TITLE PAGE

Title:

A Contemporary Review of Severe Aortic Stenosis

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Abstract:

Severe aortic stenosis (AS) is the most common form of valvular heart disease in the developed world with a rising prevalence due to an ageing Australian population. Transcatheter aortic valve implantation (TAVI) offers a less invasive option for the treatment of severe AS with evidence supporting of TAVI compared to medical therapy in inoperable patients, and superior to surgical aortic valve replacement (SAVR) in high-risk patients. Equal outcomes have been observed in all-comer intermediate risk populations. The Heart Team utilises a shared decision-making approach between physicians and surgeons in risk stratifying patients and reduces the intrinsic bias that may occur if decisions are made in isolation. Geriatric assessment is useful in identifying pre-operative frailty, a major risk factor for death post aortic valve intervention. In severe AS, a decision can be made collaboratively to pursue TAVI, SAVR, a Ross Procedure, or conservative management.

The learning curve associated with TAVI has improved markedly with overall complication rates decreasing around the world. Contemporary changes in practice such as conscious sedation without general anaesthesia, expedited recovery and early discharge will likely improve cost-effectiveness. In 2018, TAVI is a well-established procedure in Australia that has revolutionised the management of severe AS. In the future with an expanding elderly population, the number of patients to benefit from transcatheter therapies for severe AS is hypothesised to increase 4-10 fold. Heart Team assessment is crucial in patients with severe AS to direct appropriate management.

Keywords:

aortic stenosis; transcatheter aortic valve implantation; heart team; interventional cardiology; cardiac surgery

Introduction

Aortic stenosis (AS) the most common form of valvular heart disease in the developed world, has a growing prevalence due to a progressive elderly population.¹ The majority of AS occurs by calcific degeneration of the aortic valve leaflets leading to obstruction of blood flow from narrowing of the aortic orifice. Severe AS leads to an increase in afterload, causing progressive hypertrophy of the left ventricle, and a decrease in systemic and coronary blood flow. The natural history of AS consists of a prolonged latent period during which morbidity and mortality is low. However, once symptoms of angina, syncope or heart failure develop,

average survival decreases rapidly with a high-risk of sudden death.² AS prevalence increases with age, with 7% affected over the age of 65. Australia has an ageing population with 1.9% of all citizens over the age of 80, with this number expected to expand in the future.³

Until recently the two management options for severe aortic stenosis were surgical aortic valve replacement (SAVR) or medical (palliative) therapy. SAVR involves a midline sternotomy approach with perioperative use of a cardiopulmonary bypass machine. In the post-operative period, patients typically require 24-48 hours in an intensive care unit (ICU) followed by an inpatient stay of up to 10-14 days to allow for recovery and mobilisation. Elderly patients or those with multiple co-morbidities often require an extended period of rehabilitation and respite post discharge. SAVR remains the gold standard treatment for low risk patients. However, for patients over the age of 75, perioperative morbidity and mortality after SAVR period can be unacceptably high. Predictors of poor outcome for SAVR include elderly patients with co-morbidities such as chronic renal failure, chronic obstructive airways disease and diabetes mellitus. One Australian analysis demonstrated a mortality rate of 9% at 30 days in patients over 80 years of age.⁴ Historically, these results have impacted elderly patients with up to a third denied surgery purely based on their age.

Evolution of TAVI

Transcatheter aortic valve implantation (TAVI) offers a less invasive option for the treatment of severe AS and was first performed by Alain Cribier and colleagues in 2002.⁵ The TAVI procedure is similar process to femoral access coronary angiography, with the majority of

procedures performed with local anaesthetic and sedation. The use of a cardiopulmonary bypass machine is not required.

Large calibre sheaths are placed in the femoral artery, with a pacing wire positioned in the right ventricle to allow for rapid temporary pacing. A further wire is placed across the native aortic valve via a retrograde approach, with the bioprosthesis positioned below the coronary arteries at the aortic annulus. The transcatheter aortic valve is delivered by high pressure balloon dilatation with rapid ventricular pacing or by self-expanding mechanical devices. The native valve leaflets are overcome by the transcatheter aortic valve stent, and the new bioprosthetic leaflets immediately functioning during systole and diastole. Effectiveness of the TAVI position is assessed post deployment by contrast aortography, direct invasive measurement of haemodynamics and transthoracic (TTE) or transoesophageal echocardiography (TOE). After satisfactory deployment, the femoral artery puncture site is closed with the use of specialised percutaneous devices.

