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Short Report protocol

Cost effectiveness of Transcatheter Aortic Valve Implantation (TAVI) for Aortic Stenosis in patients who cannot undergo surgery

Produced by: West Midlands Health Technology Assessment Collaboration
Unit of Health Economics and
Unit of Public Health, Epidemiology & Biostatistics
University of Birmingham
Edgbaston
Birmingham B15 2TT

Authors: Rosanna Orlando[1]
Mary Pennant[2]
Stephen Rooney[3]
Sue Bayliss[2]
Ahamedali Hassan[2]
David Moore[2]
Pelham Barton[1]

[1]Unit of Health Economics, University of Birmingham
[2]Unit of Public Health, Epidemiology & Biostatistics, University of Birmingham
[3]Department of Cardiac Surgery, Queen Elizabeth Hospital, Birmingham

Correspondence to: Pelham Barton
Unit of Health Economics,
University of Birmingham
Edgbaston
Birmingham B15 2TT

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Assessment Question

The objective of this short report is to determine the cost-effectiveness of transcatheter aortic valve implantation (TAVI) compared to Standard Therapy in patients who require aortic valve replacement but are high risk or not fit for conventional surgery.

Background

Aortic stenosis is the commonest indication for aortic valve replacement. The majority of cases of aortic stenosis are secondary to either calcific degeneration or congenital bicuspid aortic valve.

Aortic stenosis

Aortic stenosis is a degenerative condition in which the aortic valve becomes progressively narrowed leading to gradual obstruction of left ventricular outflow at the level of the aortic valve. The prevalence of this pathology increases with age, the majority of people treated being above 60 years of age.[1] Chronic aortic stenosis causes pressure overloading of the left ventricle which becomes hypertrophied to maintain the stroke volume and cardiac output. Under these circumstances the patient may remain asymptomatic for many years. However with longstanding hypertrophy the ventricle will eventually become less compliant and symptoms of breathlessness, angina or collapse will develop. In the late stages of aortic stenosis the left ventricle will dilate. For patients who present in congestive heart failure mean survival is less than a year.

Different outcome measures are used to assess the severity of the condition and these are based on clinical assessment. They include the following:

- The New York Heart Association (NYHA) heart failure classification is used to classify the severity of breathlessness: from class I, in which the patient has no limitation in daily physical activity, to class IV, in which the patient is breathless at rest. NYHA is a functional classification system linking the patient's symptoms and quality of life to normal life qualities (www.americanheart.org).

- Haemodynamic assessment may involve measurement by echocardiography and/or Doppler. Aortic valve area (cm^2) is assessed relative to body surface area (in m^2). Aortic valve area <0.6 cm^2/m^2 indicates severe aortic stenosis. Transaortic gradient (mmHg) measures the blood volume flow rate through the aortic valve. Peak transaortic valve gradient >64 mmHg and mean transaortic valve gradient >40 mmHg indicates severe aortic stenosis.[2]

Treatments for aortic stenosis (in the absence of TAVI)

Surgical aortic valve replacement is the reference treatment for aortic stenosis with around 60,000 operations conducted in Europe annually.[1] Surgical aortic valve replacement involves replacing the diseased valve with a prosthetic mechanical or biological valve through a median sternotomy and using cardiopulmonary bypass. This surgical procedure consists of an incision along the sternum, after which the sternum itself is divided to provide access to the heart and lungs for surgery. The cardiopulmonary bypass is a circulatory support technique that temporarily takes over

the function of the heart and lungs during surgery, maintaining the circulation of blood and oxygen delivery to the body's tissues.[2]

Surgical risk of existing treatments

Surgical aortic valve replacement carries a very high risk for some patients, particularly those who are elderly and/or who suffer from concomitant illnesses. Risk factors include age over 80, previous cardiac surgery, chronic obstructive airways disease, peripheral vascular disease, previous stroke with residual deficit, poor left ventricular function, renal failure, diabetes and hypertension.[3]

