Conventional aortic valve replacement for high-risk aortic stenosis patients not suitable for trans-catheter aortic valve implantation: feasibility and outcome

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Abstract

Objective: High-risk patients with aortic stenosis are increasingly referred to specialist multidisciplinary teams (MDTs) for consideration of trans-catheter aortic valve implantation (TAVI). A subgroup of these cases is unsuitable for TAVI, and high-risk conventional aortic valve replacement (AVR) is undertaken. We have studied our outcomes in this cohort.

Methods: Data prospectively collected between March 2008 and November 2009 for patients (n = 28, nine male) undergoing high-risk AVR were analysed. The mean age was 78.4 ± 9.2 years. The mean additive EuroSCORE (European System for Cardiac Operative Risk Evaluation) was 10.0 ± 3.6 and mean logistic EuroSCORE was 19.9 ± 18.8. Three patients had undergone previous coronary artery bypass grafting (CABG).

Results: The mean ejection fraction was 51 ± 16%, mean valve area 0.56 ± 0.19 cm², and mean peak gradient 91 ± 27 mmHg. Ascending aortic, right axillary artery and femoral artery cannulation was used in 64%, 29% and 7% of cases, respectively. Median cross-clamp and cardiopulmonary bypass times were 84 (68—143) min and 111 (94—223) min. The median (range) inserted valve size was 21 (19—25) mm. Median intensive care and overall hospital stay were 5 (2—37) and 11 (5—44) days, respectively. In-hospital mortality was 4% (one patient). Postoperative complications included re-operation for bleeding (7%), renal failure (21%), tracheostomy (14%), sternal wound infection (7%), atrial fibrillation (25%) and permanent pacemaker implantation (7%). Kaplan—Meier survival at median follow-up of 359 (148—744) days was 81% (one further death of non-cardiac aetiology). Quality-of-life assessment at follow-up also yielded satisfactory results.

Conclusions: MDT assessment of high-risk aortic stenosis in the era of TAVI has increased the number of referrals. Conventional open surgery remains a valid option for these patients, with acceptable in-hospital mortality and early/midterm outcomes but high in-hospital morbidity.

Keywords: Aortic valve; Aortic stenosis; Trans-catheter valve; Surgery

1. Introduction

Aortic stenosis remains the most common cause of adult valvular heart disease, the prevalence increasing with age [1,2]. Average survival of patients treated conservatively has historically been reported as 2–5 years from the onset of symptoms [3]. More recent studies have confirmed the dismal prognosis of severe aortic stenosis. Advanced age, reduced left-ventricular ejection fraction, congestive heart failure and renal insufficiency appear to be independent predictors of reduced survival [4]. Asymptomatic patients with very severe aortic stenosis also share a poor prognosis with a high event rate and a risk of rapid functional deterioration [5]. Early surgery offers a therapeutic option to improve clinical outcomes via decreasing cardiac mortality and improving symptoms [6].

Even though surgical aortic valve replacement (AVR) continues to be the treatment of choice for aortic stenosis, nearly one-third of assessed patients with severe symptoms do not proceed to surgery, as the estimated surgical risk is exceedingly high [7]. The advent of trans-catheter aortic valve technology has offered the potential of an alternative less invasive treatment option for these patients [8]. A position statement was published jointly by the European Association of Cardio-thoracic Surgery and the European Society of Cardiology regarding trans-catheter aortic valve implantation (TAVI) in 2008 [9]. TAVI may offer an alternative option for patients with severe symptomatic aortic stenosis.
at high risk or with contraindications for surgery. In line with recommendations, referred patients are assessed by a local multidisciplinary team (MDT) of cardiac surgeons and cardiologists prior to being offered TAVI. At our centre, we have held such MDT meetings since 2008. High-risk patients are referred from across the northwest of England to our institution for consideration of TAVI. Following discussion at these meetings, patients are declined TAVI, offered continuing medical management, and entered into follow-up for re-assessment at a later date, offered TAVI, or in certain cases, offered conventional surgical AVR. We report our experience of performing conventional surgical AVR in this group of high-risk patients originally referred for consideration of TAVI.

2. Patients and methods

2.1. Patients

Since the introduction of the MDT assessment process for high-risk patients with aortic valve disease at our centre, 141 patients have been considered for TAVI. Of these patients, 23 (16.3%) have been declined TAVI, 22 (15.6%) have been entered into follow-up for re-assessment at a later date, 57 (40.4%) patients have been accepted for TAVI and 39 (27.7%) patients have been accepted for conventional AVR. To date, TAVI has been performed in 53 patients and conventional AVR in 28 patients.

