

Transcatheter aortic valve implantation is still inappropriate in low-risk, young patients: a UK perspective

The PARTNER 3 and Evolut LRT trials have provided the evidence base for transcatheter aortic valve implantation in low-risk patients. However, there are still issues with durability, long-term follow up and complications before their widespread use can be considered appropriate in this group.

Suvitesh Luthra¹

Sunil K Ohri¹

Author details can be found at the end of this article

Correspondence to:

Suvitesh Luthra;
drsl00@gmail.com

Transcatheter valve implantation has been approved for the treatment of aortic stenosis in low-risk patients in the USA and Europe. There have been calls for its approval in the UK and a lot of pressure has been put on the National Institute for Health and Care Excellence to endorse it for low-risk patients with severe calcific aortic stenosis.

There are still significant concerns regarding this technology despite short-term data from two trials on which the American Food and Drug Administration and the European CE mark approvals were based. This has implications for patients, policy makers, healthcare providers and the NHS. Expanding the indications for transcatheter aortic valve implantation without substantial long-term evidence could cause significant disruptions to a well-established healthcare economics and service delivery model, increase inappropriate use and may harm low-risk, young patients.

Transcatheter aortic valve implantation has been a lifesaving technology for patients who are older or infirm, who require aortic valve replacement but are deemed too high risk for surgery. It has been a phenomenal success in patients at high to intermediate surgical risk where it reduces procedural mortality, length of hospital stay, morbidity of surgery, readmissions and prolongs life (Mack et al, 2015; Leon et al, 2016). These developments were welcomed by surgeons as they meant that they did not have to operate on very high-risk patients. There has been an exponential increase in case volumes in the USA, Europe and the UK (Durko et al, 2018).

The Food and Drug Administration approved transcatheter aortic valve implantation for low-risk cases in August 2019 despite a lack of long-term data (Wu et al, 2020). The European CE mark was approved for the Edwards Sapien 3 transcatheter aortic valve in low-risk patients soon after. Three of the four randomised controlled trials for transcatheter aortic valve implantation in low-risk patients were sponsored by a single device manufacturer (Medtronic). The approvals were based on two pivotal trials (PARTNER 3; Mack et al, 2019, and Evolut LRT; Popma et al, 2019). Both of these were industry funded and their scientific validity has been questioned (Freemantle et al, 2019; Luthra and Ohri, 2020). Such generous support and funding with proper independent oversight for a new technology with so much at stake would have been welcome. Both trials concluded that not only was transcatheter aortic valve implantation non-inferior but was in fact superior to surgical aortic valve replacement in low-risk groups. However, the trials had older patients (mean age 74.8 years) and short follow up (1 year for PARTNER 3 and 2 years for Evolut LRT). The change in guidance for transcatheter aortic valve implantation in low-risk patients does not stipulate a minimum age, anatomy or risk profile for patients undergoing this procedure and leaves the decision about whether to perform transcatheter aortic valve implantation or surgery to the discretion of local multidisciplinary heart teams (Coylewright et al, 2020).

How to cite this article:

Luthra S, Ohri SK.
Transcatheter aortic valve implantation is still inappropriate in low-risk, young patients: a UK perspective. Br J Hosp Med. 2021. <https://doi.org/10.12968/hmed.2020.0059>

Transcatheter aortic valve implantation in the UK

Transcatheter aortic valve implantation was rolled out in the UK at a consensus meeting in December 2008 in London, organised by the Department of Health Heart Team,

in collaboration with the NHS Improvement Programme and the clinical networks in England. The UK TAVI Steering Group was established in 2008, with representation from professional specialist societies (Society for Cardiothoracic Surgery in Great Britain and Ireland and British Cardiovascular Intervention Society), government (Department of Health), commissioners (National Specialist Advisory Group) and regulators (National Institute for Health and Care Excellence). A joint statement from the British Cardiovascular Intervention Society and the Society of Cardiothoracic Surgeons (2008) was released and subsequently a guidance document for clinical governance, research and audit of this new technology was circulated to all commissioning groups in England (Sethi et al, 2009). This was based on the National Institute for Health and Care Excellence (2008) guidance supporting appropriate use of transcatheter aortic valve implantation. The last update of this guidance (National Institute for Health and Care Excellence, 2017) was based on evidence of efficacy and safety from PARTNER2 (Edwards Lifesciences) and CoreValve (Medtronic) trials. Transcatheter aortic valve implantation numbers have increased from 66 (2007) to 4458 (2018–19) from 35 UK centres (80 procedures per million population, British Cardiovascular Intervention Society, 2020). For the same year, almost 5000 isolated aortic valve replacements were performed, which has remained constant over the last decade. The National Institute for Health and Care Excellence guidance needs an urgent update with the new evidence.

