Transcatheter aortic valve implantation (TAVI)

for patients with symptomatic severe aortic stenosis

Technology Guidance from the MOH Medical Technology Advisory Committee (MTAC)

Guidance Recommendations

The Ministry of Health's MTAC has recommended subsidy for

- ✓ Transcatheter aortic valve implantation (TAVI) may be considered in patients with symptomatic severe aortic stenosis (AS) who are inoperable or have an unacceptably high risk for SAVR with significant comorbidities.
- ✓ Patient selection should be carried out by a multidisciplinary heart team, which must at minimum include an interventional cardiologist and a cardiac surgeon. The team should determine the risk level of each patient based on:
  - The estimated risk of mortality of 11% or greater within 30 days of surgery according to the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) risk assessment; OR
  - Other patient characteristics that preclude surgery such as frailty and cognitive function. Where appropriate, objective tools should be used to assess these characteristics.
- ✓ TAVI should be conducted by a multidisciplinary heart team that has met the applicable TAVI training and accreditation standards prescribed by the institution.
- ✓ The TAVI procedure should be performed via transfemoral delivery, unless it is contraindicated or not feasible, in catheterisation labs or hybrid operating theatres equipped with early in-hospital access to cardiac and vascular surgical support for the emergency treatment of complications and subsequent patient care.
- ✓ Consistent with the standard arrangements in place for clinical governance and audit, details of final surgical risk assessments of all patients who receive TAVI including STS-PROM score, type of TAVI device and clinical outcomes, should be properly recorded.

Subsidy status

Subsidies for the abovementioned indications apply only to the devices listed in the Annex. TAVI should not be subsidised if the patient has received the TAVI implant subsidy within the preceding five-year period.

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Factors considered to inform the recommendations for subsidy

Technology evaluation

1.1 The MOH MTAC ("the Committee") considered evidence presented for the technology evaluation of TAVI for patients with symptomatic severe aortic stenosis. The evaluation was conducted in consultation with clinical experts in interventional cardiology and cardiothoracic surgery from the public healthcare institutions. Available clinical and economic evidence for TAVI was considered in line with the registered indication.

1.2 The evidence was used to inform the Committee's deliberations around five core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Overall benefit of the technology to the patient and/or the system;
- Cost-effectiveness (value for money), which covers the incremental benefit and cost of the technology compared to existing alternatives
- Estimated annual technology cost and the number of patients likely to benefit from the technology
- Organisational feasibility, which covers the potential impact of adopting technology, especially barriers for diffusion

1.3 Additional considerations, such as ethical or social issues related to adoption of the technology, may also inform the Committee's deliberations.

Clinical need

2.1 The Committee noted that symptomatic severe AS is a chronic condition where the narrowed aortic valve critically obstructs blood flow from the left ventricle to the aorta and can lead to heart failure. Only aortic valve replacement can treat or alter the disease course. Patients with symptomatic severe AS who do not undergo aortic valve replacement have a poor prognosis.

2.2 The Committee noted that patients with symptomatic severe AS can be stratified by their estimated risk of surgical mortality to weigh the risks of the intended intervention against the natural history of the disease. In

patients who are inoperable and cannot undergo conventional surgical aortic valve replacement (SAVR) surgery, standard therapy comprising medical management with or without balloon aortic valvuloplasty (BAV) offers symptomatic relief only. For patients with symptomatic severe AS with high surgical risk, conventional SAVR is the current standard of care. TAVI is a viable option to standard therapy in patients who are inoperable, and a less invasive alternative to SAVR in patients with high surgical risk.

Clinical effectiveness and safety

3.1 The Committee noted that TAVI is a minimally invasive procedure that replaces the stenosed aortic valve with a bioprosthetic aortic valve deployed using a catheter, preferably by transfemoral access through the femoral artery. Other access routes include transapical (through the apex of the heart), transaortic (through the aorta), or transaxillary/subclavian (through the left axillary artery via a small incision beneath the clavicle) access.

3.2 The Committee noted that there are two main comparators for TAVI: i) standard therapy in patients who are inoperable (Society of Thoracic Surgeons Predicted Risk of Mortality, STS-PROM ≥11%), and ii) SAVR in patients with high surgical risk (STS-PROM 8 to <11%). Safety and clinical effectiveness outcomes were categorised according to the prevailing Valve Academic Research Consortium outcomes.

