Central regional anaesthesia in patients with aortic stenosis – a systematic review

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ABSTRACT

INTRODUCTION: Aortic stenosis is a valvular lesion that poses several haemodynamic challenges for the anaesthesiologist. The use of central regional anaesthesia is traditionally regarded as contraindicated in patients with severe aortic stenosis due to its sympatholytic effect, potentially causing loss of vascular tone and ultimately diminished cardiac output. The aim of this paper was to review current literature to find evidence for or against the use of neuroaxial blockade in patients with aortic stenosis.

METHODS: We searched PubMed for relevant articles, using the following MeSH terms: "aortic valve stenosis", "epidural anesthesia", "spinal anesthesia" and "epidural analgesia". Only English language literature was included. Papers concerning aortic stenosis and obstetrical anaesthesia were excluded.

RESULTS: There are no randomised clinical trials on the subject, and existing literature is extremely sparse. Four retrospective studies and eight case reports counting a total of ten patients were found. All report successful use of neuroaxial blockade in patients with aortic stenosis, without severe haemodynamic alterations. In addition, data indicate that postepidural analgesia improves outcome compared with conventional analgesia.

CONCLUSIONS: To the best of our knowledge, there is no clinical evidence supporting the notion that central regional anaesthesia has any adverse effects on patients with aortic stenosis. Carefully managed neuroaxial blockade could become a useful alternative to general anaesthesia in this patient group. However, evidence is sparse and of questionable quality. Large prospective randomised clinical trials are required to establish best practise.

Aortic stenosis (AS) is the most common valvular lesion with increasing incidence that is linked to an aging population [1, 2]. Valvulopathy is diagnosed using ultrasound Doppler, and severe AS is defined as an aortic valve area (AVA) < 1.0 cm^2 combined with a mean aortic valve gradient > 40 mmHg [2, 3]. AS causes pressure overload due to outflow obstruction resulting in increased left ventricular working load. Over time, this causes a reduced diastolic compliance and increased myocardial oxygen consumption. A reduced filling time and decreased subendocardial blood supply cause ischaemia. Thus, ventricular filling is dependent on a preserved preload and maintenance of sinus rhythm (SR) [1, 4-6].

Due to the significant risk of perioperative morbidity and mortality, AS poses a considerable challenge to the anaesthesiologist. Managing anaesthesia during surgery requires maintenance of cardiovascular stability to avoid hypotension and ischaemia [7-12]. General anaesthesia (GA) is often preferred to central regional anaesthesia (CRA) as the latter is considered relatively contraindicated in patients with AS. This concern rests on theoretical considerations and a great deal of caution rather than on evidence [3, 5, 12-15]. Theoretically, CRA may cause a rapid and massive decline in systemic vascular resistance (SVR) due to its potent sympatholytic effect, leading to hypotension and a reduction in coronary perfusion, changes for which patients with severe AS are unable to compensate sufficiently. However, GA may cause an even more pronounced cardiovascular effect than CRA due to an induction-triggered hypotension with a decrease in venous return and reduced vascular tone in combination with its negative inotropic effect [3, 16]. In addition, the use of muscle-relaxant drugs and positive airway pressure in the intubated patient during GA could theoretically cause an even greater haemodynamic change, which is deleterious to the patient with AS [17-19]. Also, well-documented advantages are associated with CRA compared with GA, such as lower postoperative mortality rates. In addition, CRA alone or in combination with GA reduces the incidence of pulmonary complications and cardiac dysrhythmias as well as the levels of stress hormones [20]. Furthermore, a reduced need for opioids minimises nausea, vomiting and obstipation, allowing for an earlier mobilisation. Lastly, CRA is a useful alternative in situations where GA should be avoided, such as expected difficult airway management, incomplete preoperative fasting or severe adipositas [3].

To the best of our knowledge, the concern related to the use of CRA in patients with AS is based on historical, theoretical considerations rather than on clinical evidence [3, 5, 12-14]. It is a contentious issue that is debated daily in the clinical forum with several local hospital guidelines in Denmark noting that CRA is contraindi-

SYSTEMATIC REVIEW

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KEYPOINTS

Aortic stenosis is the most common valvular lesion worldwide.

Applying general anaesthesia to a patient with aortic stenosis can be a challenge because the stenotic heart cannot compensate for significant falls in blood pressure.

