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REVIEW

Aortic Stenosis and Non-Cardiac Surgery

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ABSTRACT

Advances in surgical and anesthetic techniques associated with closer perioperative monitoring appear to allow non-cardiac elective surgical procedures possible with acceptable risk in patients with severe aortic stenosis. A correct diagnosis of the severity of aortic stenosis is mandatory in preoperative evaluation of these patients. Recent published data suggest that at least for “asymptomatic severe aortic stenosis” patients with preserved LV systolic function and no other significant valvular pathology, a reappraisal of the grading of the severity of AS in general and reassessment of perioperative risk during elective non-cardiac surgery is needed.

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Key words: Non-cardiac surgery; Anaesthesiology; Aortic stenosis; Echocardiography; Hemodynamic

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INTRODUCTION

Aortic stenosis has become the most frequent type of valvular

heart disease in Europe and North America in relation to the increased life expectancy in elderly population. Data from Euro Heart Survey on Valvular Heart Disease suggest that moderate to severe degenerative calcific aortic stenosis affects 2-3% of patients aged > 65 years and 7-10% aged > 80 year^[1]. The need for non-cardiac surgery (NCS) in patients with aortic stenosis (AS) increased significantly in the last two decades. These patients are at high risk of major cardiovascular events or death in perioperative period, therefore, in the case of elective interventions, guidelines suggest deferral of non-cardiac surgery after valve replacement^[2,3]. Not uncommonly however patients with untreated aortic stenosis undergo non-cardiac surgery. The main cause of non adherence to guidelines are asymptomatic cardiac status, patient refusal to valve replacement, urgency- emergency of non-cardiac surgery and finally prohibitive risk arising from the cardiac surgery related to multiple patient comorbidities^[4]. In patients with known aortic valve disease, since disease progression is highly variable, a careful clinical and echocardiographic evaluation must be obtained closely to surgical procedure.

PATHOPHYSIOLOGY

Severe AS (defined as aortic valve area < 1 cm², 0.6 cm²/m² body surface area) has been reported a high risk factor for perioperative myocardial infarction and cardiovascular mortality in patients undergoing non-cardiac surgery^[5]. In aortic stenosis as long as the increase of left ventricular wall thickness allows to maintain a normal wall stress, ejection fraction is preserved.

However, if the hypertrophic process is inadequate and relative wall thickness does not increase in proportion to pressure, wall stress increases and ejection fraction falls due to increased afterload. Primitive depression of myocardial function may occur in in natural history of aortic stenosis. The differential diagnosis between these two conditions is often clinically difficult. Hemodynamic demands related to non-cardiac surgery in AS patients may be not coped due to limited capability of left ventricle to increase stroke volume in the presence of critically decreased aortic valve area. Hypotension related to inappropriate blood loss and/or spinal anaesthesia, which may cause an uncontrollable decrease in systemic vascular resistance may be detrimental in these patients. Moreover it must be

stressed that a significant coronary artery disease has been reported in about 50% of patients with severe aortic stenosis. Decreased diastolic coronary flow may be critical, in particular in patients with coronary artery disease, leading to severe myocardial ischemia and irreversible ventricular dysfunction. Independently from the presence of coronary artery disease, in the case of hemodynamic derangement, if not appropriately managed, cardiac output may become irreversibly depressed and cardiac arrest may ensue.

Although spinal anaesthesia is not absolutely contraindicated for patients with aortic stenosis, these patients are more susceptible to the potential hazard of sudden hypotension as a result of the reduced systemic vascular resistance caused by the sympathetic blockade. Although a 'target blood pressure value' to define intraoperative arterial hypotension has not been universally stated, a percentage decrease $> 20\%$ in mean arterial pressure, or mean arterial pressure values < 60 mmHg for cumulative durations of 30 minutes, is associated with an elevated risk of post-operative myocardial infarction, stroke, and death. The use of invasive arterial monitoring in order to provide beat-to-beat measurement and enable rapid correction of hypotension is essential to avoid potential irreversible hemodynamic derangement.

GUIDELINES

The current American College of Cardiology/American Heart Association and European Society of Cardiology guidelines^[2,3] consider patients with severe, asymptomatic aortic stenosis (AS) at elevated risk for non-cardiac surgery. Therefore they should have elective non-cardiac surgery postponed or cancelled. Aortic valve replacement is suggested before elective but necessary non-cardiac surgery. Transcatheter valve implantation may be a reasonable alternative in high risk patients with serious co-morbidities^[6]. Percutaneous balloon aortic valvuloplasty may be both a bridge to non-cardiac surgery in hemodynamically unstable adult patients with aortic stenosis who refuse or are at high risk for aortic valve replacement surgery or need urgent non-cardiac surgery^[7].