Post TAVI patients are returned to a coronary care unit and can be mobilised 4 hours post procedure. In uncomplicated transfemoral TAVI cases, there is no requirement for routine intensive care unit admission. In the absence of conduction disturbance, patients are monitored with telemetry overnight, and can be discharged within 48 hours after the procedure. As TAVI valves are bioprosthetic, anticoagulation with vitamin-K antagonists is not required. Dual antiplatelet therapy including aspirin and clopidogrel is recommended for 3-6 months, with aspirin continued lifelong. In patients requiring anticoagulation for chronic atrial fibrillation, antiplatelet and anticoagulant therapies are tailored depending on patient bleeding and thromboembolic risk.

The Heart Team

The Heart Team is a new concept in the treatment of cardiovascular diseases to identify the best management option for an individual patient. The Heart Team utilises a shared decision-making approach between physicians and surgeons in risk stratifying patients. The benefit of the Heart Team is that it allows multiple different teams to deconstruct a patient's presentation and reduces the intrinsic bias that may occur if these complex decisions are made in isolation. In severe AS, a decision can be made collaboratively to pursue TAVI, SAVR or conservative (palliative) management.

Members of the heart team may include (but are not limited to): an interventional cardiologist, cardiothoracic surgeon, imaging cardiologist with echocardiographic experience and specialised training, general physician, geriatrician, cardiac anaesthetist, general practitioner, nursing and allied health staff (see image 1)¹⁵. Collaborative decision making occurs at multiple levels between these members including complex case discussions, with decisions recorded and enacted.

Patients who are referred for assessment of severe AS are evaluated by the heart team to: risk stratify patients with the help of validated risk scores such as the STS and EuroScore; identify management options which are appropriate; and educate and convey these deliberations to the patient and family, acting in the best interests of the patient.

There is increasing interest on the impact of frailty, an overall marker of functional reserve, cognitive function and nutritional status. The presence of frailty at an advanced age makes it unlikely that aortic valve intervention will improve quality of life or survival. Frailty can be assessed by cognitive testing, mobility assessment and functional activities with the use of standardised scales.⁷ It is essential that the Heart Team identifies frailty, as it is a marker of poor outcomes including death. In one prospective cohort study, the presence of frailty had

an odds ratio of 3.72 (95% C.I. 2.54-5.45) of mortality at 1 year post aortic valve intervention^{7, 8}.

Severe Aortic Stenosis Diagnosis

Patients with suspected AS are recommended to undergo TTE to assess valvular morphology and biventricular size and systolic function. Severe AS is defined on TTE as a reduced aortic valve area (AVA) of $<1.0\text{cm}^2$, peak velocity of $>4\text{m/s}$ and a mean gradient of greater than 40mmHg across the valve. The dimensionless index also provides further information to assess severity, and is defined as a ratio of the left ventricular outflow tract time-velocity to that of the aortic valve jet (Table 1)⁶. TAVI is considered for patients provided they do not have severe comorbidities (end stage renal failure, severe COPD, debilitating stroke, active malignancy, dementia) indicating a survival of <1 year.

Further evaluation of patients with severe AS in addition to TTE includes: coronary angiography to assess concomitant coronary artery disease, aortic tortuosity and iliofemoral access; and, multi-slice computed tomography (MSCT) of the heart, aortic valve, aorta and peripheral vessels to direct femoral or alternative access.⁶ Patients referred to a cardiologist are subsequently discussed by the Heart Team where a consensus is reached for the appropriate treatment strategy. The Heart Team has improved outcomes in the management of severe AS and other cardiac conditions, with major local and international guidelines recommending a Heart-Team approach.^{6, 9}