The use of central regional anaesthesia is regarded as contraindicated in patients with aortic stenosis because of the theoretical risk of uncontrollable central vasodilatation resulting in cardiac failure.

This review investigates the literature on central regional anaesthesia in patients with aortic stenosis. Only few case reports exist on the subject, none of which report adverse outcomes.

No data in the reviewed literature suggest that central regional anaesthesia should not be used in patients with aortic stenosis. However, large prospective randomised controlled trials are lacking on the subject.

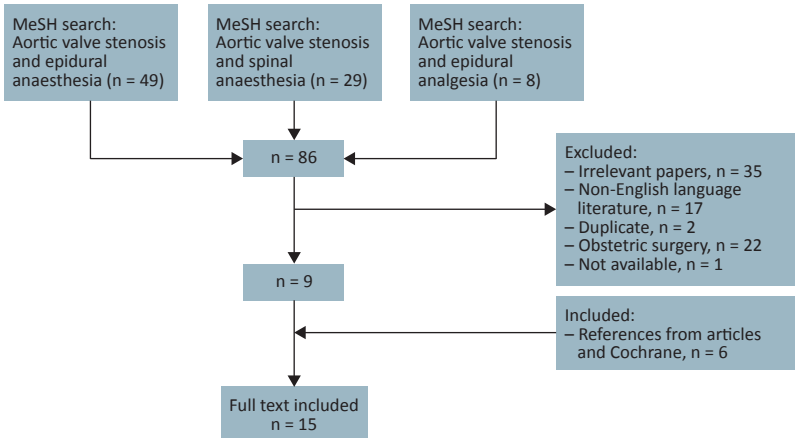
cated in patients with AS [21-23]. Patients with AS, who are typically older and more fragile, are withheld CRA due to existing dogmas and thus do not achieve the possible benefits of CRA. The aim of this paper was to review relevant literature to establish the best evidence for use of CRA in patients with AS.

METHODS

Using MEDLINE in October 2016, we identified literature by searching PubMed for articles. The search strategy in PubMed included the following MeSH terms: Aortic Valve Stenosis AND Anesthesia Epidural, Aortic Valve Stenosis AND Anesthesia, Spinal Aortic Valve Stenosis AND Analgesia, Epidural. Abstracts and full-text papers were reviewed. Additional records were obtained from other sources such as systematic reviews identified through PubMed and references from articles found.

FIGURE 1

Flow chart of study selection.



The inclusion criteria for eligibility of studies were: 1) articles published in English language until 20 October 2016, 2) Patients with AS having a neuroaxial blockade and receiving intrathecal anaesthetics ± opioids and not just opioids alone. Articles on obstetrical anaesthesia were excluded due to their specialised nature and the rare incidence of AS in this group of patients.

RESULTS

The process used for selection of articles is shown in **Figure 1**. A total of 15 articles were found to be relevant and were subjected to review. There were no prospective randomised clinical trials (RCT) comparing GA and CRA in patients with AS undergoing non-cardiac surgery. In all, four retrospective studies, two prospective studies, one review and eight case reports concerning the topic were found.

Case reports

Demographics and severity of aortic stenosis

Table 1 outlines patient demographics and the severity of AS. In all, ten patients were described in the case reports. Their age ranged from 45 to 92 years of age (average 75.7; median 78.5 years). A total of eight of the ten patients suffered comorbidities, commonly cardiovascular and respiratory disease. Concerning the severity of AS, four patients had asymptomatic severe AS and one patient suffered symptomatic severe AS; this information lacked for five patients. The ultrasound Doppler data were not consistently specified. The median AVA was 0.6 cm^2, data were missing for two patients [16, 24]. The aortic valve inlet (Ao) was either stated as peak Ao (mean: 90.2 mmHg) or mean Ao (mean: 52.8 mmHg); this information was missing for one patient [25].

