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Transcatheter Aortic Valve Implantation (TAVI) at the MUHC: a Health Technology Assessment

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Report prepared for the Technology Assessment Unit (TAU)

of the McGill University Health Centre (MUHC)

by

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Invitation.

This document was developed to assist decision-making in the McGill University Health Centre. All are welcome to make use of it. However, to help us estimate its impact, it would be deeply appreciated if potential users could inform us whether it has influenced policy decisions in any way.

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Contexte:

La sténose aortique sévère est une maladie incapacitante, accompagnée d'un taux de mortalité élevé. Le seul traitement efficace est le remplacement chirurgical de la valve aortique. Cependant, un âge avancé ou la présence de comorbidités importantes peuvent rendre impossible cette chirurgie. Mais récemment, une procédure a été développée selon laquelle une prothèse valvulaire peut être insérée, soit par un cathétérisme artériel rétrograde, ou soit par insertion transapicale au travers de la paroi thoracique.

Cette procédure fut approuvée de façon préliminaire au CUSM en 2007 à la condition que celle-ci fasse l'objet d'une révision formelle à l'intérieur d'une année. Ce rapport se fonde ainsi sur une revue systématique de la littérature et sur l'examen des dossiers des 12 premiers cas réalisés au CUSM.

Revue de la littérature :

Cette procédure fut introduite en 2002 et aucune étude randomisée n'existe sur ce sujet. Par contre, il existe 16 séries de cas et un registre multicentrique important décrivant cette procédure chez 1 262 patients. Enfin, des rapports non-publiés de deux autres registres sont aussi disponibles.

La revue des évidences disponibles nous indique que cette procédure s'accompagne d'un taux de mortalité à 30 jours de 8-10% et une mortalité subséquente approximativement de 24% et 35% après une et deux années, respectivement. Des complications sérieuses généralement bien gérées peuvent résulter de cette procédure chez 25% à 30% des cas. Enfin, les survivants peuvent s'attendre à une amélioration marquée de leur condition physiologique et symptomatique.

Expérience du CUSM :

Entre le 1er décembre 2007 et le 1er octobre 2009, 12 patients ont subi cette procédure au CUSM. Chez un patient, après que la valve se fut déplacée, l'on procéda à l'installation d'une nouvelle valve sous chirurgie à cœur ouvert. Par contre, pour les 11 autres patients, cette valve fut positionnée avec succès. Chez ces patients, la surface valvulaire estimée était augmentée et le gradient systolique moyen, diminué. Cette procédure n'entraîna aucun décès. Chez un patient, la dialyse fut stoppée sept semaines après la procédure à cause d'une qualité de vie médiocre. Les autres patients montrent une fonctionnalité améliorée, n'ont pas de signe de déficience cardiaque et présentent un état de santé aussi bon que leurs comorbidités et leur âge le permettent.

Les complications comprennent une tamponnade cardiaque suite à la perforation du ventricule droit, quatre complications au niveau de l'artère fémorale ainsi que le bris d'un cathéter qui nécessita une chirurgie pour son extraction. Toutes ces complications furent traitées efficacement dans la salle de cathétérisme.

Coûts :

Le coût moyen net par patient fut estimé à 24 024 $ et si l'on assume un achalandage de 30 patients par année, l'impact budgétaire anticipé serait de 720 719 $. Enfin, les données actuelles sont insuffisantes pour estimer le coût-efficacité.

Discussion :

Sans une étude randomisée de référence, la mortalité en l'absence de cette intervention ne peut être connue. Cependant, chez les patients symptomatiques tels ceux de ce rapport, il est probable que le taux de survie ne dépasse pas 2 à 3 ans. Ainsi il est probable, mais sans grande certitude, que cette intervention prolonge la vie des patients avec une amélioration marquée de leur condition physiologique et symptomatique.

Recommandations :

- Cette technologie est efficace et le CUSM devrait continuer de la supporter financièrement.
- Puisque cette procédure est relativement récente et que la sélection des patients de même que sa réalisation sont critiques pour sa réussite, la division cardiovasculaire devrait maintenir à jour un registre de tous les cas, incluant les suivis.
- Ce registre devrait être étudié par le CUSM dans environ une année de façon à réévaluer la décision de supporter financièrement cette technologie.

