Management of severe symptomatic aortic stenosis in the age of COVID-19 recovery

Key Paper Summary

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The new status quo

The care of patients with aortic stenosis (AS) globally has been turned topsy-turvy in the world of COVID-19.

Most hospitals have put elective procedures on hold, despite the fact that non-treatment puts these patients at greater risk of mortality/cardiovascular deterioration (Smith) and that elderly patients with AS are a high-risk group for infection with the virus.

The post-COVID-19 care of these patients face challenges that affect patients, health systems, personnel and providers:

- There are many more patients on the waiting list than there were pre-pandemic
- Hospital resources are impaired, e.g. there are COVID-19 patients who occupy hospital beds, and there is an overload of non-COVID-19 patients who are awaiting treatment. There is a requirement to maximise organisational and economic efficiencies
- Staff may still be recovering, or slow to return from diverted responsibilities
- There may be a lack of clinical specialists or supplies

It will be of the utmost importance that hospitals employ processes and procedures that adhere to clearly defined clinical pathways that maintain patient safety, plan clinical outcomes, maximise resource utilisation, plan for safe, early discharge and provide patient satisfaction.

Those features that make transcatheter aortic valve implantation (TAVI) the treatment of choice for all-risk patients who suffer from severe, symptomatic AS (ssAS) pre-COVID-19 are of even greater significance during the COVID-19 recovery phase.

This paper summarises the evidence base that supports this statement.

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European landscape

Acute care institutions around the world have been reconfigured in response to the COVID-19 pandemic.

As we enter the COVID-19 recovery phase, it will be a priority that hospitals have had address the backlog of patients for whom care may have to have been placed on hold.

It has never been more critical that a hospital display maximum efficiency in delivering best clinical care to their patients – from shortening waiting lists and minimising stay in hospitals to enabling low-level re-hospitalisation.

A key focus will be on those patients who suffer from AS.

The European population is progressively ageing, with an accompanying increased prevalence of chronic degenerative disease,[1] of which one of the most common is cardiovascular disease (CVD),[2] including AS.

This age-related increase in CVD translates to an increased prevalence of vascular heart disease (VHD) in an elderly population.[3]

In 2016, d'Arcy and colleagues in the OxVALVE population Cohort Study[4] concluded that AS was present in 1.3% of individuals aged 65 years and older, rising to 4.1–5.2 in the over 75s.[5]

Tragically, one in three of these patients do not undergo treatment,[6] without which the 3-year survival rate is less than 30%.[7]

In high- to medium-risk populations (including those deemed inoperable), there are currently 115,000 patients eligible for TAVI in the EU annually.[8] The expansion to younger, low-risk patients has the potential to cause this number to increase to over 175,000 – with major implications for healthcare resource planning.[8]

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Choices

Cardiology societies and associations – the Italian Society of Interventional Cardiology and the European Society of Cardiology – have issued guidelines and consensus statements on the management of ssAS in the COVID-19 world.

The most common treatment for ssAS is aortic valve replacement, performed either surgically (surgical aortic valve replacement [SAVR]) or non-invasively (TAVI) (either transfemorally or transapically).

Many patients and clinicians prefer a non-invasive intervention, i.e. TAVI performed under local anaesthetic, compared with SAVR, under general anaesthetic.

So what is the evidence base for the preferred TAVI approach, specifically the SAPIEN 3™ platform?

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TAVI with the SAPIEN 3™ valve system vs SAVR: what is the evidence?

Since 2011, key PARTNER™ (**P**lacement of **A**o**R**tic **T**ra**N**scathet**ER** valves) trials have compared clinical outcomes of TAVI with those of SAVR in patients with ssAS, at high, intermediate and low surgical risk.

High risk[9]

In patients with ssAS who are at high risk for operative complications and death, SAVR and TAVI with the SAPIEN™ valve system were associated with similar mortality from any cause at 30 days and 1 year and produced similar improvements in cardiac symptoms.