Patients were declined TAVI for the following reasons: one patient had a previous mechanical mitral valve replacement with a short aorto-mitral membrane, one patient had a small aortic root, one patient had a dilated aorta of 4.4 cm, five patients had severe multivessel peripheral vascular disease and one patient underwent emergency AVR prior to obtaining an MDT opinion. Of the remaining patients, who had multiple major co-morbidities and in whom TAVI was more appropriate (in the MDT’s opinion), the lack of a steady funding stream for TAVI dictated a surgical approach. Of note, these patients had severe symptoms of aortic stenosis, warranting treatment including recurrent syncpe, recurrent pulmonary oedema and biventricular failure.

To determine in-hospital and late mortality, data from hospital records and respective general practitioners were used.

2.2. Surgical technique

A standard anaesthesia technique was used with single-lumen endotracheal intubation and routine haemodynamic/monitoring lines. Exposure was gained through a median sternotomy in all cases. Cardiopulmonary bypass was established with right axillary artery, ascending aorta and two-stage right-atrium venous cannulation with systemic hypothermia at 32 °C. Axillary cannulation was the vascular access of choice in the presence of atherosclerosis of the ascending aorta to minimise aortic manipulation. Cold blood cardioplegia was delivered via the antegrade, retrograde and direct coronary ostial route (depending on the presence of aortic regurgitation). The left ventricle was vented via the right superior pulmonary vein and CO₂ insufflation was routinely used. Accessed via an oblique aortotomy, the native aortic valve was excised and meticulous decalcification of the annulus carried out. AVR was carried out by a standard operative technique using 2/0 Ethibond (Ethicon Inc., Somerville, NJ, USA) interrupted horizontal mattress sutures, with Teflon pledgets on the ventricular side. Aortotomy was closed with Prolene (Ethicon Inc., Somerville, NJ, USA) sutures in two layers and CoSeal glue (Baxter Biosurgery Europe, Germany) applied. Transoesophageal echocardiography was used to assess valve performance and for early detection of insufficient myocardial blood supply as well as monitoring of intracardiac air at weaning. Thorough de-airing through a left-ventricular vent and the ascending aorta was carried out prior to weaning from bypass. Six patients required concomitant coronary artery bypass graft surgery and one patient required removal of a left-atrial thrombus.

2.3. Quality of life

Postoperative quality of life was determined using the self-administered EQ5D questionnaire. This is a two-part questionnaire, which asks patients to assign a score of 1–3 (1 = no problem, 2 = some problem and 3 = extreme problem) to specific dimensions of quality of life. These include ‘mobility’, ‘self-care’, ‘usual activities’, ‘pain/discomfort’ and ‘anxiety/depression’. Patients then provide a score from 0 (worst imaginable health state) to 100 (best imaginable health state) on a visual analogue scale (VAS) as an overall score for self-perceived quality of life. This constitutes the EQ VAS [10]. The results for specific dimensions and overall quality of life in the study population were compared to the age-matched general population in the UK.

2.4. Statistical analysis

Continuous variables were compared using the unpaired t-test. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) v 12.0 software package for Windows (SPSS; Chicago, IL, USA).

3. Results

The preoperative characteristics of the 28 patients, who underwent conventional AVR, are displayed in Table 1. The mean age was 78 years, nine (32%) patients were male and mean EuroSCORE (European System for Cardiac Operative Risk Evaluation) and logistic EuroSCORE were 10.0 ± 3.6 and 19.9 ± 18.8, respectively. Patients with co-morbidities included seventeen (61%) with hypertension, seven (25%) with diabetes mellitus, six (21%) with chronic obstructive pulmonary disease and five (18%) with previous myocardial infarction. Four (14%) patients had previously undergone cardiac surgery.

Mean left-ventricular ejection fraction was 51 ± 16%, mean aortic valve area was 0.56 ± 0.2 cm² and mean peak aortic valve gradient was 91 ± 27 mmHg. Ascending aortic, right axillary artery and femoral artery cannulation was used in 18 (64%), eight (29%) and two (7%) patients, respectively. Median aortic cross-clamp and cardiopulmonary bypass times...
were 84 (68–143) min and 111 (94–223) min, respectively. Median intensive care unit stay was 21 (19–25) mm.

Postoperative outcomes are displayed in Table 2. Mean blood loss was 579 ± 352 ml. Blood transfusion and blood products were administered to 16 (57%) and six (21%) patients, respectively. Median extubation time was 7 (4–32) h. This does not account for patients extubated after requiring subsequent reintubation (one patient with respiratory failure and one patient with a floppy membranous trachea) or tracheostomy for respiratory weaning (two patients). Median intensive care unit stay and total hospital stay were 5 (2–37) days and 11 (5–44) days respectively. We note that median intensive care unit stay for patients undergoing tracheostomy was 26 (11–37) days. In-hospital mortality was (4%) (one patient). The following complications occurred: two (7%) patients needing re-operation for bleeding, four (14%) with tracheostomy, six (21%) with lower respiratory tract infection, one (4%) with sepsis, seven (25%) with atrial fibrillation, two (7%) with sternal wound infection, two (7%) requiring permanent pacemaker implantation and six (21%) with renal failure requiring haemofiltration.