Neuroaxial anaesthetic management

Concerning surgery and neuroaxial management, seven non-cardiac surgeries and three cardiac surgeries were reported (**Table 2**). There were five hip surgeries, of which four were performed in continuous spinal anaesthesia (CSA) and one in epidural anaesthesia (EA). The patient who had a hip repair in EA received the epidural catheter upon hospitalisation as part of a fast-track regimen aiming for analgetic control. The catheter was titrated with 12.5 mg bupivacaine over 45 minutes, which was followed by infusion of 0.125 mg/ml bupivacaine. On the day of surgery, consecutive boluses of local anaesthetics (LA) were administered for surgical anaesthesia [16]. A lumbar discectomy was performed under combined spinal epidural anaesthesia (CSEA) which was chosen due to its effective segment coverage and the possibility of bolus administration in the epidural catheter. The patient was recommended aortic valve replacement before surgery, but refused this intervention. A

bolus of 8 mg hyperbaric bupivacaine was injected, using a spinal needle, caudally to the already inserted and tested epidural catheter. After assessment of spinal hit, the epidural was injected in half boluses of 8 ml of 0.19% ropivacaine and dexmedetomidine 50 microgram at a 10-minute interval [17]. Abdominal hysterectomy was performed under the coverage of EA to the level of T6. As part of the analgesic regimen, the EA was performed postoperatively three times daily with 10 ml 0.125% bupivacaine [26]. Three aortic valve replacement surgeries were performed in thoracic EA; all patients were on autonomous breathing [24, 27, 28].

Haemodynamics

Data on haemodynamics and fluid loss are presented in **Table 3**. The majority of the non-cardiac surgery patients were monitored invasively. Two of the patients who had hip surgery in CSA [29] had a Flo-Trac connected to monitor stroke volume and cardiac index. Guided by the haemodynamic monitoring, the patients were optimised with intravenous (IV) fluids both prior to and during surgery. None of the patients had vasoconstrictive drugs administered. The patients all remained haemodymanically stable, both peri- and postoperatively. One patient developed an episode of supraventricular tachycardia postoperatively. The episode was successfully converted to SR with 6 mg of adenosine [25]. Neither blood loss nor fluid administration was commented on in the cardiac surgeries. However, no adverse haemodynamic alterations were reported in this group of patients.

Studies and reviews

Non-cardiac surgery

Ho et al [30] reported no adverse clinical outcomes (cardiovascular, renal, thromboembolic and blood loss) for patients with asymptomatic AS (n = 22; American Society of Anaesthesiologist's group (ASA) III-IV) undergoing hip surgery under hypotensive epidural anaesthesia (HEA). Besides injection of 20-25 ml 0.75% plain bupivacaine or a combination of 12.5 ml 0.75% bupivacaine with 12.5-27.5 ml 2% lidocaine in the epidural catheter, the patients received simultaneous administration of IV epinephrine (3.0 ± 0.9 microgram/min), titrated to a systolic blood pressure (BP) of 60-100 mmHg. The mean hypotensive period was 91 ± 43 minutes (mean ± standard deviation (SD)) and heart rate was maintained at a mean value of 70 ± 11.

A review by McDonald [6] investigated studies/case reports in the period from 1966 to 2004 for adverse outcomes in patients with AS receiving CRA. The evidence on the topic was sparse; no RCTs were reported, nor did any retrospective studies compare GA with CRA. Only seven case reports with a total of ten patients were found in the period from 1993 to 2003. Of those, six patients involved Caesarean section/vaginal delivery. All cases were reported as successful with the use of CRA in patients with moderate to severe AS (epidural for Caesarean section, CSA for hip surgery and Caesarean section, intrathecal sufentanil for extracorporal shockwave lithotripsy).

Two smaller studies [31, 32] observed no significant difference in outcome for AS patients versus controls

TABLE 1

Case reports: demographic details.

