and 7 ml of lidocaine solution were injected in each needle to block C2, C3 and C4 nerve roots. The superficial cervical plexus was anesthetized along the posterior border of the sternocleidomastoid muscle with 10 ml of the same local anesthetic solution.

The patient was breathing spontaneously with oxygen delivered by a nasal probe. The left carotid artery was exposed and a clamping test procedure showed good tolerance with no changes in mental status or motor response. Carotid endarterectomy was completed without an intraluminal shunt.

During the 70-min surgical procedure the patient received 2 mg of midazolam and was fully cooperative. His neurological status, determined by continuous observation of his responsiveness and motor ability, stayed normal. Arterial blood pressure, heart rate and ST-segment changes remained within 10% of their initial values.

Immediately after the end of carotid endarterectomy, general anesthesia was induced with etomidate 0.3 mg/kg, fentanyl 2 μg/kg and pancuronium 0.1 mg/kg. The trachea was intubated and the patient was mechanically ventilated. A pulmonary artery catheter was placed via the right internal jugular vein. A bladder catheter and a rectal temperature probe were inserted. Anesthesia was maintained with an intravenous infusion of midazolam 0.1 mg/kg and fentanyl 2 μg/kg per hour.
The surgical exposure technique was median laparotomy. Aortic repair was achieved by resection of the aneurysm and placement of a bifurcated prosthetic graft. The duration of aortic clamping was 75 min. Hemodynamic parameters and urine output were kept within normal limits by fluid loading and vasoactive drugs. No neurological monitoring was available during the aortic phase of the combined surgery.

At the end of the surgical procedure, the patient was admitted to the ICU. He was weaned from mechanical ventilation and the trachea was extubated during the following four hours. Physical examination revealed an intact neurological status. Postoperatively the patient had no surgical, cardiac or neurological complications. He was discharged from the ICU on the second postoperative day and from the hospital on the tenth day.

**Discussion**

The use of regional anesthesia for CEA followed immediately by general anesthesia for cardiac surgery has been cited in a single case report. This sequential anesthesia approach has not been previously described for combined CEA and major abdominal aortic surgery. In our case, the sequential use of cervical block and general anesthesia for concomitant CEA and aortic aneurysm resection was successful and well tolerated by the patient. It also provided adequate surgical conditions, hemodynamic stability and efficient neurological monitoring during the CEA phase of the combined surgery.

Several studies cited the value of direct assessment of central nervous system function and the ability to determine the need for intra-luminal shunting as major advantages of regional anesthesia for CEA. Although neurological function under general anesthesia can be monitored by such methods as electroencephalogram, somatosensory evoked potentials and transcranial Doppler ultrasound, these techniques are not always available and direct evaluation of neurological function in awake patients is a reliable alternative. Even more, a conscious patient during CEA allows the surgeon to assess the need of an intra-luminal shunting. Placement of shunts has associated morbidity and
also may make removal of the carotid plaque more difficult\textsuperscript{11}.

Although large carotid surgery trials did not show an effect of regional anesthesia on outcomes, these trials did not include patients with combined carotid and major vascular surgery\textsuperscript{12}. Patients undergoing concomitant CEA and abdominal aortic surgery are still at risk of perioperative neurological complications\textsuperscript{13,14}. If both surgical procedures are achieved under general anesthesia, a neurological insult during carotid surgery may be undetected and aggravated by the hemodynamic and metabolic modifications during aortic surgery. The sequential anesthesia approach described in this case provides the opportunity to postpone the aortic surgery should the CEA be associated with a non-reversible neurological deficit or other unexpected complications.

The anesthesia approach for combined CEA and abdominal aortic surgery described in this case carried some risks. First, carotid surgery under regional anesthesia may be associated with anxiety or residual pain. These conditions increase myocardial oxygen consumption and may lead to cardiac ischemia in patients with severe coronary stenosis. Second, deep cervical plexus block may be complicated by a hematoma of the neck and by an intravascular or intrathecal injection of the local anesthetic\textsuperscript{14}. None of these complications was observed in our patient. Third, the patient was kept awake during CEA, but there was no follow-up neurological monitoring during aortic surgery where neurological deterioration could have happened. If somatosensory evoked potentials or transcranial Doppler ultrasound were used from the beginning, the patient would have been neurologically monitored for both procedures. Unfortunately, these techniques are not available in our institution.

In conclusion, the combination of cervical plexus block for carotid surgery followed by general anesthesia for aortic surgery was safe and efficient in a patient undergoing concomitant CEA and abdominal aortic aneurysm resection. This sequential anesthesia approach may be an interesting alternative to general anesthesia, allowing better neurological monitoring in patients with severe carotid and aortic diseases and providing the opportunity to postpone the aortic surgery should the CEA be associated with a non-reversible neurological deficit. Larger studies
are needed to identify the disadvantages and the benefits of sequential regional and general anesthesia for combined carotid and abdominal aortic surgery.

References

EHLERS-DANLOS SYNDROME: COMPLICATIONS AND SOLUTIONS CONCERNING ANESTHETIC MANAGEMENT

BARRETT A. JOHNSTON*, KAITLIN E. OCCHIPINTI*, AMIR BALUCH** AND ALAN D. KAYE***

Introduction

Ehlers-Danlos syndrome (EDS) is a heterogeneous group of connective tissue disorders organized into six clinical subtypes and eleven variants¹. Each subtype is based on the severity of clinical symptoms, the pattern of inheritance and the underlying genetic defect. The complex cascade and the many proteins involved in the synthesis of collagen provide ample opportunity for mutations to occur and generate faulty collagen. All of the gene mutations that have been identified for specific subtypes of EDS involve the synthesis of collagen, collagen-modifying proteins/enzymes and tenascin-X²³. Consequently, these mutations lead to dysfunctional collagen and cause the classical signs and symptoms of EDS. The most noticeable symptoms are those involving tissues with an abundance of collagen: skin, ligaments, joints, and vessels. The most common clinical symptoms observed in varying degrees in all subtypes of EDS include hyperextensibility and severe fragility of the skin, hypermobile joints, and easy bruising. However, some subtypes have unique signs and symptoms pathognomonic to that subtype and incur their own prognosis. Management of EDS incorporates prevention of complications involving injury to the skin, vessels and joints⁴.

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The anesthesiologist must be extremely careful as there is constant risk of causing preventable injuries. Common, yet necessary, tasks including cannulation of veins, insertion of endotracheal tubes, and intramuscular injections become interventions with exaggerated and unavoidable risks5.

Epidemiology

Ehlers-Danlos Syndrome (EDS) is estimated to affect 1 in 5000 people6. A higher value has been reported in the black population7. It has a polygenic etiology with the most common types being autosomal dominant, but an X-linked recessive and several autosomal recessive patterns have also been identified89.

The first clinical description of EDS in 1892 dates back to a Russian dermatologist, Dr. Tschernogobow. Drs. Ehlers and Danlos, Danish and French dermatologists, further expanded on the condition. Later, the genetic heterogeneity of EDS was established in the 1960s, and the first molecular defects in collagen biosynthetic pathways were delineated in 197210.

