

# Heart Valve Surgery in a Very High-Risk Population: A Preliminary Experience in Awake Patients

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**Background and aim of the study:** Heart valve surgery in high-risk patients is associated with considerable morbidity and mortality. Epidural anesthesia without mechanical ventilation has been proposed to reduce invasiveness. An analysis was conducted in very high-risk heart valve patients of mid-term survival free from complications, and patient satisfaction of regional anesthesia use, without mechanical ventilation.

**Methods:** A prospective follow up study was conducted in 50 patients (24 females, 26 males; mean age  $74 \pm 10$  years; range: 43-89 years) who underwent heart valve surgery with epidural anesthesia without endotracheal intubation. Preoperatively, all patients were in NYHA class III or IV; eight patients (16%) had undergone a previous cardiac procedure. The median Additive and Logistic EuroSCORE were 14.5 and 52%, respectively. Twenty-seven patients underwent aortic valve replacement, 10 mitral valve replacement, 10 mitral valve repair, two double valve replacement, and one patient ascending aorta replacement. Associated surgical procedures included coronary artery bypass grafting in 12 patients (24%), ascending aorta replacement in three (6%), and left ventricle reshaping in two (4%). Radiofrequency ablation to treat chronic atrial fibrillation (AF) was performed in 15 patients (30%). All patients were prospectively followed up, and a six-month quality

Today's patients undergoing heart valve surgery are not only of greater age but also suffer from complex cardiac, pulmonary and systemic diseases. Among these high-risk patients, postoperative survival as well as cardiac, neurocognitive, pulmonary and renal dysfunctions continue to thwart the efforts of surgeons.

of life assessment was performed in all survivors.

**Results:** Procedures were performed without mechanical ventilation in completely awake and conscious patients. There were two in-hospital and two long-term deaths (8%). Three patients had had previous cardiac surgery (two double valve replacements, two complex mitral valve surgery). Among survivors, 34 (71%) had an uneventful postoperative outcome, except for AF in nine cases. Eight patients required revision for bleeding; two of these were redo cases. The most consistent postoperative complication was acute renal failure in 16 patients, five of whom had previous chronic renal failure. Three patients required mechanical ventilatory support, and none had a cerebrovascular accident. Patients were discharged home after a mean of  $10 \pm 5$  days (including ICU stay; median 9 h). At follow up, all patients were in NYHA class I/II, and all survivors expressed their satisfaction with epidural anesthesia.

**Conclusion:** Heart valve surgery while on cardiopulmonary bypass is feasible and safe using epidural anesthesia. By maintaining autonomic ventilation, a low mid-term morbidity and mortality was observed in patients in whom there was an unacceptable operative risk.

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Postoperative clinical decline also significantly reduces the quality of life (QOL) of survivors after surgery. In aiming to improve patient management, the use of epidural anesthesia has been proposed during beating-heart coronary surgery (1), with the advantages being based on stress response (2), coronary blood flow redistribution (3,4), cardiac stress and hemodynamic stability (5,6), and pulmonary function, including ventilation and perfusion (7). Currently, few data exist on the management and postoperative outcome in patients undergoing heart valve surgery on cardiopulmonary bypass (CPB) while in a conscious state. Thus,

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an analysis was conducted of a cohort of very high-risk patients undergoing cardiac surgery, in order to assess the effect of epidural anesthesia without mechanical intubation on mortality, morbidity and satisfaction of the clinical management.

## Clinical material and methods

### Patients

All patients with confirmed heart valve disease were potentially eligible for the study, including those with severe pulmonary, renal, vascular and combined cardiac diseases. Patients requiring emergency surgery were excluded from the study, but no other exclusion criteria were considered.

Between February 2004 and January 2006, 50 consecutive high-risk patients (24 females, 26 males; mean age  $74 \pm 10$  years, median age 75 years, range: 43 to 89 years) underwent heart valve surgery under epidural

anesthesia, without endotracheal intubation. All patient data were prospectively collected and updated in the authors' database. Patient demographics, operative characteristics and short- to mid-term outcomes are listed in Tables I, II, and III, respectively.

All patients were in NYHA class III-IV, and eight (16%) had undergone a previous cardiac procedure. The median Additive EuroSCORE was 14.5 (range: 6 to 21) and the Logistic EuroSCORE (% mortality) 52% (range: 12.48-89.83%). Twenty-seven patients underwent aortic valve replacement (AVR), 10 mitral valve replacement (MVR), 10 mitral valve repair, two double valve replacement, and one patient an ascending aorta replacement. Associated surgical procedures included coronary artery bypass grafting (CABG) in 12 patients (24%), ascending aorta replacement in three (6%), and left ventricle reshaping in two (4%). Radiofrequency ablation to treat chronic atrial fibrillation (AF) was performed in 15 patients (30%).