Reference	Patient, age, sex and past medical history, additional to AS	AS pathology, TTE and ECG
Bundgaard-Nielsen et al, 2005 [16]	80-yr-old female Stroke Cardiac arrest 2 mo.s earlier	Asymptomatic severe AS Ao = 88-90 mmHg EF: normal ECG: SR
Holyachi et al, 2012 [26]	45-yr-old, female Hashimoto's thyroiditis Euthyroid on medication	Bicuspid aortic valve NYHA II AVA = 1.9 cm^2 Ao = 31 mmHg Vmax = 3.8 m/s ECG: normal
Collard et al, 1995 [25]	84-yr-old male, HF NYHA III AF HT DM	AVA < 0.8 cm^2 EF = 25% Severe global hypokinesis ECG: AF Q waves V_1-V_3
	84-yr-old female HF NYHA III Severe COPD CLL Anaemia	Asymptomatic severe AS AVA = 0.45 cm^2 Peak Ao: 95 mmHg
López et al, 2016 [29]	92 yr-old female HT Mitral regurgitation	AVA = 0.6 cm^2 Peak Ao = 85.4 mmHg ECG: SR
	66-yr-old female	Asymptomatic severe AS AVA = 0.45 cm^2 Peak Ao = 95 mmHg
Kim et al, 2014 [17]	77-yr-old female	Asymptomatic severe AS AVA = 0.79 cm^2 Ao = 88/53 mmHg EF: normal
Mukherjee et al, 2009 [27]	85-yr-old male NYHA III Left ventricular dysfunction: EF 50% Pulmonary HT FEV1 < 60%	Symptomatic severe AS AVA = 0.5 cm^2 Max/mean Ao = 72/56 mmHg AAD = 24 mm
Petridis et al, 2012 [28]	74 yr-old male NYHA III CABG Peripheral artery disease Severe COPD FEV1 = 41%	AVA: 0.59 cm^2 Max/mean Ao = 106/69 mmHg AAD = 22 mm EF = 66%
Schachner et al, 2003 [24]	70-yr-old male HT	Mean Ao: 55 mmHg

AAD = aortic annulus diameter; AF = atrial fibrillation; Ao = aortic valve gradient; AS = aortic stenosis; AVA = aortic valve area; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; CLL = chronic lymphocytic leukaemia; DM = diabetes mellitus; ECG = electrocardiogram; EF = ejection fraction; FEV1 = forced vital capacity, 1st sec; HF = heart failure; HT = hypertension; NYHA = New York Heart Association; SR = sinus rhythm; TTE = transthoracic echocardiogram; Vmax = maximum upstroke velocity.

TABLE 2

Case reports: perioperative reports.

Reference	Surgery	Type of CRA	Local anaesthetic, concentration and dose
Bundgaard-Nielsen et al, 2005 [16]	Hip repair	Epidural L2-L3	Day before surgery: 2.5 mg/ml bupivacaine: 5 ml × 2 Followed by infusion: bupivacaine/morphine: 0.125 mg/50 µg/ml 4 ml/h Preoperatively: 15 mg bupivacaine with 1 mg morphine × 2, 35-min interval Intraoperatively: 15 mg bupivacaine with 1 mg morphine × 2, 50-min. interval
Holyachi et al, 2012 [26]	Abdominal hysterectomy	Epidural T11-T12	Preoperatively: 2% lidocaine: 5 ml + 0.5% bupivacaine: 5 ml Intraoperatively: 0.5% bupivacaine: 5 ml Post-operatively: 0.125% bupivacaine: 10 ml
Collard et al, 1995 [25]	Hip repair	CSA L3-L4	Preoperatively: 0.5% plain bupivacaine: 2.5 mg × 2, 5-min. interval Intraoperatively: 0.5% bupivacaine: 2.5 mg × 3, 90, 135, 180 min. after initial dose
	Hip repair	CSA L3-L4	Preoperatively: 2% plain lidocaine: 20 mg × 2, 5-min. interval
López et al, 2016 [29]	Hip repair	CSA L3-L4	2 × 2 mg isobar 0.5% bupivacaine, 5-min. interval
	Hip repair	CSA L3-L4	4 × 2 mg isobar 0.5% bupivacaine, 5-min. interval
Kim et al, 2014 [17]	Lumbar discectomy	CSEA; epidural L1-L2 Spinal L4-L5	Spinally: 0.5% hyperbaric bupivacaine: 8 mg Epidurally: 0.19% ropivacaine: 4 ml + 50 µg dexmedetomidine × 2, 10-min. interval
Mukherjee et al, 2009 [27]	TA-AVI	Thoracic epidural, T2-T3	0.2% ropivacaine: 5 + 25 ml, 10-min. interval Epidurally: 0.2% ropivacaine: 10 ml/h + fentanyl 2 µg/ml Post-operatively: infusion 0.2% ropivacaine: 6 ml/h
Petridis et al, 2012 [28]	TA-AVI	Thoracic epidural, T2-T3	Epidurally: 10 ml/h of a mixed solution of bupivacaine: 20 ml 0.5%, 20 ml 2%, + fentanyl: 5 ml 0.100 mg/2 ml, with addition of 2 ml 0.9% NaHCO3 + 3 ml NaCl
Schachner et al, 2003 [24]	Aortic valve replacement with CPB	Thoracic epidural, C7-T1	20 ml 0.75% ropivacaine + 25 µg sufentanil Epidurally: 0.75% ropivacaine: 5 ml/h + sufentanil: 1 µg/ml Post-operatively: 0.2% ropivacaine + sufentanil: 0.5 µg/ml