Clinical benefits of TAVI included significantly shorter stays in the intensive care unit and in the hospital. The New York Heart Association (NYHA) functional class and 6-minute walk distance were strikingly improved at 1 year in both study groups, although, at 30 days, the benefits were greater with TAVI than with SAVR.

Intermediate risk[10]

The PARTNER 2™ S3i trial using the SAPIEN XT™ valve system in patients at intermedicate surgical risk demonstrated three key results: (1) TAVI was non-inferior to SAVR with respect to the primary endpoint of all-cause mortality and disabling stroke for up to 2 years and resulted in a similar degree of lessening of cardiac symptoms; (2) bioprosthetic valve gradients were lower and the areas were greater with the SAPIEN XT™ valve compared with surgical valves, whereas the incidence of paravalvular aortic regurgitation was higher after TAVI than after SAVR; (3) several benefits with regard to secondary endpoints were associated with TAVI, including low risk of bleeding events, acute kidney injuries, new-onset atrial fibrillation and more rapid early recovery that resulted in shorter stays in the ICU and hospital.

Also in 2016, a third-generation valve system (SAPIEN 3™) observational study demonstrated superiority of TAVI compared with SAVR with regard to the composite outcome of mortality, stroke and regurgitation at 1 year,[11] suggesting that TAVI might be the preferred treatment alternative to SAVR in intermediate-risk patients.

Low risk[12]

The clinical benefits of TAVI compared with SAVR were extended to patients at low surgical risk in the multicentre, randomised PARTNER 3™ trial, reported in 2019, using the SAPIEN 3™ valve system. Results demonstrated superiority for TAVI for the composite endpoints of all-cause mortality, stroke and cardiovascular rehospitalisation at 1 year and for multiple pre-specified secondary endpoints.[12]

The SAPIEN 3™ valve was approved in the EU for use in patients with ssAS, independent of surgical risk. (press release)

In March 2020, the principal investigators of the PARTNER 3™ trial reported the clinical and echocardiographic outcomes at 2 years at an American College of Cardiology Congress.[13]

Among low-risk patients with AS, TAVI superiority to SAVR at reducing primary endpoint events (death, stroke and re-hospitalisation) demonstrated at Year 1 was sustained at Year 2 (37% reduction). TAVI was associated with:

- Lower incidence of stroke and atrial fibrillation and a shorter hospital stay compared with SAVR
- Fewer re-hospitalisations compared with SAVR
- Larger improvements in patients' quality of life compared with SAVR
- A statistically insignificant need for new, permanent pacemakers within 30 days
- Higher incidence of mild paravalvular aortic regurgitation compared with SAVR; incidence of moderate-to-severe paravalvular aortic regurgitation was rare and similar between treatment groups
- Increased valve thrombosis, especially between 1 and 2 years[13]
- No significant deterioration in valve function between 1 and 2 years in either group[13]
- Replacement valve durability is absolutely critical in this low-risk population (because they have a lower mean age than those at intermediate or high risk), and the Year 10 evaluation of valve deterioration will be key.

The authors concluded that, on the basis of what is now known, TAVI with the SAPIEN 3™ valve system is the treatment of choice in all-risk patients with ssAS – the only TAVI device with proven superiority over SAVR.

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The PARTNER 3™ Trial plan is summarised in Figure 1 and the comparison summary of primary and secondary endpoints of TAVI vs SAVR is shown in Table 1.

Figure 1: PARTNER 3™ Trial plan (adapted from Ref. 13)

