Review article

Percutaneous aortic valve replacement: overview and suggestions for anesthetic management☆

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Anesthesia; Cardiac; Aortic valve replacement; Transcutaneous; Atrioventricular block

Abstract Transcutaneous aortic valve replacement (AVR) is increasingly used for high-risk patients with severe aortic stenosis, who have high operative mortality for surgical placement during cardiopulmonary bypass (CPB). Retrograde transfemoral AVR is usually performed during sedation, whereas antegrade transapical AVR is done with general anesthesia. Both procedures can be carried out without CPB. Extended hemodynamic monitoring, including pulmonary artery catheterization and transesophageal echocardiography, may be useful. Transfemoral AVR requires placement of a transvenous right ventricular pacing lead. Typical complications include local bleeding, obstruction of the coronary ostia, and neurological insult due to embolization of sclerotic material. Aortic regurgitation due to paravalvular leakage or inadequate device expansion also may occur. Renal function may deteriorate on excessive application of contrast medium. Atrioventricular blocks may occur later rather than after conventional AVR which tend to occur immediately.

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1. Introduction

Aortic valve replacement (AVR) is the treatment of choice for patients with severe degenerative aortic stenosis, offering both symptomatic relief and a potential for improved long-term survival. Patients presenting with aortic stenosis increasingly are elderly with significant comorbidities. As a result, AVR using conventional open-heart surgery with median sternotomy and cardiopulmonary bypass (CPB) may be associated with unacceptably high mortality and morbidity in certain patients.

Although most patients are treated for symptomatic and critical aortic stenosis, less invasive procedures would be beneficial. Intervention could be extended to patients for whom the risk of surgical intervention is currently prohibitive [1]. Possible steps to minimize perioperative risk are to avoid sternotomy, CPB, and mechanical ventilation. Therefore, alternative modes of valve replacement strategies have been developed. After studies in animals [2,3], in 2002 Cribier et al. were the first to implant a transcutaneous, catheter-mounted aortic valve using the

Financial disclosure: Dr. U. Schäfer does consulting work and receives honoraria from CRS™, CoreValve Inc, Irvine, CA, USA. Dr. M. Heringlake receives scientific support and honoraria from Edwards Lifescience, Irvine, CA, USA and Covidien Healthcare, Mansfield, MA, USA.

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antegrade transfemoral venous route [4]. This approach is very challenging [5]; the retrograde arterial approach then was introduced (ie, transfemoral-AVR [6] and transapical AVR [7]).

Initial results show at least comparable mid-term morbidity and mortality rates to those with conventional isolated AVR (Table 1). Accordingly, as numbers increase [1], cardiac anesthesiologists will be confronted with this patient group with increasing frequency. For both procedures, no CPB per se is needed; one may speculate that in the near future anesthesiologists with no experience in cardiac anesthesia may be caring for these patients.

2. Technical aspects

Transcatheter AVR, especially transapical AVR, requires a special operating room (OR). The so-called “hybrid OR” [8] is a standard OR with an additional fluoroscopic angiography system equal to any standard catheterization laboratory. It combines all aspects of sterility needed for conventional surgery with the imaging techniques of a catheterization laboratory. Excellent imaging is required for exact positioning of the valve. In the event of emergency conversion to conventional surgery, CPB should be readily available. Transfemoral AVR procedures are typically performed in the catheterization laboratory. In the majority of cases, the anesthesiologist is confronted with limited space in an unfamiliar surrounding.

3. Patients

Aortic stenosis is the most common valvular heart disease and its prevalence is increasing with age [9]. Approximately 2% to 5% of elderly individuals aged >75 years present with signs of severe aortic stenosis and are scheduled for elective AVR. Excellent results have been achieved with conventional isolated AVR in the last few years, with operative mortality rates of 5% to 10% noted in octogenarians [9,10]. Mortality risk may increase excessively in the presence of additional factors. A strong link between operative mortality and the following predictive factors has been seen [9]: advanced heart failure with severe left ventricular (LV) dysfunction; comorbidities, eg, respiratory dysfunction, renal dysfunction, and peripheral or coronary arterial atherosclerosis; and need for urgent surgery.

Beside “technical” inclusion criteria such as certain aortic annulus and ascending aorta diameter [6,11,12], a combination of risk factors or scoring systems [5] also have been used as inclusion criteria. There are no published guidelines for patient selection, and percutaneous AVR remains investigational [13]. Therefore, patients presenting for percutaneous TF-AVR or TA-AVR are high-risk patients with high operative mortality, and usually they have been refused for standard AVR.

Exclusion criteria include sepsis or acute endocarditis; excessive femoral, iliac, or aortic atherosclerosis; calcification or tortuosity (for transfemoral AVR); aortic aneurysm; bleeding diathesis or coagulopathy; recent myocardial infarction (MI) or cerebrovascular accident; mitral or tricuspid valvular insufficiency (> grade II); LV or atrial thrombus; uncontrolled atrial fibrillation; and previous aortic valve replacement. In addition, patients with echocardiographic aortic valve annulus diameter < 20 mm or > 27 mm and ascending aorta diameter > 45 mm were excluded [5,6,11]. Some of these contraindications have been abandoned [12]. For example, after evaluation of the feasibility of transapical valve-in-a-valve implantation in animals [14], the first human case was reported [15]. There is ongoing discussion as to whether certain valve malformations such as bicuspid aortic stenosis could be an exclusion criterion, as stent deployment may be impaired [16].

During preoperative assessment, the anesthesiologist should be especially aware of signs of severely reduced LV systolic function, pulmonary arterial (PA) hypertension,
respiratory dysfunction, especially chronic obstructive pulmonary disease, renal dysfunction or failure, and history of neurological insult. In addition, many patients have had previous cardiac surgery and may be at increased risk of bleeding.

4. Monitoring

Beside standard monitoring, invasive arterial and central venous blood pressures, no clear recommendations for hemodynamic monitoring have been published. A PA catheter for measuring PA pressure and mixed venous oxygen saturation may be used to detect ventricular dysfunction and provide valuable data on global oxygen balance [17]. As with conventional AVR, the decision to insert a PA catheter should be based on the comorbidities of the individual patient.

Transesophageal echocardiography (TEE) is extremely helpful in determining acute changes in myocardial performance during the procedure, to determine the position and correct function of the prosthetic valve, and most important – to rule out residual aortic regurgitation and paravalvular leakages [18]. During transapical AVR performed with general anesthesia, TEE should be included [19]. Unfortunately, in patients undergoing transfemoral AVR without general anesthesia, use of TEE during the procedure is limited. In cases where TEE may not be used, intraoperative and postoperative transthoracic echocardiography may help determine the etiology of hemodynamic instability. As there is no access to the ascending aorta for epicardial echocardiography during both procedures, this technique, which is helpful during conventional aortic surgery [20,21], cannot be used as an alternative.

5. Procedure

Currently, more than 30 companies work in the development of stent-fixed valves. Two devices have been introduced into clinical practice for sutureless transcatheter AVR, ie, the CoreValve Revalving System (CRSTM; CoreValve, Inc., Irvine, CA, USA) and the Edwards-Sapien valve (Edwards Lifesciences, Inc., Irvine, CA, USA).

The CoreValve aortic valve prosthesis consists of a trileaflet bioprosthetic porcine pericardial tissue valve mounted and sutured in a self-expanding nitinol stent. Nitinol, a nickel-titanium alloy, is a shape memory metal. The balloon expandable Edwards-Sapien valve is constructed from a tubular slotted stainless steel stent with an attached bovine pericardial trileaflet valve.

Both valves have received CE mark approval (consumer safety certification of the European Union) for transfemoral implantation, while for the transapical approach only the Edwards Sapien valve has been approved.

6. Transfemoral aortic valve replacement

In the beginning, transfemoral AVR was commonly performed during general anesthesia [11]. Since no CPB is required, deep sedation is sufficient [5]. A combination of propofol (0.3-1.5 to 3 mg/kg/hr) and remifentanil (1 to 6 μg/kg/hr) works well. Currently there are no data available comparing general anesthesia and deep sedation. An individualized approach is recommended.

Premedication consists of aspirin, clopidogrel, and antibiotics for procedural prophylaxis. Aspirin (100 mg) and clopidogrel (75 mg) are recommended for 6 months, with lifelong aspirin (100-300 mg) [22]. Placement of an intravenous (IV) right ventricular pacing lead is mandatory and functionality should be tested before the procedure. A transthoracic pacemaker is not recommended. Two methods of transfemoral AVR have been published, but as antegrade transfemoral venous access carries the risk of injury to the mitral valve, retrograde transfemoral AVR is used nearly exclusively. Vascular access is obtained either with or without standard surgical cut-down of the subclavian artery, external iliac artery, or common femoral artery. A stiff guidewire is placed in retrograde fashion into the LV. Using fluoroscopic guidance and rapid pacing (150-200 bpm) to minimize ventricular outflow, balloon dilatation of the stenotic valve is performed. After the balloon catheter is withdrawn again, the device is advanced and positioned within the native valve. The CoreValve revalving system is a self-expanding device and needs only additional balloon dilatation for modelling into the aortic root, while the Edwards-Sapien valve has to be expanded actively during rapid pacing. After expansion correct positioning and function is verified with fluoroscopic angiography and/or TEE (Fig. 1A-C) [23].

7. Transapical aortic valve replacement (TA-AVR)

The TA-AVR is performed during general anesthesia. Initially one-lung ventilation was instituted using a double-lumen tube, but this approach has been abandoned. A left anterolateral intercostal incision is used to expose the LV apex and the pericardium is incised and retained. In addition, temporary epicardial ventricular pacing wires are placed. With the heart continuously beating, the apex is punctured and the aortic valve passed in antegrade fashion using a soft guidewire. A superstiff guidewire is inserted and positioned across the aortic root and anchored in the descending aorta. A balloon valvuloplasty catheter is positioned using fluoroscopic and/or TEE guidance. A valvuloplasty is performed to optimize the valve area for device placement. The balloon catheter is withdrawn and a 33-French transapical delivery sheath is inserted followed by the valve. After de-airing and proper
positioning, the valve is implanted during ventricular rapid pacing (Fig. 1D). Sometimes repeated dilatations are necessary to minimize paravalvular leakage. After correct positioning and function have been verified, the myocardium is closed using sutures placed at the outset and the thorax is closed.
Fluoroscopy time is usually less than 20 minutes, with procedure time around 180 minutes [7,12,24]. The transapical technique is considered safer in patients with severe peripheral vascular disease or increased risk of stroke as fewer aortic manipulations are necessary. During both procedures, the anesthesiologist monitors hemodynamics, especially during balloon valvuloplasty and device deployment, as they might not recover immediately after cessation of rapid pacing. New or increased aortic regurgitation might complicate the situation. In addition, ventricular fibrillation is possible and immediate electrical defibrillation and cardiopulmonary resuscitation is necessary.

8. Perioperative and postprocedural care

More than 1,200 transfemoral AVR for both CoreValve and Edwards-Sapien valves and about 450 transapical AVR have been performed. As greater numbers of patients are treated, the number of complications presumably will decrease. The physician responsible for periprocedural care should be aware of certain risks. During implantation, embolization of atherosclerotic plaques is possible due to pre-dilation and detachment or fragmentation. Migration of the valve stent into the ascending aorta or the aortic arch is possible, with the need of conversion to standard surgery. Studies have reported a mortality rate of up to 15%, stroke at 0.4% to 4.6%, MI at 0.2% to 6.5%, and cardiac perforation at 0.3% to 1.8% after balloon valvuloplasty [25,26]. Published short-term and midterm results of percutaneous AVR and isolated conventional AVR are summarized in Table 1.

During antegrade transfemoral AVR, where a transseptal puncture is performed and the mitral valve is crossed using a balloon flotation catheter, there is a risk of tethering or traumatizing the anterior leaflet of the mitral valve. This situation may lead to acute severe mitral regurgitation [26]. The retrograde approach avoids potential mitral leaflet complications. A severe complication shared by all three approaches is the obstruction of the coronary ostia with subsequent MI [27].