Pathogenesis and Molecular Genetics

Ehlers-Danlos Syndrome is a clinically and genetically heterogeneous group of conditions. Traditionally, it was subdivided into eleven variants. The latest classification of EDS, the Villefranche Nosology, was developed at a consensus conference in 199710. Currently six subtypes, based on the severity of the clinical symptoms, the pattern of inheritance and the underlying biochemical and molecular defect are recognized11 [Table 1]4. The classical types (EDS I, EDS II) and the hypermobile type (EDS III) are found in 90%. The vascular type (EDS IV) occurs in 3-10%. The kyphoscoliosis, arthrochalasis, and dermatosparaxis types represent very rare conditions12.
<table>
<thead>
<tr>
<th>Type</th>
<th>Protein</th>
<th>Inheritance</th>
<th>Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classic (type I/II)</td>
<td>Type V procollagen</td>
<td>AD</td>
<td>Major: hyperextensible skin, widened atrophic scarring, joint hypomobility. Minor: easy bruising, smooth/velvety skin, molluscoid pseudotumors, subcutaneous spheroids, hypotonia, complications of joint hypomobility, surgical complications, positive family history</td>
</tr>
<tr>
<td>Hypermobility (type III)</td>
<td>Unknown</td>
<td>AD</td>
<td>Major: generalized joint hypomobility, mild skin involvement. Minor: recurring joint dislocations, chronic joint pain, positive family history</td>
</tr>
<tr>
<td>Vascular (type IV)</td>
<td>Type III procollagen</td>
<td>AD</td>
<td>Major: excessive bruising, thin and translucent skin, arterial/intestinal/uterine fragility or rupture, characteristic facial appearance. Minor: acrogeria, early-onset varicose veins, hypomobility of small joints, tendon and muscle rupture, arteriovenous or carotid-cavernous sinus fistula, pneumo(hemo)thorax, positive family history, sudden death in close relative</td>
</tr>
<tr>
<td>Kyphoscoliotic (type VI)</td>
<td>Lysyl hydroxylase</td>
<td>AR</td>
<td>Major: severe muscular hypotonia at birth, generalized joint laxity, kyphoscoliosis at birth, scoliosis and scoliosis of the globe. Minor: tissue fragility, easy bruising, arterial rupture, marfanoid habitus, microcornea, osteopenia, family history</td>
</tr>
<tr>
<td>Arthrochalasis (type VIIA/VIIIB)</td>
<td>Type I procollagen</td>
<td>AD</td>
<td>Major: severe generalized joint hypomobility with recurrent subluxation, congenital bilateral hip dislocation. Minor: skin hyperextensibility, tissue fragility, easy bruising, muscular hypotonia, kyphoscoliosis, mild osteopenia, occasionally fractures</td>
</tr>
<tr>
<td>Dermatosparaxis (type VIIIC)</td>
<td>Procollagen-N-proteinase</td>
<td>AR</td>
<td>Major: severe skin fragility, sagging, redundant skin, excessive bruising. Minor: soft, doughy skin texture, premature rupture of membranes, large herniae</td>
</tr>
</tbody>
</table>
Specific mutations of genes for collagen, collagen-modifying enzymes and tenascin have been described in most types \(^{11}\). Collagens are structurally related, extracellular matrix proteins that are essential for development and organogenesis, cell attachment, platelet aggregation and for providing tensile strength to the connective tissues in bone, skin, ligaments and tendon. These collagen proteins are homo- or heterotrimeric molecules that share unique triple-helical domains. The presence of glycine in every third position of each chain is necessary for the formation of a stable collagen helix. The fibrillar collagens are the most widespread and abundant class of collagens and include types I, II, III, V and XI. Precursor molecules, known as procollagens, initiate the biosynthesis of collagen within the fibroblast. These procollagens align and bond from the C- to the N-terminal end of the molecule and, through a series of enzymatic modifications, the triple-helix is formed. Individual collagen molecules then spontaneously assemble into fibrils which are stabilized by covalent cross-linking. A disturbance anywhere along this process can lead to connective tissue instability\(^{4,10}\).

EDS involves collagen types I, III, and V. Type I collagen is the major collagen type in the body and has a wide distribution. A mutation resulting in structural abnormality of type I will result in the arthrochalasis type of EDS, whereas, a mutation leading to abnormal processing collagen results in the kyphoscoliosis or dermatosparaxis type. In the kyphoscoliotic form, there is a deficient activity in the collagen-modifying enzyme lysyl hydroxylase-1, and, in the dermatosparaxis type, the mutation involves the enzyme procollagen-N-proteinase. Type III collagen is an essential component of many connective tissues found in blood vessels, the gastro-intestinal tract, the uterus and the skin. A mutation in type III collagen, whether structural or haplo-insufficient, results in the vascular type of EDS. Type V collagen is co-expressed with type I in many connective tissues and its mutation results in 50% of classic type of EDS. In rare instances, a mutation causing the substitution of glycine in the procollagen chain of type I collagen has also been identified as a cause of classic EDS\(^6\).

Previously, EDS has been considered solely as a disease of collagen.
Zweers et al, however, recently demonstrated that a deficiency of
Tenascin-X may also contribute to the pathogenesis of EDS. Tenascin-X
(TNX) is a large extracellular matrix protein developmentally associated
with collagen fibrils and is thought to maintain homeostasis of the
extracellular matrix. Its deficiency is associated with fragmentation of
elastic fibers, reduction of collagen, failure of fibroblasts to correctly
deposit collagen type I, and loose packing of collagen fibrils. It was also
determined that an autosomal recessive type of EDS due to TNX
deficiency is associated with some cases of dominantly inherited
hypermobility type of EDS. Moreover, elastic fiber abnormalities in
hypermobility type EDS are specific for TNX-imploinsufficient
individuals.\textsuperscript{10,11}

Clinical Features

The diagnosis of Ehlers-Danlos Syndrome is based primarily on
clinical criteria. Clinical manifestations are present, to varying degrees, in
each subtype of the condition\textsuperscript{1}. The principle clinical features include
easy bruising and generalized connective tissue fragility, skin
hyperextensibility, delayed wound healing with atrophic scarring, and
joint hypermobility\textsuperscript{13,14} [Table 2] These features are secondary to the
disruption of tissues rich in collagen, such as skin, ligaments, and joints\textsuperscript{2}.

\begin{table}
\centering
\caption{Characteristics of EDS}
\begin{tabular}{|c|}
\hline
\textbf{Principle Clinical Features} \\
\hline
Easy bruising \\
Joint hypermobility \\
Skin hyperextensibility \\
General connective tissue fragility \\
Delayed wound healing + atrophic scarring \\
\hline
\end{tabular}
\end{table}

Easy bruising is typically the initial manifestation. Bleeding from the
gums following brushing of the teeth, or excessive bleeding after minor
trauma are common presentations\textsuperscript{4,9,15}. Vascular fragility may cause of
nonpalpable purpura. \(^{16}\)

Hematological studies such as the platelet count, bleeding time, and coagulation tests are usually normal. \(^4\) However, the Rumpel-Leede (or Hess) test may be positive, indicating capillary fragility. To apply the Rumpel-Leede test, the physician applies a blood-pressure cuff to the upper arm and inflates to a level between the diastolic and systolic pressure values. In a patient whose blood pressure is 120/80, the cuff may be inflated to 100 mmHg, for example. After pressure is maintained for 5 minutes and released, the number of petechiae are counted, with greater than 10 spots recorded as abnormal (positive) \(^{9,15}\).

Skin hyperextensibility should be tested at a neutral site such as the volar surface of the forearm as it less subjected to mechanical forces or scarring. To determine the amount of hyperextensibility, the skin is pulled up until the clinician feels resistance. It may be difficult to assess hyperextensibility in the skin of young children due to large amounts of subcutaneous fat. \(^4\)

Tissue fragility results in splitting of the skin following relatively minor trauma. Areas particularly at risk are the knees, elbows, shins, forehead and chin. Lacerations and incisions heal slowly. Widened atrophic scars, “cigarette-paper scars”, are also a manifestation of tissue fragility. \(^3,8,9\). Additionally, in areas of repetitive trauma, hemosiderin deposition may lead to dark discoloration of the skin. \(^4\)

\(\text{Table 3}\)

The nine-point Brighton hypermobility score (Ref. 9) One point may be gained for each side for maneuvers 1-4 so that the hypermobility score will have maximum of nine points if all are positive. A score of 4/9 indicates widespread hypermobility.

<table>
<thead>
<tr>
<th>Ability</th>
<th>Left</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passively dorsiflex the fifth metacarpophalangeal joint to 90°</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Oppose the thumb to the volar aspect of the ipsilateral forearm</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hyperextend the elbow to 10°</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hyperextend the knee to 10°</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Place hands flat on the floor without bending knees</td>
<td>1</td>
<td></td>
</tr>
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</table>

Max possible score: 9
Joint hypermobility often affects large and small joints and can be assessed using the Beighton scale [Table 3]. A score of \( \geq 4.9 \) defines widespread joint hypermobility.

The Beighton criteria can also be used to diagnose joint hypermobility syndrome [Table 4]. Hypermobility may lead to occasional or frequent dislocations of joints. Those most commonly involved are the shoulder, hip and patella\(^4\). Joint hypermobility also leads to chronic musculoskeletal pain and possibly premature degenerative joint disease\(^17\).

