TITLE: Transcatheter Aortic Valve Implantation: A Critical Appraisal of a Health Technology Assessment and Comparison with a Rapid Review

DATE: 21 April 2010

CONTEXT AND POLICY ISSUES:

In January 2010, CADTH's Health Technology Inquiry Service completed a rapid review on the clinical effectiveness, cost-effectiveness, and guidelines for use of percutaneous heart valve replacement (both aortic and pulmonary valves). Concurrent with the completion of CADTH's rapid response report, the Technology Assessment Unit of the McGill University Health Centre (MUHC) published an evaluation of transcatheter aortic valve implantation (TAVI). The MUHC report included a systematic review of the literature, a case series report of the first 12 patients who underwent TAVI at MUHC, and estimates of the average net cost per patient and annual budget impact of adopting the procedure.

This report will summarize and critically appraise the MUHC TAVI health technology assessment (HTA) report and compare its methodology and findings to that of CADTH's rapid response report.

RESEARCH QUESTION:

How does the MUHC HTA on transcatheter aortic valve implantation align with findings from CADTH's percutaneous heart valve rapid response report?

METHODS:

The MUHC TAVI report was summarized and critically appraised using Oxman and Guyatt's Index of the Scientific Quality of Research Overviews.
SUMMARY:

Findings of the MUHC TAVI Report

The purpose of the MUHC TAVI report was to assess the clinical benefit and potential harm associated with TAVI through a systematic literature review and assessment of clinical data from the first 12 patients who underwent the procedure at their centre. Individual studies were identified through searches of MEDLINE and EMBASE online databases. The database searches were limited to English and French publications from 2002 onward. There was no restriction on study design, but studies had to be published in peer-reviewed journals and case series reports had to include 10 or more cases in order to be included. Further, in order to be included, the surgical insertion of the valve had to involve trans-femoral or trans-apical routes. Studies which used a trans-septal approach to valve insertion were excluded as this approach is no longer used in practice. Online databases of HTA reports were also searched to identify any existing reports.

The search identified three systematic reviews, one guidance document from the National Institute for Clinical Excellence, and 17 research publications, 16 of which were described as case series reports (n=616) and one of which was described as a report from a multicentre registry (n=646). Across the 17 publications, data from 1262 patients were available. Data from the 16 case series were pooled to determine the mortality rate at 30 days, the late mortality rate, functional improvement, and complication rate. In addition to the published data, unpublished data were also obtained from the SOURCE Registry, which includes 30 day follow-up data on 1380 TAVI’s performed at 32 centres in Europe, and from the Canadian Transcatheter Aortic Valve Implantation Program (CTAVIP), which included 339 TAVI’s performed in six hospitals in Canada. Outcomes of the 12 cases undergoing TAVI at MUHC were also reported. The outcome data from the various data sources are listed in the Table 1.

Table 1: Outcomes from the Data Sources Included in the MUHC TAVI Report

<table>
<thead>
<tr>
<th></th>
<th>Case Reports (16 studies of 616 patients)</th>
<th>Registry Report (1 study of 646 patients)</th>
<th>SOURCE Registry (1380 patients)</th>
<th>CTAVIP (339 patients)</th>
<th>MUHC Cases (12 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success Rate*</td>
<td>93%</td>
<td>97%</td>
<td>94%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>30-day Mortality</td>
<td>10%</td>
<td>8%</td>
<td>8.5%</td>
<td>10.4%</td>
<td>0%</td>
</tr>
<tr>
<td>Late Mortality</td>
<td>Six Months (assessed in 6 studies): Range: 3% to 26% - data not pooled</td>
<td>Not reported</td>
<td>Not reported</td>
<td>One Year: 24%</td>
<td>One death approximately seven weeks post-surgery (unrelated to procedure)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Two year: 35%</td>
<td></td>
</tr>
<tr>
<td>Functional Improvement</td>
<td>80% to 100% in those cases that reported this outcome - data not pooled</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>All surviving patients reported to be functionally improved according to NYHA Class</td>
</tr>
<tr>
<td>Complications</td>
<td>Described as variable and expected in</td>
<td>Not reported</td>
<td>Major access site complication:</td>
<td>Major access site complication:</td>
<td>7 Serious procedure related complications</td>
</tr>
</tbody>
</table>
The authors of the MUHC TAVI report stated that the included systematic reviews differed in their conclusions, with one report stating that TAVI should receive provisional recognition for insurance and another stating that because of safety concerns and a lack of a well defined target population, reimbursement of TAVI could not be defended.

Based on the included cases series and registry data, the authors of the MUHC TAVI report summarized that TAVI could be carried out with an expected mortality rate of 8% to 10% at 30 days, but that the mortality rate at one to two years was much less certain. They further stated that serious, but manageable complications could be expected in 25% to 30% of cases. They went on to conclude that TAVI is a feasible procedure that can provide relief of symptoms in those that survive, but did note that the mortality risk was high and the long-term prognosis was uncertain. The mortality rate in absence of TAVI was described as unknown due to the absence of data from randomized controlled studies.