Surgical risk assessment tools

- The European System for Cardiac Operative Risk Evaluation (EuroSCORE) calculates the predictive operative mortality of patients that undergo cardiac surgery. For high risk patients, the more accurate logistic EuroSCORE is used. This model is most commonly used in Europe; this type of scoring system also considers particular combinations of the risk factors (www.euroscore.org). Euroscore is limited in risk stratifying patients for aortic valve replacement as it is essentially designed to risk stratify patients undergoing CABG. However it is the most widely used system in the UK. It is also straightforward to use – by completing an online scoresheet with various patient factors the logistic euroscore will be provided for you in the form of a predicted mortality percentage.
- STS score is a risk model developed by the Society of Thoracic Surgeons based on clinical and demographic data in an adult population and used to predict operative mortality and morbidity after cardiac surgery. This scoring system has been developed in USA. The high surgical risk is defined by an STS risk score of 10% or higher (on a scale of 0% to 100%, with higher scores indicating greater surgical risk). The model is based on clinical and epidemiological data of a given population who have received cardiac surgery (www.sts.org). This is quite a sophisticated model that gives not only mortality rosk but also risk of major morbidity such as prolonged ventilation, stroke and renal failure
- The Ambler Risk score has been developed in UK and is able to predict the risk of in-hospital mortality for patients undergoing heart valve surgery. This scoring system seems to be the more accurate on target population considered in this report. In real practice surgeons evaluate the surgery mortality risk according to more than one risk scoring system and different associated clinical conditions. (http://www.ucl.ac.uk/statistics/research/riskmodel/index.html)

The British Cardiovascular Intervention Society (BCIS) and the Society for Cardiothoracic Surgery (SCTS) state that the patient's operative risk should be assessed by a multidisciplinary team (MDT). The multidisciplinary team should comprise two cardiac surgeons, two interventional cardiologists, an imaging specialist, cardiothoracic anaesthetists and experienced nurses who assess the cost/benefit ratio of open heart surgery and TAVI. The usual "High risk" patient eligible for TAVI will have a logistic EuroSCORE of ≥ 20 or an STS score of ≥ 10.[2]

Interventions which do not involve open surgery

Percutaneous balloon valvuloplasty has a limited role in the treatment of severe aortic stenosis in adult patients. It may be considered to provide palliative treatment for patients with considerable co-morbidity as relief of symptoms is likely to be temporary.[2]

Transcatheter aortic valve implantation

Transcatheter Aortic Valve Implantation (TAVI) is a procedure used as an alternative to open heart surgery for people with severe aortic stenosis. In highly developed nations, the request for valve surgery is increasing among older people, who may present with more co-morbidities and a higher incidence of concomitant coronary artery disease TAVI may allow aortic valve replacement to be undertaken in some of these patients who would previously have been considered too high risk for aortic valve replacement. This is highly specialised technology and is relatively new: the first human case was in 2002. There is a UK TAVI registry; the number of TAVI per year included in this registry was 67 in 2007, 272 in 2008 and 533 in 2009.[4] TAVI is currently restricted to high risk patients with severe aortic stenosis and absolute contraindications for surgery.[5]

TAVI aims to implant a bioprosthetic aortic valve at the site of the native aortic valve through a percutaneous route. The choice of the vascular route has been developed in order to reduce surgical trauma and the use of cardiopulmonary bypass associated with valve replacement. During the procedure, a biological valve is crimped into a delivery catheter. The delivery catheter is inserted either in the femoral artery through a small incision at the top of the leg (known as transfemoral, percutaneous, endovascular and transluminal approach) or between the ribs through the apex of the heart (known as transapical or transventricular approach).The valve is guided to the heart using radiological visual guidance. Usually the route of choice is the tarnsfemoral as this is deemed to be the least invasive for the patient. The transapical route is used if the transfemoral route is limited by atherosceloris or small calibre.[2]

A balloon catheter is advanced via the arterial system or the left ventricle over a guide wire and positioned within the opening of the aortic valve. The existing aortic valve is dilated in order to make room for the prosthetic valve. The new valve, mounted on a metal stent, is manipulated into position and is either self expanding or deployed using balloon inflation. Deployment leads to obliteration of the existing aortic valve.

TAVI may be carried out under general anaesthesia or spinal aneasthesia. The procedure requires a combination of echocardiography and fluoroscopic imaging to ensure accurate deployment of the valve. Prophylactic antibiotics and anticoagulation medication are administered before and during the procedure.[2]

Surgeons and cardiologists involved in TAVI undergo dedicated training in both patient assessment as well as the clinical procedure. In addition the valve companies provide a high level of technical support and proctors with considerable experience until the new centre has enough experience to run an independent programme.