### Table 4

**Beighton criteria for joint hypermobility syndrome (JHS)** (Ref. 8) JHS is diagnosed in the presence of two major criteria, or one major and two minor criteria, or four minor criteria. Two minor criteria will suffice where there is an unequivocally affected first-degree relative.

<table>
<thead>
<tr>
<th>Major</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>• Beighton score of ( \geq 4.9 ), or more (either currently or historically).</td>
<td></td>
</tr>
<tr>
<td>• Arthralgia for longer than 3 months in four or more joints.</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Minor</th>
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</thead>
<tbody>
<tr>
<td>• A Beighton score of 1-3 out of 9 (0-3 if aged 50+).</td>
<td></td>
</tr>
<tr>
<td>• Arthralgia in 1-3 joints, or back pain or spondylosis, spondylolisthesis.</td>
<td></td>
</tr>
<tr>
<td>• Dislocation in more than one joint, or in one joint on more than one occasion.</td>
<td></td>
</tr>
<tr>
<td>• Three or more soft tissue lesions (e.g. epicondylitis, tenosynovitis or bursitis).</td>
<td></td>
</tr>
<tr>
<td>• Marfanoid habitus (tall, slim, arm span &gt; height, arachnodactyly).</td>
<td></td>
</tr>
<tr>
<td>• Skin striae, hyperextensibility, thin skin or abnormal scarring.</td>
<td></td>
</tr>
<tr>
<td>• Eye signs: drooping eyelids, or myopia, or anti-mongoloid slant.</td>
<td></td>
</tr>
<tr>
<td>• Varicose veins, or hemia, or uterine/rectal prolapse.</td>
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</tbody>
</table>

Cardiovascular manifestations range from no apparent lesion to arterial aneurysms, arterial rupture without aneurysm, varicose veins, aortic regurgitation, mitral valve prolapse and conduction disturbances\(^8,9\). Floppy mitral valve syndrome and the combination of mitral and tricuspid insufficiency due to redundant chordae tendineae or valve cusps have been reported\(^9,15\). There does not seem to be a particular succession of cardiovascular lesions\(^8,9\).
Other common manifestations to all types of EDS are a result of the deficiency in collagen, such as spontaneous pneumothorax, diverticula of the intestine or bladder, meaeosphagus, megatrachea, and megacolon. Diaphragmatic, umbilical and inguinal hernias are common\textsuperscript{9,15}.

Some signs and symptoms are more characteristic of certain subtypes based on the specific deficiency present [Table 1]\textsuperscript{4}. In classic EDS (type I/II), the skin is described as very soft and "velvety"\textsuperscript{8,9}. Molluscoid pseudotumors and subcutaneous spheroids are present. Also, prematurity due to premature rupture of the membranes is more frequent than in the general population. In severe cases, aortic and bowel rupture may occur. In the hypermobility type of EDS (type III), joint hypermobility with recurrent dislocations is a much more prominent feature than skin changes\textsuperscript{4}.

The vascular type of EDS (type IV) is the most clinically significant since it has the most severe presentation and is the only form with an increased risk of death. Complications are relatively rare in childhood, but 25% of these patients have some type of complication by age 20 and greater than 80% have some form of complication by age 40\textsuperscript{19}. Some manifestations early in life may include premature rupture of membranes in the mother, congenital clubfoot, or congenital hip dislocation. Furthermore, the median lifespan is 48 years\textsuperscript{20}. This type of EDS is the result of mutations in type III collagen which is abundant in major blood vessels, skin, and hollow viscera. Diagnosis is based on presence of two of the following: thin, translucent skin, arterial/intestinal/uterine rupture, easy bruising, and characteristic facial appearance\textsuperscript{21}. The typical features of joint hypermobility and skin hyperextensibility seen in most forms of EDS are relatively unusual in type IV. The connective tissue matrix of major vessels and viscera is more likely to be affected. In fact, 70% of arterial collagen is composed of type III collagen\textsuperscript{20}. Arterial rupture may take the form of tears, dissection or fistula formation. Medium-sized arteries of the thorax and abdomen are the most commonly involved\textsuperscript{19}. Cystic medial necrosis of the proximal aorta is prevalent\textsuperscript{7}. Hollow visceral rupture is also a complication of this form of EDS. There are reports of gastric, small intestine, and large intestine perforation/rupture, with the
sigmoid colon at particular risk. Facial dysmorphism consists of a slender face, with prominent bones, sunken cheeks, a thin nose, thin lips, eyelid telangiectasia, periorbital pigmentation, lobeless ears and possible bulging eyes. The skin is not hyperelastic but thin and translucent, showing a visible pattern over the chest, abdomen, and extremities. Other skin changes may include acrogeria or an excessive wrinkling and thinness of the skin over the hands and feet. Less usual skin manifestations include keloid formation, Raynaud phenomenon and elastosis perforans serpiginosa, which is seen as keratotic plugs within an annular lesion particularly on the neck and antecubital fossae. Obstetrical complications are frequent and these patients should be considered high-risk. Some of these complications include uterine rupture usually in the third trimester, vaginal lacerations, prolapse of uterus and bladder, premature delivery because of cervical insufficiency or fragility of membranes.

The kyphoscoliotic form of EDS (type VI) can be recognized by severe muscle hypotonia and joint hypermobility at birth. Severe, progressive kyphoscoliosis is usually present. These patients may also demonstrate ocular fragility that may lead to retinal detachment, bleeding and rupture of the ocular globe, and microcorneata.

In the arthrochalasia type of EDS (type VIIA/B), severe joint hypermobility and congenital bilateral hip dislocation is frequently present. The skin is only moderately hyperextensible and there is usually only mild to moderate bruising. This presentation is in sharp contrast to the dermatosparaxis type of EDS (type VIIC), where severe bruising and extreme fragility and laxity of the skin are present during childhood. Other characteristic features include large fontanels, short stature, typical facies with epicanthic folds, downslanting palpebral fissures, puffy eyelids, blue sclera, and micrognathia.

**Therapy**

There is no causal therapy available for EDS, however, a series of preventative guidelines based on common sense and clinical experience
can be applied to all forms. For example, patients with skin fragility should wear protective pads or bandages over the forehead, knees, and shins, to minimize skin lacerations. In the instance that dermal wounds do occur, these should be closed without tension and preferably in two layers. Subcutaneous stitches should be applied generously and cutaneous stitches should be left in place twice as long as usual. Additional use of adhesive tape to adjacent skin can help prevent stretching and dehiscence of the scar. Currently, no cases of adverse outcomes with removal of the tape have been reported.

Protective pads and bandages can help prevent bruises and hematomas. Patients with pronounced bruising should avoid contact sports and heavy exercise. In addition, supplementation with ascorbic acid, a cofactor for cross-linking of collagen fibrils, may decrease the tendency of bruising. DDAVP (vasopressin) has also been found to be useful in those with chronic bruising and epistaxis by normalizing the bleeding time.

Cardiac abnormalities should be considered in EDS patients. Patients with mitral valve prolapse and regurgitation require antibiotic prophylaxis for bacterial endocarditis. Because patients with EDS are prone to cardiac conduction abnormalities and aortic dilatation and dissection, a baseline echocardiogram with aortic diameter measurement is recommended prior to the age of 10 years. Follow-up studies can then be performed in those with abnormal findings.

Prophylactic measures are of special importance for patients with the vascular type of EDS. Drugs that interfere with platelet function should be avoided. Invasive vascular procedures, such as arteriography and catherization, should be replaced by ultrasonography and/or subtraction angiography due to the risk of vascular rupture. Surgical interventions are generally discouraged; if unavoidable, careful manipulation of vascular and other tissues is imperative. Moreover, women with type IV EDS should be counseled about the increased risk of uterine rupture, bleeding, and other complications of pregnancy.

Finally, in order to cope with the limitations of the disorder, emotional support and psychological therapy may be indicated for all
types of EDS. Approximately 36% of patients with EDS were found to have a decline in psychological well-being compared to 14% in healthy controls. For this reason, support groups are available and can be beneficial to all those affected by the illness, including families.