All patients were followed up prospectively to monitor patient satisfaction for the entire clinical management.

The study protocol was approved by an institutional review board, and all patients provided their written, informed consent.

### Physical and mental status

Physical and mental status were assessed with the generic Short Form-36 (SF-36) (8,9). Postoperatively, assessments were performed by mailed questionnaires complementary to the clinical outcome at one-year follow up.

Table I: Demographic details of the patients.

Parameter	No. of patients
Female gender	24 (48)
Age (years)	
Male	$71 \pm 10$ (range: 43-84; median 73)
Female	$77 \pm 8$ (range: 60-89; median 77)
EuroSCORE	
Logistic	52% (range: 12.88-89.83%)
Additive	14.5 (range: 6-21)
NYHA class	
I-II	0 (0)
III-IV	50 (100)
ASA class $\geq$ III	50 (100)
Hypercholesterolemia	15 (30)
PVD	6 (12)
COPD	20 (40)
Obesity	6 (12)
Previous AMI	7 (14)
CAF	26 (52)
Tobacco use	6 (12)
EDV $>80$ ml/m <sup>2</sup>	28 (56)
Ejection fraction	
30-50%	11 (22)
$<30\%$	15 (30)
Hypertension	28 (56)
Pulmonary hypertension	31 (62)
CRF	17 (34)
CAD	12 (24)
Previous neurological event	8 (16)
Diabetes	3 (6)

Values in parentheses are percentages.

ASA: American Society of Anesthesiologists; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; CRF: Chronic renal failure; EDV: End-diastolic volume; PVD: Peripheral vascular disease

Table II: Operative data of patients.

Parameter	No. of patients
CPB time (min)	$128 \pm 41$
Cross-clamp time (min)	$87 \pm 30$
AVR	27 (54)
Mitral valve repair	10 (20)
MVR	10 (20)
Double valve replacement	2 (4)
Ascending aorta replacement	1 (2)
Associated surgical procedures	
Coronary artery bypass grafting	12 (24)
Ascending aorta replacement	3 (6)
Left ventricle reshaping	2 (4)
Pulmonary veins ablation	15 (30)
Redo	8 (16)
Preoperative IABP	5 (10)

Values in parentheses are percentages.

AVR: Aortic valve replacement; CPB: cardiopulmonary bypass; IABP: Intra-aortic balloon pump; MVR: Mitral valve replacement.

### Epidural analgesia

All epidural procedures were performed by an experienced epidural anesthetist. Epidural puncture was made at the T1-T2 or T2-T3 interspaces as described previously (10). Heparin was administered at least 60 min after catheter insertion (7,11). Block was assessed by temperature and pinprick discrimination. Based on blood pressure (>70 mmHg), cardiac rate (>60 bpm) and degree of consciousness, adjunctive doses of ropivacaine were administered during surgical field preparation and before incision; this ensured preemptive analgesia without hemodynamic response to incision (11). After skin incision, 0.2% ropivacaine infusion (up to 6 ml/h) was started and maintained during surgery and for the first two postoperative days. A sensory block was observed between the neck and abdomen (including both arms); this allowed radial artery and right gastroepiploic artery harvesting without local anesthesia (if required). Patients received oxygen (5 l/min) via a facemask during surgery, but no additive sedation nor intravenous analgesic agents; no muscle-paralyzing agents were used. During surgery, the patient and physician held brief conversations, except for times of aortic cannulation and valve implant. At such times, patients were totally conscious and cooperative with the surgeon's suggestions.

### Surgical technique

Surgery was performed via a median sternotomy with CPB, using a flow rate of  $\geq 2.4$  l/m<sup>2</sup>, and mild hypothermia at 34°C. CPB was instituted using a crys-

talloid primer, and albumin (200 ml) added in all cases.

A standard arterial cannulation was performed in the distal region of the ascending aorta; if an ascending aorta aneurysm was present, the preferred cannulation site was the common femoral artery. A two-stage venous cannula was inserted into the right atrium and inferior vena cava for aortic valve patients, and a separate bi-caval cannulation for mitral valve patients. In all aortic valve patients a vent was inserted through a purse-string suture positioned on the pulmonary artery trunk. Routinely, soon after sternotomy, CO<sub>2</sub> was inflated at 4 l/min into the cardiothoracic wound (12-14).

Myocardial preservation consisted of antegrade and retrograde cold blood cardioplegia, repeated at 20-min intervals. When required, conduits harvested included the left, right, or both internal mammary arteries either in situ and y-graft and, when necessary, the non-dominant arm's radial artery or the right gastroepiploic artery.