CPB = cardiopulmonary bypass; CRA = central regional anaesthesia: CSA = continuous spinal anaesthesia; CSEA = continuous spinal and epidural anaesthesia; TA-AVI = transapical aortic valve implantation.

undergoing hip surgery. Despite few included patients, no data pointed to GA being more beneficial than CRA in either patient group.

Cardiac surgery

Bottio et al [33] conducted a single-centre non-randomised prospective follow-up study in 50 high-risk patients (New York Heart Association (NYHA) III-IV) with confirmed heart valve disease (not AS specifically). They underwent heart valve surgery on cardiopulmonary bypass with epidural anaesthesia while on spontaneous ventilation. Epidural insertion was made at the T1-T2 or T2-T3 interspaces and an infusion of 0.2% ropivacaine (up to 6 ml/h) was maintained during surgery and the first two postoperative days. Blood pressure was maintained with phenylephrine. Collected data showed a mean intensive care unit (ICU) stay of 9 hours, which is significantly lower than when this surgery is performed in GA. There were two in-hospital and two long-term deaths. The 46 surviving patients had all improved their functional status to NYHA I-II at the end of the study period.

In a comparative, non-randomised study, Amat-Santos et al [34] investigated the clinical outcome following transapical transcatheter aortic valve implantation in patients with severe symptomatic AS who either received thoracal epidural analgesia (TEA) perioperatively or an intercostal catheter (non-TEA) inside the surgical wound at the end of the intervention. Both groups maintained the catheter for at least three days after the procedure (receiving continuous infusion with bupivacaine + fentanyl). All patients were intubated before the procedure. Results showed that the TEA group experienced significantly less pain both peri- and postoperatively. There were no fatal pulmonary complications in the TEA group compared with seven in the non-TEA group, where the intubation time was also significantly longer. Furthermore, the 30-day mortality rate was significantly higher in the non-TEA group (22.9% versus 2.7%, $p < 0.001$), and the 1-year mortality remained significantly higher in the non-TEA group (31.1% versus 10.8%, $p = 0.005$).

Jakobsen et al [35] studied perioperative haemodynamic changes in elderly patients undergoing coronary artery bypass grafting (CABG) and/or aortic valve replacement due to AS. Patients were randomised to receive GA ± high thoracic epidural anaesthesia (HTEA). The group receiving supplementary HTEA had a significantly improved perioperative cardiac performance (higher stroke volume index and central venous oxygenation without increases in heart rate or mean arterial pressure) compared with the non-HTEA group.

DISCUSSION

The existing literature on the use of CRA in patients with AS is sparse. Clinical experience with the use of CRA in

TABLE 3

Case reports: haemodynamic information.