3.3 Key randomised clinical trials (RCTs) included in the evidence base were PARTNER 1B for patients who were inoperable, and PARTNER 1A and US CoreValve for patients with high surgical risk.

3.4 The Committee agreed that TAVI is likely to have an acceptable safety profile:

a. In patients who were inoperable, TAVI via transfemoral access was similar to standard therapy in 30-day all-cause or cardiac mortality, all stroke rates, major bleeding and permanent pacemaker implantation. However, TAVI via transfemoral access was associated with higher major vascular complication rates and higher major stroke rates when compared with standard therapy.
b. In patients with high surgical risk, TAVI via any access route was non-inferior to SAVR in 30-day all-cause mortality and stroke rates at one to five years. Furthermore, compared with SAVR, TAVI was

associated with higher rates of major vascular complications, moderate or severe aortic regurgitation or paravalvular aortic regurgitation, but shorter hospitalisation and intensive care unit (ICU) stay.

3.5 The Committee acknowledged that the evidence showed that TAVI via any access route is likely to be clinically effective in patients who are inoperable. At one to five years, TAVI via transfemoral access was associated with lower all-cause or cardiac mortality and rehospitalisation rates when compared with standard therapy. TAVI via transfemoral access was also associated with greater improvements in disease-related and generic quality of life (QoL) up to one-year follow-up, with a substantially greater proportion of patients with improved functional capacity at one to five years when compared with standard therapy.

3.6 The Committee acknowledged that in patients with high surgical risk, the evidence showed that TAVI via any access route and SAVR had similar all-cause mortality after two years. There was no significant difference in sustained functional capacity improvements and rehospitalisation rates between TAVI and SAVR at up to five-year follow-up. Greater improvements in disease-related and generic QoL were reported for TAVI via any access route at 30 days, but this relative benefit diminished by six months. The Committee agreed that TAVI may not provide substantial additional benefits for all patients with high surgical risk, but a subgroup of patients with unacceptably high surgical risk (STS-PROM ≤11% or with patient characteristics that preclude surgery such as frailty and cognitive function) is likely to have a high unmet clinical need which may be addressed by TAVI, if it was assessed to be a clinically appropriate option by the multidisciplinary heart team.

3.7 The Committee noted that key limitations of the clinical evidence include the use of early generation TAVI devices in the trials with follow-up of up to five years, incomplete reporting in the studies, and limited longer-term TAVI valve durability data beyond five years, due to its uncertain implications in younger patients.

Cost-effectiveness

4.1 The Committee agreed that TAVI via transfemoral access is likely to be cost-effective in patients who are inoperable based on published economic evidence showing consistent cost-effective results. When compared with

standard therapy, published incremental cost-effectiveness ratios (ICERs) ranged from S$11K (AUD$12K) to S$51K (¥3.9 million) per quality-adjusted life year (QALY) gained.

4.2 A local de novo cost-effectiveness model comparing TAVI via transfemoral access and SAVR in patients with high surgical risk (STS-PROM 8% to <11%) from the healthcare system perspective was developed based on evidence from key randomised controlled trials PARTNER 1A and US CoreValve which had long-term follow-up of up to five years. The model was simulated over a time horizon of five years in the base case.

4.3 The Committee considered that the ICER is high in patients with high surgical risk at >$105,000 per QALY. Value-based pricing (VBP) negotiations with manufacturers were needed to lower the ICER, and the cost-effectiveness was likely to be further improved in a subgroup of patients with unacceptable high surgical risk. The Committee noted that the key drivers of the model were the large cost difference between TAVI and SAVR, and the all-cause mortality rates which converged after two years. The ICER was also sensitive to the cost of paravalvular aortic regurgitation.

Estimated annual technology cost

5.1 The Committee noted that based on the projection of about 12 inoperable patients a year who would benefit from government subsidy, the estimated annual cost to the Government for subsidising TAVI was $1 million to <$3 million.

5.2 The Committee also noted that based on a projection of about 27 high-risk patients a year who would benefit from government subsidy, the estimated annual cost to the Government for subsidising TAVI was about <$1 million. The actual cost for the subgroup of patients with unacceptable high surgical risk is expected to be minimal.