EXECUTIVE SUMMARY

Background

Severe aortic stenosis is a disabling disease with a high mortality. The only effective treatment is surgical replacement of the aortic valve. However, advanced age or serious comorbidities may render this impossible. Recently a procedure has been developed whereby a valve prosthesis can be inserted either via retrograde arterial catheterization or by trans-apical insertion through the chest wall.

This procedure was given preliminary approval at the MUHC in 2007 on the understanding that it would be the subject of a formal review within approximately one year. This report is based on a systematic review of the literature and examination of the records of the first 12 cases undertaken at the MUHC.

Literature review

This procedure was introduced in 2002. There are no randomized controlled trials. Published in peer reviewed literature there are 16 case series and one substantial multicentre registry describing the procedure in a total of 1,262 subjects. Unpublished reports from two other registries are also available.

Review of this evidence indicates the procedure can be carried out with an anticipated 30 day mortality of 8-10%, and a subsequent mortality of approximately 24% and 35%, at one and two years respectively. Serious but mostly manageable complications can be expected in 25-30% of procedures. Survivors can be expected to experience substantial physiological and symptomatic improvement.

MUHC experience.

Between December 1, 2007 and October 1,2009 12 patients have undergone this procedure in the MUHC. In one the valve became displaced and a new valve was installed using open heart surgery. In the remaining 11 the valve was successfully positioned. In these the estimated valve area was increased and mean systolic gradient diminished. There have been no procedure related deaths. In one patient dialysis was discontinued seven weeks after the procedure because of poor quality of life. The remaining patients are functionally improved, have no evidence of heart failure and are in as good health as can be expected in the light of their comorbidity and age.

Complications include one cardiac tamponade secondary to perforation of the right ventricle, four femoral artery related complications, and one catheter fracture that required surgical removal. All vascular complications were treated effectively in the catheterization room.

Costs.

The average net cost per patient was estimated to be $24,024. Assuming a turnover of 30 per year the anticipated budget impact would be $720,719. There are insufficient data on which to estimate cost effectiveness.

Discussion

Without a randomized control study the mortality in the absence of this intervention can not be known. However, it is probable that in symptomatic patients such as these, survival would be less than 2-3 years. Thus, it is probable but not yet certain that this intervention will prolong survival. In survivors there is significant functional and symptomatic improvement.

Recommendations

- This is an effective technology that should continue to be funded by the MUHC.
- Since this is a relatively new procedure, and one in which both the selection of patients and its execution are crucial for success, the Cardiovascular Division should maintain a registry, including follow-up, of all cases.
- The register should be examined by the MUHC in approximately one year at which time the decision to continue funding should be reviewed .

BACKGROUND

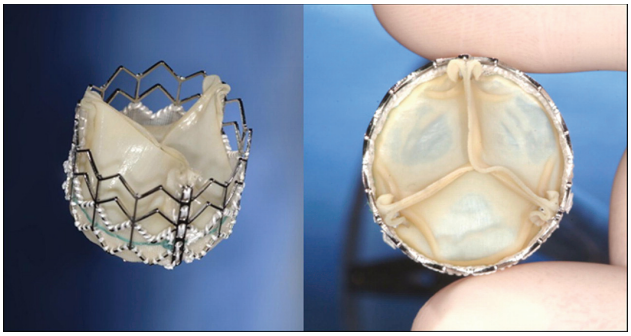
Calcific aortic stenosis is a disease of the elderly in which progressive deposition of calcium in the cusps of the aortic valve cause thickening and stiffness with consequent obstruction to the outflow of blood. The process is progressive and when it becomes severe causes left ventricular hypertrophy, myocardial ischaemia, heart failure, fainting attacks, and death which is sometimes sudden. It is a common abnormality, affecting between two and seven percent of individuals over the age of 65 in the USA[1, 2].

When intervention becomes necessary, the only effective measure is to replace the aortic valve, which until recently necessitated open heart surgery. However, in this elderly population, patients are not uncommonly too frail to undergo this procedure. Under these circumstances the only treatment up to now, other than medication, has been trans-aortic balloon angioplasty. This procedure, however, brings only temporary relief [3], and carries a risk of serious procedure related complications, ranging from 5% [4], >10%[3] to 25 %[5].