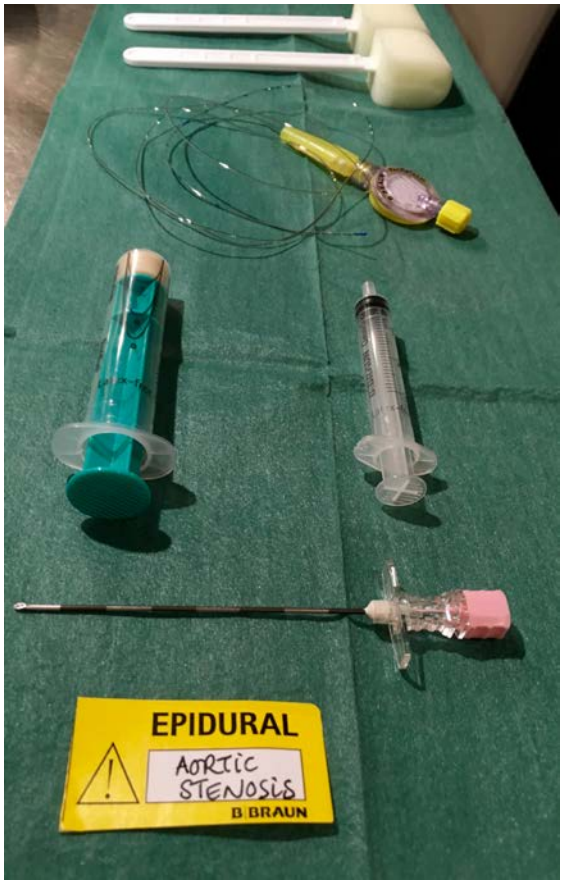
Reference	Type of monitoring	Haemodynamic alterations	Blood loss, IV-fluid administration	Comments
Bundgaard-Nielsen et al, 2005 [16]	Non-invasive BP	Stable	800 ml loss 1,500 ml IV-fluid + 600 ml SAG-M	–
Holyachi et al, 2012 [26]	Non-invasive BP	Stable	500 ml loss 1,000 ml IV-fluid	–
Collard et al, 1995 [25]	Invasive arterial and PA-catheter: CVP + PAP	Stable	700 ml loss 1,900 ml IV-fluid + 1 U erythrocytes	–
	Invasive arterial and PA-catheter: CVP + PAP	Stable, but one episode of SVT	200 ml 1,200 ml IV-fluid	
López et al, 2016 [29]	Invasive arterial, including measure of SVI, CI, SVV	Stable No need for vasoactive drugs	300 ml loss 500 ml IV-fluid	–
	Invasive arterial, including measure of SVI, CI, SVV	Stable No need for vasoactive drugs	400 ml loss 750 ml IV-fluid	
Kim et al, 2014 [17]	Invasive arterial and CVP	Stable	No loss 850 ml IV-fluid	–
Mukherjee et al, 2009 [27]	–	–	–	Invasive arterial monitoring NIV PEEP 10 cmH2O to avoid pneumothorax Heparin discontinued day before surgery 5,000 IU heparin for BACT > 2,000 sec Patient refused blood transfusion, religious reasons Haemodynamic alterations and fluid loss not commented The patient was alive and doing well at 30-day follow-up
Petridis et al, 2012 [28]	–	–	–	Invasive arterial and CVP Full-face plastic mask Aspirin discontinued day before surgery 3,500 IU heparin for BACT > 200 sec Haemodynamic alterations and fluid loss not commented The patient was alive and doing well at 30-day, 3-month and 1-yr follow-ups
Schachner et al, 2003 [24]	–	–	–	Monitored in a "standard fashion" – arterial line Haemodynamics stable with moderate use vasopressors Fluid loss not commented 30,000 IU heparin given before cannulation of aorta Uncomplicatated surgery and < 24 h stay in the ICU

BACT = baseline activated clotting time; BP = blood pressure; CI = cardiac index; CVP = central venous pressure; ICU = intensive care unit; IV = intravenous; NIV PEEP = non-invasive ventilation with end expiratory positive pressure; PA = pulmonary artery; PAP = pulmonary artery pressure; SAG-M = saline, adenine, glucose and mannitol solution; SVI = stroke volume index; SVV = stroke volume variation.

patients with AS seems limited to hospitals with a liberal attitude towards its use, e.g. where it is included as part of a fast-track regimen in patients with hip fractures [16]. No RCTs were found on the subject; only a few case reports were identified along with some small retrospective studies. This is surprising taking into account the steadily increasing incidence of AS and the many well-documented benefits of CRA for many types of surgeries as well as its use as an analgesic. In fact, there exists no evidence-based recommendations for the preferred anaesthetic regimen in patients with AS.

The reviewed literature reports consistently positive results for the use of CRA in patients with AS. The case reports show positive outcomes and no adverse haemodynamic alterations during surgery. There is a significant risk of publication bias in case reports, and their value as scientific evidence is limited, however helpful when designing RCTs. Common to all case reports, the patients were optimised intravascularly prior to surgery, and the anaesthetic drugs were given in small, incremental doses, so that haemodynamic alterations could be monitored strictly and managed with IV fluid. This may explain why there was no need for vasoconstrictor drugs for the non-cardiac surgery.