Blood pressure was maintained at 70-100 mmHg with phenylephrine, and arterial partial oxygen pressure maintained at 150-250 mmHg.

On completion of CPB, the heart chambers and great vessels were de-aired routinely by venting the ascending aorta, pulmonary inflation via a face mask with the patient in the Trendelenburg position, shaking of the heart, venting the left ventricle apex by a needle, and venting the left atrium through the left atrial incision for mitral valve patients. The aortic vent was removed when the patient had been completely weaned from CPB. The mean CPB and cross-clamp times were  $128 \pm 41$  min and  $87 \pm 30$  min, respectively.

Typically, soon after starting CPB the patients stopped breathing and sighing, but on closing the CO<sub>2</sub> washout, approximately 10 min before weaning from CPB, autonomic ventilation was spontaneously re-enhanced.

Postoperatively, each patient was transferred to the intensive care unit (ICU), and subsequently administered an infusion of 0.2% ropivacaine, 1 µg/ml fentanyl, and 1 ml lidocaine at a rate of 6-10 ml/h, via the epidural catheter. Before transferring the patient to the ward, the anesthesiologist performed a clinical and a neurologic examination aimed at evaluating sensory perception and excluding spinal cord compression (15). Any new cerebrovascular events, defined as a postoperative new focal neurologic deficit, persisting more than 72 h after onset, diagnosed by clinical findings, confirmed by a neurologist or brain imaging (CT or MRI), were noted before discharge or death. Transient neurologic events, intellectual impairment, and confusional or irritable states were included in this category.

Postoperatively, patients received continuous oral

Table III: Outcome of heart valve surgery.

Condition/outcome	No. of patients
In-hospital stay (days)	10 ± 5
ICU stay (h)	9 ± 6
Postoperative IABP	2 (4)
Death	
In-hospital	2 (4)
During follow up	2 (4)
ARF	16 (32)
AMI	2 (4)
Infections	2 (4)
Prolonged mechanical ventilation	3 (6)
New neurological event	0 (0)
Bleeding	8 (16)
AF	22 (44)
Pneumothorax	0 (0)
Sternal dehiscence	0 (0)
A-V block with pacemaker	1 (2)
Median troponin I (µg/l)	9 (range: 3-100)

Values in parentheses are percentages.

AMI: Acute myocardial infarction; ARF: Acute renal failure; IABP: Intra-aortic balloon pump.

anticoagulation with warfarin (target International Normalized Ratio 2.0-3.0). Treatment was normally started on Day 2 and continued until the third postoperative month. Patients with chronic AF and/or with left atrial and/or ventricular dilatation were anticoagulated indefinitely. The epidural catheter was removed postoperatively as indicated clinically, and always before anticoagulation became active. A meticulous neurologic assessment was maintained for at least 12 h after catheter removal. Finally, arterial troponin I (a marker of myocardial damage) was monitored on the morning of Days 1 and 2, and several times daily if a high level was detected in the first sample.

### Follow up

Follow up data were collected monthly via patient visits, questionnaires, or telephone interviews. Follow up was closed in June 2006, and was 100% complete. The median follow up period was 14 months. When patients died during follow up the date of death was recorded and the cause documented. Qualitative variables were expressed regarding absolute and relative frequencies as percentages. Quantitative variables were described using the median as the measure for centralization; maximum and minimum values were provided as measures of dispersion.

Recognized guidelines (16) for reporting morbidity and mortality were used to define postoperative complications and prosthesis-related events. The severity of symptomatic impairment was assessed according to the NYHA classification. The preoperative surgical risk was assessed by using Additive and Logistic EuroSCORE gradings.

## Results

### Perioperative mortality

Two female patients (4%), aged 76.5 and 85.6 years, died perioperatively ( $\leq 30$  days). Both women were in NYHA class III-IV, and had Additive EuroSCOREs of 17 and 21, respectively. The younger patient had undergone double valve replacement; the older patient also had concomitant treatment of chronic AF. Both patients had revision for bleeding during the first postoperative hours and were mechanically ventilated. Both had a complicated course and died due to low cardiac output syndrome (Table III).

### Survival

Two patients (4.2%) died during the follow up period ( $>90$  days after hospital discharge). The first patient, a 76-year-old woman, was readmitted to the ICU at 80 days after surgery with acute and massive gastrointestinal bleeding, which provoked her sudden death. The second patient, a 78-year-old woman, was

readmitted to the hospital for a septic sternal dehiscence and acute renal failure (ARF), and died from low cardiac output syndrome. The actuarial freedom from cardiac-related death was 94% at 12 months; the overall two-year survival was 92%.