In 2002 Cribier and colleagues carried out the first successful transcatheter aortic valve implantation (TAVI) [6], and this procedure, with various modifications is now being increasingly used. A recent reviewer reports that prior to 2008 more than 2,400 aortic prostheses had already been implanted in this way[7].

The prosthesis can be introduced by retrograde catheterization of the femoral artery, or if the access vessels are too diseased, directly into the left ventricle through a chest wall incision. A third approach, using retrograde transvenous catheterization to enter the right ventricle, and then the left ventricle via trans-septal puncture has been largely abandoned.

There are two percutaneous aortic valves available for clinical use; the CoreValve Revalving System and the Cribier-Edwards Sapien Aortic Valve. The latter has been used for the first 12 cases at the MUHC. It consists of a balloon expandable stainless steel stent to which a bovine tri-leaflet pericardial valve is attached. The valve is placed in position either via the femoral artery or the left ventricular apex, depending on the presence and extent of peripheral vascular disease.



From: http://content.onlinejacc .org/cgi/content-nw/full/53/20/1829/FIG1

Neither prosthesis is licensed in Canada, or the USA. In the USA the devices are marketed under a Humanitarian Device Exemption (HDE) [7], and in Canada they are used under "special access" regulations. At the MUHC approval was given in late 2007 to carry out a limited number of cases on the understanding that the procedure would be the subject of a formal review in approximately one year. The first procedure was carried out in December 2007 and a total of 12 had been completed by October 1, 2009. The present review is undertaken at the request of Mr Gary Stoopler, Administrative Director of the Surgical and Medical Missions of the MUHC.

To determine the health benefits and risks of this procedure we carried out a systematic review of the literature (See Appendix 1), and reviewed the clinical data of the first 12 cases undertaken at the MUHC. .

LITERATURE REVIEW

The method employed is described in Appendix 1. No randomized controlled trials have

yet been published. In peer reviewed literature we identified three systematic reviews [7-9], an Interventional Procedures Guidance advisory [10]. , 16 case series[13,15,16,19-31] and one substantial multicentre registry based report involving a total of 1,262 subjects [11] totalling 17 publications describing percutaneous aortic valve replacement in 1,262 subjects. These are summarized in Table 1. In addition, we reported some findings from two substantial unpublished registries. The SOURCE Registry is a record of events up to 30 days following 1380 procedures (428 trans-femoral, 522 trans-apical) carried out in 32 European centres [12]. The Canadian Transcatheter Aortic Valve Implantation Program reports 339 procedures (transfemoral 168, trans-apical 172) carried out in six Canadian hospitals[13].

RESULTS (See Table 1)

The average age of patients in the case series summarised in table 1 varied from 78 to 85 years. These were seriously ill patients with numerous comorbidities and in general, this procedure appears to have been reserved for patients who required intervention, but for whom open surgery was considered too dangerous. The EuroSCORE risk score which purports to predict surgery-related mortality risk averaged 24%.

Most procedures consisted of retrograde catheterization carried out from an incision in the left femoral artery, while in a small number the valve was passed through the apex of the left ventricle via an incision in the chest wall. Both approaches were included in meta analysis.

The procedure was carried out successfully in 93% of the case reports , 97% in the registry based report [11], and 94% in the SOURCE registry[12].

Mortality,30 day.The average 30 day mortality was 10% in the case reports(Table 1), 8% in the registry based report[11] , 8.5% in the SOURCE registry[12], and 10.4% in the Canadian registry[13]. Most, but not all these deaths were procedure related, but patients were old and frail and several authors report significant mortality in patients awaiting

intervention.

Mortality, late. Reporting of late mortality in the case series was too inconsistent to permit of meta analysis. In the six studies that reported mortality at six months, mortality had not increased above the 30 day rate in three[15,16,21], but had increased significantly in three others [19,20,28](see Table 1). In two of the larger studies, mortality at approximately one year was 19%[29] and 28%[28]. The Canadian registry reports mortality rates of 24% and 35% at one and two years, respectively[13]. It is clear from the descriptions that much of the delayed mortality was unrelated to the surgical procedure and was associated with the advanced age and high comorbidity of these patients.

Functional improvement. All reports that include haemodynamic measurements indicate reduced trans-valvular gradients and increased valve areas post-operatively . In those reports that recorded functional improvement there was marked improvement in from 80% to 100% of patients..

