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Summary

Transcatheter aortic valve implantation: Evaluation of the evidence and synthesis of organizational issues

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Context

Aortic valvular stenosis, or narrowing of the valve orifice, is a progressive disease that generally affects patients over the age of 65 years in Western countries and is usually caused by degenerative calcification. Aortic stenosis causes increasing resistance against the ejection of blood from the left ventricle towards the aorta. After symptoms appear (dyspnea, angina, syncope), the disease rapidly progresses causing severe limitation of physical capacity, heart failure, and high risk of mortality. Aortic stenosis represents the third most common cardiovascular disease among adults and the most frequent cardiac valve illness among elderly persons in the industrialized world. Its prevalence is estimated at 2.8% in the population aged 75 and older in the United States. In Quebec, the number of octogenarians will double to about 780,000 persons by 2035, representing about 9% of the total population. Aortic stenosis will thus become more frequent and is expected to have an increasingly important impact on the Quebec health care system.

Until recently, the only effective therapy for severe or symptomatic aortic stenosis was surgical valve replacement, but about a third of elderly patients can be refused this procedure due to their health status or aortic anatomy, which renders surgery too risky. In 2002, a percutaneous technique for implanting an aortic valve was developed, allowing the delivery by catheter and deployment of an aortic valve bioprosthesis, without recourse to open-heart surgery. Since then, the number of transcatheter aortic valve implantations (TAVIs) carried out worldwide has increased at a rapid rate. However, there are no Canadian clinical practice guidelines specific to TAVI, and the criteria for selection of patients raise important questions.

Currently in Quebec, several institutions either have already set up a TAVI program or are in the process of doing so. A narrative review of the literature up to 2009 and an analysis of the Quebec experience was published in 2010 by a working group of the Réseau québécois de cardiologie tertiaire (RQCT). Following the release of this document, the ministère de la Santé et des Services sociaux (MSSS) recommended that this procedure be used only for patients who cannot be treated by traditional surgical methods due to an excessive risk of complications and be offered only by university hospitals or institutes with experienced multidisciplinary teams (performing a minimum of 30 procedures a year). Also, the MSSS gave the Institut national d'excellence en santé et en services sociaux (INESSS) the mandate to perform an evaluation of TAVI.

The objectives of this evaluation are to:

1. Synthesize, via a systematic review, the recent evidence on effectiveness, safety and economic issues related to TAVI using the Cribier-Edwards / Edwards SAPIEN or CoreValve bioprostheses for adult patients with severe, symptomatic aortic stenosis, with an emphasis on clinical results at 1 year; and to
2. Synthesize, via a narrative review, the principal organizational aspects of delivering this procedure, including the selection of patients before implantation and key considerations concerning ethics and the patient's perspective.

Methods

A systematic search of the scientific literature published between January 2008 and January 2011 was carried out using bibliographic databases, 2008 being the year when clinical results on mortality at 1 year began to become available. Given the relative lack of publications from registries, on quality of life and

regarding economic issues, we also selected several oral presentations from scientific conferences. Using primary research articles and registry reports that provided survival data at 1 year as the main source of information, we examined clinical results for TAVI patients at 30 days and at 1 year.

In order to summarize issues pertaining to organizational aspects and patient eligibility, we retrieved relevant information from the following sources: 1) the most recent expert consensus documents from North America and Europe; 2) health technology assessment (HTA) reports published between 2008 and 2010, and the 2011 update of a report by the National Institute for Health and Clinical Excellence (NICE); 3) relevant articles retrieved from our literature search; and 4) a key research article and accompanying editorial, published in June 2011, concerning cohort A of the PARTNER randomized controlled trial.

Results

In the systematic review of clinical results, 17 studies met our selection criteria: 13 were research studies (1 randomized controlled trial, 4 controlled cohort studies, 8 case series), and 4 were analyses of registries (2 national, 2 from industry), which can be considered as case series. Most studies were from outside North America. In the clinical trial (PARTNER B cohort), 179 patients were randomized to transfemoral TAVI, and 179 were randomized to medical treatment (most of the patients in this group also underwent balloon aortic valvuloplasty (BAV) for aggravation of their aortic stenosis). We also retained 3 HTA reports and 2 systematic reviews.

In each of the 17 studies, the patients eligible for TAVI were considered either inoperable, not suitable for surgery or at high surgical risk. In almost every study, it was indicated that patient selection was based on the consensus decision of a multidisciplinary team. In general, TAVI patients were elderly (with a mean age of at least 81 years) and the majority were in New York Heart Association (NYHA) class 3 or 4, but the extent of surgical risk varied greatly across studies.

Based on our systematic review of effectiveness, safety and economic issues related to TAVI, we noted the following:

1. Effectiveness of TAVI at 1 year is promising with regard to survival. However, clinical results (survival at 1 year, adverse events in the first 30 days and in the first year) vary greatly across the 17 studies. This variability is also noted in HTA reports and other systematic reviews. The variability is partly a result of heterogeneous patient selection criteria, but points to an overall uncertainty regarding risks and net benefits.
2. Globally, survival at 1 year varies from 63% to 87% in the research studies and from 76% to 85% in the registries. In cohort B of the PARTNER trial, the absolute difference in survival between patients randomized to transfemoral TAVI and those randomized to medical treatment / BAV was 19% (69% versus 50%, respectively).
3. Impact on quality of life and functional status (NYHA classification, 6-minute walking test) at 1 year is promising, according to a subgroup of 7 and 8 studies respectively, including the randomized controlled trial.
4. Among adverse events, the risk of stroke is of great concern (7.8% for major stroke at 1 year in the PARTNER B cohort) given the associated high rate of morbidity and mortality.
5. Risk of readmission to hospital due to deterioration in clinical status following the procedure was only reported in the PARTNER B trial and was 22.3% in the first year after TAVI.
6. There are a number of important limitations in the current scientific literature on TAVI:
    - The overall level of evidence is moderate, given that only one relatively small randomized controlled trial is available and that it has some limitations in terms of methodology and generalizability, a major one being the very high recourse to BAV in the medical group, a procedure now rarely used in Quebec. The non-randomized clinical studies are supportive, but represent lower quality evidence.