Low-Flow Low-Gradient Aortic Stenosis

AVA is useful for the diagnosis of severe AS, however, this needs to be measured with mean pressure gradient, stroke volume, valve calcification and left ventricular size and wall

thickness to determine severity. Low-flow low-gradient AS with reduced left ventricular ejection fraction (LVEF) is defined as an AVA of $<1\text{cm}^2$, mean gradient $<40\text{mmHg}$, LVEF $<50\%$ and a stroke volume index (SVI) $\leq 35\text{mL/m}^2$. Dobutamine stress echocardiography is useful in this setting to determine severe AS from pseudosevere AS (defined as an increase in AVA $>1\text{cm}^2$ post infusion) often accompanied by left ventricular contractile reserve⁶. Low-flow Low-Gradient AS with preserved LVEF often affects elderly females, with small left ventricular size and left ventricular hypertrophy. It is defined as an AVA $<1\text{cm}^2$, mean gradient $<40\text{mmHg}$, SVI $\leq 35\text{mL/m}^2$ and an LVEF $\geq 50\%$. In this group measurement of aortic valve calcification by MSCT is useful in determining severity and outcome⁶.

Evidence

Inoperable & High-Risk Patients

The original first case reports and randomised control trials (RCTs) were performed in inoperable or high-risk patients. High surgical-risk is defined as patients who have high 30-day mortality. This is performed by individual evaluation of validated risk scores in cardiac surgery including the Society of Thoracic Surgeons (STS $>8\%$) and EuroSCORE.

The first major RCT of TAVI in severe AS was the PARTNER 1B trial¹⁰, comparing TAVI to medical therapy for patients deemed inoperable. The study demonstrated a statistically significant decrease in all-cause mortality of 20% ($p<0.001$), equalling a number needed to treat of five patients at one year to prevent one death (Table 2).¹⁰

Subsequently, there have been several RCTs that have compared TAVI to SAVR in high surgical-risk populations. Both the PARTNER 1A and CoreValve US PIVOTAL trials were prospective, multicentre RCTs which proved non-inferiority of TAVI compared to SAVR (Table 2).^{11, 12} The CoreValve US PIVOTAL study was initially developed to assess for non-

inferiority of TAVI compared to SAVR, however the apparent benefit of TAVI achieved a statistically significant result of superiority ($p=0.04$).¹¹ Overall, both studies demonstrated comparable one-year mortality and stroke rates. For secondary endpoints, both trials demonstrated non-inferiority of TAVI compared to SAVR, including an improvement in symptoms of New York Heart Association (NYHA) class II or less at 30 days Class II ($p < 0.001$).^{11,12}

Both the PARTNER and CoreValve US PIVOTAL populations have been followed up for an extensive period of time between 2-5 years. Overall, follow up of these populations have shown a sustained benefit over time compared to SAVR.

Intermediate & Low-Risk Patients

Given the success of high-risk RCTs, the utility of TAVI in severe AS for intermediate risk surgical populations, defined as an STS of $<8\%$, has been evaluated in two large RCTs. The PARTNER 2 and SURTAVI trials both demonstrated non-inferiority of TAVI compared to SAVR, with comparable rates of mortality and stroke between both groups.^{13, 14} The PARTNER 2 trial subset of patients who underwent a transfemoral TAVI compared to SAVR, interestingly had a statistically significant reduction in death from any cause or stroke ($p=0.05$). Furthermore, hospital admission length and ICU admission duration were significantly less for the TAVI cohort than SAVR ($p<0.001$).¹³

The NOTION trial was multicentre RCT which used an “*all-comer*” approach to emulate a real-world population randomised to TAVI vs SAVR. In this intention to treat analysis, there was no significant difference between both groups over a two year follow up period.¹⁵

Overall, the evidence from RCTs comparing TAVI to SAVR is supportive of TAVI being superior to medical therapy in inoperable patients, and superior to SAVR in mortality in high-

risk patients. There are studies suggesting the cost of TAVI is favourable compared to SAVR in high to intermediate risk patients.¹⁶ Therefore according to international guidelines, TAVI is the recommended treatment strategy for severe AS over SAVR in inoperable and high-risk patients, with the Heart Team to consider the best management option with TAVI or SAVR for intermediate risk patients.⁶

Multiple trials are now recruiting to assess the outcome of SAVR compared to TAVI in low risk populations (The Partner 3 Trial - NCT02675114, Feasibility of Transcatheter Aortic Valve Replacement in Low-Risk Patients with Symptomatic Severe Aortic Stenosis - NCT02628899, Medtronic Evolut Transcatheter Aortic Valve Replacement in Low Risk Patients - NCT02701283, Notion-2 Trial - NCT02825134).