Complications. In the case series that reported complications, the rates of serious complications were very variable (Table 1). Meaningful meta analysis of their frequency was not possible. Complications reported included stroke, major bleeds requiring transfusion, vascular problems at the site of access , vascular collapse requiring support, cardiac tamponade, ventricular fibrillation, infection , and myocardial infarction.

The rates of some complications reported by the two registries are as follows: Major access site complications 7%[12] and 13%[13]; Valve migration, malposition and embolisation, approximately 1.8%[12] and 7%[13]; Stroke 2.5%[12] and 2.3%[13]; Renal failure requiring dialysis 8.7%[12] and 2.6%[13]; need for a permanent pacemaker 7%[12]; Sepsis 2.9%[13].

Aortic regurgitation. While minor degrees of aortic regurgitation at follow-up were common, severe regurgitation requiring further intervention was very infrequent. Thus, the Canadian registry reports some regurgitation in approximately 80%, though in only 6.6% were these considered moderate, and in none severe[13].

Summary of the literature, leads us to conclude with confidence that this procedure can be carried out with an anticipated 30 day mortality of 8-10%, Prediction of late mortality is much less certain but rates of 24% and 35%, at one and two years are reasonable approximate estimates. Serious but mostly manageable complications can be expected in 25-30% of procedures. In almost all survivors, physiological and symptomatic improvement can be expected..

Systematic reviews differ in their conclusions. A French review carried out by the *Haute Autorité de Santé* (HAS) recommended that the procedure and the prosthesis should receive provisional recognition for insurance, for a period during which data should be collected and followed by a subsequent re-evaluation. Furthermore, the procedure should be limited to certain teams[8].

In the most recent systematic review, from Belgium, the authors reviewed all publications up to December 2008, and concluded that, "A reimbursement of the percutaneous aortic valve can currently not be defended because of patient safety concerns, and a poorly defined target population" [7].

MUHC EXPERIENCE

Patient selection:

At the MUHC patients with severe symptomatic aortic valve stenosis are referred for transcatheter aortic valve implantation when age and co-morbidities constitute an unacceptable risk for open heart surgery. Every patient is evaluated by a

multidisciplinary team consisting of two interventional cardiologists (Drs. Martucci and Beaudry), two cardiac surgeons (Drs. De Varennes and Lachappelle), two general cardiologists (Drs Crelinsten and Brophy), a critical care specialist (Dr Goldberg), and a clinical nurse (Ms. Comptois).

Preoperative tests include a transthoracic echocardiogram, a right and left heart diagnostic catheterization and angiogram, an iliofemoral contrast angiogram, and a computed tomographic angiogram. Only patients who urgently require intervention and are refused surgery on the grounds of risk are accepted. Patient preference for a percutaneous approach is not considered a valid reason for the procedure if a surgical option exists.

The procedure has not yet been approved for general use and can only be used under "special access" regulations . These require that once a case is accepted at the MUHC, it is presented to an international panel made up of all the percutaneous aortic valve implanters in North America via video-conference on a biweekly basis. After each case has undergone local and international assessment, the case is sent to the Therapeutic Products Directorate, of the Department of Health and Welfare, Ottawa, Canada for approval for compassionate use.

Procedure:

The procedure is performed in the catheterization laboratory with operating room ventilation standards, using full operating room-like sterile precautions. The procedure is performed under general anesthesia with transesophageal echocardiographic and fluoroscopic guidance. Because of the risk of peripheral vascular complications there is always a team of vascular surgeons on stand by. Once the procedure is completed the patient is transferred to the coronary care unit and ultimately to the cardiology floor.

Results: (See Table 2).

Between December 1, 2007 and October 1, 2009, 12 patients have undergone transcatheter aortic valve implantation at the MUHC.

Mortality**:** There have been no procedure related deaths and there has been no mortality in the first 30 post-procedure days. In one patient who was on dialysis, this was discontinued seven weeks after the procedure because of poor quality of life. (She had no symptoms of heart failure and her death four days later was due to hyperkalemia). All the remaining patients are reported to be alive, to have no evidence of heart failure, and to be in as good health as can be expected in the light of their comorbidity and age.