Anesthetic Management

Because of the many clinical manifestations of EDS, patients with the condition must be held in special consideration when requiring any anesthetic procedure throughout the perioperative period.

Pre-operatively the patient's EDS subtype should be determined as each hold different challenges. For example, type III patients will be much more prone to joint dislocations, whereas, type IV patients can have deadly vascular complications. All patients should be typed, cross-matched and evaluated for clotting abnormalities due to the propensity to bleed. The anesthesiologist must be prepared for a rapid transfusion. EDS may also predispose to certain cardiac abnormalities. While most are thought to be relatively mild, a detailed cardiac evaluation should be completed prior to any surgical procedure. Particular attention must be paid to conduction abnormalities, most commonly atrial fibrillation secondary to mitral regurgitation and atrial enlargement, which can be continually assessed intra-operatively with ECG monitoring. Furthermore, prophylactic antibiotics may be dispensed to guard against subacute bacterial endocarditis if mitral valve disease is detected. Finally, the cervical spine is evaluated for any atlantoaxial instability due to a laxity in the ligaments.

Peri-operatively many problems arise due to tissue fragility and the propensity for hemorrhage and hematoma formation, therefore, the number of needle sticks should be minimized. According to the National Institute for Clinical Excellence, all central monitoring devices should be inserted under ultrasound guidance to safeguard against rupturing an underlying aneurysm, dissection and rupture. Additionally, these monitors should be used for the minimum amount of time necessary. Anesthetic technique should avoid hypertension since arterial walls are already
weakened. Tissue fragility may also pose a problem with intubation. Any instrumentation of the nose, mouth, or esophagus must be carefully performed with awareness of the patient’s increased susceptibility to bleeding which may potentially lead to a compromised airway. In fact, simple laryngoscopy may damage the gums, mucosa, and airway. Appropriate assessment of endotracheal tube placement should be performed immediately by chest auscultation, CO₂ and O₂ saturation monitoring, and possibly chest X-ray. Fiberoptic intubation should be considered to minimize trauma and to insure proper placement. Airway and dental conditions (i.e. loose teeth) should be evaluated for any defects that may cause intubation difficulties or trauma. If the use of a mask is necessary, the pressure applied to it should be closely monitored to avoid excessive bruising on the face. Vaseline may be considered in this case for protection. Low airway pressures with assisted or controlled ventilation should be maintained due to a higher risk of pneumothoraces.

Skin hyperextensibility is yet another feature that poses a problem for the anesthesiologist. Increased skin laxity impedes vessel fixation for inserting catheters. Furthermore, it may interfere with IV and ET tube placement. Moreover, when taping the IV of ET tube, extra care should be taken to insure proper fixation and to protect against the increased fragility of the skin. Skin hyperelasticity can hide significant vessel trauma and extravasation. Finally, care must be taken with movement and positioning of the patient due to bruising and joint dislocations.

Post-operatively, the same considerations apply. There is an 8-60% chance of pleural effusion experienced by EDS patients in the ICU. There is also a high incidence of surgical emphysema due to accidental tracheal puncture in the peri-operative period. As previously mentioned, all cannulae should be removed as soon as possible. Central venous catheter erosions can result in pleural effusion and pericardial tamponade. These consequences have a 74% incidence of mortality.

All intramuscular and subcutaneous injections, including use of local anesthesia, should be avoided due to the propensity for hematoma formation and bleeding. Also, it has been found that people with EDS may be less likely to gain analgesia from the use of regional anesthetics.
However, use of epidural blocks in obstetric patients has been found to be safe and efficacious. 

Summary

Ehlers-Danlos syndrome is an inherited disorder that results in dysfunctional collagen bundles. These dysfunctional collagen bundles are most noticeable in tissues rich with collagen fibers-skin, vessels, GI, and ligaments. Until gene therapy advancements can correct the underlying gene mutations causing faulty collagen, the mainstay of treatment is prevention of traumatic injury. The success of anesthetic management in patients with EDS requires and understanding of the role of collagen in the various tissues of the body. Collagen-rich tissue fragility, skin hyperextensibility, joint hypermobility, hematoma formation and cardiovascular disease are just some of the complications that need to be accounted for before every anesthetic procedure involving EDS patients. Anesthesiologists should be keenly that any physical manipulation of EDS patients incurs risks of trauma.

References

EHLERS-DANLOS SYNDROME TYPE IV

– Anesthetic Considerations –

– Case Report –

MEI-YING LIANG*, EVA HANKO**
AND M. SAEED DHAMEE***

Abstract

This report describes the anesthetic management of a patient with Ehlers-Danlos syndrome type IV. This is one of the rare genetic disorder which can present both in emergency and as a scheduled surgical case.

Key words

Anesthetic management, Ehlers-Danlos syndrome type IV, Vascular EDS.

Introduction

Ehlers-Danlos syndrome is a group of inherited connective tissue disorders characterized by skin extensibility, joint hypermobility and tissue fragility. There are six major types, with a prevalence 1:560000 to 1:5000\(^1\). Type IV EDS (also known as Vascular EDS), has a high incidence of vascular damage. The arteries are extremely fragile, can have

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multiple aneurysmal formations, spontaneous rupture and dissection. There also high risk of intestinal and uterine ruptures.²

Case report

A thirty-six year old man presented with acute swelling and severe pain of his left arm 18 hours after playing golf. After evaluation with ultrasound of his left upper extremity vasculature, a diagnosis of compartment syndrome was made. He was brought to the operating room for an emergency fasciotomy. Patient was in severe distress due to pain in his left arm. He admitted to easy bruising and slow healing.

On physical examination, he had a long facial contour, long prominent nose and translucent skins. He had long fingers, but with little skin hyperextensibility. His vital signs were within normal limits. His past history was significant that he was diagnosed with Ehlers-Danlos syndrome type IV after a spontaneous rupture of his azygos vein leading to a hemothorax. He had splenectomy done following splenic artery rupture after pushing a car. He had a hepatic artery aneurysm which was treated by embolization. He also gave a history of spontaneous dissection of distal superior mesenteric artery which was treated conservatively.

At age 32, the diagnosis of Ehlers-Danlos syndrome type IV was established after skin biopsy and fibroblast culture, showing deficiency of collagen III. He had a positive family history of Ehlers-Danlos syndrome type IV. His father died at age 36 years with intra-abdominal hemorrhage of unknown etiology, and his sister died at age of 32 from complications of EDS with a positive history of EDS-IV.

Patient was taken to the operating room. General anesthesia was induced with rapid sequence method using propofol, succinylcholine and fentanyl. Under direct view, his trachea was intubated gently with a 7 mm ID endotracheal tube. Anesthesia was maintained with sevoflurane, oxygen and nitrous oxide. Intra-operative management was also focused on controlling the blood pressure as he had a known pre-existing aneurysm of superior mesenteric artery. Intra and postoperative course was uneventful, and he was discharged home the following day.
Discussion

Ehlers-Danlos syndrome is a group of inherited connective tissue disorders characterized by skin extensibility, joint hypermobility and tissue fragility. There are six major types, with prevalence 1:560000 to 1:5000\(^1\). Type IV EDS, also known as vascular EDS, has a high incidence of vascular damage\(^2\). The mutations within the triple-helical coding region of COL 3 A1 (collagen III gene) leading to glycine substitutions and exon skips are the most common. Sometimes deletions of collagen III gene can be seen as well\(^3\). The arteries of these patients are extremely fragile. They can have multiple aneurysm formation and spontaneous rupture and dissection\(^4\), with the high risk of bowel perforation and uterine rupture\(^5\).

Patient with Ehlers-Danlos syndrome type IV can (1) have distinctive features. They have thin, long thin nose, sunken checks and bulging or protruding eyes and thin lips. (2) Very thin and translucent skin. (3) Tendency to bruise easily, delay in wound healing and (4) rupture of vessels, especially the middle sized arteries, and rupture of viscera such as intestine and uterine. Spontaneous rupture of arteries is the most common presenting symptom. Most patients develop these complications before age of 40. Median age in these patients is 48 years\(^2\).