Thirty-four surviving patients (71%) had an uneventful postoperative outcome, except for AF in nine cases in whom the median Additive and Logistic EuroSCOREs were  $14.4 \pm 2.7$  and  $50 \pm 19\%$ , respectively. Eight patients required a revision for bleeding (two were redo cases). The most common postoperative complication was ARF in 16 patients; five of these patients also suffered chronic renal failure. Only three patients required mechanical ventilatory support; in two cases this was due to low cardiac output syndrome (both patients died), and in the third patient to primitive respiratory distress. None of the patients had any postoperative neurological dysfunction, although such risk was present in eight patients preoperatively. The mean hospital stay was  $10 \pm 5$  days, and median ICU stay 9 h. The median troponin I level observed was  $9 \mu\text{g/l}$  (range: 3 to  $100 \mu\text{g/l}$ ). On completion of follow up, all survivors were in NYHA class I-II, and all were in sinus rhythm. Thus, all survivors had improved their functional status, and none had suffered any thromboembolic event, hemorrhage, or valve-related complications.

All survivors completed the postoperative SF-36; the mean postoperative mental component score (MCS) was 49.64, and the mean postoperative physical component score (PCS) was 42.12.

## Discussion

As the world's population continues to age, and cardiovascular disease is recognized as the leading cause of mortality among older patients, considerable interest has been directed towards different anesthesia-related surgical approaches, management, and outcomes. It is believed that the present study is the first to provide useful insights into anesthesia-related differences of in-hospital and mid-term postoperative outcome in selected high-risk patients with unselected cardiac valve diseases. Moreover, the analysis lends credence to the notion that epidural anesthesia, without endotracheal intubation, might have a substantial role in cardiac surgery, especially for patients who are at very high risk and have an Additive EuroSCORE  $>10$ .

### Mortality

Recently, Toumpoulis et al. (17) showed that the Standard EuroSCORE predicts, with good discrimination, hospital mortality, morbidity and length of stay, as well as three-month mortality. Moreover, the logis-

tic EuroSCORE has been shown to be a better risk predictor, especially in high-risk patients, and has gained wide acceptance in Europe, North America, and Japan (18,19). Based on the EuroSCORE, the calculated postoperative mortality in the present population was 50%, but by using epidural anesthesia (without endotracheal intubation) and a meticulous surgical approach this value fell to only 4%. Mortality was in fact much lower than was reported by Collart et al. in a patient population of mean age  $83 \pm 2$  years (20). With additive and logistic EuroSCOREs of  $9.5 \pm 2.3$  and 15.1% (significantly lower than in the present series), these authors noted an operative mortality of 8.8% (20). Thus, epidural anesthesia without mechanical ventilation, may guarantee more promising results by improving patient management.

### Morbidity

#### *Postoperative neurological complications*

Roach et al. (21) identified two outcomes, namely "fatal cerebral injury and non-fatal", and "new deterioration in intellectual function or new onset of seizures". Among the present patients, no serious adverse cerebral events were observed, despite advanced age, proximal aortic atherosclerosis, previous stroke and transient ischemic attack, pulmonary disease, and history of hypertension being considered strong risk factors for adverse cerebral outcomes (22-24). A history of previous neurological disease was identified in eight of the present patients, none of whom had reported a postoperative cerebral event. A stroke may also be related to careless manipulation of the atherosclerotic ascending aorta (25-29). Among the present patients, proximal aortic atherosclerosis, as detected by palpation and by ultrasonographic scanning, was identified in almost 60% of cases, and this prompted the use of several maneuvers to limit neurological impairments. In fact, the proximal anastomosis was routinely avoided by using only those artery conduits that had been harvested in skeletonized fashion and anastomosed according to the y-graft technique. In addition, moderate hypothermia was used routinely during CPB (34-35°C). Diabetes, by impairing brain blood flow autoregulation, may ultimately become a neurological risk factor (26,28,30). Three of the present patients had diabetes, and none reported a new cerebral event.

The use of a left ventricular vent has also been described as a particular risk factor, as air may be introduced into the cardiac chambers during its insertion. The present authors' policy is always to use a pulmonary artery vent which may lead to heart unloading without complete drainage, leaving the left ventricular apex completely filled, and simplifying the de-airing maneuvers.

Thus, the avoidance of general anesthesia and endotracheal intubation, both of which prevent neurological evaluation during the procedure, and use of the above-described maneuvers, led to reduction in the number of major and minor neurological complications encountered.