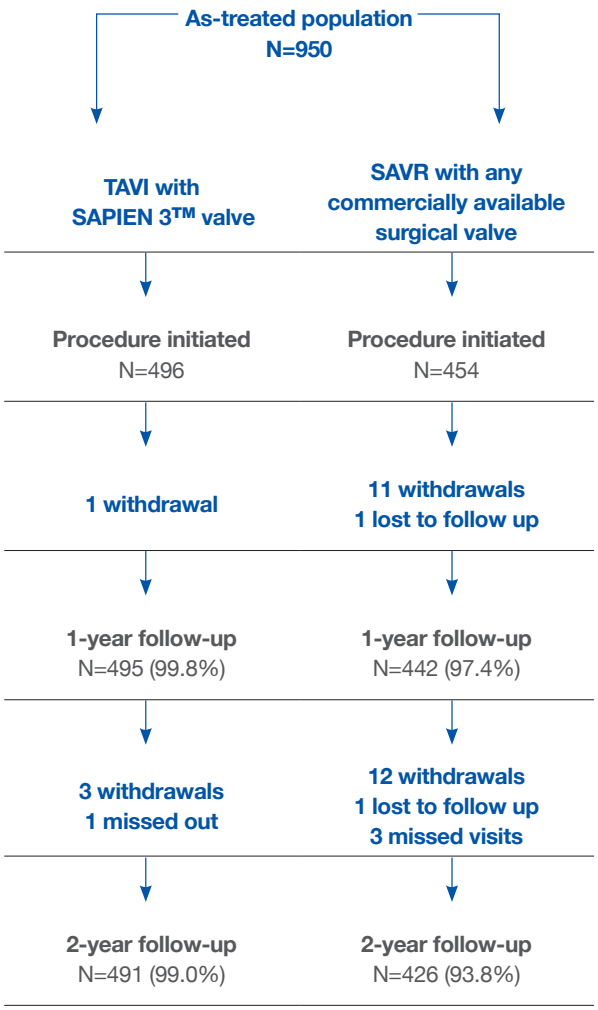

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Table 1: (a) Primary endpoints at Years 1 and 2, TAVI vs SAVR (PARTNER 3™ trial)

Endpoint	1-Year follow-up[12,14]		2-Year follow-up[13]	
	TAVI N=496 (%)	SAVR N=454 (%)	TAVI N=496 (%)	SAVR N=454 (%)
All-cause mortality, all stroke, rehospitalisation	8.5	15.1	11.5	17.4
All-cause death	1.0	2.5	2.4	3.2
All stroke	1.2	3.3	2.4	3.6
Death or disabling stroke	1.0	3.1	3.0	3.8
Rehospitalisation (valve related or procedure related, including heart failure)	7.3	11.3	8.5	12.5

(b) Primary and secondary endpoints at 30 days, TAVI vs SAVR (PARTNER 3™ trial) (adapted from Refs 12 and 14)

Endpoint	30-day follow-up	
	TAVI N=496 (%)	SAVR N=454 (%)
Primary endpoint		
Composite of death, stroke and rehospitalisation	4.2	9.3
All-cause death	0.4	1.1
All stroke	0.6	2.4
Rehospitalisation	3.4	6.5
Secondary endpoint		
Major vascular complications	2.2	1.5
Rehospitalisation due to heart failure	0.2	0.9
New-onset atrial fibrillation	5.0	39.5
Life-threatening, disabling or major bleeding	3.6	24.5
New permanent pacemaker	6.5	4.0
Discharged to home/self-care	95.8	73.1
Median length of hospital stay	3 days	7 days

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Further key points from the Mack PARTNER 3™ studies:

Optimising organisational efficiencies

Procedure time (in minutes) has been shown to be reduced from 208.3 for SAVR to 58.6 for TAVI.[14]

Because the SAPIEN 3 TAVI procedure is less invasive with fewer clinical complications than SAVR, both median intensive care time and median total length of stay (LOS) are reported to be lower than SAVR.[14] LOS was reported to be 7 and 3 days for TAVI and SAVR, respectively.[14]

96% of transfemoral (TF) TAVI patients are discharged within 30 days compared with 73% of SAVR patients.[12]

Patient safety, quality of life and health outcomes

Patient-related benefits and patients' quality of life have been found to improve the fastest following TAVI at 30-days post-procedure with the SAPIEN 3™ valve compared with SAVR: quicker discharge home (96% for TAVI vs 73.1% for surgical aortic valve replacement [SAVR]);[12] improved health status, as measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ) instrument (a 38% change from baseline for TAVI compared with 13% for SAVR), and improved 6-minute walk distance (+17.2 metres from baseline with TAVI vs -15.2 for SAVR).[14]