Diagnosis of this syndrome is based mainly on above four clinical features, but definite diagnosis is made on skin biopsy and culture of skin fibroblast, which show mutations within the triple-helical coding region of COL 3 A1 (collagen III gene). Glycine substitutions and exon skips are the most common mutations and some times deletions can be seen as well\(^3\). It is a monogenic disease, transmitted as an autosomal dominant trait. Affected individuals have a 50% chance of passing EDS on the each child\(^6\).

The choice of anesthesia in emergency situation can be general or regional, depending on the site of injury. Even though epidural analgesia has been reported to be used successfully in a patient for labor and delivery\(^7\), bleeding is always a danger because of the fragility of the tissue and difficulty to obtain hemostasis. Often times these patients are presented with a full stomach in an emergency situation with internal
bleeding from a dissecting aneurysm. In these situations, general anesthesia is recommended. Since general anesthesia exposes the patient to the risk of aspiration, laryngeal airway mask is less favorable. LMA can put more pressure on the fragile soft tissue in the pharynx which can cause bleeding from the fragile vessels. Intra-operative management was focused on stabilizing patient’s blood pressure, as these patient always carried great risk of spontaneous visceral or arterial aneurysm rupture\textsuperscript{8,9}. Prophylactic use of DDAVP under consultation of a hematologist has been reported\textsuperscript{10}. In that case report, patient had an increased bleeding tendency with subconjunctival bleeding even after sneezing. Our patient bruised easily, but his coagulation panel was normal, we did not give DDAVP.

In summary, we have described the clinical features and anesthetic management of a patient with Ehlers-Danlos syndrome type IV with multiple episodes of past arterial aneurysm ruptural and/or dissections. Patient was managed with general anesthesia with no peri-operative complications.
References

PARADOXICAL VOCAL CORD MOTION:
AN ALARMING STRIDOR FOR
A BENIGN CONDITION

- Case Reports -

ABDUL-LATIF HAMDAN*, ROGER V. MOUKARBEL**
AND MARWAN YOUSSEF**

Abstract

Paradoxical vocal cord motion presents a challenge to medical practitioners in various specialties. Physicians in general and anesthesiologists should suspect this condition in a patient presenting with stridor or a history of choking or asthma not responding to medical treatment. Women are usually more affected than men and more often there is history of anxiety and/or a precipitating factor such as cough or hyperventilation. Accurate diagnosis relies on visualizing adduction of the vocal cords during inspiration or throughout the respiratory cycle using fiberoptic nasopharyngeal laryngoscopy or telescopic examination.

The etiology varies from organic causes such as brainstem compression or lower motor neuron injury to non-organic causes such as malingering or conversion disorders. The pathophysiology is believed to be accentuation of the glottic closure reflex.

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Many modalities of treatment are available ranging from sedation, voice therapy and breathing exercises to Heliox administration, Botulinum toxin type A injection, intubation and at times tracheostomy.

**Key Words:** Stridor, Paradoxical Vocal Cord Motion, Asthma.

**Introduction**

Paradoxical vocal cord motion is rare entity that presents a challenge to medical practitioners in various specialties. Pulmonary physicians describe it as factitious asthma or hysterical asthma because of poor response to bronchodilators. Otolaryngologists have used terms such as irritable larynx syndrome or functional airway obstruction with the belief that it is a hyperfunctional disorder of the thyrearytenoid muscle precipitated by the inhalation of chemical or other irritants. Anesthesiologists often refer to this entity as episodic paroxysmal laryngospasm witnessed following endolaryngeal manipulation. This diversity in terminology has further confused the diagnosis of this frustrating condition, yet the clinical presentation remains the same, alarming and frightful. Anesthesiologists are often mislead by the symptoms. What is paradoxical Vocal Cord Motion?

We would like to present two cases of paradoxical vocal cord movement, discuss the clinical presentation, pathophysiology, diagnosis and treatment of this rare entity.

**Case Reports**

Case 1: A 62 year old lady not known to be hypertensive, cardiac or diabetic presented with history of choking sensation precipitated by emotional stress or cough. Patient also described stridor with inability to breath during the attack which lasts for minutes and subsides on no treatment. Patient is known to have allergic rhino sinusitis for which she received antihistamines with decongestants. She also reported history of heartburns and regurgitation suggestive of gastro-esophageal reflux for
which she received a proton-pump inhibitor. Patient was suffering from severe depression because of chronic illness that has affected her son. Fiberoptic nasopharyngeal laryngoscopy revealed normal vocal cords mobility with absence of glottic or supraglottic lesions. Laryngeal videoendostroboscopy was normal. Patient was admitted to the hospital for assessment and work-up of her condition. During her stay she suffered from a stridorous attack. Repeated nasopharyngeal laryngoscopies during the attack revealed adduction of the true vocal cords during inspiration and expiration. Patient was reassured and given a positive feedback that she is doing well and consequently the vocal cords resumed normal function and started abducting during inspiration. Patient was informed about her condition and was discharged home on an anxiolytic medication. On follow-up she did well and reported complete resolution of her symptoms.

Case 2: A 90 years old lady presented with history of stridor and inability to breath that affected her daily activity. The attacks came sporadically with no obvious precipitating factor. She denied any other complaints and did not suffer from any chronic illnesses except for hypertension and gastro-esophageal reflux disease for which she was receiving treatment. Patient underwent in and outside hospital all kinds of diagnostic work-up including magnetic resonance imaging (MRI) of the head and neck, Computerized Tomography (CT) of the neck and chest, esophagoscopy and bronchoscopy, all of which were normal. Fiberoptic nasopharyngeal laryngoscopy revealed initially mild abduction of the true vocal cords during inspiration and few seconds later adduction during which she became stridorous (Figure 1 and Figure 2). Patient was reassured during the attack and subsequently the symptoms subsided in few seconds and the true vocal cords resumed normal mobility. Laryngeal video-endostroboscopy did not show any abnormality. Patient was advised psychoanalysis and voice therapy.
Fig. 1
A fiberoptic laryngoscopic view of a 74 year old female with paradoxical vocal cord movement showing complete adduction of the true vocal cords during inspiration resulting in an audible stridor. Please note the diamond shape appearance posteriorly.

Fig. 2
A fiberoptic laryngoscopic view of the same patient when she was symptom free, i.e. not during the attack.
Definition

In early 1974 Christopher et al was the first to report involuntary adduction of the vocal cords during inspiration\(^4\), however the term paradoxical was used only in 1978 by Rogers et al. Since then sporadic attacks of stridor during activity have been associated with the entity of paradoxical vocal cord motion\(^5\). Adults are affected more than pediatrics with a major predominance for middle-aged females in the paramedical field. Affected males are usually achievers and invariably there is a positive history of anxiety or personality disorder\(^6\). Juvenile paradoxical vocal cord dysfunction has also been reported with an average age of 14.5 years. Girls are again more affected than boys (82%), and close to half of them play competitive sports and have history of important social stress\(^7\).

Patients usually describe a choking sensation with inability to breath resulting in an audible inspiratory and /or expiratory sound, i.e. stridor. Wheezing may or may not be present. They may describe tightness in the neck and sometimes in the chest. The attack usually may last seconds to minutes. More often there is a precipitating or an inducing factor such as hyperventilation, cough, panting, phonatory tasks or the inhalation of irritants or perfume, or any oropharyngeal or laryngeal manipulation prior or post extubation. Stress by itself is commonly reported prior to the attacks\(^8\).

All of our patients had history of choking and inability to breathe. In one case the attacks were precipitated by cough, and emotional stress whereas in the other there were no precipitating factors. Change in voice quality, dysphonia or complete aphony may occur but was not present in our cases.

Many co-existing physiologic abnormalities and diseases may be present. These include brainstem abnormalities, functional disorders, neurologic compromises, cystic fibrosis and vagal neuropathy\(^9,10,11\). Asthma is very commonly associated with paradoxical vocal cord motion. Close to 10% of patients with asthma may have paradoxical vocal cord
motion and almost half of patients with paradoxical vocal cord motion have asthma. None of our cases had history of asthma, however both had allergic rhino sinusitis. Gastro-esophageal reflux disease has been attributed to most benign as well as malignant vocal cords lesions. It plays a major role in both organic and functional voice disorders and has been incriminated heavily in most hyperfunctional laryngeal disorders. In our two cases, patients had history of gastro-esophageal reflux disease that was treated with a proton pump inhibitor.

