Percutaneous aortic valve replacement for severe aortic stenosis

Part B: Addendum to technology assessment

- Draft criteria and provisional thresholds for patient selection
- Provisional Key Performance Indicators (KPIs) to monitor PAVR service
- Cost model

May 2008
# Contents

**Addendum 1 - Draft criteria and provisional thresholds for patient selection**

1.1 Introduction .................................................................................................................. Page 3
1.2 Criteria to assess capacity to benefit ............................................................................... Page 3
1.3 Criteria to assess procedural risks and contraindications ............................................ Page 4
1.4 Pre-procedural screening ............................................................................................... Page 6
1.5 Characteristics of patients in case series ....................................................................... Page 7

**Addendum 2 - Provisional Key Performance Indicators (KPIs) to monitor PAVR service**

2.1 Introduction .................................................................................................................. Page 11
2.2 Effectiveness outcomes ................................................................................................. Page 11
2.3 Efficiency outcomes ..................................................................................................... Page 12
2.4 Equitability .................................................................................................................. Page 12
2.5 Safety .......................................................................................................................... Page 12
2.6 Timeliness/access ......................................................................................................... Page 12
2.7 Patient quality of life outcomes .................................................................................... Page 12

**Addendum 3 - Cost Model** .......................................................................................... Page 13

**References** ..................................................................................................................... Page 14
Addendum 1:

Criteria and provisional thresholds for selecting patients for PAVR procedures (to be discussed with clinicians)

1.1 Introduction

When recommending a treatment or proposing policy, clinicians and policy makers need to balance the expected benefits from a procedure with the known risks for individual patients. Any scheme that attempts to standardise these decisions is limited by the quality of the existing data and the extent to which the results of trials performed in groups of selected patients can be applied to individuals within a more general or less restricted population. The reliability of risk assessment relates to this external validity of the trials, coupled with the ability of specific scores, such as the EuroSCORE (see Box), to discriminate between people at high or low risk of adverse operative events or mortality in groups other than those for whom it was designed.

Bazian has drafted the following provisional referral criteria based on the populations included in case series studies that were assessed as part of the health technology assessment. To date, this is the best available evidence for the PAVR procedure. These criteria should be seen as broad domains of interest, based on the current case series evidence, within which clinicians and policy makers can agree specific thresholds for offering the service.

1.2 Criteria to assess capacity to benefit (long term and short term)

The evidence for benefit comes from case studies and series of PAVR in people with severe symptomatic aortic stenosis, who are unsuitable for surgery. The indirect comparator for this group is supportive or conservative management.

The thresholds marked* for this analysis come from the case series listed in the full report;

Patients should have:

- a capacity to benefit from treatment i.e. low survival or severe symptoms without treatment
  - provisional threshold: classic symptoms syncope, angina or dyspnoea with
    *Severe or critical aortic stenosis (valve area <1cm² mean gradient across valve >40mmHg, aortic jet velocity >4m/s) and NYHA symptoms grade III or IV
• *been refused surgery (confirmed by cardiothoracic surgeon) i.e. likely to benefit from PAVR when compared to supportive care
  - provisional threshold: same operative mortality and comorbidity considerations that would prohibit cardiothoracic surgery. e.g. *a surgical cardiothoracic operative mortality risk (log EuroSCORE) > about 20% and other agreed contraindications to an open AVR
• function unlimited by other comorbidities
  - provisional threshold: no dementia, severe stroke or neurological disease that are the major cause of limitation to function
• reasonable life expectancy
  - provisional threshold: *no progressive disease with life expectancy less than 1 year

1.3 Criteria to assess procedural risks and contraindications to PAVR

Risks were assessed prior to enrollment for the case series and published as inclusion or exclusion criteria for the studies.