A special problem may be aortic regurgitation due to paravalvular leakages or inadequate device expansion. Minor regurgitation immediately after insertion of the valve may be acceptable in patients with preserved ventricular function and it typically disappears after several hours. Moderate and high-grade regurgitation normally is treated with additional device dilatation. In case of severely depressed LV function, TEE may underestimate the true severity of the situation and special emphasis regarding systemic cardiopulmonary function is essential to rule out acute heart failure. During transapical AVR, there is a constant risk of systemic air embolism with catastrophic clinical consequences. Local bleeding problems at the catheter insertion site may require surgical repair. Anticoagulant loading therapy with clopidogrel and aspirin during transfemoral AVR may increase bleeding problems [6] and may be life-threatening in the event that conversion to conventional on-pump AVR is indicated.

Postprocedural care in patients after TF-AVR or TA-AVR differs from care given after conventional surgical AVR. While postoperative patients undergoing AVR with CPB are often hypovolemic and show a typical post-CPB inflammatory response with decreased systemic vascular resistance, leading to the need for relatively high amounts of fluids and vasopressor therapy, patients after percutaneous AVR are at risk of hypervolemia, especially if residual aortic regurgitation is present. Thus, adequate hemodynamic monitoring and detailed hemodynamic care is necessary. Special attention to renal function is required, especially in patients with preoperatively reduced kidney function, as the nephrotoxic effects of the contrast medium may aggravate the situation. For patients at risk, preventive strategies to reduce the likelihood of contrast medium-induced nephropathy include preprocedural and periprocedural IV hydration therapy and use of the lowest dose possible of low-osmolarity contrast medium. The use of nephroprotective agents such as N-acetylcysteine or theophylline is controversial, but may be considered in certain patients [28,29]. Loop diuretics increase renal injury after application of radiocontrast dye [30]; these drugs should be used cautiously.

Atrioventricular conduction blocks are a well-known complication of aortic valve surgery. It is noteworthy that after transfemoral AVR and transapical AVR, blocks may develop up to one week post-procedure, necessitating permanent pacemaker insertion [16].

9. Summary

Transcutaneous AVR, whether using the transfemoral or the transapical route, is an innovative approach. Anesthesiologists caring for these patients either during or after the procedure should have sound knowledge of the procedure and its risks and complications. As different specialties and personnel, including cardiac surgeons, cardiologists, anesthesiologists, OR nurses, and technicians have to work together in unfamiliar surroundings, cooperation, collaboration, and experience are of paramount interest for success.

Before transcutaneous AVR may be recommended for a wider patient group, properly designed, prospective, randomized clinical trials comparing transfemoral AVR, transapical AVR, and conventional surgical AVR are necessary to determine long-term outcome.

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1. Introduction

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References


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Case series: Anesthesia for retrograde percutaneous aortic valve replacement – experience with the first 40 patients

[Présentation de cas : L’anesthésie pour un remplacement valvulaire aortique percutané rétrograde : notre expérience avec les 40 premiers patients]

Ronald M. Ree MD FRCPC, John B. Bowering MD FRCPC, Stephan K. W. Schwarz MD PhD FRCPC

Purpose: To describe both the evolution and the main associated complications in the anesthetic management of the initial 40 patients at our centre who underwent percutaneous retrograde aortic valve replacement, a novel technique utilizing a catheter-guided femoral artery approach.

Clinical features: With institutional Research Ethics Board approval, we retrospectively reviewed the medical records of the first 40 patients who underwent percutaneous retrograde aortic valve replacement between January 2005 and March 2006. Information obtained included patient characteristics, anesthetic management, details of the procedure, and complications. All procedures were scheduled to be performed in the cardiac catheterization laboratory. The first four patients received monitored anesthesia care, and the subsequent 36 underwent general anesthesia. There were no anesthesia-related adverse events. The prosthetic valve was placed successfully in 33/40 patients (83%). Median anesthetic time was 3.5 hr (range, 1.25–7.25 hr). Thirty-two/40 patients required vasopressor support. The most common, serious procedural complications were myocardial ischemia and arrhythmia following rapid ventricular pacing, hemorrhage from vascular injury secondary to the placement and removal of the large-bore sheath in the ilio-femoral artery, aortic rupture, and prosthetic valve maldeployment; 30-day mortality was 13% (n = 5/40).

Conclusions: Percutaneous retrograde aortic valve replacement is a novel procedure that presents the anesthesiologist with unique challenges. Careful preoperative assessment, intraoperative monitoring appropriate for a major vascular procedure, and meticulous management of hemodynamics are imperative for a successful outcome. Serious complications, including major hemorrhage from vascular injury as well as arrhythmia and myocardial ischemia following rapid ventricular pacing, must be anticipated and managed in an expeditious fashion.

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Objectif: Décrire l’évolution et les principales complications associées à la prise en charge anesthésique des premiers 40 patients de notre centre à subir un remplacement valvulaire aortique percutané rétrograde, une technique innovante utilisant une approche échoguidée par l’artère fémorale.

Éléments cliniques: Une fois le consentement du Comité d’éthique de la recherche obtenu, nous avons révisé de façon rétrospective les dossiers médicaux des 40 premiers patients à avoir subi un remplacement valvulaire aortique percutané rétrograde entre janvier 2005 et mars 2006. Les caractéristiques des patients, la prise en charge anesthésique, les détails de l’intervention et les complications faisaient partie des renseignements obtenus. Toutes les interventions étaient prévues dans le laboratoire de cœdétérisation cardiaque. Les quatre premiers patients ont reçu une séduction sous surveillance, et les 36 suivants une anesthésie générale. Il n’y a pas eu d’événements indésirables provoqués par l’anesthésie. La

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prothèse valvulaire a été positionnée avec succès chez 33/40 patients (83%). Le temps d’anesthésie médian était de 3,5 h (extrêmes, 1,25 – 7, 25 h). Un vasopresseur a été nécessaire chez 32/40 patients. Suite à l'intervention, les complications graves les plus fréquentes étaient l’ischémie myocardique et l'arythmie à la suite d'un entraînement ventriculaire rapide, l'hémorragie provoquée par une lésion vasculaire due au positionnement et le retrait de la gaine à grand diamètre dans l’artère ilio-fémorale, la rupture aortique et le mauvais déploiement de la prothèse valvulaire. La mortalité à 30 jours était de 13 % (5/40).

Conclusion : Le remplacement valvulaire aortique percutané rétrograde est une intervention nouvelle qui présente à l’anesthésiologiste des défis spéciaux. Une évaluation préopératoire attentive, un monitorage peropératoire adapté à une intervention vasculaire majeure et une prise en charge méticuleuse de l’hémodynamique sont absolument nécessaires à un devenir réussi. Des complications graves, notamment une hémorragie majeure causée par une lésion vasculaire ainsi que de l’arythmie et une ischémie myocardique suite à un entraînement ventriculaire rapide doivent être anticipées et pris en charge rapidement.

AORTIC stenosis is the most common cardiac valvular lesion in the developed world. Its etiology may be congenital or acquired. Both forms of stenosis result in a valve with calcified, restricted leaflets. Once aortic stenosis becomes symptomatic, it carries a poor prognosis and is poorly managed with medical Therapy. Surgical aortic valve (AV) replacement is effective in prolonging life and improving symptoms; however, the procedure can be associated with significant perioperative risk, especially in the elderly with decreased functional reserve and multiple co-morbidities. Surgery may also carry an unacceptable risk due to extensive calcification of the ascending aorta. Whereas balloon valvuloplasty represents an alternative therapeutic option, the reduction in stenosis is modest and temporary.

Percutaneous approaches to AV replacement have been investigated since 1992. In 2002, Cribier et al. reported a successful percutaneous valve replacement via an antegrade transseptal approach through the femoral vein. However, due to arrhythmias and possible mitral valve injury, the antegrade approach is technically challenging and not well tolerated by some patients. A percutaneous retrograde approach for replacing the AV has been developed at our centre by Webb et al. Vascular access is achieved through the femoral artery. The prosthesis, which is mounted on a catheter-guided stainless steel mesh stent, is maneuvered in a retrograde fashion into the ascending aorta and placed through the native AV before deployment. Here, we report on the evolution in the anesthetic management of the initial 40 patients undergoing this novel procedure, and we summarize the associated major perioperative complications encountered.

Methods
With approval of the institutional Research Ethics Board, we retrospectively reviewed the charts, anesthetic records, and procedural database of the initial 40 patients who underwent percutaneous retrograde aortic valve replacement at our centre (St. Paul’s Hospital, The University of British Columbia, Vancouver, B.C.) between January 2005 and March 2006. Patient characteristics, anesthetic management, details of the procedure, and complications were noted. Prior to the calculation of descriptive statistics and data comparisons, we used the Kolmogorov-Smirnov test and assessed kurtosis and symmetry of continuous data to test if values came from a Gaussian distribution. Unless otherwise stated, data are presented as mean ± SD or median [interquartile range], as appropriate. Descriptive data on AV area and mean transaortic gradient, before and after prosthetic valve placement, were compared with the Mann-Whitney test; P < 0.05. Descriptive statistics and comparisons were calculated using Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA, USA) and Prism version 4 (GraphPad, San Diego, USA) software.

Patient selection
The Therapeutic Products Directorate (Health Canada, Health Products and Food Branch; Ottawa, Ontario, Canada) approved the procedure for compassionate clinical use in patients considered unsuitable for conventional surgery by a team of cardiologists and cardiac surgeons. Patients with severe symptomatic aortic stenosis were referred for a percutaneous procedure due to multiple comorbidities and/or surgical risk (logistic EuroSCORE ≥ 20%, indicating a 30-day predicted mortality ≥ 20% with operative management). Patient preference for a percutaneous procedure was not considered an indication. The interventional cardiology team obtained informed consent for the procedure from all patients.

Percutaneous valve replacement procedure
A detailed description of the technical aspects of this procedure, from an interventional cardiology perspective, has recently been published. Patients received clopidogrel 600 mg and aspirin 325 mg orally prior to the procedure. Antibiotic prophylaxis with either intravenous vancomycin (1 g) or cefazolin (1 g) was
TABLE 1  Preoperative patient characteristics

<table>
<thead>
<tr>
<th>Patients</th>
<th>n = 40 (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>81 ± 8</td>
</tr>
<tr>
<td>Female gender</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>Body mass index (kg·m⁻²)</td>
<td>27 ± 6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23 (58%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (23%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>28 (70%)</td>
</tr>
<tr>
<td>Severe chronic obstructive lung</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>disease</td>
<td></td>
</tr>
<tr>
<td>History of cerebral ischemic</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>event</td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>8 (20%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>Never smoked</td>
<td>19 (48%)</td>
</tr>
<tr>
<td>Estimated GFR &lt; 60 mL·min⁻¹·1.73 m²</td>
<td>20 (50%)</td>
</tr>
<tr>
<td>Permanent pacemaker</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>Aortic calcification</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>Prior thoracotomy</td>
<td>14 (35%)</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>NYHA 3 or 4</td>
<td>37 (93%)</td>
</tr>
<tr>
<td>Angina</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Aortic valve area (cm²)</td>
<td>0.6* (range, 0.3–1.2)</td>
</tr>
<tr>
<td>Transaortic mean gradient</td>
<td>46 ± 18</td>
</tr>
<tr>
<td>(mmHg)</td>
<td></td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>18 (45%)</td>
</tr>
<tr>
<td>grade 3 or 4</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction &lt; 50%</td>
<td>9 (23%)</td>
</tr>
<tr>
<td>Logistic EuroSCORE (%)</td>
<td>25 ± 15</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>23 (58%)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD, where appropriate; *median. GFR = glomerular filtration rate; NYHA = New York Heart Association.

administered. All procedures were performed by an interventional card iologist in the cardiac catheterization laboratory. Femoral access was achieved percutaneously, and the ilio-femoral artery was progressively dilated to accommodate either a 22 or a 24 Fr sheath, depending on the size of the prosthesis to be placed. Heparin 70 U·kg⁻¹ iv was administered following arterial cannulation. The femoral vein was also cannulated to allow a pacing lead to be positioned in the right ventricle. Balloon valvuloplasty of the AV was then performed in a standard manner.¹¹ A Cribier-Edwards valve was mounted on a balloon at the tip of a deflectable steering catheter (Edwards Lifesciences Inc., Irvine, CA, USA). The guiding catheter was used to guide the device up the abdominal and thoracic aorta to the AV. Prior to deployment, the correct placement of the prosthesis across the AV was confirmed by fluoroscopy, aortography, and also, after the initial patients (who received transthoracic echocardiogra-

phy; cf. below), routine transesophageal echocardiography.