**Diagnosis**

A high index of suspicion is needed to unravel a patient’s condition. Proper awareness of this entity can spare the patient needless diagnostic tests and invasive therapeutic interventions. Inappropriate and dangerous long-term treatment can also be avoided. Diagnosis of paradoxical vocal cord motion relies on the proper visualization of the inspiratory and expiratory activity of the true vocal cords during a stridorous attack. This visualization can be seen using either indirect or direct laryngoscopy. Fiberoptic nasopharyngeal laryngoscopy or telescopic examination of the larynx will reveal paradoxical adduction of the vocal cords during inspiration or throughout the respiratory cycle. A persistent posterior diamond shaped chink as seen in our cases is invariably present. Although pathognomonic, abnormal adductory vocal fold movement during asymptomatic periods of normal breathing have been documented. Laryngeal electromyography of the thyroarytenoid and posterior cricoarytenoid muscles has also shown an increase in activity. This brings up the question whether paradoxical vocal cord motion is a chronic disease or an episodic one. A question that remains to be answered.

Videolaryngoscopy may show a posteriorly positioned epiglottis in 36% of the cases, significant anteroposterior constriction in 41% and abnormal false vocal cords adduction in 45%. These findings strongly suggest an increase in muscle tension pattern described earlier by Koffman et al. In our first case there was antero-posterior constriction...
and mild false cords adduction during inspiration. Posterior glottic changes such as interarytenoid edema and frank pachyderma have also been reported and explained on the basis of laryngopharyngeal reflux disease\textsuperscript{7,14}. The vocal cord functional pattern is usually normal during vocalization except in cases of dysphonia or aphonia where edema of the membranous component of the true cords can be seen. These endoscopic findings are in parallel with the acoustic analysis results reported by Murray et al showing an increase in perturbation parameters and an increase in noise to harmonic ratio\textsuperscript{17}. None of our cases had vocal changes or presented with dysphonia.

A laryngeal video-endostroboscopic study conducted on fifty adults with history of paradoxical vocal cord motion seen between the attacks revealed unstable zero phase reflecting an increase in cycle to cycle variation in frequency, decreased amplitude of vibration, decreased mucosal waves and asymmetry\textsuperscript{15}. These findings further support the hypothesis that paradoxical vocal cord motion is a continuum of laryngeal instability. Laryngeal video-endostroboscopy performed on the two cases presented did not show any abnormalities.

Metacholine/histamine bronchoprovocative tests have also been used for the diagnosis of paradoxical vocal cord motion with failure of response to anti-asthmatic medications\textsuperscript{18}. Flow volume loops study shows attenuation of the inspiratory flow suggesting an extrathoracic airway obstruction. Blood gases are usually within normal.

Radiologic investigation with computed tomography and magnetic resonance imaging of the head, neck and chest are usually normal and non revealing\textsuperscript{8}, as shown in case 2.

The differential diagnosis of paradoxical vocal cord motion includes laryngeal dyskinesia, bilateral vocal cord paralysis, hereditary abductor paralysis, interarytenoid web and cricoarytenoid joint fixation. Patients with exertional dyspnea should also be investigated for paradoxical vocal cord motion. Multiple system atrophy and autonomic dysfunction disorders such as Shy-Drager syndrome have had also nocturnal stridor or sleep apnea syndrome\textsuperscript{19}. 
Classification and Pathophysiology

In the early seventies, paradoxical vocal cord motion also described as episodic laryngospasm was considered under the classification scheme of hyperkinetic laryngeal function reported by Morrison et al. Muscular tension dysphonia, chronic cough, throat clearing and globus pharyngeus were other symptoms listed as secondary to hyperactivity of intrinsic laryngeal muscles. In 1997, Maschka et al from the University of Iowa came with a more complete classification of paradoxical vocal cord motion. These were grouped according to the etiology as being (a) organic such as brainstem compression, upper or lower motor neuron disorders or movement disorders, and (b), non-organic such as factitious or malingering paradoxical vocal cord motion and conversion disorders.

The pathophysiology of paradoxical vocal cord motion is believed to be neurophysiological keeping in mind the psychological background of the patients affected. It is believed to be due to accentuation of the glottic closure reflex. There is an augmentation of the normal physiologic response triggered by an extrinsic or intrinsic stimulant such as an inhaled irritant, allergies, reflux, stress or other emotional triggers.

It starts by excitation of sensory receptors in the upper aerodigestive tract followed by mediation of this afferent information to the brainstem by sensory neuropeptides. This information is integrated at the level of the nucleus tractus solitarius before it is communicated by second order neurons to the efferent limb that starts at the nucleus ambiguus to generate the glottic closure reflex. This theory is substantiated by the fact that laryngospasm can be induced in animals by injecting substance P (a class of sensory neuropeptide) into the nucleus tractus solitarius. Interference with the laryngeal innervation due to surgical manipulation, local trauma to the larynx or endotraheal manipulation has also been reported to induce paradoxical vocal cord motion in patients following thyroidectomy.
Treatment

The most important element in the treatment of paradoxical vocal cord motion is patient's education. Knowing that many cases are self-limiting with an average duration of symptoms 40.5 months is comforting. Psychoanalysis followed by psychotherapy to unravel psychological disorders and emotional disturbances is necessary for each case.

Many modalities of treatment ranging from simple sedation, laryngeal control therapy to tracheostomy have been reported in the literature. Speech and voice therapy combined with breathing exercises with or without nasolaryngoscopic biofeedback are extremely useful. The usage of Heliox (80% helium, 20% Oxygen) to reduce the stridor and continuous positive airway pressure to splint the upper airway have also been described. Anti-allergic and anti-reflux therapy should always be contemplated as adjunctive therapy. Botulinum toxin type A injection into each cord is also an alternative in patients who are cooperative. As an anesthesiologist, intubation and possible tracheostomy should be avoided and should be kept as the last resort only in patients who desaturate and fail.

Conclusion

As a physician dealing with the upper airway, the entity of paradoxical vocal cord motion should always be kept in mind in patients presenting with an acute alarming stridor or a chronic history of wheezes not responding to the conventional asthmatic medications. A prior history of asthma and/or depression or psychological disturbances should prompt the caring physician to request close observation for possible examination of the patient during the attack. A laryngoscopic visualization of the vocal cords dysfunction is essential for a proper diagnosis, a rightful step that will spare the patient unnecessary and elaborate tests and interventions such as intubation or possible tracheostomy.
References

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PARADOXICAL VOCAL CORD MOTION:
A POSTOPERATIVE DILEMMA

- A Case Report -

KATHERINE KINGHORN* AND SAEED DHAMEE**

Abstract

Paradoxical vocal cord motion (PVCM) is a dysfunction more often seen by otolaryngologists, but of which the anesthesiologist must also be aware of in order to prevent inappropriate invasive airway interventions. For the anesthesiologist, PVCM is most often seen as inspiratory stridor during the postoperative recovery period. Unfortunately, inspiratory stridor can also be a sentinel of impending respiratory failure, and so it is crucial that the serious etiologies be efficiently ruled out. Presented is a case of postoperative PVCM, diagnosed by direct fiberoptic examination, in which timely recognition of this benign, psychogenic postoperative complication resulted in effective and appropriate noninvasive management.

Case Report

A 25-year old, 91 kg, 73 inch tall male with right shoulder instability secondary to motor vehicle accident, presented for shoulder arthroscopy. Past surgical history was significant for one prior shoulder arthroscopy under general anesthesia without complication. He had no known

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medication allergies and was otherwise healthy.

Interscalene block was performed in the preoperative holding area for postoperative pain management. The brachial plexus was located using a peripheral nerve stimulator, and 45 ml of 0.5% bupivacaine with 1:200,000 epinephrine was injected. No cardiovascular or central nervous system effects were observed upon administration of the block.

During transfer to the operating room, the patient complained of difficulty breathing and was noted to be tachypneic and anxious. Pulse oximetry was 100% on room air at the time of arrival in the OR. General anesthesia was induced intravenously with 180 mg of propofol followed by 100 mg of succinylcholine. Intubation was accomplished atraumatically following direct laryngoscopy. Anesthesia was maintained with sevoflurane and muscle relaxation was achieved with rocuronium. Intraoperative anesthetic course was uneventful. The trachea was extubated immediately upon arrival to the post anesthesia care unit (PACU).