Patients should have:

• suitable anatomical dimensions of the valve and ascending aorta
  - provisional threshold: *Core valve – aortic annulus diameter (20–23mm); sinotubular junction diameter (45mm or less) and diameter of ascending aorta (30mm or less at 3cm above annulus). *Edwards valve – aortic annulus diameter (19 – 24mm)
• no limitation to access for technical reasons
  - provisional threshold; *Internal lumen diameter of access artery appropriate for sheath or femoral iliac or aortic atherosclerosis, calcification or tortuosity or other vascular disease that precludes access
    - *porcelain aorta absent
    - *severe chest deformation absent
    - *aortic aneurysm absent
• an assessment of their overall risk from PAVR (as this is a new procedure, it is not clear yet from long term studies if there is a group of patients, amongst those enrolled in the case series, in whom the risk of the procedure is so great that balance of risk and benefit is in favour of supportive care)
provisional items for estimating this procedural risk should be collected using registry data analogous to the EuroSCORE (see Box) and could include: a measure of renal function e.g. creatinine clearance; a threshold for LV function and "no history of recent MI and other agreed criteria"

**In addition patients should not have:**

- *hypersensitivity or contraindication to medications
- *contraindication to general anaesthesia (majority of included studies used general anaesthesia for PAVR; general anaesthesia may also be required to manage complications, e.g. rescue surgery)
- *bleeding diathesis or coagulopathy
- *sepsis or active endocarditis
- *uncontrolled AF
- *LV or atrial thrombus, or
- *a history of previous AVR surgery

---

**Box: EuroSCORE**

The EuroSCORE is used to predicted operative mortality in people undergoing cardiac surgery. The following variables are considered:

<table>
<thead>
<tr>
<th>Patient related factors</th>
<th>Cardiac related factors</th>
<th>Operation-related factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>unstable angina</td>
<td>emergency</td>
</tr>
<tr>
<td>gender</td>
<td>LV function</td>
<td>other than isolated CABG</td>
</tr>
<tr>
<td>chronic pulmonary disease</td>
<td>recent MI</td>
<td>surgery on thoracic aorta</td>
</tr>
<tr>
<td>extracardiac arteriopathy</td>
<td>pulmonary hypertension</td>
<td>post-infarct septal rupture</td>
</tr>
<tr>
<td>neurological dysfunction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>previous cardiac surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>creatinine &gt; 200µmol/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>active endocarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>critical preoperative state</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1.4 Pre-procedural screening

Two case series describe pre-procedural tests as including some of the following:
Transthoracic echo, transoesophageal echo, carotid and arteriovenous duplex ultrasonography, and
computed tomography angiography.

Optional investigation included; cardiac MRI, invasive cardiac evaluation with coronary arteriography
and left ventriculography and ileo-femoral contrast angiography where indicated.
### 1.5 Characteristics of patients in case series

<table>
<thead>
<tr>
<th>Author</th>
<th>Study design</th>
<th>Inclusion criteria</th>
<th>Type of anaesthesia</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Jaegere, 2007¹</td>
<td>Case series, CoreValve</td>
<td>Patient 1 (female): no previous medical history except for hip replacement, SAS, moderately impaired LVF, no significant aortic or mitral regurgitation, no CAD. Log Euroscore 19.7%. Classified as high risk and rejected for surgery because of age, renal function, subsequent risk for neurocognitive dysfunction and renal failure after surgical VR. Patients 2-4: limited further info: 3 and 4 had both had prior CABG/PCI, 3 with no other comorbidities or history, 4 with COPD. Euroscores; 11.66, 26.32, 22.59% respectively.</td>
<td>Dissociated anaesthesia (sedation and analgesia, no intubation and ventilation)</td>
<td>Patient 1: Reduction in peak velocity over valve at day 5 and reduction in peak gradient. Grade 1 aortic regurg after implantation. Patients 2–3: outcomes not discussed.</td>
</tr>
<tr>
<td>Grube et al, 2006²</td>
<td>Case series, CoreValve</td>
<td>Inclusion criteria: all of the following: 1) native AS with valve area &lt;1 cm² and/or native aortic valve regurg grade 3 or more by echo, 2) valve annulus between ≥20 and ≤23 mm, 3) diameter of the ascending aorta 3 cm above annulus of ≤30 mm, and 4) contraindication to surgery because of concomitant comorbid conditions assessed and agreed to by both an independent cardiologist and a cardiovascular surgeon. Exclusion criteria: any of the following: hypersensitivity or contraindication to any study medication, sepsis or active endocarditis; excessive femoral iliac, or aortic atherosclerosis, calcification or tortuosity; aortic aneurysm, bleeding diathesis, coagulopathy. Baseline risk estimated using log EuroSCORE. Preintervention screening: included transthoracic and transoesophageal echo, carotid and...</td>
<td>General anaesthesia.</td>
<td>20% in-hospital mortality. Symptom improvement in 18 who survived to 30 days.</td>
</tr>
</tbody>
</table>
arteriovenous duplex ultrasonography, computed tomography angiography, optional cardiac MRI, invasive cardiac evaluation with coronary arteriography and left ventriculography