To prevent movement and possible ejection of the device during valve deployment, rapid right ventricular pacing was used to minimize pulsatile flow through the AV at the time of prosthesis implantation.¹⁵ Test pacing was first performed at a rate of 220 min⁻¹. The rate was reduced until reliable capture was observed and a reduction in systolic arterial pressure less than 60 mmHg was achieved (Figure 1). Following placement of the valve prosthesis, angiographic (and later also transesophageal echocardiographic; cf. below) examinations were performed to assess prosthetic valvular function and coronary artery patency. If a significant paravalvular leak was identified, balloon dilatation of the prosthesis was performed to further expand the mesh stent.

Anesthetic management

The anesthetic management underwent a significant evolution during the initial multidisciplinary learning curve associated with this novel procedure. On the day of the first scheduled procedure, the anesthesiologist on call was asked to help in the administration of conscious sedation in the cardiac catheterization laboratory. The initial four procedures were then carried out under monitored anesthesia care. As it became evident that patients regularly required surgical vascular repair at the access site (cf. below), the following 36 procedures were performed under general endotracheal anesthesia. It also became evident that endotracheal intubation facilitated the use of routine intraoperative transesophageal echocardiography (not done in the first four patients) to aid in the confirmation of accurate prosthetic valve function and placement. In
TABLE II  Anesthetic management and intraoperative characteristics

<table>
<thead>
<tr>
<th>Patients</th>
<th>n = 40 (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of anesthetic</td>
<td></td>
</tr>
<tr>
<td>Monitored anesthesia care</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>36 (90%)</td>
</tr>
<tr>
<td>Maintenance agent(s)</td>
<td></td>
</tr>
<tr>
<td>Desflurane</td>
<td>18 (46%)</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>Desflurane &amp; propofol</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Desflurane &amp; propofol &amp; remifentanil</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Desflurane &amp; remifentanil</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>Sevoflurane &amp; propofol</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Sevoflurane &amp; remifentanil</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Duration</td>
<td></td>
</tr>
<tr>
<td>&lt; 2 hr†</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>2–3 hr</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>3–4 hr</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>4–5 hr</td>
<td>10 (25%)</td>
</tr>
<tr>
<td>&gt; 5 hr</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>Vasopressors used</td>
<td></td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>30 (75%)</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>12 (30%)</td>
</tr>
<tr>
<td>Dopamine</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Epinephrine‡</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Calcium chloride§</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Minimum</td>
<td></td>
</tr>
<tr>
<td>intraoperative systolic blood pressure§</td>
<td></td>
</tr>
<tr>
<td>70–79 mmHg</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>80–89 mmHg</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>90–99 mmHg</td>
<td>14 (35%)</td>
</tr>
<tr>
<td>100–109 mmHg</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>110–119 mmHg</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>&gt; 119 mmHg</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Intraoperative transfusion</td>
<td></td>
</tr>
<tr>
<td>1 U packed red blood cells</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>2 U packed red blood cells</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>3 U packed red blood cells</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>&gt; 3 U packed red blood cells</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>

*Two (of the first four) patients received monitored anesthesia care for the valve placement, then general anesthesia for vascular repair. †The two patients whose procedure lasted less than two hours both suffered an intraoperative cardiac arrest. ‡Epinephrine and calcium chloride were used as resuscitative agents during the intraoperative cardiac arrests. §Indicates blood pressure in the prepping stage of the procedure. One patient underwent massive transfusion (19 U of packed red blood cells, 20 U of platelets, 9 U of fresh frozen plasma, and 10 U of cryoprecipitate; cf. body text).

As mentioned, transesophageal echocardiography, performed by a dedicated specialized cardiologist, was introduced as a routine monitoring modality in these patients. Intraoperative hypotension (systolic arterial pressure < 90 mmHg) was treated with intravenous crystalloid infusion as well as phenylephrine and/or ephedrine boluses. For persisting hypotension, phenylephrine, norepinephrine, and/or dopamine infusions were prepared and administered as indicated.

Following the procedure, tracheal extubation was undertaken when the patients were awake in the cardiac catheterization laboratory, whereas others were transferred, ventilated, to the cardiac care unit (CCU). All patients were monitored overnight in the CCU.

Results

The patients’ preoperative baseline characteristics are listed in Table I. Fifty-eight percent of patients had a logistic EuroSCORE ≥ 20% (cf. Methods: Patient selection); the mean logistic EuroSCORE was 25 ± 15% [95% confidence interval (CI), 20.2–29.8%]. The remainder were accepted due to significant comorbidities, including advanced age (> 85 yr), involvement of more than one valve, severe chronic obstructive pulmonary disease, multiple cerebrovascular accidents and carotid atherosclerosis, marked pulmonary hypertension, and debilitating arthritis that was felt to preclude rehabilitation after open heart surgery.

The prosthesis was placed successfully in 33/40 patients (83%). The reasons for an unsuccessful procedural outcome included an inability to deliver the prosthesis to the correct position in five patients and deployment in the aortic arch in two patients (Figure 2).

Patients tolerated general anesthesia well, with no anesthesia-related complications. Table II summarizes details on the anesthetic management of these patients. Reduced doses of anesthetic agents appropriate for the advanced age, multiple co-morbidities, and severe valvular disease of these patients were used and carefully titrated. For the management of hypotension, phenylephrine was administered to 30 patients, while ephedrine was used in 12 patients. Dopamine was used in a single individual as an adjunct to phenylephrine and ephedrine. Eight patients required no vasopressors. Epinephrine and calcium chloride were used in two instances during resuscitation following cardiac arrest.

Two patients sustained complications related to rapid ventricular pacing. Both occurred after pacing for balloon valvuloplasty, but prior to placement of the prosthetic valve. Ventricular fibrillation occurred in one patient who responded immediately to external
defibrillation. The second patient developed profound hypotension. Asystolic cardiac arrest ensued and, despite attempted resuscitation with epinephrine (3 mg), calcium chloride (1 g), and pacing, the patient died.

Following successful placement of the prosthetic valve, patients’ hemodynamic parameters improved, with the median calculated AV area increasing from 0.6 cm² (interquartile range, 0.5–0.7 cm²) to 1.7 cm² (interquartile range, 1.4–2.0 cm²; Mann–Whitney test, P < 0.0001; patients with available post data on the AV area, n = 32) and the mean transaortic gradient decreasing from 49 mmHg (median; interquartile range, 32–60 mmHg) to 11 mmHg (interquartile range, 9–16 mmHg; Mann–Whitney test, P < 0.0001; patients with available post data on the mean transaortic gradient, n = 32). Paravalvular aortic insufficiency, when present, was graded mild in severity. In association with improved hemodynamics, five patients required intravenous antihypertensive therapy after deployment of the prosthesis. Upon completion, all patients who had experienced no procedural complications were extubated and transported to the CCU. The median anesthetic time for the procedure was 3.5 hr (range, 1.25–7.25 hr).

Significant morbidity and mortality developed from vascular complications secondary to the placement and removal of the large-bore sheath in the ilio-femoral artery. One of the early patients in this case series died intraoperatively due to aortic rupture from the steering catheter. Another death resulted from postoperative multi-organ failure following a hemorrhagic cardiac arrest after femoral sheath removal and subsequent massive transfusion (cf. Table II). Overall, procedural blood loss was variable. Five patients required intraoperative transfusion of packed red blood cells, while eight additional patients were transfused during their hospital stay (cf. Tables II and III). As a result, the routine availability of a vascular surgeon to repair the femoral access site in the cardiac catheterization laboratory was incorporated as part of the standard management of these procedures.

Table III summarizes the in-hospital, post-procedure outcomes. The 30-day mortality was 13% (5/40 patients). Infection occurred in four patients. These included one case of *Staphylococcus aureus* septicemia, one case of infection at the access site after complex vascular repair, and urinary tract infections in two patients. All of these patients recovered with antibiotic therapy.

One patient experienced a postoperative cerebrovascular event. This individual made a full neurologic recovery.

**Discussion**

In this case series, we report on the first experiences with anesthesia for patients undergoing percutaneous retrograde AV replacement. Although surgical AV replacement is beneficial for improving patient symptoms and increasing life expectancy, it poses a
TABLE III  In-hospital complications

<table>
<thead>
<tr>
<th>Patients</th>
<th>n = 40</th>
<th>(100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inability to deliver the prosthesis valve</td>
<td>5</td>
<td>(13%)</td>
</tr>
<tr>
<td>Prosthetic valve malposition</td>
<td>2</td>
<td>(5%)</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>1</td>
<td>(3%)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>13</td>
<td>(33%)</td>
</tr>
<tr>
<td>Postoperative infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Access site</td>
<td>4</td>
<td>(10%)</td>
</tr>
<tr>
<td>Staphylococcus aureus septicemia</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>UTI</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>TIA/CVA within 30 days</td>
<td>1</td>
<td>(3%)*</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>5</td>
<td>(13%)</td>
</tr>
<tr>
<td>Intra-procedural mortality</td>
<td>1</td>
<td>(3%)</td>
</tr>
</tbody>
</table>

*Complete resolution with no neurologic sequelae.
TIA = transient ischemic attack; CVA = cerebrovascular accident; UTI = urinary tract infection.

significant risk to the elderly with multiple medical problems, rendering these patients poor operative candidates. Patients may also be nonsurgical candidates due to marked aortic calcification or previous cardiac surgery. In these individuals, percutaneous AV replacement may become an alternative in the management of aortic stenosis. Other inherent potential advantages of the percutaneous approach compared to open heart surgery include avoidance of cardiopulmonary bypass and aortic cross clamping, avoidance of sternotomy and minimization of surgical stimulation, reduction in the need for postoperative ventilation and intensive care unit stay, and possible associated cost savings.

The anesthetic management of the initial four procedures carried out at our institution consisted of monitored anesthesia care with conscious sedation, in accordance with the original plan of the interventional cardiology team. We found, however, that performing the procedure under general endotracheal anesthesia offered distinct advantages. These include the facilitation of routine intraoperative transesophageal echocardiography to assist in the precise placement of the prosthesis prior to deployment and to assess for complications following placement. General anesthesia also allowed for improved patient tolerance of prolonged procedures and eased the process of surgical repair of the access site at the end.

The anesthetic risks for patients with severe aortic stenosis are well documented. We found that percutaneous AV replacement, however, carries with it unique additional challenges. Rapid ventricular pacing used during this procedure assists with the precise placement of the valve prosthesis. Induced ventricular tachycardia, however, does not allow sufficient diastolic time for the hypertrophied ventricle to fill, producing a temporary state of decreased coronary perfusion in the face of increased myocardial oxygen demand. This has the potential of inducing profound arrhythmias and myocardial ischemia. Although rapid ventricular pacing was tolerated by most, two patients sustained significant complications. Our current practice, therefore, is to minimize pacing duration and to stabilize the patients’ blood pressure with vasopressors prior to repeat pacing. We have found that close communication between the cardiologist and the anesthesiologist is critical during this part of the procedure. Alternative methods of temporarily reducing cardiac output during valve deployment include administration of adenosine, balloon occlusion of venous return to the right or left atria, as well as electrically inducing ventricular fibrillation. However, each of these techniques is associated with its own set of complications.

Vascular injury was a significant cause of morbidity and mortality. All patients now undergo preoperative imaging of their vascular access sites to determine if the ilio-femoral artery lumen is sufficient to allow placement of the guiding catheter. Imaging also delineates the extent of any arterial calcification and tortuosity that may impair catheter advancement or surgical repair. Thirty-three per cent of our patients experienced procedural blood loss significant enough to warrant perioperative transfusion of red blood cells. Major vascular trauma must be anticipated as an intraoperative complication of this procedure. Hemorrhage also should be anticipated postoperatively, however, since ongoing bleeding from ilio-femoral vascular injury may be insidious and present in a delayed fashion (e.g., as retroperitoneal hematoma). Other perioperative complications to be anticipated by the anesthesiologist include cardiac tamponade, coronary artery ostia occlusion during device deployment, coronary artery embolization, and other complications associated with prosthetic valve maldeployment.