Technical outcome : In one case the valve prolapsed into the left ventricle and a new valve was installed by open heart surgery. In the remaining 11 the valve was successfully positioned. In these the estimated valve area was increased, from mean 0.7 to 1.2 cm^2 (normal, 2.0 to 3.0 cm^2)[3], and the mean systolic aortic gradient was diminished, from mean 55.9 to 13.1 mmHg). Post-procedure aortic regurgitation was absent or mild except in one patient in whom it was estimated to be "mild-moderate".

Complications : Serious procedure related complications were common. They included:

- One valve displacement, with conversion to open heart surgery and satisfactory recovery .
- One cardiac tamponade secondary to perforation of the right ventricle,
- Four iliofemoral artery related complications.
- One catheter fracture that required surgical removal.

All vascular complications were treated effectively in the catheterization laboratory.

Function : Of the 11 surviving patients, there have been no readmissions for heart failure or other cardiac related symptoms. All are reported to be functionally improved. At present nine are in New York Heart Association (NYHA) Functional Class I, and two in Class II, (down from 10 in Class III and one in Class IV).

Summary of the MUHC experience therefore, indicates that both the selection process and the interventions carried out so far appear to be highly satisfactory. The outcomes compare favourably with the published literature.

COST ESTIMATES

Estimates of the cost and budget impact are based on data supplied by the manufacturers and by the Department of Finance of the MUHC (M. Nicolas Robert). The duration of hospital stay of each patient for the six months preceding and following valve implantation was provided by the Department of Quality Management (Mme. Doris Dubé). The details of cost estimates are reported in Appendix 2.

Procedure Costs: The average cost per procedure was made up of the following components :

Evaluation, including clinical work up and tests =…… $3,714.20

Procedure, including hospital costs and supplies =……. $2,355.75

Non-reusable equipment = ……. $20,000.00

Total . $26,069.95

Preliminary evidence (Appendix 2) indicates that there is a reduction in hospital usage following the procedure, estimated at $2,046.00 per patient. Assuming that this benefit is maintained in the future, average net cost per patient ($26,069.95 -$2,046)=……**$24,023.95**

Estimated turnover. According to the report of the Groupe de Travail of the Réseau Québécois de Cardiologie Tertiaire[14] the provincial demand for this procedure is likely to be 200 per year. Following their recommendation that cases should be managed according to their RUIS of origin, the McGill RUIS should receive 46 cases per year. We will arbitrarily assume for the purpose of this initial estimate, a turnover of 30 per year.

Budget impact.Assume 30 procedures / year

($24,023.95 x 30) = ……..**$720,718.50**

Cost Effectiveness**.** There are too few follow-up data following valve placement and too much uncertainty as to the length and quality-of-life that would be experienced by these patients in the absence of the procedure , for any meaningful estimate of cost effectiveness to be undertaken.

DISCUSSION

The effectiveness of this procedure can be judged by its influence on morbidity and mortality. As regards the former there is no question that the survivors experience significant improvement in function and, although this has not been reported , in quality of life.

Survival Gain**.** If we judge the effectiveness of this procedure in terms of survival , we have to know the survival that could be expected in the absence of intervention, which is unknown. However, there is no question that the prognosis for patients with severe aortic stenosis who receive only medical treatment is poor.

Several authors report that deaths occur while awaiting surgery [15-17], and one author reports a 30% mortality at six months in patients who refused intervention[18]. In one study the four-year mortality of patients in whom the valve area was 0.6 cm was 76%[19]. In another, 55 patients with haemodynamically severe stenosis who refused operation

had a mean average survival of 23 months, while the mean survival after the onset of left heart failure was 11 months [2]. All patients in the MUHC series were reported to be in failure.

The onset of symptoms (heart failure, angina, blackouts) is reported to indicate a poorer prognosis . In one study the mortality rate at one and two years after the onset of one or more of these symptoms was 26% and 48% [20]. The Task Force of the American College of Cardiology and American Heart Association concluded that following the development of angina, syncope, or heart failure, the average survival is <2 to 3 years. [3]. It should be noted that all MUHC patients undergoing this procedure were symptomatic.

Although the mortality in the absence of surgery remains unknown these reports suggest that it would be high. Thus, in addition to symptomatic improvement for the 90% short-term survivors, it seems probable that this procedure may result in extension of life as well. However, this cannot be certain on the basis of present evidence.