Organisational feasibility

6.1 The Committee noted that the appropriate accreditation and training, institutional TAVI registries and audit framework are in place in public healthcare institutions (PHIs) to ensure safe and effective TAVI procedures.

The Committee agreed that TAVI procedures should be conducted in catheterisation labs or hybrid operating theatres equipped with early in-hospital access to cardiac and vascular surgical support for the emergency treatment of complications and subsequent patient care.

6.2 The Committee also noted that an expansion of regulatory approval for use in the lower surgical risk groups could potentially lead to the leakage across patient risk groups.

Additional considerations

7.1 Longer term valve durability remains limited and may be an increasingly pertinent concern given its growing use of TAVI in younger patients. These may include patients with end stage renal failure (ESRF) and those with lower surgical risk. In these patients, it is unclear how often the valve would need to be replaced in their lifetime. The Committee agreed that this is likely due to the short innovation cycle of TAVI which could limit the generation of longer-term evidence for current TAVI models.

7.2 The Committee further noted that although patients with ESRF could experience futility with TAVI and be at high risk for more frequent TAVI replacements, the use of TAVI in this patient subgroup could still be justified due to a lack of ideal alternatives, and favourable outcomes with TAVI from some published literature and clinical experience. However, the Committee remained concerned about the high risk for frequent repeat TAVI procedures in this group of patients due to premature TAVI valve failure before the typical five-year valve durability. To address this, the Committee took reference from the reimbursement criteria from Medicare Benefits Schedule, Australia and agreed that it was necessary to strengthen the patient selection process for TAVI subsidy eligibility by limiting TAVI implant subsidy to once per patient in a five-year period. This requirement would also help to mitigate the high risk of potential leakage into patients of lower risk groups.

7.3 The Committee agreed that the multidisciplinary heart team should assess a patient's eligibility for TAVI based on considerations including but not limited to clinical eligibility, likely overall benefit from TAVI, and valve durability (particularly in younger patients). Where appropriate, objective tools should be used to assess other surgical risk and other patient characteristics that preclude surgery.

Recommendation

8.1 Based on the evidence presented, the Committee recommended subsidy for TAVI in patients with symptomatic severe AS who are inoperable or have an unacceptably high risk for SAVR with significant comorbidities.

8.2 Patient selection should be carried out by a multidisciplinary heart team, which must at minimum include an interventional cardiologist and a cardiac surgeon. The team should determine the risk level for each patient based on:

- The estimated risk of mortality of 11% or greater within 30 days of surgery according to the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) risk assessment; OR
- Other patient characteristics that preclude surgery such as frailty and cognitive function. Where appropriate, objective tools should be used to assess these characteristics.

8.3 TAVI should be conducted by a multidisciplinary heart team that has met the applicable TAVI training and accreditation standards prescribed by the institution.

8.4 The TAVI procedure should be performed via transfemoral delivery, unless it is contraindicated or not feasible, in catheterisation labs or hybrid operating theatres equipped with early in-hospital access to cardiac and vascular surgical support for emergency treatment of complications and subsequent patient care.

8.5 Consistent with the standard arrangements in place for clinical governance and audit, details of final surgical risk assessments of all patients who receive TAVI including STS-PROM score, type of TAVI device and clinical outcomes, should be recorded.

8.6 The Committee agreed that only TAVI devices listed in the Annex would be eligible for subsidy in patients with symptomatic severe AS who are inoperable or have an unacceptably high risk for SAVR, in accordance with the Committee's subsidy recommendation. TAVI should not be subsidised if the patient has received the TAVI implant subsidy within the preceding five-year period.

ACE
agency for
care effectiveness

About the Agency

The Agency for Care effectiveness (ACE) is the national health technology assessment agency in Singapore residing within the Ministry of Health. It conducts evaluations to inform the subsidy of treatments, and produces guidance on the appropriate use of treatments for public hospitals and institutions in Singapore. When using the guidance, the responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional. This guidance is based on the evidence available to the Committee as of 4 November 2020 and 17 March 2021.This guidance is not, and should not be regarded as a substitute for, professional/medical advice. Please seek the advice of a qualified healthcare professional on any medical condition.

Find out more about ACE at www.ace-hta.gov.sg/about

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