However these recommendations are based on few, non recent, small observational studies. In patients with severe aortic stenosis who refuse cardiac surgery or are otherwise not candidates for aortic valve replacement, was reported a mortality risk associated with non-cardiac surgery close to 10%^[4,8].

The optimal management of asymptomatic patients with severe AS is even more controversial, with few available data to determine the best clinical approach. There have been only a few observational studies that have examined the impact of severe AS on the postoperative outcomes in patients undergoing NCS. According to guidelines low to intermediate risk surgery, including orthopaedic surgery, can be safely performed in asymptomatic patients. Since major orthopaedic surgery (elective hip or knee replacement or surgery for hip fracture) is not uncommonly associated with high blood losses that may critically impair hemodynamic in AS should we consider it effectively an intermediate risk surgery? In high risk patients not candidate for aortic valve replacement or TAVI, elective surgery under strict haemodynamic monitoring should be performed only if strictly needed.

ELECTIVE SURGERY

As previously reported in the case of elective non-cardiac surgery, the presence of symptoms has been considered a key for decision making. In symptomatic patients, aortic valve replacement should

be considered before elective surgery. In patients who are not candidates for valve replacement either due to high risks associated with serious co-morbidities or those who refuse, non-cardiac surgery should be performed only if is essential. However current guidelines are based on limited and dated studies.

A small study published in 1987^[9] reported the perioperative course of 48 (mean age, 73 years, 36 symptomatic) consecutive patients with significant aortic stenosis who underwent a non-cardiac operation or diagnostic procedure. At Doppler echocardiography average peak instantaneous gradient was 76 mmHg and a calculated aortic valve area of 0.61 cm². Seven patients (14%) had one or more transient perioperative events, including intraoperative hypotension in five. No intraoperative deaths occurred.

Similarly a retrospective chart audit of all patients with AS (55 patients 32 male, 23 female, mean age 73 yr, mean aortic valve area 0.9 cm²) who underwent non-cardiac surgery in Hamilton between 1992 and 1994 did not show difference in the risk of cardiac complications compared with matched controls^[10]. The study demonstrated however differences in perioperative management between patients with aortic stenosis and controls.

In the study by Torsher *et al*^[11] studied 19 patients with severe AS (aortic valve area index < 0.5 cm²/m² or mean gradient > 50 mmHg) underwent 28 surgical procedures: 22 elective and 6 emergency. The type of anesthesia was general in 26 procedures and continuous spinal in 2. Intraarterial monitoring of blood pressure was used in 20 of the 28 surgical procedures. The anesthesia team was aware of the severity of the AS and integrated this into the anesthetic plan. Two patients (elective operation in 1 and emergency in 1) had complicated postoperative courses and died. There were no other intraoperative or postoperative events.

Kertai *et al*^[12] studied 108 patients with moderate (mean gradient, 25 to 49 mmHg) or severe (mean gradient, $> \text{or} = 50$ mmHg) aortic stenosis and 216 controls who underwent non-cardiac surgery between 1991 and 2000. The main outcome measure was the composite of perioperative mortality and nonfatal myocardial infarction. The composite end-point was significantly more frequent in patients with aortic stenosis (14% [15/108] vs 2% [4/216], $P < 0.001$). Severe aortic stenosis were more commonly followed by perioperative complications compared with moderate aortic stenosis (31% [5/16] vs 11% [10/92], $P = 0.04$). After adjusting for cardiac risk factors, aortic stenosis remained a strong predictor of the composite endpoint (odds ratio = 5.2; 95% confidence interval: 1.6 to 17.0).

In a recent paper Agarwal *et al*^[4] studied the outcome in patients with aortic stenosis undergoing non-cardiac surgery compared to a matched control group. AS was classified moderate (valve area: 1.0-1.5 cm²) or severe (valve area: < 1.0 cm²). Patients were included in the study if they had a preoperative echocardiogram within 90 days before undergoing NCS. Dobutamine stress echocardiography was used to identify AS in low flow-low gradient patients. 4 matched control patients without AS for each patient with AS undergoing NCS were identified using propensity score matching. The propensity score matching used the 6 revised cardiac risk index criteria, in addition to age and sex. A composite of 30-day mortality and postoperative myocardial infarction was considered as primary outcome.

Twenty-nine patients underwent urgent surgery. The reason for non adherence to Guidelines suggesting AVR (or TAVI) in 79% undergoing elective surgery are reported in Table 1.