Other Forms of Aortic Valve Disease

Patients with pure aortic regurgitation (AR) have not been included in the aforementioned TAVI trials as this is a different disease process often affecting a younger population. In patients where there is mixed calcific trileaflet aortic valve disease with severe AS and co-existent AR, TAVI may be appropriate. Bicuspid aortic valve disease is prevalent in 0.5-2% of the population and is the most common indication for SAVR in patients less than 70 years of age. Bicuspid AS is associated with aortopathy and eccentric annular calcification. Registries of TAVI in bicuspid aortic valve patients has yielded unacceptable rates of paravalvular aortic regurgitation (PAR) and vascular complications.¹⁷ It must be emphasised that this group has largely been excluded from RCTs and SAVR remains standard of care for this group. Structural deterioration of a pre-existing bioprosthesis in the aortic position leading to severe AS or severe AR can be treated with valve-in-valve TAVI insertion (Figure 3 - D).

Surgical Aortic Valve Replacement

Interestingly, in the TAVI era the absolute number of patients undergoing SAVR has increased, reflecting the requirements of an ageing population.¹⁸ Patients deemed by the Heart Team to undergo SAVR for severe AS can have mechanical or bioprosthetic valve insertion. The choice of valve is dependent upon age, compliance, bleeding risk, patient and surgeon preference. There has been a paradigm shift with a decrease in the age of which a bioprosthetic valve is considered appropriate. This is due to the recognition that a percutaneous valve-in-valve TAVI is a management option for future bioprosthetic valve failure or degeneration.¹⁸

In a subset of young patients with a long life-expectancy the Ross Procedure may be performed. This involves replacing the diseased aortic valve with the patient's own pulmonary valve. In turn, a pulmonary allograft is then placed in the pulmonic position. Australian data has demonstrated superior long-term survival with the Ross Procedure compared to mechanical prosthesis in specialised centres.¹⁹

Alternative Access TAVI

In patients with unsuitable femoral anatomy, alternative access routes can be used including transapical, direct aortic, subclavian artery, transcarotid or transcaval access without the need for cardiopulmonary bypass.²⁰ Cardiothoracic surgeons are the primary operator for transapical and direct aortic access, with procedures performed in hybrid theatres. The alternative access routes for TAVI have not been compared, however retrospective evidence suggest subclavian access may be the safest option where there is unsuitable femoral anatomy.²¹

Asymptomatic Severe Aortic Stenosis

Management of asymptomatic patients with severe AS remains controversial. The current evidence does not provide adequate data to recommend intervention (SAVR or TAVI) in this group of patients, despite the risk of sudden death.²² In physically active individuals, careful exercise testing may unmask symptoms and allow for risk stratification to improve decision making. Similarly, the TAVI UNLOAD trial (NCT02661451) is recruiting a challenging group of symptomatic patients with moderate AS and reduced LVEF to assess if TAVI is of benefit.

Complications of TAVI

The learning curve for TAVI has improved markedly worldwide with overall complication rates decreasing in major registry analysis (Table 3).²⁰ Notwithstanding there are several complications relevant to Heart Team and patient decision making in the setting of severe AS.

Vascular Complications

Early trials yielded high rates of major vascular complications between 3-9% due to large sheath sizes, calcified and small calibre anatomy. These complications delivered significant morbidity and led to increased mortality.²³ The advent of pre-operative three-dimensional imaging with MSCT reconstruction (Figure 4) , ultrasound guided arterial puncture, and use of balloon crossover techniques to ensure adequate vessel haemostasis has decreased complication rates.²⁴ Despite these improvements, vascular complications remain the “Achilles Heel” of TAVI with rates in intermediate risk groups still as high as 6%²⁵.