### Critical Appraisal of the MUHC TAVI Report

The MUHC TAVI report was evaluated using Oxman and Guyatt’s Index of the Scientific Quality of Research Overviews. The methods used to identify the relevant literature were stated in the report and were reasonably comprehensive. While inclusion and exclusion criteria for the individual studies were described, it was not clear how these criteria were applied to study selection and it was not clear if measures were taken to avoid bias in the selection of studies. The authors did not report any criteria for validity assessment of the included studies. Thus, it was not clear if or how this was carried out. However, the validity of the included studies would have likely been considered low given that all included studies were case series. The methods used to pool data across the studies were not reported and the pooled results were described.
as a “weighted mean”. The findings of the studies did appear to be appropriately combined in order to address the research question. The conclusions of the report appeared to be supported by its findings, with the exception of one. The authors stated that TAVI “probably causes some overall extension of life.” Since there was no comparator group data presented (i.e., no data to describe duration of survival in absence of TAVI), it is unclear whether this statement is supported by the data. According to the Index’s rating scheme, this report would be considered to potentially have minor to major flaws. This is mainly because of lack of detail in reporting methods used to select studies for inclusion, assess quality of the included studies, and pool data for the analysis.

Comparison with the CADTH Rapid Response Report

The methods used in the CADTH rapid response report on percutaneous heart valve replacement differed from the MUHC TAVI report in a number of ways. First, the CADTH report was not a systematic review in that the literature was selected by one individual who also prepared the report. The MUHC TAVI report is described as a systematic review, but it is not clear if more than one individual selected the literature for inclusion and prepared the report. The language used in the report (i.e. plural) would suggest more than one individual was involved. In addition, the CADTH report was not restricted to aortic valve replacement; it included pulmonary valve replacement as well. Further, the CADTH report did not specifically exclude studies that used the trans-septal approach to valve insertion, whereas the MUHC report did as they stated that this approach was no longer used in practice. While there was no restriction on study design in the MUHC TAVI report, the CADTH report did not include case series unless they were captured by an HTA, systematic review, or meta-analysis (i.e. it was specified that individual studies had to include a comparator). The inclusion of other types of observational studies was restricted to those not already included in the HTA reports that had been identified and selected for inclusion. This is a standard approach used in CADTH’s rapid responses to avoid duplicate reporting of study findings. In terms of the literature search, the CADTH rapid response report did not search EMBASE, did not include French language studies, and went back to 2004. The MUHC TAVI report did search EMBASE, included French language studies, and searched back to 2002. The earliest case series included in the MUHC report was from 2007. Guidelines were summarized in the CADTH rapid response, but not in the MUHC report. The MUHC TAVI report pooled data where possible across the case series, while no pooling was done in the CADTH rapid response. Pooling is not typically carried out in CADTH’s rapid response reports.

The CADTH rapid response report included a HTA report that summarized findings of three other HTA reports and 25 case series or case reports of percutaneous aortic valve replacement. In addition, two cohort studies and two case control studies were included in the CADTH rapid response report. One of the two cohort studies was also included in the MUHC TAVI report, but it was classified as a case series and data on the patients undergoing alternate treatments (surgical valve replacement or symptomatic treatments) were not reported. The other cohort study was not included in the MUHC TAVI report. For the case control studies included in the CADTH rapid response report, one of the two studies was also included in the MUHC TAVI report, but was described as a case series, without reporting data from the control patients. Another difference was that the MUHC TAVI report included data which were obtained from their own centre and from unpublished registries. Thus, there were some differences in the included literature and the manner in which some studies were classified in the two reports.
Thirty day mortality was presented in both reports. The pooled estimate of 30 day mortality from the MUHC TAVI report was 10%. In the HTA report included in the CADTH rapid review, the 30 day mortality was 12% to 25% using trans-arterial retrograde insertion and 8% to 18% using the trans-apical approach. In the observational studies included in the CADTH rapid response, the 30 day mortality ranged from 9.5% to 25%. Conclusions of the CADTH rapid response were drawn in relation to other treatment options (surgical valve replacement, medical management, or valvuloplasty) and it was stated that the comparative safety and efficacy of percutaneous valve replacement were unknown. It was further concluded that there were methodological limitations to the available data, but that functional status appeared to improve with successful valve placement. The potential for major complications in those undergoing the procedure was noted. These concluding statements are similar to those of the MUHC report, even though the MUHC report addressed a slightly different question in that no comparator was used and the CADTH rapid response included pulmonary valve insertion as well as TAVI.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

In summary, despite addressing slightly different research questions and differences in the methodologies used in the two reports (the MUHC TAVI report was a systematic review while the CADTH report was a rapid review), the conclusions about the use of TAVI to treat patients with severe aortic stenosis who would not otherwise be surgical candidates for aortic valve replacement are similar. Both reports described the procedure as feasible and recognized the risks associated with undergoing the procedure and the potential for symptomatic relief. No information on cost-effectiveness was identified by either report. An update to the CADTH rapid review is currently underway and is due to be completed in May, 2010.

PREPARED BY:
Health Technology Inquiry Service
Email: htis@cadth.ca
Tel: 1-866-898-8439
REFERENCES:

