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REVIEW ARTICLE

Is Transcatheter Aortic Valve Replacement Taking the Path of Disruptive Innovation Technology?

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ABSTRACT

Transcatheter aortic valve replacement (TAVR) has become the treatment of choice for patients with severe symptomatic aortic stenosis (AS) at high risk and potentially also at moderate surgical risk. The theory of disruptive innovation has proven to be a powerful tool for thinking about innovation-driven growth. The question on hand is whether TAVR represents a disruptive innovation that might change the future of surgical aortic valve replacement (SAVR). This review follows the evolution of TAVR according to the model of disruptive innovation and assesses the prospect of a paradigm shift in the management of AS.

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KEYWORDS Aortic stenosis; disruptive innovation; transcatheter aortic valve replacement

Introduction

Transcatheter aortic valve replacement (TAVR) has become the treatment of choice for patients with severe symptomatic aortic stenosis (AS) that are at high risk and potentially also at moderate surgical risk.[1–6] Initially, TAVR was offered mostly to older patients with AS, who were previously excluded from valve replacement therapy, due to elevated surgical risk and/or excessive frailty. Recently, it became apparent that TAVR adoption is about to expand its reach by becoming available to patients with lower risk.[7] This expanded application was due to results from the latest clinical trials, which showed that TAVR was equivalent and potentially superior to SAVR for treating patients with intermediate risk.[4–6] Nonetheless, the European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA) guidelines have not yet adopted TAVR as the treatment of choice in patients at moderate risk. Thus, the question has arisen of whether TAVR represents a disruptive innovation. More specifically, whether TAVR will be adopted in low-risk patients still needs to be confirmed in a randomized study, two trials are currently ongoing. The answer to this question is important, because it might predict, or even define, the future of TAVR and the scope of TAVR utilization, particularly among patients with severe AS who are not necessarily elderly and/or at high surgical risk.

First, let's remind ourselves of the theory of disruptive innovation, which was intellectualized by Clayton Christensen and Joseph Bower in their seminal paper that appeared in 1995 in the Harvard Business Review[8] and later was reiterated and revised.[9] In the business sector, "disruption" describes a process whereby a small company (i.e., a venture) with few resources is able to mount a successful challenge to established, incumbent businesses. First, as the incumbents focus on improving their products and services for their most demanding (and usually most profitable) customers, they exceed the needs of some segments and *ignore* the needs of others. Next, entrants that prove disruptive begin by successfully targeting those overlooked segments; they gain a foothold by delivering more suitable functionality, frequently at a lower price than that offered by the incumbents. Incumbents, which are focused on chasing higher profitability in more demanding segments, tend not to respond vigorously. Entrants then move upmarket, delivering the performance required by the incumbent's mainstream customers, but preserving the advantages that drove their early success. When mainstream customers start adopting the entrant's offerings in volume, disruption has occurred.

Discussion

The evolution of TAVR innovation

Now let's get back to the TAVR story. The TAVR can be regarded from a business outlook, assessed as a healthcare saga, or viewed as the culmination of both. One should not expect to find a contradiction between the two viewpoints, because expanding clinical needs should lead to a growing business activity and vice versa. Nevertheless, I believe it is vital to follow the path of the TAVR evolution to address the question at hand, which is whether TAVR is indeed a disruptive innovation.

The first question that needs to be addressed relates to the target of disruption, in other words, "what are we disrupting?"

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The instinctive answer by many would be "we are disrupting the surgical aortic valve replacement (SAVR)"—but is this really the case? Initially, it was certainly not the case, because TAVR was offered and/or restricted to patients that *were not* candidates for the SAVR or patients at high risk of experiencing a poor surgical outcome. Thus, during its infancy in evolution, TAVR was innovative, but far from being considered disruptive to SAVR. Patients offered the TAVR were mostly older individuals with AS combined with multiple co-morbidities, who were traditionally excluded from any treatment option, particularly open heart surgery. Thus, these patients with excessive morbidity and mortality risks were left with "no option," because no curative treatment was previously available for them. Consequently, the TAVR technique was initially considered for addressing those patients, i.e. the "ignored customers," according to the classic initial phase of the disruptive innovation theory.