As a result of the lessons learned in the management of this first series of patients, anesthesiology involvement now routinely begins preoperatively, as all patients these days are seen in the anesthesia pre-assessment clinic for preoperative consultation and optimization. Whereas it remains difficult to decide when a patient, deemed by definition to be a nonsurgical candidate, is in fact a non-anesthetic candidate, our observation that there were no adverse events specifically related to anesthesia is somewhat reassuring. However, due to the number of observed and potential procedural and perioperative complications, all patients now receive invasive arterial and central venous pressure monitoring, in addition to the feno-
ral access secured by the cardiology team. Finally, the construction at our centre of a new operating theatre dedicated to advanced cardiac procedures has very recently allowed us to perform these procedures in the main operating room suite (with cardiopulmonary bypass pumps in close proximity/on standby), as opposed to (from an anesthesiologist's perspective), a remotely located cardiac catheterization laboratory. We believe that the comprehensive perioperative involvement of anesthesiology as part of a multidisciplinary team has significantly contributed to the improved outcomes achieved after the first series of patients.21

In summary, percutaneous replacement of the AV by a retrograde femoral approach is a new and exciting development in the treatment of aortic stenosis. Although it represents an intriguing alternative for those patients not considered candidates for conventional surgery, there are a number of significant concerns, as this case series demonstrates. Whereas the vast majority of these sick patients tolerated general anesthesia well, serious and, at times, spectacular complications, including major hemorrhage from vascular injury, arrhythmia and myocardial ischemia following rapid ventricular pacing, and prosthetic valve maldeployment, must be anticipated by the anesthesiologist and, where possible, managed in an expeditious fashion. To an extent, these complications may be part of a learning curve that accompanies any novel technique such as this.21 Future developments that may improve patient safety with this procedure include smaller profile catheters and sheaths that minimize trauma to the vascular access site, alternative methods of reducing left ventricular outflow during device placement that may be more cardioprotective, and the use of intracardiac echocardiography to possibly allow this procedure to be performed under local anesthesia.

Acknowledgements
We would like to thank our interventional cardiology colleagues, Drs. John G. Webb and Sanjeevan Pasupati, for helpful comments and their kind assistance in the acquisition and provision of patient data and images.

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Case Reports/Case Series

Case series: Anesthesia for retrograde percutaneous aortic valve replacement – experience with the first 40 patients

[Présentation de cas : L’anesthésie pour un remplacement valvulaire aortique percutané rétrograde : notre expérience avec les 40 premiers patients]

Ronald M. Ree MD FRCPC, John B. Bowering MD FRCPC, Stephan K. W. Schwarz MD PhD FRCPC

Purpose: To describe both the evolution and the main associated complications in the anesthetic management of the initial 40 patients at our centre who underwent percutaneous retrograde aortic valve replacement, a novel technique utilizing a catheter-guided femoral artery approach.

Clinical features: With institutional Research Ethics Board approval, we retrospectively reviewed the medical records of the first 40 patients who underwent percutaneous retrograde aortic valve replacement between January 2005 and March 2006. Information obtained included patient characteristics, anesthetic management, details of the procedure, and complications. All procedures were scheduled to be performed in the cardiac catheterization laboratory. The first four patients received monitored anesthesia care, and the subsequent 36 underwent general anesthesia. There were no anesthesia-related adverse events. The prosthetic valve was placed successfully in 33/40 patients (83%). Median anesthetic time was 3.5 hr (range, 1.25–7.25 hr). Thirty-two/40 patients required vasoressor support. The most common, serious procedural complications were myocardial ischaemia and arrhythmia following rapid ventricular pacing, hemorrhage from vascular injury secondary to the placement and removal of the large-bore sheath in the ilio-femoral artery, aortic rupture, and prosthetic valve maldeployment; 30-day mortality was 13% (n = 5/40).

Conclusions: Percutaneous retrograde aortic valve replacement is a novel procedure that presents the anesthesiologist with unique challenges. Careful preoperative assessment, intraoperative monitoring appropriate for a major vascular procedure, and meticulous management of hemodynamics are imperative for a successful outcome. Serious complications, including major hemorrhage from vascular injury as well as arrhythmia and myocardial ischemia following rapid ventricular pacing, must be anticipated and managed in an expeditious fashion.

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Objectif: Décrire l’évolution et les principales complications associées à la prise en charge anesthésique des premiers 40 patients de notre centre à subir un remplacement valvulaire aortique percutané rétrograde, une technique innovante utilisant une approche échoguidée par l’artère fémorale.

Éléments cliniques: Une fois le consentement du Comité d’éthique de la recherche obtenu, nous avons révisé de façon rétrospective les dossiers médicaux des 40 premiers patients à avoir subi un remplacement valvulaire aortique percutané rétrograde entre janvier 2005 et mars 2006. Les caractéristiques des patients, la prise en charge anesthésique, les détails de l’intervention et les complications faisaient partie des renseignements obtenus. Toutes les interventions étaient prévues dans le laboratoire de cathétérisation cardiaque. Les quatre premiers patients ont reçu une sédation sous surveillance, et les 36 suivants une anesthésie générale. Il n’y a pas eu d’événements indésirables provoqués par l’anesthésie. La

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Financial support: Supported by departmental/institutional funds. Dr. Schwarz is recipient of the 2006 Canadian Anesthesiologists’ Society (CAS) Research Award and the 2006-2008 CAS/Abbott Laboratories Ltd Career Scientist Award in Anesthesia.

Conflicts of interest: none.
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prothèse valvulaire a été positionnée avec succès chez 33/40 patients (83%). Le temps d’anesthésie médian était de 3,5 h (extrêmes, 1,25 – 7, 25 h). Un vasopresseur a été nécessaire chez 32/40 patients. Suite à l’intervention, les complications graves les plus fréquentes étaient l’ischémie myocardique et l’arythmie à la suite d’un entraînement ventriculaire rapide, l’hémorragie provoquée par une lésion vasculaire due au positionnement et au retrait de la gaine à grand diamètre dans l’artère ilio-fémorale, la rupture aortique et le mauvais déploiement de la prothèse valvulaire. La mortalité à 30 jours était de 13 % (5/40).

**Conclusion** : Le remplacement valvulaire aortique percutané rétrograde est une intervention nouvelle qui présente à l’anesthésiologiste des défis spéciaux. Une évaluation préopératoire attentive, un monitoring peropératoire adapté à une intervention vasculaire majeure et une prise en charge méticuleuse de l’hémodynamique sont absolument nécessaires à un devenir réussi. Des complications graves, notamment une hémorragie majeure causée par une lésion vasculaire ainsi que de l’arythmie et une ischémie myocardique suite à un entraînement ventriculaire rapide doivent être anticipées et pris en charge rapidement.

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ORTIC stenosis is the most common cardiac valvular lesion in the developed world. Its etiology may be congenital or acquired. Both forms of stenosis result in a valve with calcified, restricted leaflets. Once aortic stenosis becomes symptomatic, it carries a poor prognosis and is poorly managed with medical therapy. Surgical aortic valve (AV) replacement is effective in prolonging life and improving symptoms; however, the procedure can be associated with significant perioperative risk, especially in the elderly with decreased functional reserve and multiple co-morbidities. Surgery may also carry an unacceptable risk due to extensive calcification of the ascending aorta. Whereas balloon valvuloplasty represents an alternative therapeutic option, the reduction in stenosis is modest and temporary.

Percutaneous approaches to AV replacement have been investigated since 1992. In 2002, Cribier et al. reported a successful percutaneous valve replacement via an antegrade transseptal approach through the femoral vein. However, due to arrhythmias and possible mitral valve injury, the antegrade approach is technically challenging and not well tolerated by some patients. A percutaneous retrograde approach for replacing the AV has been developed at our centre by Webb et al. Vascular access is achieved through the femoral artery. The prosthesis, which is mounted on a catheter-guided stainless steel mesh stent, is maneuvered in a retrograde fashion into the ascending aorta and placed through the native AV before deployment. Here, we report on the evolution in the anesthetic management of the initial 40 patients undergoing this novel procedure, and we summarize the associated major perioperative complications encountered.

**Methods**

With approval of the institutional Research Ethics Board, we retrospectively reviewed the charts, anesthetic records, and procedural database of the initial 40 patients who underwent percutaneous retrograde aortic valve replacement at our centre (St. Paul’s Hospital, The University of British Columbia, Vancouver, B.C.) between January 2005 and March 2006. Patient characteristics, anesthetic management, details of the procedure, and complications were noted. Prior to the calculation of descriptive statistics and data comparisons, we used the Kolmogorov-Smirnov test and assessed kurtosis and symmetry of continuous data to test if values came from a Gaussian distribution. Unless otherwise stated, data are presented as mean ± SD or median [interquartile range], as appropriate. Descriptive data on AV area and mean transaortic gradient, before and after prosthetic valve placement, were compared with the Mann-Whitney test; P < 0.05. Descriptive statistics and comparisons were calculated using Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA, USA) and Prism version 4 (GraphPad, San Diego, USA) software.

**Patient selection**

The Therapeutic Products Directorate (Health Canada, Health Products and Food Branch; Ottawa, Ontario, Canada) approved the procedure for compassionate clinical use in patients considered unsuitable for conventional surgery by a team of cardiologists and cardiac surgeons. Patients with severe symptomatic aortic stenosis were referred for a percutaneous procedure due to multiple comorbidities and/or surgical risk (logistic EuroSCORE ≥ 20%, indicating a 30-day predicted mortality ≥ 20% with operative management). Patient preference for a percutaneous procedure was not considered an indication. The interventional cardiology team obtained informed consent for the procedure from all patients.

**Percutaneous valve replacement procedure**

A detailed description of the technical aspects of this procedure, from an interventional cardiology perspective, has recently been published. Patients received clopidogrel 600 mg and aspirin 325 mg orally prior to the procedure. Antibiotic prophylaxis with either intravenous vancomycin (1 g) or cefazolin (1 g) was
TABLE 1 Preoperative patient characteristics

<table>
<thead>
<tr>
<th>Patients</th>
<th>n = 40 (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>81 ± 8 (38%)</td>
</tr>
<tr>
<td>Female gender</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>Body mass index (kg·m⁻²)</td>
<td>27 ± 6 (58%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23 (58%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (23%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>28 (70%)</td>
</tr>
<tr>
<td>Severe chronic obstructive lung disease</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>History of cerebral ischemic event</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>8 (20%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>Never smoked</td>
<td>19 (48%)</td>
</tr>
<tr>
<td>Estimated GFR &lt; 60 mL·min⁻¹·1.73 m⁻²</td>
<td>20 (50%)</td>
</tr>
<tr>
<td>Permanent pacemaker</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>Aortic calcification</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>Prior thoracotomy</td>
<td>14 (35%)</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>NYHA 3 or 4</td>
<td>37 (93%)</td>
</tr>
<tr>
<td>Angina</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Aortic valve area (cm²)</td>
<td>0.6* (range, 0.3–1.2)</td>
</tr>
<tr>
<td>Transaortic mean gradient (mmHg)</td>
<td>46 ± 18 (45%)</td>
</tr>
<tr>
<td>Mitral regurgitation grade 3 or 4</td>
<td>18 (45%)</td>
</tr>
<tr>
<td>Ejection fraction &lt; 50%</td>
<td>9 (23%)</td>
</tr>
<tr>
<td>Logistic EuroSCORE (%)</td>
<td>25 ± 15 (58%)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD, where appropriate; *median. GFR = glomerular filtration rate; NYHA = New York Heart Association.

administered. All procedures were performed by an interventional cardioligist in the cardiac catheterization laboratory. Femoral access was achieved percutaneously, and the ilio-femoral artery was progressively dilated to accommodate either a 22 or a 24 Fr sheath, depending on the size of the prosthesis to be placed. Heparin 70 U·kg⁻¹ iv was administered following arterial cannulation. The femoral vein was also cannulated to allow a pacing lead to be positioned in the right ventricle. Balloon valvuloplasty of the AV was then performed in a standard manner. A Cribier-Edwards valve was mounted on a balloon at the tip of a deflectable steering catheter (Edwards Lifesciences Inc., Irvine, CA, USA). The guiding catheter was used to guide the device up the abdominal and thoracic aorta to the AV. Prior to deployment, the correct placement of the prosthesis across the AV was confirmed by fluoroscopy, aortography, and also, after the initial patients (who received transthoracic echocardiography), routine transesophageal echocardiography.