While in the PACU, the patient’s vital signs remained within normal limits; he denied pain. His breathing remained spontaneous and unlabored. Approximately one and one-half hours after tracheal extubation, the patient was transferred to stage II recovery. Soon after arrival, the patient became anxious, indicating to the nurse that he was having difficulty breathing and complaining of a sore throat. Inspiratory stridor was first noted at this time. Vital signs were blood pressure 145/80 mmHg respiratory rate 18 breaths per minute, pulse 95 beats per minute, and pulse oximeter 100% on room air. Aerosolized racemic epinephrine was administered. A chest radiograph demonstrated an elevated right hemidiaphragm and was otherwise unremarkable. Upon treatment with midazolam, and subsequently with alfentanil, the patient’s inspiratory stridor resolved completely.

As the sedation began to wear off, the patient again became distressed, stridorous, and anxious, using accessory muscles to breathe. His respiratory rate ranged from 18-32 breaths per minute, blood pressure 143-158/80-103 mmHg, and heart rate 95-109 beats per minute. Pulse
oximeter reading was consistently 99-100% on either room air or 2 liters of oxygen via nasal cannula.

An otolaryngology consult was requested. Direct visualization of the airway with a flexible fiberoptic laryngoscope demonstrated paradoxical vocal cord motion and otherwise normal anatomy. The patient was admitted for overnight observation. He was evaluated by a speech therapist, whose physical exam noted phonation on inspiration. He was discharged the following day with follow up planned with speech therapy. After discharge, the patient’s symptoms spontaneously cleared over the ensuing two weeks.

Discussion

Paradoxical vocal cord motion is a functional abnormality causing bilateral adduction of the vocal folds on inspiration, resulting in the classic inspiratory stridor\textsuperscript{1,2}. Other synonyms for this condition include hysterical stridor, psychogenic stridor, Munchausen’s stridor, spasmodic croup, atypical asthma, and benign vocal fold dysfunction. Paradoxical vocal cord motion is considered a type of conversion disorder. A conversion disorder, as defined by the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), is a subtype of somatoform disorder characterized by one or more neurologic complaints that cannot be explained by any known neurologic disorder, in addition, the onset or exacerbation of symptoms must be associated with psychologic factors\textsuperscript{2}. Risk factors for paradoxical vocal cord motion include female gender, working in the health care professions, middle age, a diagnosis of asthma, and having an ongoing upper respiratory infection. Patients with other psychiatric diagnoses, including depression or anxiety disorders, are also at increased risk\textsuperscript{3}. An awareness of paradoxical vocal cord motion as one of the etiologies of postoperative stridor is necessary to avoid unnecessary airway intervention in these patients. Pervious reports have described reintubation and even tracheostomy in patients eventually diagnosed with paradoxical vocal cord motion\textsuperscript{4}.
The differential diagnosis for postoperative inspiratory stridor includes laryngospasm, allergic airway edema, laryngeal stridor (commonly from residual relaxant effect), intubation injury, and mass lesion or foreign body\textsuperscript{[5]}. Given the potentially serious nature of these etiologies, immediate management should be undertaken with the urgency appropriate to the possibility of impending respiratory failure. Medical interventions may include nebulized neomycin epinephrine, antihistamines, corticosteroids, intravenous or topical lidocaine, and confirmation of reversal of neuromuscular blockade. If the index of suspicion for paradoxical vocal cord motion is high, a trial of anxiolytic therapy is appropriate. Resolution of stridor suggests the diagnosis.

The diagnosis of paradoxical vocal cord motion is made by a combination of relevant history and physical examination including direct fiberoptic examination. If fiberoptic examination of the airway is not performed during an episode of the stridor, it can be considered a diagnosis of exclusion after other, more serious etiologies have been ruled out. Our patient did not complain of shortness of breath nor did he exhibit stridor until after admission to stage II recovery. It is possible that once the sedative effects of general anesthesia had dissipated, the awareness of decreased pulmonary function from ipsilateral phrenic nerve block caused the anxiety that triggered the paradoxical vocal cord motion. Treatment of paradoxical vocal cord motion includes reassurance and short term anxiolytic therapy, as well as education. A good prognosis is associated with the presence of an identifiable stressor, a sudden onset of symptoms, a good premorbid adjustment, and a lack of accompanying medical disorder\textsuperscript{[26]}

Perioperative anesthetic management of patients with a history of paradoxical vocal cord motion should include measures to reduce the number of possible triggers. Preoperative psychological consultation is advisable. Anesthetic techniques which avoid tracheal intubation should be considered\textsuperscript{[4]} as mechanical stimulation of the airway has been suggested as a trigger\textsuperscript{[7]}. Adequate anxiolysis in the perioperative period may be preventative.
References

EVALUATION OF REMIFENTANIL IN
ENDOSCOPIC RETROGRADE
CHOLANGIO-PANCREATOGRAPHY

N. EL BITAR* AND S. SFEIR**

**Background and objective:** Endoscopic retrograde cholangiopancreatography (ERCP) is a painful procedure that requires transient analgesia and conscious sedation. Remifentanil an ultrashort, very potent narcotic, is eliminated by plasma esterases, and does not interfere with liver function. It does not accumulate and is free of residual depression.

Our aim is to find out if remifentanil can provide safe and effective sedation in ERCP, without undue technical difficulty secondary to sphincter spasm.

**Patients and Methods:** Thirty five patients, ASA I-II and III, scheduled to undergo elective ERCP were divided randomly in two groups: Midazolam-remifentanil group (group I), received remifentanil a loading dose of 0.2 µg/Kg/min over 5 minutes and a maintenance dose of 0.1-0.15 µg/Kg/min to achieve an adequate level of sedation and analgesia. Midazolam-fentanyl group (group II), received intermittent doses of midazolam and fentanyl guided by level of sedation. All patients were premedicated with midazolam 0.05 mg/kg IV, in divided doses as per patient tolerance, before starting the procedure. Sedation was assessed depending on Ramsey scale of sedation. SpO2, blood pressure, heart rate, respiratory rate, dosages of the medications, peroperative amnesia and operative time were recorded. Operator and patient satisfaction were rated on a scale of 1 to 4.

**Results:** There were statistically significant differences in the level of sedation (p = 0.003), patient satisfaction (p = 0.01) and the amount of

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midazolam used (p < 0.01) in favor of group I. Operator satisfaction was the same in the two groups. There was no statistically significant difference between the two groups regarding the peri-operative amnesia. The technical difficulty (catheterization of ampulla, duration of procedure, need of parasympatholytics...) was comparable in the two groups, as judged by the operator.

There was one case of mild desaturation in group I that responded to stimulation. No other respiratory or cardiovascular events were noted.

**Conclusion:** We recommend remifentanil in ERCP. Vigilance, however, must be exercised in titration and supervision of patients.

**Keywords:** Cholangio-pancreatography, Endoscopic Retrograde, remifentanil, conscious sedation.

**Introduction**

Endoscopic retrograde cholangio-pancreatography (ERCP) is a painful procedure that requires transient analgesia and sedation. Techniques used to achieve this goal implemented a variety of protocols including; among others', combinations of narcotics, benzodiazepines and propofol.

Remifentanil is an ultrashort acting, synthetic opioid. It has a methyl ester linkage and is metabolized by nonspecific blood and tissue esterases. In adult patients, it has a rapid clearance (CL) and short terminal half-life (T1/2), approximately 4 min that is independent of infusion duration and of hepatic and renal function. The resulting carboxylic acid metabolite, GR90291, has approximately 1/4, 600 the potency of remifentanil as a micro-opioid agonist in anesthetized dogs. In humans, GR90291 is eliminated primarily via renal excretion with a terminal half-life of approximately 1.5-2 hours.

Low doses of remifentanil were used for conscious sedation, results in analgesia with negligible changes in neurocirculatory end-points, and should provide near ideal conditions for this procedure, provided sphincter spasm does not lead to detectable clinical difficulty. The narrow
margin of safety regarding depression of spontaneous respiration should be considered rigoursly.