634 patients with AS undergoing NCS were matched to 2536 controls. 244 patients had severe AS and 390 patients moderate AS.

Table 1 Reason for non adherence to Guidelines suggesting AVR in patients with AS undergoing non cardiac surgery.

Advanced age	27%
Cancer surgery	12%
Low risk surgery	15%
Multiple comorbidities	51%
Patient refusal	3%
Spinal anesthesia	8%
Tolerated recent surgery	20%

The categories are not mutually exclusive. A single patient may belong to several categories.

Thirty-day mortality was 2.1% for AS patients compared with 1.0% in non-AS controls ($P = 0.036$). Postoperative myocardial infarction was more frequent in patients with AS compared with controls (3.0% vs 1.1%; $P = 0.001$). Combined primary outcome was significantly worse for both moderate and severe AS patients compared with respective controls (4.4% vs 1.7%; $P = 0.002$; and 5.7% vs 2.7%; $P = 0.02$, respectively). High-risk surgery, symptomatic severe AS, coexisting mitral regurgitation, and preexisting coronary disease were significant predictors of primary outcome in patients with AS. 30-day mortality rate although lower in the severe AS group (1.6%) in comparison to moderate AS group (2.3%) was not statistically different. In comparison with the non-AS group (2.7%), the incidence of primary outcome was significantly higher in the symptomatic severe AS group (8.3%; $P = 0.007$). This difference was largely attributable to the higher incidence of postoperative MI. In severe AS incidence of coronary artery disease (71.4%) was significantly higher among patients experiencing primary outcome in comparison with those without the primary outcome (40.4%; $P = 0.02$). Patients with primary outcome and moderate AS had more frequently depressed LV ejection fraction < 40% (35.3%) and moderate or severe mitral regurgitation (29.4%) as compared with those without the primary outcome. These results suggest that patients with moderate AS and high risk features like depressed ejection fraction, a greater degree of stenosis, or coexisting mitral regurgitation were more prone to developing primary outcome as compared with others without high-risk features. In conclusion the authors state that although AS is considered an high risk preoperative risk factor, prognosis is not significantly worse than in matched control in elective non-cardiac surgery.

In a study from the Danish Health Care System 2823 patients with AS were compared to 2823 matched controls^[13]. 1722 subjects in each group underwent elective non-cardiac surgery. 30 day mortality has been 3.8% in AS patients in comparison to 2.9% in controls, a non-statistically significant difference. Similarly MACE was not different in the two groups. Of particular relevance was the similar rate of complications between symptomatic and asymptomatic patients.

EMERGENCY-URGENCY SURGERY

In the case of urgent non-cardiac surgery guidelines suggest that in patients with severe AS, such procedures should be performed under close haemodynamic monitoring. Few studies reported the results of emergency surgery in patients with AS. In the investigation by Andersson *et al*^[13] among 2823 patients 40% underwent emergency surgery. Overall mortality in AS patients was significantly higher (21.4%) than in elective surgery (3.8%) However the difference was significantly lower in patients with AS undergoing emergency surgery and matched controls (21 vs 17%, $p < 0.01$). Symptomatic patients had a two folds risk of death in comparison to asymptomatic.

Table 2 Comparison in mortality between patients with and without AS undergoing Surgery for hip fracture.

	Mortality	Moderate/severe AS	Controls
Adunski et al	In hospital	6.50%	3.2%
Mc Brien et al	30 day	16.20%	7.40%
	1 year	58.6%	22.20%
Kesami et al	30 day	14.70%	4.20%
	1 year	48.80%	14.10%
Rostagno*	In hospital	7.50%	2.80%

*Unpublished data.

Although near 30% of patients included in the study by Agarwal *et al*^[4] underwent urgent surgery, results are not reported separately therefore we have no information regarding the risk related to different types of surgery in AS patients.

Among common emergency non-cardiac surgical procedures treatment of hip fracture has a prominent epidemiological role. Since the incidence of severe aortic valve stenosis in patients who need surgery for hip fracture is comprised between 5 and 10%^[14] and that in Italy every year at least 70 000 patients undergo surgery for hip fracture, it may be estimated that between 3 500 and 7 000 of them suffer from severe aortic stenosis. Despite the “epidemic” relevance of this situation only few studies examined the prognostic role of aortic stenosis on hospital and mid-term survival in in this frail group of patients. The main concern in patients with hip fracture is that the diagnosis is frequently omitted since only few centres have the availability of bed side echocardiography service to evaluate and confirm the severity of AS in patients with systolic murmurs. SIGN guidelines in 2009^[15] suggested that echocardiography “should be performed if aortic stenosis is suspected, to allow confirmation of diagnosis, risk stratification and any future cardiac management”. However, they state that the need for echocardiography “should not delay surgery unduly” and that if delays are to be avoided, “rapid access to an echocardiography service is recommended”. The cost of setting up and maintaining such a service may be offset by reducing delays and improving outcomes. Nevertheless despite these recommendations only a negligible proportion of patients with hip fracture undergo pre operative echocardiography.

Pelikka *et al*^[16] reported that surgery may not pose any additional risks for patients with aortic stenosis. Other authors reported a trend towards general anaesthesia versus spinal anaesthesia in hip fracture patients with varying severity of aortic stenosis; invasive monitoring was also used in some patients. A warning to the surgeon of high patient cardiac risk may prompt more efficient surgery and less blood loss and consideration of less invasive techniques.

Adunsky *et al*^[17] reported a two-fold increase of in hospital mortality (6.5 vs 3.2 %) in aortic stenosis (average aortic valve area 0.97 cm²) in comparison to patients without aortic stenosis.

Recently Keswani *et al*^[18] in a retrospective case-control study in patients with hip fracture compared 65 subjects with aortic stenosis to 129 matched controls. Both cardiac and non-cardiac complications were significantly more frequent in AS patients than in controls. Moreover both 30 day and 1 year mortality were significantly higher in AS group (14.7 % vs 4.2 % at 30 days and 46.8 vs 14.1 % at 1 year respectively). Moderate/severe aortic stenosis and chronic kidney disease were the only independent predictors of 1 year mortality. In the study of Mc Brien *et al*^[19] 272 patients with hip fracture and previously undiagnosed AS were compared to 3698 patients with hip fracture and no AS. Patients with severe AS were more frequently treated in general anaesthesia (66.7%) and had arterial line positioning for continuous

hemodynamic monitoring. Thirty day mortality was 10% in AS in comparison to 6.25% in moderate AS and 7.4% in control group, while at 1 year mortality in the three groups were 36.7%, 21.9% and 22.2% respectively. Time from trauma to surgery was not significantly different in patients undergoing echocardiography for diagnosis of AS and control patients (average 5 days). Preliminary data from our institution about 54 consecutive patients referred for hip fracture between 2012 and 2014 and diagnosed moderate/severe AS show a 7.5% in hospital mortality in comparison to 2.8% of patients without AS (Table 2).

CONCLUSION

Advances in surgical and anesthetic techniques (avoidance of intraoperative hypotension and treating it aggressively with phenylephrine, avoidance of tachycardia with aggressive management of intraoperative arrhythmia) with closer perioperative monitoring appear to allow non-cardiac elective surgical procedures possible with acceptable risk in patients with severe aortic stenosis. A correct diagnosis of the severity of aortic stenosis is mandatory in preoperative evaluation of patients candidate to non-cardiac surgery. On the basis of echocardiographic evaluation, adverse events during non-cardiac surgery occurred primarily in patients with an AVA < 0.7 cm² and a mean gradient > 50 mm Hg and normal left ventricular function. Although data at present are limited, non-cardiac surgery is associated with a poorer outcome also in low-flow low- gradient AS. Dobutamine stress echocardiography should be used to identify this high risk subgroup. Asymptomatic patients with AS with an AVA > 0.8 cm², and preserved LV systolic function should not be labeled as high risk for a non-cardiac surgery. Therefore at least for “asymptomatic severe aortic stenosis” patients with preserved LV systolic function and no other significant valvular pathology, a reappraisal of the grading of the severity of AS in general and reassessment of perioperative risk during elective non-cardiac surgery is urgently needed^[20]. Samarendra and Mangione^[20] suggest to label high risk for non-cardiac surgery AS patients with a mean gradient ≥ 45 mmHg, left ventricular systolic dysfunction, symptoms due to AS, associated mitral regurgitation, increase ≥ 18 mmHg in mean gradient during exercise echo stress and significant concomitant coronary artery disease.

For patients who need urgent/emergency non-cardiac surgery at present data are limited and not uniform. AS in these patients is often previously undiagnosed and only preoperative careful evaluation with echocardiographic examination may reveal its presence and severity. AS is usually associated with a higher risk of perioperative death and myocardial infarction. Preoperative detection of valve disease may lead to change anesthesiologic strategy (from spinal to general anesthesia in particular in patients with hip fracture) and adoption of close hemodynamic monitoring that may limit perioperative complications.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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