To prevent movement and possible ejection of the device during valve deployment, rapid right ventricular pacing was used to minimize pulsatile flow through the AV at the time of prosthesis implantation. Test pacing was first performed at a rate of 220 min⁻¹. The rate was reduced until reliable capture was observed and a reduction in systolic arterial pressure less than 60 mmHg was achieved (Figure 1). Following placement of the valve prosthesis, angiographic (and later also transesophageal echocardiographic; cf. below) examinations were performed to assess prosthetic valvular function and coronary artery patency. If a significant paravalvular leak was identified, balloon dilatation of the prosthesis was performed to further expand the mesh stent.

Anesthetic management

The anesthetic management underwent a significant evolution during the initial multidisciplinary learning curve associated with this novel procedure. On the day of the first scheduled procedure, the anesthesiologist on call was asked to help in the administration of conscious sedation in the cardiac catheterization laboratory. The initial four procedures were then carried out under monitored anesthesia care. As it became evident that patients regularly required surgical vascular repair at the access site (cf. below), the following 36 procedures were performed under general endotracheal anesthesia. It also became evident that endotracheal intubation facilitated the use of routine intraoperative transesophageal echocardiography (not done in the first four patients) to aid in the confirmation of accurate prosthetic valve function and placement. In

FIGURE 1 Femoral arterial pressure tracing showing marked hypotension and decreased pulsatile flow during rapid right ventricular pacing. EKG = electrocardiogram.
TABLE II Anesthetic management and intraoperative characteristics

<table>
<thead>
<tr>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 40 (100%)</td>
</tr>
<tr>
<td>Type of anesthetic</td>
</tr>
<tr>
<td>Monitored anesthesia care</td>
</tr>
<tr>
<td>General anesthesia</td>
</tr>
<tr>
<td>Maintenance agent(s)</td>
</tr>
<tr>
<td>Desflurane</td>
</tr>
<tr>
<td>Sevoflurane</td>
</tr>
<tr>
<td>Desflurane &amp; propofol</td>
</tr>
<tr>
<td>Desflurane &amp; propofol &amp; remifentanil</td>
</tr>
<tr>
<td>Desflurane &amp; remifentanil</td>
</tr>
<tr>
<td>Sevoflurane &amp; propofol</td>
</tr>
<tr>
<td>Sevoflurane &amp; remifentanil</td>
</tr>
<tr>
<td>Duration</td>
</tr>
<tr>
<td>&lt; 2 hr†</td>
</tr>
<tr>
<td>2–3 hr</td>
</tr>
<tr>
<td>3–4 hr</td>
</tr>
<tr>
<td>4–5 hr</td>
</tr>
<tr>
<td>&gt; 5 hr</td>
</tr>
<tr>
<td>Vasopressors used</td>
</tr>
<tr>
<td>Phenylephrine</td>
</tr>
<tr>
<td>Ephedrine</td>
</tr>
<tr>
<td>Dopamine</td>
</tr>
<tr>
<td>Epinephrine‡</td>
</tr>
<tr>
<td>Calcium chloride‡</td>
</tr>
<tr>
<td>Minimum</td>
</tr>
<tr>
<td>intraoperative systolic blood pressure§</td>
</tr>
<tr>
<td>70–79 mmHg</td>
</tr>
<tr>
<td>80–89 mmHg</td>
</tr>
<tr>
<td>90–99 mmHg</td>
</tr>
<tr>
<td>100–109 mmHg</td>
</tr>
<tr>
<td>&gt; 110 mmHg</td>
</tr>
<tr>
<td>Intraoperative transfusion</td>
</tr>
<tr>
<td>1 U packed red blood cells</td>
</tr>
<tr>
<td>2 U packed red blood cells</td>
</tr>
<tr>
<td>3 U packed red blood cells</td>
</tr>
<tr>
<td>&gt; 3 U packed red blood cells</td>
</tr>
</tbody>
</table>

*Two (of the first four) patients received monitored anesthesia care for the valve placement, then general anesthesia for vascular repair. †The two patients whose procedure lasted less than two hours both suffered an intraoperative cardiac arrest. ‡Epinephrine and calcium chloride were used as resuscitative agents during the intraoperative cardiac arrests. §Indicates blood pressure in the prepping stage of the procedure. ‼One patient underwent massive transfusion (19 U of packed red blood cells, 20 U of platelets, 9 U of fresh frozen plasma, and 10 U of cryoprecipitate; cf. body text).

As mentioned, transesophageal echocardiography, performed by a dedicated specialized cardiologist, was introduced as a routine monitoring modality in these patients. Intraoperative hypotension (systolic arterial pressure < 90 mmHg) was treated with intravenous crystalloid infusion as well as phenylephrine and/or ephedrine boluses. For persisting hypotension, phenylephrine, norepinephrine, and/or dopamine infusions were prepared and administered as indicated.

Following the procedure, tracheal extubation was undertaken when the patients were awake in the cardiac catheterization laboratory, whereas others were transferred, ventilated, to the cardiac care unit (CCU). All patients were monitored overnight in the CCU.

Results

The patients’ preoperative baseline characteristics are listed in Table I. Fifty-eight percent of patients had a logistic EuroSCORE ≥ 20% (cf. Methods: Patient selection); the mean logistic EuroSCORE was 25 ± 15% [95% confidence interval (CI), 20.2–29.8%]. The remainder were accepted due to significant comorbidities, including advanced age (> 85 yr), involvement of more than one valve, severe chronic obstructive pulmonary disease, multiple cerebrovascular accidents and carotid atherosclerosis, marked pulmonary hypertension, and debilitating arthritis that was felt to preclude rehabilitation after open heart surgery.

The prosthesis was placed successfully in 33/40 patients (83%). The reasons for an unsuccessful procedural outcome included an inability to deliver the prosthesis to the correct position in five patients and deployment in the aortic arch in two patients (Figure 2).

Patients tolerated general anesthesia well, with no anesthesia-related complications. Table II summarizes details on the anesthetic management of these patients. Reduced doses of anesthetic agents appropriate for the advanced age, multiple co-morbidities, and severe valvular disease of these patients were used and carefully titrated. For the management of hypotension, phenylephrine was administered to 30 patients, while ephedrine was used in 12 patients. Dopamine was used in a single individual as an adjunct to phenylephrine and ephedrine. Eight patients required no vasopressors. Epinephrine and calcium chloride were used in two instances during resuscitation following cardiac arrest.

Two patients sustained complications related to rapid ventricular pacing. Both occurred after pacing for balloon valvuloplasty, but prior to placement of the prosthetic valve. Ventricular fibrillation occurred in one patient who responded immediately to external...
with the median calculated AV area increasing from 0.6 cm² (interquartile range, 0.5–0.7 cm²) to 1.7 cm² (interquartile range, 1.4–2.0 cm²; Mann–Whitney test, P < 0.0001; patients with available post data on the AV area, n = 32) and the mean transaortic gradient decreasing from 49 mmHg (median; interquartile range, 32–60 mmHg) to 11 mmHg (interquartile range, 9–16 mmHg; Mann–Whitney test, P < 0.0001; patients with available post data on the mean transaortic gradient, n = 32). Paravalvular aortic insufficiency, when present, was graded mild in severity. In association with improved hemodynamics, five patients required intravenous antihypertensive therapy after deployment of the prosthesis. Upon completion, all patients who had experienced no procedural complications were extubated and transported to the CCU. The median anesthetic time for the procedure was 3.5 hr (range, 1.25–7.25 hr).

Significant morbidity and mortality developed from vascular complications secondary to the placement and removal of the large-bore sheath in the ilio-femoral artery. One of the early patients in this case series died intraoperatively due to aortic rupture from the steering catheter. Another death resulted from postoperative multi-organ failure following a hemorrhagic cardiac arrest after femoral sheath removal and subsequent massive transfusion (cf. Table II). Overall, procedural blood loss was variable. Five patients required intraoperative transfusion of packed red blood cells, while eight additional patients were transfused during their hospital stay (cf. Tables II and III). As a result, the routine availability of a vascular surgeon to repair the femoral access site in the cardiac catheterization laboratory was incorporated as part of the standard management of these procedures.

Table III summarizes the in-hospital, post-procedure outcomes. The 30-day mortality was 13% (5/40 patients). Infection occurred in four patients. These included one case of Staphylococcus aureus septicemia, one case of infection at the access site after complex vascular repair, and urinary tract infections in two patients. All of these patients recovered with antibiotic therapy.

One patient experienced a postoperative cerebrovascular event. This individual made a full neurologic recovery.

**Discussion**

In this case series, we report on the first experiences with anesthesia for patients undergoing percutaneous retrograde AV replacement. Although surgical AV replacement is beneficial for improving patient symptoms and increasing life expectancy, it poses a
**TABLE III** In-hospital complications

<table>
<thead>
<tr>
<th>Patients</th>
<th>n = 40</th>
<th>(100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inability to deliver the prosthetic valve</td>
<td>5</td>
<td>(13%)</td>
</tr>
<tr>
<td>Prosthetic valve malposition</td>
<td>2</td>
<td>(5%)</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>1</td>
<td>(3%)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>13</td>
<td>(33%)</td>
</tr>
<tr>
<td>Postoperative infection</td>
<td>4</td>
<td>(10%)</td>
</tr>
<tr>
<td>Access site</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus septicemia</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>UTI</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

TIA/CVA within 30 days | 1 | (3%)* |
30-day mortality | 5 | (13%) |
Intraprocedural mortality | 1 | (3%) |

*Complete resolution with no neurologic sequelae.
TIA = transient ischemic attack; CVA = cerebrovascular accident; UTI = urinary tract infection.

significant risk to the elderly with multiple medical problems, rendering these patients poor operative candidates. Patients may also be nonsurgical candidates due to marked aortic calcification or previous cardiac surgery. In these individuals, percutaneous AV replacement may become an alternative in the management of aortic stenosis. Other inherent potential advantages of the percutaneous approach compared to open heart surgery include avoidance of cardiopulmonary bypass and aortic cross clamping, avoidance of sternotomy and minimization of surgical stimulation, reduction in the need for postoperative ventilation and intensive care unit stay, and possible associated cost savings.

The anesthetic management of the initial four procedures carried out at our institution consisted of monitored anesthesia care with conscious sedation, in accordance with the original plan of the interventional cardiology team. We found, however, that performing the procedure under general endotracheal anesthesia offered distinct advantages. These include the facilitation of routine intraoperative transesophageal echocardiography to assist in the precise placement of the prosthesis prior to deployment and to assess for complications following placement. General anesthesia also allowed for improved patient tolerance of prolonged procedures and eased the process of surgical repair of the access site at the end.

The anesthetic risks for patients with severe aortic stenosis are well documented. We found that percutaneous AV replacement, however, carries with it unique additional challenges. Rapid ventricular pacing used during this procedure assists with the precise placement of the valve prosthesis. Induced ventricular tachycardia, however, does not allow sufficient diastolic time for the hypertrophied ventricle to fill, producing a temporary state of decreased coronary perfusion in the face of increased myocardial oxygen demand. This has the potential of inducing profound arrhythmias and myocardial ischemia. Although rapid ventricular pacing was tolerated by most, two patients sustained significant complications. Our current practice, therefore, is to minimize pacing duration and to stabilize the patients’ blood pressure with vasopressors prior to repeat pacing. We have found that close communication between the cardiologist and the anesthesiologist is critical during this part of the procedure. Alternative methods of temporarily reducing cardiac output during valve deployment include administration of adenosine, balloon occlusion of venous return to the right or left atria, as well as electrically inducing ventricular fibrillation. However, each of these techniques is associated with its own set of complications.

Vascular injury was a significant cause of morbidity and mortality. All patients now undergo preoperative imaging of their vascular access sites to determine if the ilio-femoral artery lumen is sufficient to allow placement of the guiding catheter. Imaging also delineates the extent of any arterial calcification and tortuosity that may impair catheter advancement or surgical repair. Thirty-three per cent of our patients experienced procedural blood loss significant enough to warrant perioperative transfusion of red blood cells. Major vascular trauma must be anticipated as an intraoperative complication of this procedure. Hemorrhage also should be anticipated postoperatively, however, since ongoing bleeding from ilio-femoral vascular injury may be insidious and present in a delayed fashion (e.g., as retroperitoneal hematoma). Other perioperative complications to be anticipated by the anesthesiologist include cardiac tamponade, coronary artery ostia occlusion during device deployment, coronary artery embolization, and other complications associated with prosthetic valve maldeployment.