In 2019, PARTNER 3™ clinical outcome superiority of TAVI vs SAVR was supported by patient-perceived superiority. Using data from the PARTNER 3™ trial, Baron and colleagues[15] compared health status outcomes after TAVI vs SAVR in low-risk patients at Months 1, 6 and 12. They found that TAVI patients improved more rapidly than SAVR patients, showing a difference of 16% between groups in the Kansas City Cardiomyopathy Questionnaire overall summary scores at Month 1. Previous studies (in higher risk patients) have already shown TAVI to be associated with better (early) health status but this study also observed a sustained health status benefit of TAVI compared with SAVR at later time points of 6 months and 1 year.

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Financial impact of the SAPIEN 3™ platform

Shorter procedural times for TAVI compared with SAVR[14] means that between 2 and 3 more patients can be treated daily in one cathlab/hybrid room, or costs can be cut by reallocating/releasing staff.[14]

The TAVI minimalist approach limits direct procedural costs (estimated at a saving of ~€4000 over SAVR).[14,16] More importantly, it shortens the median LOS[12] (a saving of ~ €1200 over SAVR for intensive care unit LOS,[14,17] and ~ €1400 for ward LOS[14,17]), thereby minimising post-procedure costs (additional diagnostics, additional intervention and additional Intensive care unit and ward time).[14]

Potential cost savings with TAVI, resulting from lower complication rates compared with SAVR, have been quantified with the SAPIEN 3™ valve at ~€4000 per procedure.[14,18]

Re-hospitalisation has hospital costs in terms of staff, beds and procedural resources and lowering re-hospitalisation rates allows these resources to be allocated elsewhere, increasing hospital efficiency and lowering waiting lists, leading to better outcomes for patients. The SAPIEN 3™ valve leads to less hospitalisation at 30 days compared with SAVR, and it is the only TAVI system superior to SAVR for all-cause death, all stroke and re-hospitalisation at 1 year (8.5% vs 15.1%).[12]

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TAVI with the SAPIEN 3™ platform: further evidence

Further 2019 studies with the SAPIEN 3™ platform have investigated the safety and efficacy of next-day discharge, taking into consideration the individual patient characteristics and medical need.

- In the FAST-TAVI trial (**F**easibility **a**nd **S**afety of early discharge after **T**ransfemoral **TAVI**), Barbanti and colleagues in three European countries defined and validated the adequacy of a pre-specified set of risk criteria and its ability to predict timely and safe discharge properly after intervention in a prospective European, multi-centre register.[19]
  The rate of 30-day complications did not reveal any risk increase with this strategy, compared with the reported outcomes in major TAVI trials and registries.[19]
  The median LOS was 2 days: 26.8% were discharged within 1 day, 51% within 2 days and 72.6% within 3 days. The majority of patients were discharged home.[19]
- Lauck[20] and Wood[21] have described the development, implementation and evaluation of the Vancouver 3M (Multidisciplinary, Multimodality but Minimalist) Clinical Pathway for transfemoral TAVI *(Figure 2)*.
- In 2019, Wood and colleagues[21] showed that adherence to this clinical pathway at low-, medium- and high-volume TAVI centres allowed next-day discharge in 80% of patients and 48h discharge in 90% of patients, with excellent safety and efficacy outcomes.