No patients with severe AS had their aortic valves replaced prior to non-cardiac surgery, as is recommended in current guidelines [9, 36-38]. This practise is suitable for elective surgery; but in critically ill patients, the advantages of performing urgent surgery outweigh the benefits of valve replacement [39]. Although one interesting meta-analysis was found, it was unfortunately not specific for patients with AS. In the meta-analysis, Guay et al [40] analysed nine systematic Cochrane reviews which covered 40 studies on intermediate-to-



Central regional anaesthesia has traditionally been regarded as contraindicated in patients with aortic stenosis

high-cardiac risk surgeries with CRA or GA ± addition of CRA, assessing postoperative rates of deaths, chest infections, myocardial infarction and other serious adverse effects. In summary, it was shown that compared with GA (with or without supplementary CRA) CRA alone significantly reduced the mortality rate by 2.5% (p = 0.02, moderate evidence leve, due to the risk of selection bias) and the risk of perioperative pneumonia. However, patient characteristics and comorbidities were left out of the analysis, making the results difficult to extrapolate to patients with AS.

It appears that cardiac surgery with a high thoracic epidural insertion and therefore a high sympathetic blockade is manageable for patients with AS under invasive haemodynamic monitoring. However, it should be noted that two of the aortic valve replacements in the case reports were transcatheter aortic valve implantation (TAVI) surgeries [27, 28], which are less invasive than traditional cardiac surgery. The promising results presented by Amat-Santos et al suggest that epidural analgesia is well tolerated in an elderly fragile population with multiple comorbidities [34]. Apart from this study, there exists no literature investigating the potential benefits of epidural analgesia specifically in patients with AS. However, in a single-centre cohort study, Stenger et al [41] demonstrated that GA supplemented with HTEA is associated with a lower 6-month mortality and a lower frequency of cardiac infarction in elderly patients undergoing various kinds of cardiac surgery.

It is crucial that patients with AS receive proper analgesic treatment [6]. Pain elicits a stress response that activates the sympathetic nervous system, resulting in haemodynamic alterations such as tachycardia. This may create an imbalance between oxygen delivery and demand in the heart that is deleterious for patients who are dependent on a fixed cardiac output. In a prospective RCT, Scheinin et al [42] investigated pain management and perioperative cardiac events in elderly patients with cardiac risk factors or manifest cardiovascular disease undergoing hip surgery in spinal anaesthesia. Patients were randomised to preoperative epidural pain management or conventional intramuscular oxycodone. The study showed a significantly lower incidence of perioperative cardiac ischaemia in the epidural group even though there were no differences in episodes of hypotension or in the use of vasopressors during surgery. This study is supported by another prospective RCT by Matot et al [43] comparing the preoperative use of continual epidural infusion to intramuscular opioid in elderly patients with hip fracture who were at risk of or who had manifest coronary artery disease. Pre- and perioperative adverse cardiac events were significantly less prevalent in the group randomised to receive epidural analgesia. Both studies had limitations, such as limited sample size (59 and 77 patients, respectively) and one of them lacked blinding [43]. In a subgroup analysis derived from a larger RCT, Peyton et al [44] confirmed, that perioperative epidural analgesia compared with IV opioids does not significantly affect mortality or morbidity for abdominal surgery in high-risk patients. Prospective trials are required before these data can be extrapolated to patients with AS.

The retrospective study by Ho et al [30] reporting successful use of HEA to patients with asymptomatic AS needs to be interpreted with caution. The authors stressed that the results cannot be applied to patients with symptomatic AS. In a letter to the editor, Dawson [45] pointed out several weaknesses of the study, such as its retrospective design, the small patient population and the lack of a control group, devaluating its scientific validity. Sharrock et al [46] describe HEA as a safe method in elderly patients with comorbidities such as respiratory, renal and cardiac disease, but stress its deleterious effects on the preload in patients with AS.

CONCLUSIONS

There is no evidence that CRA should not be applied to patients with AS. Both cardiac and non-cardiac surgeries have been performed successfully using CRA in patients

with AS. Under the guidance of invasive monitoring and with intravascular fluid optimisation, careful titration of local anaesthetics and immediate access to treatment with vasoconstrictors in case of hypotension, the technique appears to be as safe as GA. However, the lack of proper evidence leaves the clinician without a definitive best practice. The few existing observational case reports and small retrospective studies on the subject must be interpreted cautiously. Large, prospective RCTs comparing the outcome in patients with AS undergoing surgery performed under CRA or GA are required.

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