Pacemaker Insertion

Heart block and the need for pacemaker occurs after TAVI due to direct compression of the bioprosthetic valve on the native conduction tissue. Early TAVI trials had unacceptable post

procedure pacemaker rates of >25%, with major risk factors including pre-existing right bundle branch block, low TAVI implant height and self-expandable devices.²⁶ The importance of higher TAVI implantation, improved contemporary TAVI devices and the introduction of repositionable valves has lowered the need for permanent pacemaker to <15% for most devices. Although permanent pacemaker implantation adds to the risk of procedural complications and overall cost, it likely protects the patient against bradyarrhythmias, a common finding amongst elderly patients with severe AS.²⁷

Paravalvular Aortic Regurgitation

Post procedure moderate to severe PAR is associated with an increased mortality. This was a common problem in the early generation TAVI trials reported in up to 10%–15% of patients,²⁸ where TOE guidance was often used to direct valve size. The advent of MSCT as a superior modality for annulus sizing and device selection has resulted in lower rates of PAR to <5% in the contemporary era. This is accompanied by new TAVI valves having an outer skirt adaptive seal such as the Sapien 3 (Edwards Lifesciences, Irvine USA), and repositionable delivery devices that optimise positioning, including the Evolute R and Evolute PRO (Medtronic, Dublin Ireland) (see Figure 3).

Stroke

Stroke is a devastating complication post aortic valve intervention and conveys a high-risk of short term mortality. In the original high-risk PARTNER I trial the stroke rate was over twice that of SAVR (5.5% vs 2.4% at 30 days $P=0.04$)¹⁰. However the rate of stroke has decreased over time, with a lower incidence observed in the intermediate-risk RCTs comparing TAVI vs SAVR.^{13, 25} Embolic protection devices have failed to demonstrate a reduction in stroke incidence despite a reduction in infarct volume on brain magnetic resonance imaging.²⁹

Other Complications

Infective endocarditis post TAVI conveys a high risk of in-hospital mortality with an incidence of 1.1%, the majority of organisms cultured either *enterococcus* or *staphylococcus* species. Management goals are difficult and often restricted to antibiotic therapy as the majority of patients have been deemed unfit for cardiac surgery.³⁰ Acute kidney injury (AKI) has shown to be less frequent in TAVI patients compared to SAVR.^{13,14,15} This is important as one meta-analysis demonstrated AKI after valve intervention led to a threefold increase in 12 month mortality post procedure.³¹ Catastrophic complications such as coronary obstruction, aortic dissection and left ventricular perforation are rare with TAVI at 0.2-1.1%, partly attributable to MSCT planning identifying hazardous anatomy and preparing the operator with a three-dimensional view of the access site, aorta and annulus.^{13, 25}

Cost Effectiveness

The huge impact of TAVI for the management of severe AS has seen over 300,000 procedures performed worldwide, in a global market worth billions.²⁰ This shift in uptake of the procedure has led to TAVI numbers surpassing that of SAVR for severe AS in some European nations.²⁷

There have been several studies which have performed cost-effective analysis into the utility of TAVI in the treatment of severe AS. In general, heterogeneity exists in the results between studies, with some demonstrating benefit in adopting TAVI, and others suggesting the procedure is expensive compared to traditional SAVR.¹⁶ This phenomenon is largely driven by differing costs between countries, access to medical care and the cost of the device from industry providers. For example, in the US a TAVI device costs approximately \$30,000.²⁰ It is

likely that these costs will improve over time by increasing competition between industry providers and technological improvements.

TAVI vs Medical Therapy

The evidence for inoperable patients with severe AS is robust for TAVI and favours its use. In one review evaluating eleven studies comparing TAVI to medical therapy, 9 were in favour of TAVI as cost-effective.³² This was defined as an incremental cost effectiveness ratio (ICER) of \$50,000 USD or less, under the willingness-to-pay threshold of acceptable cost effectiveness in the United States.

TAVI vs SAVR

In a recent metanalysis, eleven studies compared TAVI to SAVR, and showed no significant difference in quality adjusted life years between comparison groups. This noted marked heterogeneity in ICER between studies, with 5 determining TAVI to have favourable (or equivalent) ICERs, and 6 studies did not.¹⁶ Further research into the cost-effectiveness of TAVI compared to SAVR is required given these findings. However, there is evidence that with modest improvement of the initial cost of the device, a favourable cost-benefit ratio can be attained in comparison to SAVR. A review of the PIVOTAL trial noted that TAVI reduced the need for rehabilitation, prevented ICU admissions and reduced overall length of stay. The bulk of the admission cost related to the initial cost of the TAVI bioprosthesis. The authors concluded a modest decrease of ~\$1700 USD in outset costs would result in a favourable ICER.³³

Australian Considerations

In Australia, the uptake of TAVI has been relatively slow compared to that of the Northern Hemisphere. In late 2017, a Medicare Benefits Schedule item number was developed for TAVI. The Cardiac Society of Australia and New Zealand has developed position statements and an accreditation process for TAVI operators and centre suitability⁹. The mandatory use of a Heart Team for patient selection is the cornerstone of TAVI clinical practice, to ensure unbiased decision making and prevent indication creep. A national TAVI registry is also in development to ensure optimal patient outcomes. It is important that Australian patients have access to Heart Team assessment in a safe and timely manner and are not denied access to aortic valve intervention on the basis of geographical or funding restrictions.