| Marcheix et al, 2007<sup>3</sup> | Case series, 10 patients, CoreValve | “high risk patients with severe symptomatic AS with high or prohibitive risk with conventional surgery”. Patients underwent TEE, iliofemoral contrast angiography, and coronary angiography. Actual contraindications for surgery were pulmonary fibrosis, COPD, PVD, prior CABG, connective tissue disease, cardiac cachexia, kyphoscoliosis, renal failure, prior MVR | Unclear | Immediate improvement in valve area and pressure gradient. 30-day mortality 20%. Median NYHA improved from NYHA III to II |
| Berry et al, 2007<sup>4</sup> | Case series, 11 patients, CoreValve | Severe aortic stenosis ‘believed to be nonsurgical candidates’, or who had been declined surgical AVR by at least 2 cardiac surgeons.  
**Inclusion criteria:** SAS (valve area index ≤0.6cm<sup>2</sup>/m<sup>2</sup>), aortic annulus diameter of 20–23mm, sinotubular junction diameter ≤45mm, and either patient aged 80 and over with log EuroSCORE ≥20%, or age ≥65 years plus at least one major disincentive for surgery (previous cardiac surgery, pulmonary artery systolic pressure >60mmHg).  
**Exclusion criteria:** peripheral arterial disease associated with significant tortuosity or an internal lumen diameter ≤7mm. | General anaesthetic | 30 day mortality: 18% (2 deaths in 30 days). |
| Grube et al, 2007<sup>5</sup> | Case series, 86 patients, CoreValve | Patient was considered high risk if there was a consensus among an independent cardiologist and cardiac surgeon that “conventional surgery would be associated with excessive morbidity and mortality”.  
**Inclusion criteria:** SAS with an area <1cm<sup>2</sup> or 0.6cm<sup>2</sup>/m<sup>2</sup>, with or without aortic regurg and | General anaesthesia or with just local anaesthesia in combination with a mild systemic | Procedural mortality: 6%, 30-day mortality 12%. |
age ≥80 years or a logEuroSCORE of ≥20% for the 21F group and age ≥75 or logEuroSCORE ≥15% for the 18F group, or age ≥65 years and at least one of the following: 1. cirrhosis of liver, pulmonary insufficiency, previous cardiac surgery, pulmonary hypertension >60mmHg, porcelain aorta, recurrent pulmonary embolus, right ventricular insufficiency, thoracic burning sequelae with contraindication for open chest surgery, history of mediastinum radiotherapy, severe connective tissue disease with contraindication for surgery, or cachexia (BMI ≤ 18kg/m²); 2. echocardiographic aortic valve annulus diameter ≥20 and ≤27mm; 3. diameter of the ascending aorta ≤45mm at the sinotubular junction.

Exclusion criteria: hypersensitivity or contraindication to study meds, sepsis or active endocarditis, excessive femoral, iliac or aortic atherosclerosis, calcification, or tortuosity; aortic aneurysm; bleeding diathesis or coagulopathy; recent MI or cerebrovascular accident; mitral or tricuspid valvular insufficiency (>grade II); left ventricular or atrial thrombus; uncontrolled atrial fibrillation; previous AVR; polyarterial patients with either severe iliac or aortic vascular condition that make an insertion impossible or symptomatic carotid or vertebral arteries narrowing (>70%) disease or abdominal/thoracic aortic aneurysm; progressive disease with life expectancy <1 year; pregnancy; or creatinine clearance <20ml/min.