As a result of the lessons learned in the management of this first series of patients, anesthesiology involvement now routinely begins preoperatively, as all patients these days are seen in the anesthesia pre-assessment clinic for preoperative consultation and optimization. Whereas it remains difficult to decide when a patient, deemed by definition to be a nonsurgical candidate, is in fact a non-anesthetic candidate, our observation that there were no adverse events specifically related to anesthesia is somewhat reassuring. However, due to the number of observed and potential procedural and perioperative complications, all patients now receive invasive arterial and central venous pressure monitoring, in addition to the femo-
ral access secured by the cardiology team. Finally, the construction at our centre of a new operating theatre dedicated to advanced cardiac procedures has very recently allowed us to perform these procedures in the main operating room suite (with cardiopulmonary bypass pumps in close proximity/on standby), as opposed to (from an anesthesiologist's perspective), a remotely located cardiac catheterization laboratory. We believe that the comprehensive perioperative involvement of anesthesiology as part of a multidisciplinary team has significantly contributed to the improved outcomes achieved after the first series of patients.21

In summary, percutaneous replacement of the AV by a retrograde femoral approach is a new and exciting development in the treatment of aortic stenosis. Although it represents an intriguing alternative for those patients not considered candidates for conventional surgery, there are a number of significant concerns, as this case series demonstrates. Whereas the vast majority of these sick patients tolerated general anesthesia well, serious and, at times, spectacular complications, including major hemorrhage from vascular injury, arrhythmia and myocardial ischemia following rapid ventricular pacing, and prosthetic valve maldeployment, must be anticipated by the anesthesiologist and, where possible, managed in an expeditious fashion. To an extent, these complications may be part of a learning curve that accompanies any novel technique such as this.21 Future developments that may improve patient safety with this procedure include smaller profile catheters and sheaths that minimize trauma to the vascular access site, alternative methods of reducing left ventricular outflow during device placement that may be more cardioprotective, and the use of intracardiac echocardiography to possibly allow this procedure to be performed under local anesthesia.

Acknowledgements
We would like to thank our interventional cardiology colleagues, Drs. John G. Webb and Sanjeevan Pasupati, for helpful comments and their kind assistance in the acquisition and provision of patient data and images.

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The effect of tranexamic acid on blood loss and use of blood products in total knee arthroplasty: a meta-analysis

Haoran Zhang · Junmin Chen · Fei Chen · Wenzhong Que

Received: 13 July 2011/Accepted: 25 October 2011 © Springer-Verlag 2011

Abstract

Purpose Studies have shown that tranexamic acid (TXA) reduces blood loss and transfusion need in patients undergoing total knee arthroplasty (TKA). However, no single study has been large enough to definitively determine whether the drug is safe and effective. We report a systematic review and meta-analysis of randomised controlled trials evaluating the efficacy and safety of TXA in reducing blood loss and transfusion in TKA.

Methods A comprehensive literature search was done in Cochrane Library, MEDLINE, EMBASE, and CNKI. Two reviewers independently identified the eligible studies, assessed their methodological quality, and extracted data. The data were evaluated using the generic evaluation tool designed by the Cochrane Bone, Joint and Muscle Trauma Group. The relevant data were analyzed using RevMan 5.0.

Results Fifteen randomized controlled trials involving 842 patients were included. The use of TXA reduced total blood loss by a mean of 487 ml [95% confidence interval (CI) −629 to −344], intra-operative blood loss by a mean of 127 ml (95% CI −313−59), and post-operative blood loss by a mean of 245 ml (95% CI −410 to −80). TXA led to a significant reduction in the proportion of patients requiring blood transfusion (risk difference −0.4). There were no significant differences in deep-vein thrombosis (DVT), pulmonary embolism, or other complications among the study groups.

Conclusion Meta-analysis indicates that TXA may reduce post-operative, total blood loss and transfusion in patients undergoing TKA. TXA led to a significant reduction in the proportion of patients requiring blood transfusion.

Level of evidence Therapeutic study (Systematic review of Level I studies with inconsistent results), Level II.

Keywords Tranexamic acid · Total knee arthroplasty · Blood loss · Transfusion · Meta-analysis

Introduction

In total knee arthroplasty (TKA), there can be considerable blood loss, requiring allogeneic blood transfusion. Intra-operative and post-operative bleeding, in series of TKA, ranges from 340 to 1,500 ml [1, 27]. Minimizing bleeding and blood transfusion is desirable given its cost, risk, and potential for adverse reactions. Blood transfusion carries significant risks of immunological reactions, intravascular hemolysis, transmission of disease, renal failure, transfusion-induced coagulopathy, admission to intensive care, and even death [4, 25, 26].

A variety of blood-conserving techniques have been developed to reduce blood loss and post-operative transfusion rates, including controlled hypotension, intra-operative blood salvage, regional anesthesia, navigation, minimally invasive surgery (MIS), use of drain, and the use of erythropoietin and antifibrinolytic agents [4, 36, 43]. Antifibrinolytic agents such as tranexamic acid (TXA), aprotinin, and epsilon aminocaproic acid (EACA) are widely available agents which enhance hemostasis, thus
potentially reducing blood loss during surgery and transfusion requirements.

TXA is a synthetic derivative of the amino acid lysine and a competitive inhibitor of plasminogen activation and therefore interferes with fibrinolysis. It has been used successfully to stop bleeding after dental extraction, cardiac surgery, tonsillectomy, prostate surgery, heavy menstrual bleeding, and in patients with hemophilia [6, 9, 10, 28, 37]. TXA is more inexpensive and safer than aprotinin and more potent than EACA, with overall good penetration into major joints [11, 13]. Numerous studies have investigated their efficacy in reducing blood loss and transfusion requirements in TKA [2, 3, 8, 11–13, 17, 18, 20, 21, 24, 29, 34, 39, 41]. However, some of these studies have been criticized for poor design, low power, inconclusive results, and short follow-up. This has prejudiced the use of these potentially valuable agents in orthopedic practice.

The purpose of this review was to provide an indication of whether TXA reduce bleeding and transfusion requirements in patients undergoing TKA, as well as their effect on the rate of complication.

Materials and methods

This review was performed according to the standard described in 'Preferred reporting items for systematic reviews and meta-analyses' statement [31].

Criteria for considering studies for this review

This meta-analysis evaluated randomized controlled trials (RCTs) in any language comparing tranexamic acid agents with control (placebo or nothing) for hemorrhage and blood transfusion during perioperation. The participants were adults who had undergone TKA, regardless of the type or size of prosthesis used. Subgroup analyses were performed for patients with different characteristics. The intervention considered was the administration of intravenous TXA. Studies that involved oral or intramuscular treatment were excluded.

The primary outcomes were estimated intra-operative, post-operative, and total blood loss. The secondary outcomes were the proportion of patients who had allogeneic blood transfusion, the amount of blood units transfused per patient, complications, functional knee outcome measures, and general quality of life outcome measures.

Search strategy for identification of studies

The following exploded Medical Subject Headings (MeSH) terms were used for the initial literature search: 'Antifibrinolytics', 'Tranexamic acid', and 'Cyklokapron.' The Medline search was then refined to include clinical trials and randomised controlled trials in adult humans. The electronic databases searched were: MEDLINE (1966–March 2011), EMBASE (1980–2011 Week 12), Cochrane Library (Issue 1, 2011), and Chinese National Knowledge Infrastructure (CNKI) (1994–March 2011). No language or date restrictions were applied. Reference lists of all included studies and reviews related to the topic of the present meta-analysis were manually searched for other potentially eligible studies.

Methods of the review

Potential studies for inclusion were identified from the search results. Two reviewers (H.Z. and F.C.) independently applied the search strategy to selected references from these databases. The titles and abstracts of the articles were reviewed independently. When there was a doubt, the full article was retrieved for further scrutiny. The two authors independently assessed each full study report to see whether it met the review’s inclusion criteria, and authors were contacted for more information and clarification of data as necessary. Disagreements on inclusion of studies were resolved by the senior reviewer (J.C.) until consensus was obtained.

In order to assess the methodological quality of included studies the review authors (H.Z. and F.C.) used a modification of the generic evaluation tool used by the Cochrane Bone, Joint and Muscle Trauma Group [14] (Table 1). The methodological quality of each trial was scored and ranged from 0 to 24. Disagreements were resolved by consensus or consultation with the senior reviewer (J.C.).

Data extracted from the included studies were entered independently by two reviewers (H.Z. and F.C.). Any disagreement was resolved by the senior reviewer (J.C.). The authors of individual trials were contacted directly to provide further information when necessary. When this was not possible or data were missing through loss to follow-up, intention-to-treat principles were used.

Statistical analysis

Continuous data for each arm in a particular study were expressed as mean and standard deviation (SD), and the treatment effect as mean differences. Dichotomous data for each arm in a particular study were expressed as proportions or risks, and the treatment effect as risk differences. Relevant data were analyzed using RevMan 5.0. Heterogeneity was explored by Chi-squared test with a significance set at a $P$ value of 0.1, and the quantity of heterogeneity was measured by $I^2$ [16]. The origins of heterogeneity, if present, were analyzed according to differences in methodological quality, characteristics of participants and intervention. When the data allowed, the authors of this paper performed subgroup analysis of the
Table 1  Quality assessment items and possible scores
A. Was the assigned treatment adequately concealed prior to allocation?
2 = Method did not allow disclosure of assignment
1 = Small but possible chance of disclosure of assignment or unclear
0 = Quasi-randomised or open list/tables
B. Were the outcomes of participants who withdrew described and included in the analysis (intention to treat)?
2 = Withdrawals well described and accounted for in analysis
1 = Withdrawals described and analysis not possible
0 = No mention, inadequate mention, or obvious differences and no adjustment
C. Were the outcome assessors blinded to treatment status?
2 = Effective action taken to blind assessors
1 = Small or moderate chance of unblinding of assessors
0 = Not mentioned or not possible
D. Were the treatment and control group comparable at entry?
2 = Good comparability of groups, or confounding adjusted for in analysis
1 = Confounding small; mentioned but not adjusted for
0 = Large potential for confounding, or not discussed
E. Were the participants blind to assignment status after allocation?
2 = Effective action taken to blind participants
1 = Small or moderate chance of unblinding of participants
0 = Not possible, or not mentioned (unless double-blind), or possible but not done
F. Were the treatment providers blind to assignment status?
2 = Effective action taken to blind treatment providers
1 = Small or moderate chance of unblinding of treatment providers
0 = Not possible, or not mentioned (unless double-blind), or possible but not done
G. Were care programmes, other than the trial options, identical?
2 = Care programmes clearly identical
1 = Clear but trivial differences
0 = Not mentioned or clear and important differences in care programmes
H. Were the inclusion and exclusion criteria clearly defined?
2 = Clearly defined I = inadequately defined 0 = not defined
I. Were the interventions clearly defined?
2 = Clearly defined I = inadequately defined 0 = not defined
J. Were the outcome measures used clearly defined? (by outcome)
2 = Clearly defined I = inadequately defined 0 = not defined
K. Were diagnostic tests used in outcome assessment clinically useful? (by outcome)
2 = Optimal I = adequate 0 = not defined, not adequate
L. Was the surveillance active, and of clinically appropriate duration? (by outcome)
2 = Optimal I = adequate 0 = not defined, not adequate

trials according to the type of anesthesia, dose regimen and timing of TXA delivery, transfusion trigger, and administration of low-molecular-weight heparin.

Results

The search strategy identified 378 citations with 15 satisfying the pre-defined eligibility criteria for inclusion in the analysis (Fig. 1). Fifteen independent randomized controlled trials [2, 3, 8, 11–13, 17, 18, 20, 21, 24, 29, 34, 39, 41] reporting 842 patients at final follow-up were eligible for data extraction and meta-analysis (Table 2). These studies involved a total of 443 patients in TXA group and 399 patients in control group.

The majority of included trials were small studies with between 20 and 108 participants. However, they were relatively well designed and the quality assessment score was high in most of them, with a mode of 24, the highest possible score and a range of 14–24 [2, 3, 29]. Only one study had a score less than 20 [20].