Conclusion

In 2018, TAVI is a well-established procedure that has revolutionised the management of severe AS. In the future with an expanding elderly population, the number of patients to benefit from TAVI is hypothesised to increase 4-10 fold²⁰. Heart Team assessment is crucial in identifying patients with severe AS to direct appropriate management. Contemporary changes in TAVI practice such as conscious sedation without general anaesthesia, expedited recovery, early discharge and lower complication rates will likely improve cost-effectiveness.

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Figure Legends

Figure 1 – The Heart Team.

Figure 2 – Figure 2 – Transthoracic Echocardiographic Findings of Severe AS. The middle trace is a continuous wave Doppler through the aortic valve demonstrating a peak velocity of 4.2m/s and a mean gradient of 44mmHg.

Figure 3 – Types of TAVI Valves A: Evolut-R Valve (Medtronic, Dublin, Ireland), B: Evolut-R TAVI insertion from a transfemoral approach, C: Sapien-3 Valve (Edwards Lifesciences, Irvine, USA), D: Sapien-3 Valve-in-Valve insertion from a transfemoral approach for a degenerative Perimount bioprosthetic valve leading to severe aortic regurgitation.

Figure 4 - Multi-Slice Computed Tomography of the descending aorta & iliofemoral arteries. This is performed to determine suitability for transfemoral TAVI insertion and direct puncture sites in order to decrease the risk of vascular complications.

TABLE 1 – Severe AS Diagnosis by Transthoracic Echocardiography⁶

	Mild AS	Moderate AS	Severe AS
Aortic Valve Area (cm²)	>1.5	1.0-1.5	<1.0
Mean gradient (mmHg)	<20	20-40	>40
Peak aortic velocity (m/sec)	<3	3-4	>4
Indexed Aortic Valve Area (cm²/ m²)	>0.85	0.60-0.85	<0.60
Dimensionless Index (DI)	>0.50	0.25-0.5	<0.25

TABLE 2 – TAVI Evidence from Randomised Control Trials

Name	Design	n(total)	Comparison group	Surgical-risk average (STS %)*	Primary outcome	Mortality TAVI at specified timepoint (%)	Mortality comparison group (%)	Mortality p value 95%	TAVI approach
Partner 1B trial ¹⁰	Multicentre prospective RCT	358	Medical Management	11.6	All cause mortality at 1 year	30.7	50.7	P<0.001	Transfemoral
PARTNER 1A trial ¹²	Multicentre prospective RCT	699	SAVR	11.7	All cause mortality at 1 year	24.2	26.8	P=0.44	Transfemoral and transapical
CoreValve US trial PIVOTAL ¹¹	Multicentre prospective, RCT	795	SAVR	7.4	All cause mortality at 1 year	14.2	19.1	0.04	Transfemoral and transapical
PARTNER 2 ¹³	Multicentre prospective RCT	2032	SAVR	5.8	All cause mortality + disabling stroke at 2 years	19.3	21.1	P=0.25	Transfemoral and transapical
SURTAVI ¹⁴	Multicentre prospective RCT	1746	SAVR	4.5	All cause mortality + disabling stroke at 2 years	12.6	14.0	P>0.999	Transfemoral and transapical
STACCATO trial ³⁴	Multicentre prospective, RCT	72	SAVR	3.3	All cause mortality at 30 days	14.7	2.8	P=0.07	Transapical
NOTION ³⁵	Multicentre, prospective RCT	280	SAVR	3.0	All cause mortality + disabling stroke at 1 year	13.1	16.3	P= 0.43	Transfemoral or subclavian