Preintervention screening: "Included transthoracic and transoesophageal echo, carotid and arteriovenous duplex ultrasonography, computed tomography angiography, optional cardiac MRI, invasive cardiac evaluation with coronary arteriography and left ventriculography"
| Study               | Type         | Patients | Valve          | Inclusion Criteria                                                                                                                                                                                                                                                                                                                                 | Exclusion Criteria                                                                                                                                                                                                                      | Anaesthesia                                      | Notes                                                                 |
|---------------------|--------------|----------|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| Cribier et al, 2006 | Case series  | 27 patients, Edwards valve | (doesn’t separate out antegrade and retrograde patients).  
*Inclusion criteria:* SAS ($\leq 0.7\text{cm}^2$), NYHA IV dyspnea, who were expected to benefit from isolated valve replacement. Patients had to be “refused for standard aortic valve replacement by two independent cardiac surgeons” on the basis of their high risk for surgery (Parsonnet’s score $\geq 30$). |  
*Exclusion criteria:* vascular disease that precluded access, severe deformation of the chest, intracardiac thrombus, unprotected stenosis of left main coronary artery not amenable to percutaneous intervention, MI within 7 days, prosthetic heart valves, active infection, leucopenia, coagulopathy, active bleeding, acute anemia (Hb $<9\text{mg/dl}$). Patients who could not be fully dilated with a 23mm aortic valvuloplasty balloon and patients with a native aortic valve annulus size $>24\text{mm}$ or $<19\text{mm}$ | Mild sedation and local anaesthesia | Doesn’t separate out retro and antegrade patient outcomes |
| Webb et al, 2007    | Case series  | 50 patients, Edwards Valve | “High-risk severely symptomatic patients”, logEuroSCORE = 28%. Comorbidities included CAD, moderate to severe mitral regurg, severe lung disease, prior thoracotomy, porcelain aorta, severe pulmonary hypertension, prior cerebral ischemic events, severe debility. |  | Usually under general anaesthetic with endotracheal intubation | Successful implantation in 86%. Intraprocedural mortality was 2%. 12% mortality at 30 days in those with log EuroSCORE=28%. Different outcomes for first 25 patients v last 25 patients. Outcomes improved over time. |
Addendum 2:

Provisional Key Performance Indicators (KPIs) to monitor PAVR service

2.1 Introduction

Performance indicators are an essential part of the quality improvement focus recommended by a collaborative approach to clinical governance. These process outcomes should be selected with the agreement of those expected to record the required data and the following examples are put forward as draft suggestions.

In general we have selected measurable and specific outcomes that have evidence suggesting that they can, to some extent, be influenced by clinical decisions. Ideally these KPIs should be benchmarked against other providers and targets and time frames set so that progress towards any agreed objectives can be monitored. In discussing KPIs it is also important to have the demographic components that reliably contribute toward a measure of risk or severity for comparison.

We have broadly grouped these into six major domains of quality based on IOM report categories;

- Effectiveness
- Efficiency
- Equitability
- Safety
- Timeliness
- Patient centred outcomes

Heart disease is recognised as one of the biggest killers in the United Kingdom and has been targeted as a key area by the Government, for quality improvement within the National Health Service. The Health Care Commission and the Society for Cardiothoracic Surgery already monitor outcomes for cardiothoracic surgery including survival data.

2.2 Effectiveness outcomes

- Insertion success (operative)
- Functional improvement (NYHA symptom class at one year)
- Readmission rates in first year
2.3 Efficiency outcomes

- Procedure codes used (HRG) and tariff costs
- Length of stay, (total, critical care and HDU)

2.4 Equitability

- Compliance with agreed patient selection criteria
- Age and demographic details
- Euroscore risk or equivalent

2.5 Safety

- Complication rates e.g. bleeding within 30 days or rescue surgery
- 30–day mortality
- Mortality cause (especially non-cardiac)

2.6 Timeliness/access

- Waiting times for procedures

2.7 Patient quality of life outcomes

- Patient satisfaction
- Scores of dependency

Some of these indicators would be more easily collected if a registry of patients undergoing PAVR were initiated.
Addendum 3:

Cost model: comparison of direct and maintenance costs associated with surgical valve replacement, PAVR and conservative treatment

The draft cost model that follows illustrates a tool that Bazian can develop for commissioners and healthcare professionals. The purpose of such a model is to demonstrate direct costs associated with procedures, in this case those associated with treatment of patients with severe, symptomatic aortic stenosis. Follow up costs to a specified time can be incorporated. Importantly, the model is not a cost-effectiveness model.

The model is interactive and users can enter data that represent local populations, hospital stays, and annual maintenance costs. The cost model (an excel workbook) has been sent in an email to the SCG.
References