Transcatheter aortic valve implantation has not been approved for use in low-risk cases in the UK so far. The National Institute for Health and Care Excellence has resisted endorsement for low-risk groups for many years and generally, clinical commissioning groups have been reluctant to fund the procedure in patients for whom surgery is an option. The motivation for clinical commissioning groups has been primarily financial, as even the industry-subsidised cost of a transcatheter aortic valve implantation valve is almost ten times the cost of a surgical valve. Not all of these costs can be recuperated from reduced hospital stay, and questions remain regarding longevity of these valves, paravalvular leak rates, need for permanent pacemakers, anticoagulation with warfarin, results of valve-in-valve transcatheter aortic valve implantation therapy and effects on quality of life for young low-risk patients. So far, patients have been considered on a case-by-case basis without factoring in patient choice for transcatheter aortic valve implantation. The industry and interventional cardiology groups have aggressively pursued the agenda of mainstreaming transcatheter aortic valve implantation for low-risk groups without consideration of age.

In the authors' experience, there was a surge in transcatheter aortic valve implantation cases during the COVID-19 pandemic, largely as a result of the complete halt of surgical operating lists. Even in that situation, only high to intermediate risk, urgent cases that were confirmed COVID-19 negative and could not be discharged without intervention were considered for transcatheter aortic valve implantation, to reduce pressure on intensive care and ward beds. Even in the extenuating circumstances of the pandemic, most units have not performed transcatheter aortic valve implantation in low-risk patients.

Serious concerns for young, low-risk patients

The concerns arise from both trial and registry data (Luthra et al, 2020; Zhang et al, 2020). The trial data are highly selective, and there are no long-term data on durability of transcatheter aortic valve implantation valves. Rates of permanent pacemaker implantation and dependency are very high (up to 30–40% compared to 3–5% for surgery), and moderate to severe paravalvular leak rates are three to eight times higher than those after surgery (Luthra et al, 2020). These factors are all associated with increased late interventions and reduced life expectancy in young patients. There is increasing realisation after the GALILEO and GALILEO-4D trials (Dangas et al, 2020; De Backer et al, 2020) that these patients will also need lifelong anticoagulation with warfarin with its attendant risks of decreased quality of life, bleeding and thrombosis. GALILEO was terminated prematurely because of concerns about both the safety and efficacy of the treatment arm.

Younger patients are more likely to have unsuitable valve anatomy (bicuspid aortic valves) and need additional aortic procedures. Previous transcatheter aortic valve implantation in

this group substantially increases the risk of coronary interventions and stenting, which will likely be needed in later years as a result of their long life expectancy. The options for early transcatheter aortic valve implantation valve failures in young patients are not well established and results of subsequent interventions for these failed valves are largely unknown.

Young low-risk patients, including those with adult congenital disease with bicuspid aortic valves, women of reproductive age and pregnant women, are more likely to be attracted to 'keyhole' and 'day case' procedures, which require less time off work and away from family, despite the considerable resulting potential long-term morbidity burden of reinterventions for paravalvular leaks and early valve failures, need for anticoagulation, pacemakers and ultimately reduced life expectancy.

Impact on patients and the NHS

Around 80% of patients referred for aortic valve replacement are low risk. So far, transcatheter aortic valve implantation has been a complementary substitute for conventional surgery. Expanding the indication to low-risk surgical cases pits transcatheter aortic valve implantation against surgery as a competing, high-cost, unproven technology. Surgery has been the gold standard in this group. It is cost effective, lasts for a long time and is proven over many decades of experience from both trial and registry data.

The economic impact and cost analysis of transcatheter aortic valve implantation has been confined to intermediate and high-risk groups (life expectancy of 2–5 years), mostly from the USA. These cannot be extrapolated to young low-risk groups (life expectancy of 15–20 years). The high costs of treatment, inequity and inefficiencies in healthcare delivery, pressure from lobby groups, industry and monopolistic private insurance firms are well known in the American private healthcare system. These are not really applicable to the NHS, although industry-funded patient pressure groups and so-called thought leaders can influence the debate in the UK.

A change in use would cause major disruptions in healthcare planning, supply chains, expenditure and fiscal deficits in an already overstretched healthcare system. Significant infrastructure investments for new expensive hybrid cardiac catheter labs and staffing would be needed to meet the surge in demand. All this would be for an unproven technology at the expense of an existing, proven, cost-effective surgical alternative with excellent long-term results. There are still significant concerns regarding this technology despite the short-term data from two trials on which the Food and Drug Administration approval was based. This has significant implications for patients, policy makers, healthcare providers and the NHS. Expanding the indications for transcatheter aortic valve implantation without substantial long-term evidence and debate would cause significant disruptions and increase inappropriate use to the long-term detriment of low-risk, young patients.

Author details

¹Wessex Cardiothoracic Centre, Southampton University Hospital NHS Foundation Trust, Southampton, UK

Key points

- PARTNER 3 and Evolut LRT now provide the evidence base for transcatheter aortic valve implantation in low-risk patients.
- National Institute for Health and Care Excellence guidance for transcatheter aortic valve implantation needs to be updated to account for this new evidence.
- There are still concerns about long-term durability, anticoagulation, paravalvular leaks and pacemaker implantation rates, as a result of which wider adoption of transcatheter aortic valve implantation in low-risk groups in the UK is still inappropriate.