Cost implications

TAVI is an expensive procedure, requiring a multidisciplinary team and substantial equipment to be available during the procedure. The approximate cost of the procedure has been estimated at £18,000.[1] However, successful implantation may reduce the need for later hospitalisation, so there is likely to be some cost saving to offset against the cost of the procedure.

Economic Evaluation

The objective of this short report is to determine the cost-effectiveness of transcatheter aortic valve implantation (TAVI) compared to Standard Therapy in patients who require aortic valve replacement but are high risk or not fit for conventional surgery. The cost-effectiveness analysis will adopt the perspective of the NHS. An incremental cost-effectiveness analysis will be conducted, with survival years as the main measure of the efficacy of the technology. The result will be presented as cost per additional year gained and if possible as cost per quality adjusted life year (QALY) gained.[6]

Cost effectiveness review

Initial scoping searches have been carried out to assess the volume and type of literature relating to TAVI for aortic stenosis.

National TAVI and aortic valve replacement registry is the most updated source of data. A trial published on the New England Journal of Medicine in October 2010[7] and other cohort studies summarised in Annals of Internal Medicine[8] also in 2010 represent relevant updated evidence about short term effectiveness. Ongoing trials have been found into the TAVI clinical trials registers searches.

A model published by Bazian in May 2008[1] contains TAVI cost data, the model is not a cost-effectiveness analysis but it contains both procedure-related costs and costs that may be incurred during one year of follow up for both TAVI and medical therapy.

Bazian reported that they had found no published studies or models that had assessed the cost-effectiveness of TAVI. We will carry out an appropriate search to determine whether this is still the case. If any relevant studies or models are found, we will appraise them using standard criteria[9]. Although we do not expect to find any/many studies, if any robust evaluations are identified, we will use them to inform our model.

Economic model

An economic model will be designed to represent the pathway of patients with severe symptomatic aortic stenosis who are high risk or unfit for surgery compared to standard therapy.

The standard therapy comparator will differ depending on the type of patient. For patients at high risk, but not contra-indicated for surgery, the most appropriate comparator may be surgery whereas, for patients contra-indicated for surgery, other therapies will be more appropriate comparators. It is recognised that there is likely to be considerable areas of 'grey' where the most appropriate treatment route for a particular patients is debatable. However, in order to make modelling for this project feasible, two separate patient groups will be considered. As was done in the PARTNER trial[7], the two patient groups will be assumed to be distinct:

Group 1 – Patients who are at high risk but are not contra-indicated for surgery. The comparator for this group will be surgery.

Group 2 – Patients who are contra-indicated for surgery. The comparator for this group will be other forms of standard therapy (not surgery).

Before and during the development of the model, a steering group, with expertise in TAVI and surgical techniques and other possible comparators, will be consulted to give guidance to the technical team on clinical pathways, treatment strategies and other factors that may influence the structure and content of the model. This group will also give clinical guidance to inform the suitability of model parameters. This group is currently being formed under the direction of our clinical expert (SR).

As far as possible, the model will be populated with data derived from the literature. Data required for the model based economic evaluation may include:

- Safety data:
  - In hospital mortality and procedure related complications. Those data will refer to intra-, post- and peri-procedure (in the latter, beginning with the patient's emergence from anaesthesia and continuing through the time required for the acute effects of the aesthetic and surgical procedures to abate). This procedure safety period will be extended from the time of hospitalisation for surgery to the time of discharge
  - Impact of procedural learning curve over procedural success and outcome for patients
  - Impact of choice of the specific valve and delivery methods on clinical outcome
  - Effect of age on peri-operative complication and post-operative quality of life
  - Vascular complication rate due to malfunctioning of the aortic valve and/or developed consequent to the TAVI procedure
  - Morbidity related to TAVI and medical therapy
  - Bleeding and renal insufficiency with the procedure and without it
  - Stroke, transient ischaemic attack, and myocardial infarction
  - Complications with associated treatments

- Effectiveness data:
  - Survival Rate short term and long term
  - Overall impact of medical treatment and TAVI on health related quality of life, expressed as Quality Adjusted Life Years (QALYs) if possible
  - Procedural success rate (successful implantation of aortic valve)
  - Haemodynamic improvements
  - Cardiac symptomatic improvement (measured as NYHA)