Cause of death. The mortality rates determined from the literature review (see Table 1), include deaths from all causes, although usually, when judging the *safety* of a procedure, only the procedure related deaths are considered. However, when considering the *effectiveness* of a procedure it may be more appropriate to consider mortality from *all causes* (at least in the short term), because to put patients through this procedure would be a questionable "success" if they were due to die within the next few months from some unrelated cause. Judged on this basis, the MUHC results must be considered satisfactory, with zero deaths at 30 days and one death out of 12 patients (8%) at three months from an unrelated cause .

Thus, the effectiveness of this procedure is highly dependent on the way in which patients are selected. On the one hand it is necessary that all should suffer from severe aortic stenosis, and that frailty, age and comorbidity should be so advanced as to

exclude the option of open heart surgery. On the other hand, frailty and comorbidity should not be so severe as to make a reasonably symptom-free post-procedure survival for several months unlikely.

Cost considerations. It is probable that the expenditure of $720,719 per year will not be matched by any additional funding to the MUHC , and that this sum will come from existing budget . The health benefit that may result from this expenditure must be conjectural. However, given the same case selection and results as in the first 12 cases, it is likely to cause a substantial improvement in quality of life for possibly 27 of 30 patients for at least six months, and possibly an extension of life of improved quality for a diminishing number of patients, for several years thereafter.

Opportunity costs must also be considered. While the exact source within the budget of the approximately $720,719 can obviously not be identified, it represents resources that can not be used for other purposes. In value it is approximately equivalent to the sum required to maintain 5 hospital beds (direct costs of nursing, supplies and housekeeping) or to treat 152 bed patients for an average stay of 12 days .

CONCLUSION

In spite of a high mortality risk, and uncertain long-term prognosis, transcatheter aortic valve implantation is a feasible procedure that clearly gives survivors symptomatic relief and probably causes some overall extension of life . It can be carried out at the MUHC at a net cost of approximately **$24,024** per patient. The budget impact of the anticipated 30 patients per year would be approximately **$720,719**

RECOMMENDATIONS

- This is an effective technology that should continue to be funded by the MUHC.
- Since it is a relatively new procedure, and one in which both the selection of patients and its execution are crucial for success, the Cardiovascular Division should maintain a registry, including follow-up, of all cases.
- The registry should be examined by the MUHC in about one year at which time the decision to continue funding should be reviewed .

TABLE 1 Literature review

Author (Year)	*N*	*Prosthesis Thesis*	*Approach*	*Euro score*	*Age yr mSD*	*Procedure Success%*	*Perioperative Complications*	*30day Mort%*	*6 mth Mort%*	*Follow up(d)*	*Mort % at Folow-up*
Berry[15] (2007)	11	Core	Femoral	36	82(10)	100	Stroke 1,Major bleed 2.	18	n/a	305	27
Bleiziffer[21] (2009)	137	Core114, Ed Sap 23.	109 Femoral 23 Apical	23	81	98	Open Surgery 1, .,Resuscitation 8, Defib 2, Circl support 4, Effusion 5	12	23	97	21
Covello[22] (2009)	18	Edwards Sapien	Femoral	26	78 (8.7)	100	V Fib requiring IABP 1,Renal failure 1, Artrial fib 1, Stroke 1.	0	17	180	17
Descoutures [23](2008)	12	Edwards Sapien	Femoral	31	83(6)	83	Fem Art tear 2,Tamponade 1,Heart Block 1, Bleeding 2.	17	17	180	17
Grube[24] (2007)	86	Core	Femoral	22	82(5.9)	88	Stroke 7, Tamponade 6, MI 1,	9	n/a	n/a	n/a
Kapadia[25] (2009)	18			28	81(6)		Bleeding 7, Infection 2, , Prolonged ventilation 1, Perm pacemaker 1.	5	n/a	220	22
Spargias[26] (2008)	12	Sapien Edwards	8 Femoral 4 Apical	34	81(4.6)		Severe Aorticr regurg 1 .Cut down complications 2, Diathermy burn 1.	0	n/a	50	0
Otten[18] (2008)	39	Core		15	81(7)			3	3	395	13
Ree[27] (2009)	40	Cribier Edwards	Femoral	25	83(8)	83	Bleeding 5, Stroke 1, Infection 4,	13	n/a	n/a	n/a
Rodés[17] (2008)	22	Edwards Sapien	11 Femoral 11 Apical	26	84(7)	91	Massive Aortic Regurg 1, Severe Bleeding 1, Tamponade 1.	5	5	183	5
Svensson[28] (2008)	40	Edwards Sapien	Apical	13(sts)	83	90	MI 7,Emerg Cardiac surg 1,Stroke2,	18	n/a	143	38
Tamburino[29] (2009)	30	CoreValve	Femoral	25	82(5)	93	Tamponade 1, Bleeding 1.	7	n/a	147	7
Walther[30] (2008)	50	Edwards Sapien	Apical	28	82(5)	94		8	26	360	28
Webb[31] (2007)	50	Cribier Edwards	Femoral	28	82(7)	86	Stroke 1, MI 1, V Fib 2, Heart Block 2, Tamponade 1.	12	n/a	359	19
Webb[32] (2009)	25	SapienXT Edwards	Femoral	21	85	100	Non-disabling stroke 2, Circ support 2 (IABP 1, fem-fem 1).Bleeeding 3	0	n/a	n/a	n/a
Zierer[33] (2008)	26	Cribier-Edwards.	Apical	37	84(6.5)	100	Conversion to open surgery 2,.	15	n/a	n/a	n/a
TOTAL	616	**WEIGHTED MEAN**		24 (6.6)	82 (6.6)	93		10			
Piazza[11] (2008)	646	Core	Femoral	23	81(6.6)	97		8	n/a	n/a	n/a