References

- British Cardiovascular Intervention Society, Society of Cardiothoracic Surgeons. Transcatheter aortic valve implantation (TAVI). 2008. <https://www.bcis.org.uk/wp-content/uploads/2016/12/BCIS-SCTS-position-statement.pdf> (accessed 26 February 2021)
- British Cardiovascular Intervention Society. BCIS National Audit Adult Interventional Procedures. 1st April 2018 to 31st March 2019. 2020. <https://www.bcis.org.uk/wp-content/uploads/2020/12/BCIS-Audit-2018-19-data-ALL-4-5-2020-for-web.pdf> (accessed 26 February 2021)
- Coylewright M, Forrest JK, McCabe JM, Nazif TM. TAVR in low-risk patients: FDA approval, the new NCD, and shared decision-making. *J Am Coll Cardiol.* 2020;75(10):1208–1211. <https://doi.org/10.1016/j.jacc.2019.12.057>
- Dangas GD, Tijssen JGP, Wöhrle J et al. GALILEO investigators. A controlled trial of rivaroxaban after transcatheter aortic-valve replacement. *N Engl J Med.* 2020;382(2):120–129. <https://doi.org/10.1056/NEJMoa1911425>
- De Backer O, Dangas GD, Jilaihawi H et al. GALILEO-4D Investigators. Reduced leaflet motion after transcatheter aortic-valve replacement. *N Engl J Med.* 2020;382(2):130–139. <https://doi.org/10.1056/NEJMoa1911426>
- Durko AP, Osnabrugge RL, Van Mieghem NM et al. Annual number of candidates for transcatheter aortic valve implantation per country: current estimates and future projections. *Eur Heart J.* 2018;39(28):2635–2642. <https://doi.org/10.1093/eurheartj/ehy107>
- Freemantle N, Irs A, De Paulis R et al. Transcatheter versus surgical aortic valve replacement: what does the latest evidence tell us? *Eur J Cardiothorac Surg.* 2019;56(1):7–9. <https://doi.org/10.1093/ejcts/ezz163>
- Leon MB, Smith CR, Mack MJ et al. PARTNER 2 Investigators. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med.* 2016;374(17):1609–1620. <https://doi.org/10.1056/NEJMoa1514616>
- Luthra S, Ohri SK. Transcatheter aortic valve implantation for low-risk aortic stenosis: are we ready? *Eur J Cardiothorac Surg.* 2020;57(3):413–417. <https://doi.org/10.1093/ejcts/ezz372>
- Luthra S, Leiva-Juárez MM, Ohri SK. Surgical vs transfemoral aortic valve replacement in low-risk patients: an updated meta-analysis of trial and registry data. *J Card Surg.* 2020;35(9):2264–2274. <https://doi.org/10.1111/jocs.14802>
- Mack MJ, Leon MB, Smith CR et al. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet.* 2015;385(9986):2477–2484. [https://doi.org/10.1016/S0140-6736\(15\)60308-7](https://doi.org/10.1016/S0140-6736(15)60308-7)
- Mack MJ, Leon MB, Thourani VH et al; PARTNER 3 Investigators. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med.* 2019;380(18):1695–1705. doi: <https://doi.org/10.1056/NEJMoa1814052>
- National Institute for Health and Care Excellence. Transcatheter aortic valve implantation for aortic stenosis. Interventional procedures guidance [IPG266]. 2008. <https://www.nice.org.uk/guidance/IPG266> (accessed 26 February 2021)
- National Institute for Health and Care Excellence. Transcatheter aortic valve implantation for aortic stenosis. Interventional procedures guidance [IPG586]. 2017. <https://www.nice.org.uk/guidance/ipg586> (accessed 25 January 2021)
- Popma JJ, Deeb GM, Yakubov SJ et al; Evolut Low Risk Trial Investigators. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med.* 2019;380(18):1706–1715. <https://doi.org/10.1056/NEJMoa1816885>
- Sethi S, Daniel T, Howell J, Griffin C. A commissioning framework for transcatheter aortic valve implantation (TAVI) for severe symptomatic aortic stenosis. 2009. <https://www.bcis.org.uk/wp-content/uploads/2016/12/TAVI-National-Commissioning-Framework-FINAL-160309.pdf> (accessed 26 February 2021)
- Wu C, Vasseur B, Maisel W. The march of transcatheter aortic valve replacement therapy-US Food and Drug Administration perspectives on device approval for patients at low surgical risk. *JAMA Cardiol.* 2020;5(1):5–6. <https://doi.org/10.1001/jamacardio.2019.4383>
- Zhang X, Wang T, Lan R et al. Meta-analysis comparing results of transcatheter versus surgical aortic-valve replacement in patients with severe aortic stenosis. *Am J Cardiol.* 2020;125(3):449–458. <https://doi.org/10.1016/j.amjcard.2019.10.057>