- While the registries provide favourable “real-world” data, the registry results currently available are limited in terms of time frame and completeness of the variables included.
- Regarding durability of the bioprostheses, the longest follow-up period in the published literature is currently 3 years, in a single study.
- Effectiveness and safety are related in part to operator performance.
- The economic literature is insufficient at present (7 documents retained, with only 1 peer-reviewed) to draw conclusions about the cost-effectiveness or cost-utility of TAVI in the Quebec context.

The following conditions for a TAVI program were consistently noted in the literature consulted:

- Limiting the procedure to patients judged to be inoperable or having high surgical risk;
- Limiting the procedure to a small number of expert, specialized centres performing a high volume of procedures;
- Fostering a collaborative environment for interventional cardiologists, cardiac surgeons and other specialists in a multidisciplinary TAVI team;
- Tracking outcomes with a view to quality assurance using clinical registries that employ standardized definitions of variables and methods of reporting.

Recommendations

Considering the results of our evaluation and discussion of these with a scientific committee of Quebec clinical experts, INESSS makes the recommendations listed below.

Patient selection criteria

- TAVI can be considered for patients with symptoms attributable to severe aortic stenosis and for whom valve replacement surgery is contra-indicated or judged to be excessively risky.
- In addition, there must be a reasonable probability that quality of life (related to functional capacity, autonomy, and activities of daily living / domestic activities) would significantly improve following the procedure and be maintained for at least 1 year. Although the criterion of 1 year is unavoidably arbitrary, we believe this is a reasonable minimal length of time not only for survival, but for improved quality of life, given the associated risks of the procedure and the resources necessary for its use.
- Patient selection criteria that are clear, applicable and as objective as possible must be developed to define inoperability (that is, ineligibility for surgery) and eligibility for TAVI in order for these to be the same for all performing centres.

Patient selection process

- A multidisciplinary team, including cardiologists and cardiac surgeons, must evaluate the overall state of each patient to decide whether to offer TAVI after examining cognitive function, frailty and physical status, as well as all other relevant dimensions. The majority of patients referred for TAVI being elderly, the active implication of a geriatrician is clearly important.
- Ideally, the opinion that a patient is at excessively high risk for valve replacement surgery or that surgery is contra-indicated should be based on the consensus of at least 2 cardiac surgeons.
- The therapeutic choices considered appropriate and the results of the TAVI selection process should be clearly communicated to and discussed with the patient.
- The patient should be made fully aware of the relative novelty of TAVI and of its potential complications (cognitive difficulties, stroke, embolic events, the need for a pacemaker, readmissions to hospital, etc.).

- The fundamental importance of the patient's perspective must be taken into account with respect to the needs and expectations associated with the therapeutic choices being offered by the medical team.

Organizational issues related to the practice of TAVI

- The number of centres performing TAVI in Quebec must be limited in order to maintain a sufficient volume of procedures in each hospital. The requirements for establishing a program as well as the manner in which procedures are distributed across centres should be worked out in concrete terms.
- Adequate and dedicated funding is necessary to ensure the sustainability of TAVI programs in the different centres. This funding should cover costs related to patient selection, the TAVI procedure (including the cost of the bioprostheses) and short- and long-term follow-up of TAVI patients.

Requirements for performing centres

- Each centre should establish a multidisciplinary team made up of the following: cardiologists, cardiac surgeons, anaesthesiologists, geriatricians, rehabilitation specialists and social workers, among other health care professionals.
- Close collaboration between interventional cardiologists and cardiac surgeons is critical. At least one interventional cardiologist and at least one cardiac surgeon should be available for each TAVI procedure.
- Members of the multidisciplinary team must be appropriately trained on evaluation of TAVI eligibility and performance of the procedure according to quality standards recognized by professional associations and used to accredit institutions.
- The eligibility evaluation should be documented for all patients considered for TAVI. This should include specifying the reasons for which a patient is deemed ineligible for cardiac surgery or for which an eligible patient refuses the TAVI procedure.
- Definitions of adverse outcomes should be standardized across the province, ideally in a manner consistent with those used in other regions.
- Centres should follow up on TAVI patients by collecting information on standardized indicators of benefit (such as quality of life, functional status, cognitive function, destination on discharge and readmissions to hospital after TAVI), in addition to survival, in the short and long term.
- According to our meta-analysis of research studies, a minimal survival rate at 1 year of 65% in each centre is reasonable.

Provincial registry

- Centres performing TAVI must participate in a provincial registry. The budget allocated for TAVI should include the costs of maintaining this registry.
- The main purpose of the registry will be the collection of data regarding baseline characteristics of all patients (including those evaluated, but not treated with TAVI), the TAVI procedure, adverse events and other patient outcomes.
- Ideally, the registry would include cost variables allowing for a formal economic evaluation of TAVI in the Quebec health care context.