Quality of life data for patients in the 70–79 years and >80 years age groups is displayed in Table 3. Twenty-three (85%) out of twenty-seven patients alive at the median follow-up of 359 (148–744) days responded to the EQ5D questionnaire. The study population comprised one patient in the 60–69 years age group, eight patients in the 70–79 years age group and 14 patients in the >80 years age group. There was a minor but significant reduction in self-perceived overall health-related quality of life, demonstrated by the EQVAS score, in the study population compared with the general population in the 70–79 years (71.4 ± 21.7 vs 75.3 ± 18.5, p < 0.001) and >80 years (67.7 ± 24.0 vs 72.5 ± 18.2, p < 0.02) age groups, respectively. For specific EQ5D dimensions, comparison of the study population to the general population in the 70–79 years age group showed a significant increase in patients reporting no pain or discomfort (63% vs 44%, p = 0.003) and a non-significant increase in those reporting no problem with mobility (63% vs 60%, p = 0.75) and anxiety or depression (75% vs 75%, p = 0.97), respectively. For other dimensions in the 70–79 years age group, there was a significant reduction in patients reporting no problem in the study population compared with the general population. Comparison of the study population to the general population in the >80 years age group showed a non-significant reduction in patients reporting no pain or discomfort (36% vs 40%, p = 0.45), and a significant reduction in patients reporting no problem in all other dimensions.

4. Discussion

Local as well as published data demonstrate an increasing number of high-risk patients with advanced age and multiple co-morbidities being referred for TAVI assessment [11]. Although reports demonstrate faster postoperative recovery with similar early and midterm morbidity and mortality compared with minimally invasive AVR [12], there is still insufficient evidence reported on the long-term outcomes of TAVI. In a systematic review by Yan et al., procedure-associated 30-day mortality was shown to be 0–25%, and mortality at 6 months ranged from 18% to 48%, with overall 30-day major adverse cardiovascular and cerebral events ranging from 3% to 35% [13]. Data from the same work documented permanent pacemaker insertion and moderate-to-major paravalvular leak in 0–36% and 4–35% of patients, respectively. Based on these findings, it is concluded by the authors that the use of TAVI should be confined within the boundaries of clinical trials. Ongoing randomised trials such as the Placement of AoRTic TraNscatheterER Valve Trial (PARTNER) (ClinicalTrials.gov identifier: NCT00530894) will provide further information on long-term performance in comparison to conventional surgery for high-risk patients.
Long-term outcome is improved following conventional AVR for aortic stenosis irrespective of preoperative left-ventricular function [14]. Valve replacement surgery is only offered within our unit, if the expected benefit outweighs the potential risks of the treatment. However, preoperative determination of patient risk factors that influence outcomes following isolated AVR remains a dynamic area of research in keeping with changes in patient population characteristics and operative/postoperative management [15]. Advanced age is an important surgical risk factor, and an increasing number of elderly patients are presenting for consideration of AVR, leading many groups to investigate the outcomes of AVR in the elderly [16,17]. The effectiveness of available risk scores in predicting outcomes in high-risk cases is currently under scrutiny [18]. The need for accurate risk prediction has become even more necessary in patients considered for TAVI interventions [19]. Whilst risk of operative mortality has been shown to be best predicted by the Society of Thoracic Surgeons (STS) score [18], the logistic EuroSCORE appears to be the strongest predictor for 30-day mortality following TAVI even though it does not predict actual risk (data from Edwards SAPIENTM Aortic Bioprosthesis European Outcome (SOURCE) Registry) [20].

The impact of offering a TAVI service has had a positive effect on the volume of conventional AVR surgery carried out at our centre [21]. Even more interestingly, this increase in activity has been associated with a non-significant reduction in overall mortality despite a trend of increasing predicted risk in these patients. A percentage of patients referred for TAVI will be offered surgical AVR, as documented by other groups [11,22]. Mean logistic EuroSCORE was calculated at 19.9 ± 18.8 within the described cohort.

At our centre, every patient is assessed by an experienced aortic surgeon on an individual basis, as it is well acknowledged that available risk models fail to capture some factors important to the evaluating surgeon when estimating patient-specific mortality risk [23]. As evidenced by the successful outcome in the case of emergency conversion to conventional surgery in five out of six patients in whom the valve was misplaced [24], many patients deemed ‘too high-risk’ on initial assessment would be suitable surgical candidates. Previous cardiac surgery as well as the need for combined coronary artery bypass graft surgery should not preclude conventional AVR, and concomitant coronary revascularisation is known to improve operative and long-term survival in octogenarians. Improved mortality and neurological outcomes have been clearly reported for aortic surgery by many specialist centres using axillary artery cannulation, and we commonly use this approach for the arterial inflow of the cardiopulmonary bypass circuit to minimise aortic manipulation in this high-risk group. We also routinely provide vascular access via the left axillary route for TAVI at our centre.