Mort = Mortality, Bleed = Haemorrhage requiring transfusion, IABP = Intra-aortic Baloon Pump, Atrial fib = Atrial fibrillation, Tr-Sept = Trans-septal, A Regurg = Aortic regurgitation, Fem Art = Femoral Artery, (sts) = Society of Thoracic Surgeons, MI = Myocardial Infarction, V Fib = Ventricular Fibrillation, Circ = Circulatory, fem-fem = Femoral-Femoral.

TABLE 2 Summary of MUHC patients

PREOPERATIVE DATA									POSTOPERATIVE DATA							
Pt	Age	Sex	NY	Euro	STS	LVEF	Mean	Valve	Suggical	Hosp	Follow	NY	Aortic	LVEF	Mean	Valve
		M/F	HA	Score	%	%	grad	area	approach	days	up	HA	Regurg	%	grad	area
							mmHg	cm2			mths				mmHg	cm2
1	89	M	III	16%	15%	65	64	0.8	Femoral	5	9.0	I	Trace	55	11	1.9
2	79	M	III	19%	57%	30	50	0.7	Apex	19	9.0	II	None	30	7	1.9
3	77	M	III	40%	55%	40	27	0.7	Femoral	8	17.0	I	Mild	50	7	1.5
4	85	F	III	17%	7%	65	48	0.8	Femoral	36	17.0	I	Trace	75	13	1.5
5	85	M	III	71%	27%	20	40	0.9	Apex	26	8.0	I	Mi/mod	25	8	1.7
6	84	F	IV	45%	51%	45	38	0.9	Femoral	115	21.0		Trace			1.5
7	93	M	III	26%	16%	60	55	0.5	Femoral	5	18.0	I	None	60	9	1.7
8	75	M	III	31%	5%	20	26	0.9	Femoral	12*	4.0*	II*	Mild *	75*		
9	97	F	III	38%	21%	60	53	0.7	Apex	11	3.0	II	Mild	65	9	1.5
10	91	F	III	26%	12%	75	85	0.2	Apex	32	4.0	I	Trace	70	32	1.5
11	61	F	III	32%	6%	70	91	0.7	Femoral	5	12.0	I	Trace	70	25	1.3
12	94	F	III	18%	8%	60	75	0.6	Femoral	6	3.0	I	Mild	60	10	1.6
Mean			*I I I*			*57*	*0.8*			*I.2*			*14.3*	*1.6*		

* results following conversion to open heart surgery as described.