- Costs:
  - Procedural hospitalisation costs: the equipment, other resource use and costs associated with TAVI procedure (the procedure is generally performed in a hospital, in a cardiac operating theatre or a hybrid operating room:

sterilised and equipped with specific instrumentation needed for the procedure)

- Time and resources associated with multidisciplinary staff involved in the procedure's performance (cardiac surgeon, interventional cardiologist, anaesthetist, operating room assistant, echographist)
- Diagnosis, admission and maintenance costs of patients going under TAVI procedure and of those who stay on standard therapy (these costs will include hospital stay, ongoing medical management and readmission costs per patient)
- Repeat hospitalisation due to aortic stenosis or complications of the valve procedure (valve-related hospitalization rate)
- Outpatient resource utilisation

Literature searches to obtain data

In order to obtain data to populate the model, our starting point will be the 2008 Bazian report[1], the trial as reported in the NEJM[7], and the review of observational studies in the Annals of Internal Medicine[8].

We will update the searches in the Bazian report to ensure that up to date information is included. We consider these searches to be sufficiently robust. Wherever possible, model parameters will be chosen from studies where the data is most relevant to the decision problem.

Additional searches

Additional targeted searches may be performed on an ad hoc basis to seek information to populate parameters identified by the modellers that have not been obtained by other means.

Such information may include unit costs or prices, required to be attached to each resource item so that the overall cost per patient can be calculated. Some hospital resource utilisation and costs data are reported in the Bazian report[1] but the two main sources will be the "Unit cost of health and social care[10]" published by (PSSRU) Personal Social Services Research Unit 2009 and the NHS Reference Cost.[11]

Other sources of data

It is anticipated that data from controlled trials on long term outcomes and quality of life may not be found in the literature searches. Additionally, there does not appear to be data available from controlled trials of the effectiveness of TAVI in patients who are high risk, but not contra-indicated, for surgery (patient group 2 in the model).

In order to address these points of concern, we have made contact with the study author of the PARTNER trial. Findings for one arm of this randomised controlled trial are currently published.[7] The published data is for patients who are contra-indicated for surgery (patient group 1 in the model). The study author has provided us with data on patient quality of life at 1 year.

The other arm of the PARTNER trial involves the randomisation of patients who are high risk, but not contra-indicated, for surgery (patient group 2 in the model). We have requested data from this arm of the trial. These results are due to be presented in spring 2011 and, if it is available before March 2011, the authors have provisionally agreed to provide us with that data.

A further source of data may be the national cardiac surgery register. We will take advice from the steering group as to whether this is a useful source of data for the model and, if so, how best to access the relevant information.

Model structure and approach

The likely model structure will be based on a decision tree representing the short-term effects of TAVI. Longer term effects will be incorporated in Markov processes with a monthly time cycle. TreeAge software will be used – this software is appropriate for the model structure proposed.

Markov models are able to represent clinical situations where patients change health states or experience recurrent events over a long period of time.[12] Health states to be included in this model are likely to be based on repeat hospitalisation, mainly due to left ventricular failure.

In the base case analysis, the time horizon for the model will approximate a lifetime model. Alternative analysis will be run with a shorter time horizon of 2 years to reflect the information available from trial data.[7]

An incremental approach will be adopted with a focus on additional costs and gain in benefits. Discounting adjustments will be made to reflect the differential timing of costs and outcomes in terms of extension to the length of life associated with the procedure.

Sensitivity analysis and presentation of results

Both deterministic and probabilistic sensitivity analysis will be conducted. Deterministic analysis will include consideration of alternative scenarios and may also include unvaried sensitivity analysis in which key parameters are individually varied within their plausible range. This will help us to find the parameters that drive uncertainty.

Probabilistic sensitivity analysis considers overall parameter uncertainty by constructing distributions for values of model parameters, either singly or jointly, as required to allow for correlation between uncertainties in parameters.[13] Results will be presented in graphical formats including cost-effectiveness scatter plots and cost-effectiveness acceptability curves.[14]

Project timetable

The proposed duration for this project is 5 months

Five months Project Task	Nov 2010	Dec 2010	Jan 2011	Feb 2011	Mar 2011
Preview protocol development					
Searching and collecting studies					
Study assessment, data extraction					
Evidence synthesis					
Economic modelling					
Progress report to NCCHTA					
Writing draft report					
Internal peer review					
Final report and paper writing					

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