Accepting the inherent limitations of elderly patients completing quality of life questionnaires, our study demonstrated, in agreement with previous literature, that satisfactory quality of life may be anticipated following aortic valve surgery in this high-risk patient group. Interestingly, quality of life is affected in many patients by non-cardiac co-morbidities.

In conclusion, a proportion of patients referred for TAVI will be accepted for conventional surgery in experienced centres. These patients may exhibit low in-hospital mortality, good survival and satisfactory postoperative quality of life, but do develop significant postoperative complications — particularly renal failure, prolonged intensive care and overall hospital stays. Commissioners considering TAVI versus conventional surgery cost should consider these issues when commissioning services (TAVI is more expensive procedurally but may be significantly cheaper overall for specific subgroups of high-risk patients). Although sustained clinical and haemodynamic benefits for up to 36 months following TAVI have been demonstrated [25], the evidence base regarding the clinical benefits and cost-effectiveness of TAVI technology remains limited. Conventional surgery remains a viable therapeutic option in high-risk patients, if no absolute contraindications exist. Development of risk scores predicting operative mortality more accurately in this high-risk group of patients is pertinent, as the inaccuracy of available risk scores may hamper the definition of entry criteria in randomised trials.

### 4.1. Limitations of the study

The study evidently reflects a single-centre experience with a limited number of patients. Furthermore, our institution does not offer, at present, trans-apical TAVI and subjects were not randomised into treatment groups; hence, no conclusions may be drawn on a comparative basis, as such. Regarding our results for quality-of-life assessment, several patients providing low scores in their questionnaires included free text comments explicitly stating that their relatively poor quality of life is attributable to other causes. However, this qualitative data could not be factored into the analysis. Finally, as patients are referred from a very wide geographical area, follow-up is undertaken at their local cardiology departments. This entails different follow-up protocols, and pooled data is not suitable for analysis.


Appendix A. Conference discussion

Dr A. Franco-Cereceda (Stockholm, Sweden): It’s quite reassuring to hear this presentation amidst the TAVI hype that we’re actually experiencing right now. If we look at the EACTS Surgical Database of 2010, hospital mortality for single aortic valve replacement in octogenarians is about 6.1%. You present your data with a hospital mortality of 3.6%, which is really excellent. We also know from the Euro Heart Survey that the two most important denominators for refusing surgery to aortic stenotic patients is age above 80 and ejection fraction below 30%.

So with this in mind, I have two questions for you. The first relates to the term ‘high-risk’ patients. In my view, I think what you present in terms of octogenarians being referred for aortic valve surgery really represents a fairly standard population of patients that we see in many clinics. Before the TAVI era, these patients would have been operated on. And I would like you to elaborate on how you define the high-risk patient.

The second question relates to surgical outcomes. When operating on these high-risk patients, apparently your clinic and other clinics can achieve excellent results, and others do not. If TAVI should really teach us something it is that we should improve, and we can improve, the surgical outcomes. So could you please tell us what you do, what precautions do you take to optimize surgical outcome in these patients?

Dr Dimarakis: The definition of high-risk patients, I completely agree, is very difficult because of the limitations of the available preoperative risk scores. So although most patients have been considered, in published studies, based on the logistic EuroSCORE or STS score, these risk models fail to capture some factors important to the evaluating surgeon when estimating patient-specific mortality risk. In addition, cardiac surgeons are not the gatekeepers for patient referral to the TAVI assessment unit. As a tertiary referral centre for a very wide geographical area an important issue that arises is what type of patient cohort referring cardiologists perceive as high-risk. Prior to providing a TAVI service, I suppose that a number of cardiologists would perceive many patients as high-risk and probably inoperable and we would actually never assess them in the clinics. So I do agree that our data is biased from that point of view and furthermore we are looking at a small overall population of 140 patients. So in effect what we are seeing is a new trend of referrals as well as a change of concept from the cardiology point of view as to which patient may be assessed as a potential surgical candidate.

An indirect marker of this change of concept is the fact that we are seeing a number of transfers from patients referred for aortic valve surgery case load overall. Interestingly outcomes for mortality and morbidity have, if anything, improved over the last two years.
And coming to your second question, I believe that we do provide high level aortic service as all these cases have been carried out by one the unit’s surgeons with a specialist interest in aortic surgery. This translates to a wide armamentarium of approaches being offered on a patient-specific basis such as right axillary artery cannulation in fragile or severely atheromatous aortas. In other units this versatility may not exist. So I think the very good results are in keeping with a specialized surgeon dealing with these patients.