Our aim is to find out if remifentanil can provide safe and effective sedation in ERCP.

Patients and Methods

After institutional ethics committee approval and, written informed consent, we studied 35 patients, (24 to 93 yrs, ASA physical status I-II and III) in a prospective, randomized manner. All patients underwent elective ERCP. Exclusion criteria included patients with allergies to the drugs being used, with increased intracranial pressure, who are heavier than 150% of their ideal body weight, with severe cardiovascular or respiratory diseases (ASA grade IV or higher), a history of drug abuse and long term use of benzodiazepines or tricyclic antidepressants.

All patients fasted for at least 6 hours before the procedure.

Each patient arrived to the endoscopy unit with an IV line. SpO2 sensor and blood pressure cuff were applied to the patient. Oxygen was administered by nasal cannula (3 l/min).

All patients were premedicated with midazolam intermittent up to 0.05 mg/kg IV before starting the procedure. Patients were randomly assigned to two groups:

Group I
Midazolam-remifentanil, 18 patients to receive remifentanil for maintenance had another IV gauge #22 cath installed for uninterrupted administration of remifentanil.

The latter was started at a loading dose of 0.2 µ/Kg/min over 5 minutes and maintenance of 0.1-0.15 µg/Kg/min in order to achieve an adequate level of sedation and analgesia.

Group II
Midazolam-fentanyl group, 17 patients received additional doses of
midazolam and intermittent fentanyl to achieve an adequate level of sedation.

Elderly patients received reduced doses (30-50% reduction).

Prior to endoscopic manipulation, every patient received topical anesthesia of the pharynx with lidocaine 2% spray. During the procedure SpO2, blood pressure, heart rate, respiration, dosages of medications and operative times were recorded.

Verbal contact with the patient was maintained to assess the degree of comfort and response to stimulation.

Sedation was assessed depending on Ramsay scale of sedation. Propofol 2 mg/kg/hr was added to this protocol in cases of inadequate sedation.

Agitation or other problems were noted.

At the end of the procedure the infusion of remifentanil was stopped.

Operator and patient satisfaction were rated on a scale of 1 to 4 (4 is the ideal and 1 is the worst). Recovery time was also monitored.

Patients were visited 4 hours later on the floor to assess their satisfaction, amnesia and the presence of side effects.

Statistics

Continuous parameters were tested with the t-test for independent samples and Fisher’s exact test for categorical variables. Correlation was done using Pearson’s test. All tests are two-tailed with a confidence level of 95% ($P < 0.05$). Consequently, significances of $P < 0.05$ reflect the probability of differences that can at best be used for generating hypotheses, but do not prove them.

Results

The two groups were comparable with the respect to demographic data: age, sex, and duration of the procedure (Table I).
Table I

Patient demographic data

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group I (n = 18 patients)</th>
<th>Group II (n = 17 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[Remifentanil]</td>
<td>[Fentanyl]</td>
</tr>
<tr>
<td>Age yr (mean ± SD)</td>
<td>61 ± 17</td>
<td>64 ± 18</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>78%</td>
<td>71%</td>
</tr>
<tr>
<td>Operative time (min) (mean ± SD)</td>
<td>64 ± 25</td>
<td>53 ± 23</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.

There were statistically significant differences in the level of sedation (p = 0.003) and patient satisfaction (p = 0.01) in favor of group I. No correlation was found between age, sex and patient satisfaction or sedation level. Operators were satisfied equally regarding the two groups. The amount of midazolam used during the procedure was significantly lower in the remifentanil group (p < 0.01) (Table II), nonetheless this did not affect inadvertently the quality of amnesia. Three patients in the fentanyl/midazolam group did not support the procedure and propofol 2 mg/kg/hr was added to obtain an adequate level of sedation.

Table II

Statistical data

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group I [Remifentanil]</th>
<th>Group II [Fentanyl]</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient sedation level</td>
<td>4.9 ± 0.9</td>
<td>3 ± 1.9</td>
<td>0.003</td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td>3.8 ± 0.5</td>
<td>3 ± 1.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Operator satisfaction</td>
<td>4</td>
<td>3.7 ± 0.47</td>
<td></td>
</tr>
<tr>
<td>Perioperative amnesia</td>
<td>39.9%</td>
<td>47.1%</td>
<td>0.738</td>
</tr>
<tr>
<td>Midazolam dosage</td>
<td>1.8 ± 0.4</td>
<td>3.4 ± 1.4</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.

Continuous parameters were tested with the t-test for independent samples and Fisher’s exact test for categorical variables. Correlation was done using Pearson’s test. All tests are two-tailed with a confidence level of 95% (p < 0.05).

There were statistically significant differences in the level of sedation measured depending on Ramsey sedation scale (p = 0.0003) and patient satisfaction (p = 0.01).

Operator satisfaction was the same in the two groups.

There was no statistical significant difference between the two groups regarding the peri-operative amnesia.

There was significant difference in the amount of midazolam used during the procedure between the 2 groups (p < 0.01).

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N. EL BITAR
All patients in the remifentanil group had a recovery time less than 15 minutes while only 64.7% in the fentanyl group did (Table III).

<table>
<thead>
<tr>
<th>Group</th>
<th>RECOVERY TIME</th>
<th>RECOVERY TIME</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 15 min</td>
<td>&gt; 15 min</td>
</tr>
<tr>
<td>Group I REMIFENTANIL (N = 18)</td>
<td>18 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>Group II FENTANYL (N = 17)</td>
<td>11 (64.7%)</td>
<td>6</td>
</tr>
</tbody>
</table>

The vital signs in the two groups (respiratory rate, pulse and blood pressure) were maintained, except for one case of mild oxygen desaturation 10% in remifentanil-midazolam group that corrected rapidly upon stimulation.

 Discussion

Endoscopic retrograde cholangio-pancreatography (ERCP) is being used widely to diagnose and treat several biliary and pancreatic pathologies. Being less invasive than surgery, it has become the standard of care in a multitude of indications. This procedure entails manipulation of the biliary tract in patients who already have hepatobiliary and pancreatic derangements. Besides the discomfort of the endoscope, pain due to interventions (ex: sphincterotomy, biliary dilatation) must be alleviated.

Several techniques have been implemented for the analgesia and sedation of such patients: narcotics for pain, hypnotics for patient comfort and benzodiazepines for amnesia. Remifentanil, an ultra-short opioid is herein evaluated.

Remifentanil, an ultra-short acting opioid, that does not depend on liver for metabolism, seems to be a good alternative, as it offers titrable analgesia without putting an extra burden on an already diseased liver. The hemodynamic stability that the drug incurs is an added benefit. In
addition, the expected fast recovery would be an advantage in terms of discharging the patient, especially in ambulatory cases. A couple of caveats need to be precautioned.

The narrow margin of safety concerning depression of spontaneous respiration must be considered seriously.

Another disadvantage to consider would be the constrictive effects of morphine derivatives on the ampulla of Vater. However, if this does not surface as an added difficulty, then this possible drawback will not outweigh the advantages already mentioned.

This study showed statistically significant differences in terms of better sedation, better patient satisfaction and comparable amnesia at lower midazolam doses, in favour of remifentanil. The operators were satisfied with the adequate working conditions as concerns patients’ sedation and cooperation provided in group I, however there was no statistical difference between the two groups (Table II).

All patients were fully awake and comfortable within 15 minutes after discontinuation of remifentanil vs. 64% in group II, which is an added benefit in terms of fasttracking of patients. No patient in the remifentanil group needed additional intervention, whereas three patients in group II needed additional propofol in order to achieve adequate sedation.

The incident of mild desaturation, mentioned earlier, that occurred in one patient who received remifentanil emphasizes the need for extreme caution with the use of such a potent narcotic on patients breathing spontaneously.

No other untoward cardiovascular and respiratory events were noted in both groups.

Conclusion

Monitored anesthesia care for patients undergoing ERCP with continuous remifentanil after premedication with midazolam provides a pain free protocol with excellent patient sedation, satisfaction, amnesia,
operator satisfaction and very rapid return to consciousness, with no apparent increased technical difficulty secondary to sphincter spasm.

We recommend this technique, however vigilance must be exercised in titration and close supervision of patients.

References