#### **Perioperative myocardial injuries**

A reduced coronary blood flow response during sympathetic stimulation has been reported in patients with diabetes and atherosclerotic lesions (31-33). Nygard et al. (3) investigated coronary flow in patients with a multivessel atherosclerotic pathology, and found that a thoracic epidural anesthesia, by blocking the efferent sympathetic nervous heart innervation and relieving postoperative pain, normalizes the myocardial blood flow response to sympathetic stimulation, and improves coronary function. Twelve of the present patients had concomitant multivessel coronary disease but, except for the two who died, none experienced postoperative myocardial infarction. In fact, troponin I levels were lower in both valvular and valvular + CABG patients when compared to other patients. These observations may account for an improved coronary flow immediately after weaning from CPB and during the first hours and days after surgery. This is especially true for patients undergoing myocardial revascularization with the use of total arterial techniques, in which conduits and coronary spasms are very challenging.

#### **Perioperative pulmonary distress**

The fragility of these patients is well reported, and renal insufficiency, pulmonary hypertension, or NYHA class >II, as well as chronic obstructive pulmonary disease (COPD) emerge as risk factors (34,35). In fact, pulmonary diseases may also impair cerebral blood flow autoregulation by causing CO<sub>2</sub> retention. When prolonged mechanical ventilation is required, cerebral perfusion and oxygenation are impaired (25,26,36,37). All but one of the present patients suffered from severe pulmonary disease detected preoperatively; two of these patients were treated chronically with continuous oxygen therapy. In fact, only three patients (including the two with postoperative low output syndrome) required mechanical ventilation, and in no case was intensive ventilatory support and/or intervention for pneumothorax required. This finding compared well with the findings of another study (38) in which, when a Standard EuroSCORE >14 was detected, 13.9% of the patients showed postoperative respiratory failure that required mechanical ventilation.

### Patient management

When monitoring ICU and postoperative hospital stays, there was a marked reduction following the use of these conservative measures, especially considering that the patients were old and at very high risk. In a series of 215 consecutive octogenarian patients, Collart et al. reported a mean ICU stay of five days, and a hospital stay of 14 days (20). Compared with patients who received a general anesthesia, either at the present authors' institution or elsewhere (39), those patients operated on while conscious had shorter ICU and in-ward stays, which suggested that substantial savings might be made by using the latter approach.

In terms of CPB and cross-clamp times, no difference was found between epidural anesthesia without endotracheal intubation and conventional, general anesthesia (34).

### Postoperative QOL

Although the outcome of cardiac surgery is normally assessed in terms of mortality and morbidity, an emerging consensus is to monitor QOL, with the aim of developing new therapeutic strategies. The summary scores for the PCS and MCS, when standardized to the general US population, equate to a mean of  $50 \pm 10$  (8), while Rumsfeld et al. (40) recently reported that, by following a standard CABG procedure, a population of 1,744 patients with a mean age of 63 years showed a 4% average improvement in mental health status, and an improvement of 16% based on physical health status. These patients, even after surgery, showed calculated PCS (38.2) and MCS (46.1) values well below that observed in the general population. Apolone and Mosconi (9), in 1998, validated the SF-36 in a cohort of Italian patients with a slightly higher proportion of women (51%) than men, and a mean age of 47.7 years. Compared to the present patients, who were significantly older and unwell, the Italian population showed a significantly better PCS. However, the MCS scores for the patients compared well with those of the Italian population, and re-confirmed the benefits of epidural anesthesia in obtaining a good QOL after surgery. These data were also confirmed by the higher average MCS and PCS values obtained compared to those observed by Rumsfeld et al. (40).

### Study limitations

In this prospective, non-randomized study, the enrolled patients were limited to a single center and time-span in order to reduce the impact of temporal changes in practice, and in procedures such as valve replacement and aneurysmectomy that increase the postoperative risk of mortality and adverse events. In addition, all preoperative and postoperative examinations relating to the patients' history and new events

were assessed by a small number of specialists. The study was limited by a lack of technical experience in neuropsychological testing and the time required for such tests to be conducted; thus, an assessment of deteriorating intellectual function might be open to criticism. An additional limit was that the study was not randomized in design, and hence comparisons between patients operated on at the authors' institution were possible only by using historic, and not simultaneous, data.

*In conclusion*, based on the study results, adverse postoperative events are very rare when a high epidural anesthesia is adopted in cardiac surgery. This study may be the first to provide useful insights into the management benefits available following epidural anesthesia, as compared to general anesthesia, as a lower mortality and a lower incidence of complications were observed, together with shorter ICU and hospital stays and a reduced need for prolonged care. Further investigations are required, however, to confirm these findings.

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