The trials performed were all for primary TKA, and osteoarthritis was the most common diagnosis. The patients’ characteristics were comparable within each study group, including the pre-operative hemoglobin and hematocrit levels. A placebo (normal saline) was given in twelve studies, and only three studies used controls who did not receive any treatment [8, 12, 20]. Different doses, ranging from 10 to 30 mg/kg, and modes of TXA delivery were used. A single IV bolus given pre-operatively was used in two studies [17, 34]. Eleven studies used repeated boluses

Fig. 1 Flow chart of included and excluded studies
<table>
<thead>
<tr>
<th>Trials</th>
<th>Cases (Tx/C)</th>
<th>TXA dose</th>
<th>Control DVT prophylaxis</th>
<th>DVT screen</th>
<th>Blood transfusion protocol</th>
<th>QAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hiippala-97</td>
<td>90 (39/38)</td>
<td>15 mg/kg IV b/f TRNQT deflation then 10 mg/kg 3–4 and 6–7 h after initial dose</td>
<td>S</td>
<td>Dalteparin</td>
<td>Clinical Exam ± US</td>
<td>Hb &lt; 10 g/dL</td>
</tr>
<tr>
<td>Ido²</td>
<td>43 (21/22)</td>
<td>TXA 1 g IV just before operation and 3 h after operation</td>
<td>–</td>
<td>NA</td>
<td>Clinical</td>
<td>NA</td>
</tr>
<tr>
<td>Engel¹²</td>
<td>24 (12/12)</td>
<td>15 mg/kg IV b/f TRNQT release, 10 mg/kg after 3 h</td>
<td>–</td>
<td>Enoxaparin</td>
<td>Clinical exam ± venography</td>
<td>Hb &lt; 10 g/dL</td>
</tr>
<tr>
<td>Hiippala-95</td>
<td>29 (15/13)</td>
<td>15 mg/kg 2–5 min b/f TRNQT deflation</td>
<td>NS</td>
<td>Enoxaparin</td>
<td>Clinical exam ± venography</td>
<td>Hb &lt; 10 g/dL</td>
</tr>
<tr>
<td>Benoni²</td>
<td>96 (43/43)</td>
<td>10 mg/kg IV b/f TRNQT release and after 3 h</td>
<td>S</td>
<td>Dalteparin</td>
<td>Clinical exam ± venogram or W/Q</td>
<td>Clinical decision/ Hb &lt; 10 g/dL</td>
</tr>
<tr>
<td>Jansen²</td>
<td>42 (21/21)</td>
<td>15 mg/kg 30 min b/f inflation of TRNQT then repeated every 8 h for 3 days</td>
<td>S</td>
<td>Fraxiparin</td>
<td>Clinical exam</td>
<td>Packed Cell Volume &lt; 26% in any post-op measure</td>
</tr>
<tr>
<td>Ellis¹¹</td>
<td>20 (10/10)</td>
<td>15 mg/kg 30 min b/f defatting the limb tourniquet followed by 10 mg/kg/hr for 12 h</td>
<td>S</td>
<td>Enoxaparin</td>
<td>Clinical exam</td>
<td>Hct &lt; 27%</td>
</tr>
<tr>
<td>Tanaka³⁹</td>
<td>99 (24, 22, 27/26)</td>
<td>(a) 20 mg/kg 10 min b/f surgery</td>
<td>S</td>
<td>NA</td>
<td>Venography, 7–14 days post-op as well as perfusion lung scan</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) 20 mg/kg 10 min b/f defatination of TRNQT</td>
<td></td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(c) 10 mg/kg 10 min b/f surgery and 10 min b/f defatination of TRNQT</td>
<td></td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Velen⁴¹</td>
<td>30 (15/15)</td>
<td>10 mg/kg (to 1 g max) b/f TRNQT release and repeated 3 h later</td>
<td>NS</td>
<td>Fragmin</td>
<td>Clinical</td>
<td>Hct &lt; 28%</td>
</tr>
<tr>
<td>Good¹³</td>
<td>55 (27/24)</td>
<td>10 mg/kg IV b/f TRNQT release and 3 h later</td>
<td>S</td>
<td>Dalteparin</td>
<td>Clinical exam ± US</td>
<td>Hb &lt; 9 g/dL</td>
</tr>
<tr>
<td>Camarasa³</td>
<td>95 (35/60)</td>
<td>10 mg/kg IV b/f TRNQT release and 3 h later</td>
<td>S</td>
<td>Dalteparin</td>
<td>Clinical exam ± US</td>
<td>Hb &lt; 8 g/dL</td>
</tr>
<tr>
<td>Orpen⁴⁴</td>
<td>30 (15/14)</td>
<td>IV 15 mg/kg at cement mixing</td>
<td>NS</td>
<td>Fragmin</td>
<td>Color DUS</td>
<td>Hb &lt; 9 g/dL</td>
</tr>
<tr>
<td>MacGillivray²⁹</td>
<td>60 (20, 20/20)</td>
<td>(a) 10 mg/kg IV b/f TRNQT deflation and after 3 h</td>
<td>NS</td>
<td>Warfarin</td>
<td>Clinical ± spiral computerized tomography</td>
<td>Hb &lt; 8 g/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) 15 mg/kg IV b/f TRNQT deflation and after 3 h</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dhillon⁸</td>
<td>108 (52/56)</td>
<td>10 mg/kg IV b/f TRNQT deflation and after 3 h</td>
<td>–</td>
<td>LMWH</td>
<td>Clinical exam</td>
<td>Hb &lt; 9 g/dL and Hct &lt; 28%</td>
</tr>
<tr>
<td>Kakar²⁴</td>
<td>50 (25/25)</td>
<td>10 mg/kg IV b/f TRNQT deflation followed by 1 mg/kg/h IV till closure of the wound</td>
<td>NS</td>
<td>NA</td>
<td>Clinical exam</td>
<td>Hb &lt; 8 g/dL</td>
</tr>
</tbody>
</table>

TXA tranexamic acid, DVT deep-vein thrombosis, LMWH low-molecular-weight heparin, QAS quality assessment score, IV intravenous, W/Q scan ventilation/perfusion scan, S saline, NS normal saline, NA data not available, a, b, c indicate multiple treatment arms, DUS Doppler ultrasound, b/f before, Hb hemoglobin, Hct hematocrit, Tx treatment group, C control group, TRNQT tourniquet, EOS end of surgery, op operation

[2, 3, 8, 12, 13, 18, 20, 21, 29, 39, 41] and the remainder a prolonged infusion [11, 24]. Thirteen studies stated a transfusion trigger, which was related to a fall in either hemoglobin or hematocrit levels [2, 3, 8, 11–13, 17, 18, 21, 24; 29, 34, 41]. In one study [39], transfusion trigger was reported being based on criteria and guidelines of the National Institutes of Health Consensus Conference. One study did not mention the blood transfusion protocol [20]. All studies except those of Ido et al. [20], Tanaka et al. [39], MacGillivray [29], and Kakar et al. [24] used...
low-molecular-weight heparin for prophylaxis against deep-vein thrombosis (DVT). In six studies, screening for DVT relied on clinical assessment followed by ultrasound examination, venography, or computerized tomography in suspected cases [2, 3, 12, 13, 18, 29]. In two studies, an ultrasound examination or venogram was performed routinely [34, 39].

Post-operative drainage was measured between 24 and 48 h, when the drains were removed in most cases. There were six trials that used regional anesthesia alone [2, 12, 13, 17, 18, 41], three did not mention the type of anesthetic [8, 20, 39] and the remaining six used a combination of general and regional anesthesia [3, 11, 21, 24, 29, 34]. The prostheses were cemented in twelve trials [3, 8, 12, 13, 17, 20, 21, 24, 29, 34, 39, 41], cementless in two [2, 18], and data not available in one [11]. The amount of functional knee measures and general quality of life outcome measures was not analyzed, as there were insufficient data. Two studies reported on mortality [3, 18].

Effects of interventions

Blood loss

Total blood loss was examined in 13 studies [2, 3, 8, 12, 13, 17, 18, 21, 29, 34, 39, 41] with a total of 779 patients. The effect of TXA was similar, significantly reducing total blood loss by a mean of 486.7 ml ($P < 0.00001$). However, there was significant heterogeneity ($I^2 = 89\%$) among the studies included (Fig. 2).

Intra-operative: Six studies [2, 3, 8, 12, 17, 34] with a total of 370 patients were eligible for this outcome. These trials randomised 172 patients to receive TXA and 198 patients as controls. There were no statistically significant differences in reducing intra-operative blood loss between TXA and control groups (Fig. 3).

Post-operative: Five studies [2, 8, 17, 20, 34] including 294 patients were eligible for this outcome. The use of TXA significantly reduced post-operative blood loss, measured by drainage volume, by a mean of 245.0 ml ($P = 0.004$) (Fig. 4).

Subgroup analysis was performed on whether patients received cemented prosthesis or uncemented prosthesis. The results showed that the use of uncemented prosthesis more significantly reduced total blood loss and post-operative blood loss (Figs. 2, 4). There were also no statistically significant differences in reducing intra-operative blood loss in subgroup analysis (Fig. 3).

Transfusion requirements

Transfusion requirements were examined in 13 studies [2, 3, 8, 11-13, 17, 18, 21, 29, 34, 39, 41] with a total of 749 patients. The use of TXA led to a 37% reduction in the proportion of patients who required blood transfusion (risk difference $-0.4$, $P < 0.00001$, Fig. 5). The relative risk (RR) for blood transfusion was 0.4 ($P < 0.00001$). Analysis of 10 studies [2, 8, 11-13, 17, 18, 21, 34, 39] (564 patients) using allogeneic blood (any study in which only allogeneic blood was used) resulted in a risk difference of $-0.4$ ($P < 0.00001$).
**Fig. 3** Forest plot diagram showing the effect of TXA on intra-operative blood loss

**Fig. 4** Forest plot diagram showing the effect of TXA on post-operative blood loss

**Fig. 5** Forest plot diagram showing the effect of TXA on blood transfusion
Blood units transfused per patient

This outcome measure was available in only eleven studies [3, 8, 11–13, 17, 18, 21, 29, 39, 41]. In two studies [12, 41], the MD could not be calculated because no patient received blood transfusions in the TXA group. The use of TXA significantly reduced the average number of red blood cell (RBC) transfusions per patient when compared with patients who received placebo (MD = 1.3, P < 0.00001). However, there was significant heterogeneity among the studies included (Fig. 6).

Adverse effects

DVT and pulmonary embolism

Fourteen studies [2, 3, 8, 12, 13, 17, 18, 20, 21, 24, 29, 34, 39, 41] (822 patients) reported DVT complications. Patients receiving TXA (433 patients) had 12 episodes of DVT while 389 patients who did not receive TXA had a total of 12 episodes. The RR for DVT was 0.9 (Fig. 7).

Others

In this section, the authors of this paper compared all other reported adverse events among the groups, such as formation of hematoma, secretion from drain sites, and systemic complications. There was one trial [2] reported eleven events of hematoma in the 15 trials, seven in the TXA group and four in the control group. One trial [2]...
reported adverse events of secretion from drain sites, three in the TXA group, and two in the control group. Systemic complications included one case in the normal saline group (control group) died suddenly on the 15th post-operative day [18]. The cause of death was pulmonary embolism verified in autopsy. In the telephone survey 3 months after the operation, one had died from aggravation of a prior condition of pulmonary fibrosis [3]. In the TXA group, a patient with a history of ischemic heart disease suffered a myocardial infarction on the fourth day after operation [17], and a patient complained of chest pain and showed hypotension 3 days after surgery [2]. There were three trials [2, 8, 13] reported eight events of infections in the 15 trials, six in the TXA group and two in the control group. However, there was no statistical significance in the risk of developing infection among the groups. Overall, the results showed that the use of TXA was associated with fewer such complications. However, this did not reach a statistically significant level.

Discussion

The most important finding of this present study was that TXA reduced total blood loss and post-operative blood loss, reduced the risk of transfusion by 56%, reduced the average number of RBC transfusions per patient and did not appear to increase the risk of DVT. TXA have a trend of reduced intra-operative blood loss, but not statistically significant between TXA and control groups.