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APPENDIX 1

Methods: Literature Search

Major online databases for healthcare technology assessment [INAHTA, CRD, Cochrane, NICE, AETMIS, and CADTH] were searched for existing reports. MEDLINE [including: In-Process & Other Non-Indexed Citations] and EMBASE database searches were performed through Ovid Online. All searches were limited to citations published in either English or French since 2002 [when the technology was first introduced] to present. Keywords used in the searches included 'transcatheter aortic valve' AND ‘implantation OR replacement OR insertion' NOT 'valvuloplasty.’

We considered only data published in peer reviewed journals. Since the trans-septal approach has now been abandoned, we included only case series that described the placement of an aortic valve prosthesis via the trans-femoral and trans-apical routes. We also excluded series that included less than 10 cases. When it appeared that different publications were describing substantially the same case material we included only the most recent report.

APPENDIX 2

Costs Estimates

The costs considered are those incurred by the MUHC. They include direct costs of supplies, expendable equipment and salaries (excluding MD salaries that are not paid by the MUHC).

Evaluation

All patients with severe aortic stenosis requiring intervention, whether by surgery or percutaneous intervention, will undergo a transthoracic echocardiogram, and right and left heart catheterization with coronary angiography. The costs of these procedures are not considered.

Tests. When intervention is indicated but patients are considered incapable of undergoing open surgery they are evaluated for percutaneous valve replacement. This requires two further tests:

Iliofemoral contrast angiography [Code 8405*] =…….. $ 89.00

CT angiography [Code 8262*] =……..$ 43.40

Total =……$ 132.40

Of the first 73 patients evaluated in the MUHC, nine were selected to undergo surgery. It will be assumed that this ratio (approximately 8:1) is maintained in the future. Thus:

Cost of evaluation tests / procedure (132.40 x 8) = **$ 1,059.20**

Clinical Evaluation. As noted above, for each patient selected for this procedure eight must be evaluated. At the MUHC between December 07 and October 09 , 12 patients have undergone this procedure and approximately 96 patients have been evaluated. In addition, patients who undergo the procedure are followed up on four occasions during

the first year. Because of this increased activity it has been necessary to add one full-time clerical position and one part-time nurse to the MAUDE unit, at a cost of:

Clerical , $55,474 pa + Nursing ($48,343 x0.5) =…. $ 79,645 pa.

Assume 30 cases per year.

Cost of clinical preoperative evaluation and post-operative follow-up, per procedure ($79,645 /30) = ……. **$ 2,655.00**

Procedure costs. (Personnel plus supplies).

Catheterization suite (Code 1082*)= ……$180.00

1 Nurse($41.50/hr X 3hr) = ……...$ 124.50

2 Technicians, [Anaesthesia , Cath Lab].

($34.64/hr X 3 hr each) = ……$ 207.84

Post Cath Recovery room, {1 Nurse ($ 41.50 /hr) x 2 hr

= $83.00. Assume average 3 patients in recovery}.

Cost per procedure ($83/3) =…….. $ 27.66

Coronary care unit ($560.95 + House Keeping $44.3)

per day x 3 days = ……...$ 1,815.75

Total procedure costs……...**$ 2,355.75**

Equipment Costs(Valve, catheters, cannula)…….**$ 20,000.00**

TOTAL cost per procedure ……**$ 26,069.95**

Hospitalization costs.

The procedure might theoretically increase hospital visits due to follow-up problems, or diminish hospital usage by relieving symptoms. We were able to ascertain hospital utilization during equal periods of time, before and after valve insertion, for nine patients. (The reason for utilization, not identified). The observation period (both before

and after) for these patients averaged 7 (6-12) months. During this time the average number and duration of hospital admissions and emergency room visits were as follows:

	Before insertion.	After insertion
ER visits:	1.2	1.2
ER days:	2.3	1.7
Admissions :	1.3	0.2
Hospitalization (days):	8.4	2.8

Thus, for nine patients for an average of seven months before and seven months after valve insertion, the average number of hospital admissions was reduced from 1.3 to 0.2 and the average number of days in hospital from 8.4 to 2.8 . If this pattern is consistent for future patients there will be a saving to the hospital of 5.6 hospital days per procedure , or, assuming a day rate of ($ 321 + $44.30 house keeping), an average saving of $2,046 per procedure. With this assumption:

Net cost per patient = $26,069.95 - $2,046 = ……$24,023.95