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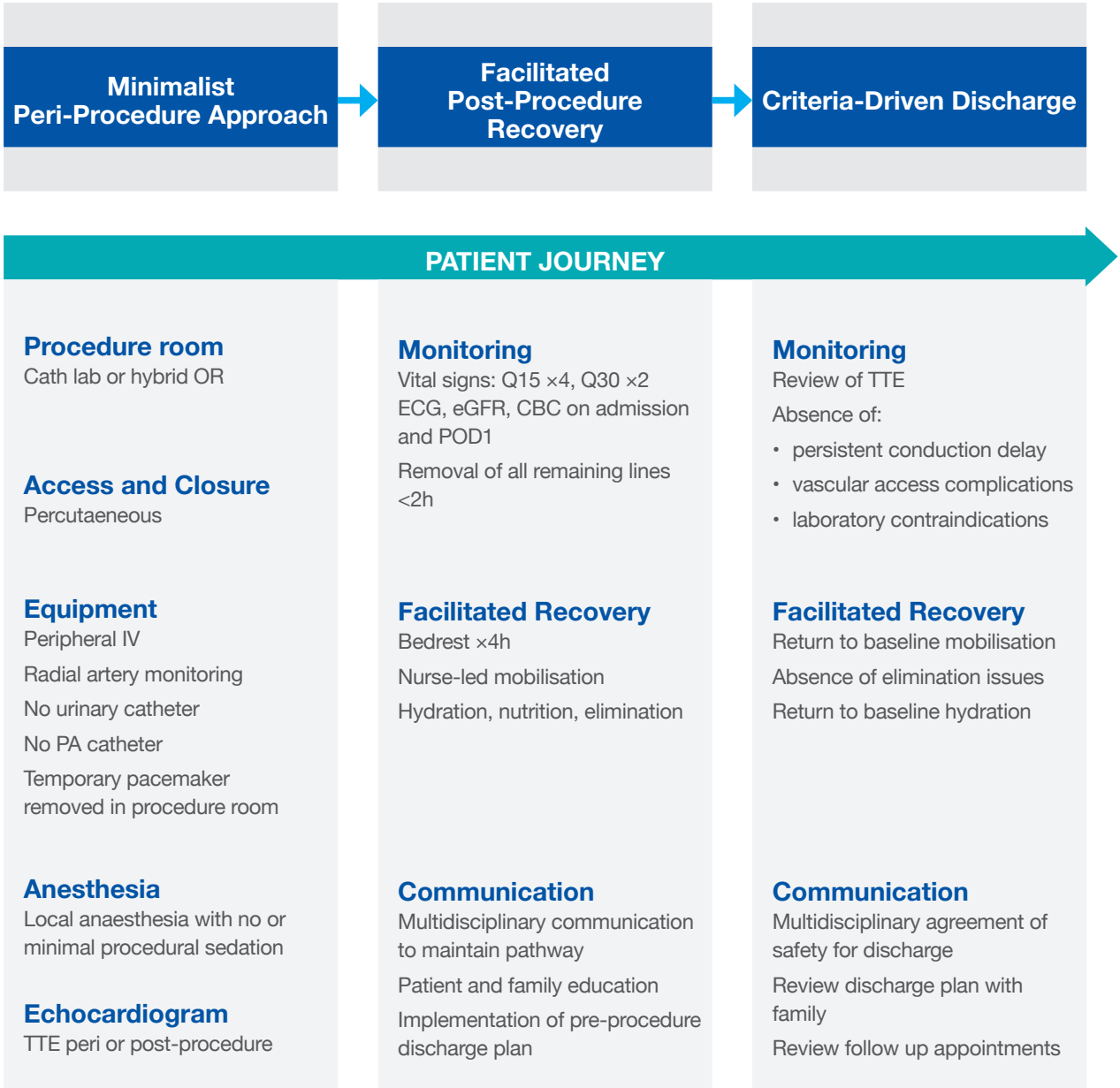
Figure 3: Vancouver 3M TAVR clinical pathway - from admission to discharge (adapted from Ref. 21)



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Conclusion

This paper has summarised the key evidence base that supports the use of the SAPIEN 3™ platform for the treatment of all-risk patients with ssAS. Snap-shot evaluations of key papers can be found in the Appendix.

The advantages of this system over SAVR in terms of organisational efficiency, economic impact and patient safety and satisfaction were of compelling impact before the COVID-19 pandemic.

This is even more the case as the world emerges from the pandemic.

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