TABLE 3 - TAVI Complications from Randomised Control Trials

Study name	Complication type	TAVI group rate (%)	Comparison group rate (%)	P-value
Partner 1B trial¹⁰	Major stroke rate	5.0	1.1	0.62
	Major vascular complication rate	16.2	1.1	<0.001
	Major acute kidney injury rate	0	1	1.00
	New onset atrial fibrillation	0.6	1.1	1.00
	New pacemaker insertion rate	3.4	5.0	0.60
PARTNER 1A trial¹²	Major stroke rate	3.8	2.1	0.20
	Major vascular complication rate	11.0	3.2	<0.001
	Major acute kidney injury rate	2.9	3.0	0.95
	New onset atrial fibrillation	8.6	16.0	0.006
	New pacemaker insertion rate	3.8	3.6	0.89
CoreValve US PIVOTAL trial¹¹	Major stroke rate	3.9	3.1	-
	Major vascular complication rate	3.9	3.1	-
	Major acute kidney injury rate	-	-	-
	New onset atrial fibrillation	-	-	-
	New pacemaker insertion rate	-	-	-
PARTNER 2¹³	Major stroke rate	3.2	4.3	0.2
	Major vascular complication rate	7.9	5.0	0.008
	Major acute kidney injury rate	1.3	3.1	0.006
	New onset atrial fibrillation	9.1	26.4	<0.001
	New pacemaker insertion rate	8.5	6.9	0.17
SURTA¹⁴	Major stroke rate	1.2	2.5	p>0.05
	Major vascular complication rate	6.0	1.1	p<0.05
	Major acute kidney injury rate	1.7	4.4	p<0.05
	New onset atrial fibrillation	12.9	43.4	p<0.05
	New pacemaker insertion rate	25.9	6.6	p<0.05
NOTION³⁵	Major stroke rate	1.4	3.0	0.37
	Major vascular complication rate	5.6	1.5	0.10
	Major acute kidney injury rate	0.7	6.7	0.01
	New onset atrial	16.9	57.8	<0.001

	fibrillation			
	New pacemaker insertion rate	34.1	1.6	<0.001

Abbreviations

AKI acute kidney injury

AR aortic regurgitation

AS aortic stenosis

AVA aortic valve area

ICER incremental cost effectiveness ratio

ICU intensive care unit

LVEF left ventricular ejection fraction

MSCT multi slice computed tomography

PAR paravalvular aortic regurgitation

RCT randomised control trial

SAVR surgical aortic valve replacement

STS society of thoracic surgeons

SVI stroke volume index

TAVI transcatheter aortic valve implantation

TOE transoesophageal echocardiography

TTE transthoracic echocardiography

Abstract:

Severe aortic stenosis (AS) is the most common form of valvular heart disease in the developed world with a rising prevalence due to an ageing Australian population. Transcatheter aortic valve implantation (TAVI) offers a less invasive option for the treatment of severe AS with evidence supporting of TAVI compared to medical therapy in inoperable patients, and superior to surgical aortic valve replacement (SAVR) in high-risk patients. Equal outcomes have been observed in all-comer intermediate risk populations. The Heart Team utilises a shared decision-making approach between physicians and surgeons in risk stratifying patients and reduces the intrinsic bias that may occur if decisions are made in isolation. Geriatric assessment is useful in identifying pre-operative frailty, a major risk factor for death post aortic valve intervention. In severe AS, a decision can be made collaboratively to pursue TAVI, SAVR, a Ross Procedure, or conservative management.

The learning curve associated with TAVI has improved markedly with overall complication rates decreasing around the world. Contemporary changes in practice such as conscious sedation without general anaesthesia, expedited recovery and early discharge will likely improve cost-effectiveness. In 2018, TAVI is a well-established procedure in Australia that has revolutionised the management of severe AS. In the future with an expanding elderly population, the number of patients to benefit from transcatheter therapies for severe AS is hypothesised to increase 4-10 fold. Heart Team assessment is crucial in patients with severe AS to direct appropriate management.

Figure 2.tif

Figure 3 - TAVI Valves.jpg

Figure 4.tiff

The Heart Team.jpg

TITLE PAGE

Title:

A Contemporary Review of Severe Aortic Stenosis

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Keywords:

aortic stenosis; transcatheter aortic valve implantation; heart team; interventional cardiology; cardiac surgery

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