These observations are consistent with those found in the cardiovascular surgery literature [38, 42] and are of particular clinical importance given the observation that from 1995 to 2004 the rates of inpatient knee replacements increased by 70% in patients over 65 in the United States [7]. Such increases will be associated with increasing bleeding risk and will place additional burden on the blood delivery system, unless methods to reduce bleeding are found. Standardized surgical technique in TKA usually includes the use of pneumatic tourniquet, resulting in reduced perioperative blood loss. Some studies showed that the post-operative blood loss with tourniquet relevantly depends on the time of deflating the tourniquet [40], and intra-operative deflation leads to higher blood loss than deflating after wound closure [30]. Current surgical techniques such as intra-operative hemodilution, autologous donation, and controlled hypotension may increase costs, pose additional logistical problems, and lead to different immunomodulatory activity [22, 32]. TXA is cheap and widely available, making them a promising therapy for the prevention of blood loss [33].

The quality assessment score for most of the studies included was high, which contributes to the strength of point estimates and conclusions drawn from the meta-analysis. The majority of included trials were of good methodological quality, they were relatively well designed, and the quality assessment score was high in most of them. There are several issues related to quality control in conducting a meta-analysis, in particular study selection and the homogeneity of the studies. A systematic review and meta-analysis with homogeneity are regarded as level Ia evidence [35]. Hence, our study focused on the use of TXA and TKA as a single group to reduce heterogeneity related to other antifibrinolytic agents and other types of operation.

The most significant result of this review was the consistency of TXA in reducing total blood loss, post-operative, and transfusion rates after TKA in the majority of studies. The results showed that multiple-dose regimen and total dose ≥30 mg/kg significantly reduced total blood loss (−520 ml vs. −361 ml and −792 ml vs. −437 ml). There were no statistically significant differences in reducing intra-operative blood loss (MD, −126.8 ml, 95% CI −312.8−59.3) between TXA and control groups. Intra-operative blood loss is the only unexpected result of this study. There have not been enough studies evaluating the efficacy of TXA in reducing intra-operative blood loss and transfusion in TKA. TXA reduced intra-operative blood loss with mean of 127 ml, difference was not statistically significant between TXA and control groups. Secondly, estimating blood loss was variable, since invisible bleeding was rarely measured. Differences in usage of the tourniquet and surgical techniques are also likely to have contributed to the differences observed between studies. There was significant heterogeneity among the studies when postoperative and total blood losses were evaluated. The variations that may have accounted for such heterogeneity include the variations in patient characteristics and different strategies for measuring outcomes. At the same time, we noticed that there were some differences in difference of the dosage, perioperative management protocols of application, type of implant and the usage of the tourniquet. These factors that vary across studies may lead to heterogeneity.

This meta-analysis showed that intravenous TXA reduced allogeneic blood transfusion requirements by 37%. Furthermore, sub-group analysis showed that this positive effect persisted regardless of whether TXA was delivered in single or multiple doses, whether the patient had low-molecular-weight heparin, regional anesthesia, a cemented TKA or total dose, and whether a transfusion protocol existed (Table 3). Interestingly, multiple-dose regimen, total dose ≥30 mg/kg, and the use of transfusion protocols produced a more profound risk reduction of blood transfusion, which is consistent with evidence from previous studies [19, 44]. Because some of the sample sizes were small in subgroup analysis, we need to be more cautious in
drew conclusions about apparent variations in the effect sizes.

One study in the meta-analysis did not support the routine use of TXA in TKA. Orpen et al. [34] randomised 29 patients to either a single dose of TXA or a similar volume of saline as a pre-operative bolus. The results were in favor of the placebo group, with a mean post-operative blood loss of 77 ml (SD 108) versus 130 ml (SD 126) for the TXA group. However, these authors and the results of our meta-analysis attribute these findings to the fact that TXA was given too low to show a significant effect, as most of the other studies administered TXA post-operatively, with overall good results.

Other meta-analyses examined the relationship between TXA and bleeding and/or transfusion after TKA. Ho and Ismail [19] included in the meta-analysis trials that studied patients undergoing either hip or knee joint arthroplasty. Blood loss was again collectively defined as ‘perioperative bleeding’, despite including the results of total bleeding as well as post-operative bleeding under this definition. However, the authors of this paper only analyzed in this meta-analysis RCTs that included patients undergoing TKA.

Cid and Lozano [5] performed another meta-analysis where the effects of TXA in TKA were evaluated. Only nine trials were eligible for this meta-analysis, which showed that the use of TXA for patients undergoing TKA is effective in reducing the requirements of allogeneic blood transfusion. However, blood loss was not included in their analysis. Zuffery et al. [44] analyzed the effect of intravenous anti-fibrinolytics, including aprotinin, TXA, and epsilon aminocaproic acid, on blood transfusion in orthopedic surgery. Their results on blood transfusion were similar to ours, especially when considering a multiple-dose regimen for TXA. However, the effect of TXA on blood loss was only briefly discussed as part of ‘other efficacy endpoints’ and was evaluated as a single group under ‘perioperative bleeding’.

Kagoma et al. [23] studied the effect of antifibrinolytics on reducing blood transfusion after total knee and hip arthroplasties. They reviewed the evidence of using aprotinin, TXA and EACA on total bleeding and transfusion rates in orthopedic surgery. Despite similar trends to our study, all three antifibrinolytics were either analyzed as a single group or their effects evaluated for knee and hip arthroplasties combined. However, we only analyzed in our meta-analysis trials that included patients undergoing TKA. In that meta-analysis, ten early related studies were included. Since that time, additional clinical studies determining the effects of TXA have been reported.

This meta-analysis does have several limitations. First, trials included in our study were designed to assess the efficacy and safety of TXA in primary TKA, where high-risk factors were excluded. These included patients with a history of cardiovascular disease, thromboembolic events, renal failure, allergy to TXA, pregnancy, bleeding diathesis, and those on warfarin or a therapeutic dose of low-molecular-weight heparin. Second, differences in surgical techniques and blood transfusion protocol are likely to have contributed to the differences observed among studies. Few studies reported the type of surgical hemostasis (i.e., gauzes packing, electrical cauteration) utilized; these techniques are known to reduce bleeding during surgery [15]. Estimating bleeding was variable, since invisible bleeding was rarely measured. It is likely that these inconsistencies across all studies contributed to the high $I^2$ values seen in statistical analyses. Third, the limitations of this meta-analysis included insufficient data to support the analysis of functional outcome scores or quality of life outcome measures as originally planned.

Based on the current evidence-base, clinicians and patients need to know the possible clinical benefit/risk of TXA, when deciding on their therapy management following TKA. According to the efficacy and safety, the analysis suggested that TXA should be indicated in patients undergoing TKA.
Conclusion

Meta-analysis of the current literature indicates that TXA significantly reduced post-operative and total blood loss after primary TKA. However, there were no statistically significant differences in reducing intra-operative blood loss. TXA led to a significant reduction in the proportion of patients requiring allogeneic blood transfusion and the average number of RBC transfusions per patient. Patients receiving TXA had no significant increase in the risk of complication rates.

Conflict of interest The authors state that they have no conflict of interest.

References

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37 C.F.R. Section 201.14
STANDARDS FOR BASIC ANESTHETIC MONITORING
Committee of Origin: Standards and Practice Parameters

(Approved by the ASA House of Delegates on October 21, 1986, and last amended on October 20, 2010 with an effective date of July 1, 2011)

These standards apply to all anesthesia care although, in emergency circumstances, appropriate life support measures take precedence. These standards may be exceeded at any time based on the judgment of the responsible anesthesiologist. They are intended to encourage quality patient care, but observing them cannot guarantee any specific patient outcome. They are subject to revision from time to time, as warranted by the evolution of technology and practice. They apply to all general anesthetics, regional anesthetics and monitored anesthesia care. This set of standards addresses only the issue of basic anesthetic monitoring, which is one component of anesthesia care. In certain rare or unusual circumstances, 1) some of these methods of monitoring may be clinically impractical, and 2) appropriate use of the described monitoring methods may fail to detect untoward clinical developments. Brief interruptions of continual† monitoring may be unavoidable. These standards are not intended for application to the care of the obstetrical patient in labor or in the conduct of pain management.

1. STANDARD I

Qualified anesthesia personnel shall be present in the room throughout the conduct of all general anesthetics, regional anesthetics and monitored anesthesia care.

1.1 Objective –

Because of the rapid changes in patient status during anesthesia, qualified anesthesia personnel shall be continuously present to monitor the patient and provide anesthesia care. In the event there is a direct known hazard, e.g., radiation, to the anesthesia personnel which might require intermittent remote observation of the patient, some provision for monitoring the patient must be made. In the event that an emergency requires the temporary absence of the person primarily responsible for the anesthetic, the best judgment of the anesthesiologist will be exercised in comparing the emergency with the anesthetized patient’s condition and in the selection of the person left responsible for the anesthetic during the temporary absence.

2. STANDARD II

During all anesthetics, the patient’s oxygenation, ventilation, circulation and temperature shall be continually evaluated.

2.1 Oxygenation –

2.1.1 Objective –

To ensure adequate oxygen concentration in the inspired gas and the blood during all anesthetics.
2.2 Methods –

2.2.1 Inspired gas: During every administration of general anesthesia using an anesthesia machine, the concentration of oxygen in the patient breathing system shall be measured by an oxygen analyzer with a low oxygen concentration limit alarm in use.*

2.2.2 Blood oxygenation: During all anesthetics, a quantitative method of assessing oxygenation such as pulse oximetry shall be employed.* When the pulse oximeter is utilized, the variable pitch pulse tone and the low threshold alarm shall be audible to the anesthesiologist or the anesthesia care team personnel.* Adequate illumination and exposure of the patient are necessary to assess color.*

3. VENTILATION

3.1 Objective –

To ensure adequate ventilation of the patient during all anesthetics.

3.2 Methods –

3.2.1 Every patient receiving general anesthesia shall have the adequacy of ventilation continually evaluated. Qualitative clinical signs such as chest excursion, observation of the reservoir breathing bag and auscultation of breath sounds are useful. Continual monitoring for the presence of expired carbon dioxide shall be performed unless invalidated by the nature of the patient, procedure or equipment. Quantitative monitoring of the volume of expired gas is strongly encouraged.*

3.2.2 When an endotracheal tube or laryngeal mask is inserted, its correct positioning must be verified by clinical assessment and by identification of carbon dioxide in the expired gas. Continual end-tidal carbon dioxide analysis, in use from the time of endotracheal tube/laryngeal mask placement, until extubation/removal or initiating transfer to a postoperative care location, shall be performed using a quantitative method such as capnography, capnometry or mass spectroscopy.* When capnography or capnometry is utilized, the end tidal CO2 alarm shall be audible to the anesthesiologist or the anesthesia care team personnel.*

3.2.3 When ventilation is controlled by a mechanical ventilator, there shall be in continuous use a device that is capable of detecting disconnection of components of the breathing system. The device must give an audible signal when its alarm threshold is exceeded.

3.2.4 During regional anesthesia (with no sedation) or local anesthesia (with no sedation), the adequacy of ventilation shall be evaluated by continual observation of qualitative clinical signs. During moderate or deep sedation the adequacy of ventilation shall be evaluated by continual observation of qualitative clinical signs and monitoring for the presence of exhaled carbon dioxide unless precluded or invalidated by the nature of the patient, procedure, or equipment.
4. CIRCULATION

4.1 Objective –

To ensure the adequacy of the patient’s circulatory function during all anesthetics.

4.2 Methods –

4.2.1 Every patient receiving anesthesia shall have the electrocardiogram continuously displayed from the beginning of anesthesia until preparing to leave the anesthetizing location.*

4.2.2 Every patient receiving anesthesia shall have arterial blood pressure and heart rate determined and evaluated at least every five minutes.*

4.2.3 Every patient receiving general anesthesia shall have, in addition to the above, circulatory function continually evaluated by at least one of the following: palpation of a pulse, auscultation of heart sounds, monitoring of a tracing of intra-arterial pressure, ultrasound peripheral pulse monitoring, or pulse plethysmography or oximetry.

5. BODY TEMPERATURE

5.1 Objective –

To aid in the maintenance of appropriate body temperature during all anesthetics.

5.2 Methods –

Every patient receiving anesthesia shall have temperature monitored when clinically significant changes in body temperature are intended, anticipated or suspected.

† Note that “continual” is defined as “repeated regularly and frequently in steady rapid succession” whereas “continuous” means “prolonged without any interruption at any time."

* Under extenuating circumstances, the responsible anesthesiologist may waive the requirements marked with an asterisk (*); it is recommended that when this is done, it should be so stated (including the reasons) in a note in the patient’s medical record.