After a series of pivotal studies, the proof of concept had been established, and TAVR was shown to be superior to the optimal medical treatment (including the palliative aortic balloon valvuloplasty procedure) among patients with AS that were at very high risk of a poor surgical outcome. TAVR was also shown to be non-inferior to SAVR among patients that could undergo surgery, but were at particularly high risk of a poor outcome. Consequently, the first TAVR device was approved by the Food and Drug Administration (FDA) in 2012 (a few years after it was approved in Europe), and it became commercially available for clinical applications. The first generation prototype, i.e. the original Cribier-Edwards device, and soon thereafter, the Sapien XT valve, exhibited significant glitches and were associated with some serious complications. For example, in the pivotal Placement of AoRTic TraNscathetER Valve (PARTNER) I trial, the peri-procedural stroke rate was 6%, vascular complications occurred in almost 20% of cases, and significant para-valvular leakage was noted in 12% of treated valves.[10,11] These complication rates would be considered unacceptable by today's standards, in our current environment of improved new generation devices and contemporary techniques.

In the CoreValve pivotal study, conducted in the United States, complications were also noted. In particular, that study reported a high need (approaching 20%) for pacemaker implants following TAVR.[12] However, that study was particularly important, because it showed for the first time that the rate of death from any cause at 1 year was significantly lower in the TAVR group than in the surgical group (14.2% vs. 19.1%). Despite these initial hurdles, TAVR fit the paradigm of a disruptive innovation, because first generation products are often unsatisfactory and must be improved with advanced modifications. Accordingly, the TAVR clinical results obtained currently with Sapien 3 and Evolut R have been much more favorable than those of the prototype valve devices.[13,14]

High-end disruptive technology

A major deviation from the classic disruptive innovation theory occurred in the TAVR pricing strategy. These devices have been expensive, in absolute and relative terms, when surgical valves are taken as a benchmark for comparison. Among inoperable AS patients, cost-effectiveness analysis of TAVR compared with standard of care (e.g., no intervention) showed that TAVR increased life expectancy at an incremental cost per life-year gained well within accepted values for commonly used cardiovascular technologies.[15] Although the pricing strategies of the two companies most dominant in producing TAVR devices (Edwards Lifesciences and Medtronic) did not follow the Christensen paradigm of disruption, the high prices could point to the formulation of an alternate theory of *disruption from above* or *high-end disruption*, rather than the *low-end disruption* that Christensen emphasized initially. The business strategy of the major TAVR-producing companies was most likely intended to position the TAVR as an exclusive product, which could enter the market at the high end. This high-end entry might have been a reasonable strategy for the industry, but it created a significant economic barrier to adoption and/or prevented widespread utilization of TAVR devices globally. Edwards Lifesciences and Medtronic initially benefitted from mutual exclusivity, because a few years earlier, they had acquired different start-up companies that had pioneered the TAVR devices (Edwards Lifesciences acquired PVT in 2004, and Medtronic purchased CoreValve in 2009). At that time, profound investments in research and development were necessary to achieve the following objectives: (1) to demonstrate the safety and efficacy of TAVR devices; (2) to fulfill the regulatory requirements; (3) to conduct large, costly, pivotal clinical trials; (4) to build the infrastructure for global manufacturing; (5) to invest in operator training; (6) to develop a marketing strategy; and (7) to continue creating updated iterations of the devices to improve procedural outcomes.

However, despite these substantial investments, one can assume that the high-end pricing strategy for TAVR devices was deliberate and disproportional to the actual financial investment in the technology. The two ventures that originally invented and developed the product made a profitable return from their investment at relatively early stages, without the need to undertake robust clinical testing, before their "exit" from the market. After integrating TAVR device production into the strategic takeover companies, TAVR sales continued to move forward and upward at a unique, rapid pace, much like the echosystem of a "start-up" company, which typically employs a backup strategy, rather than establishing a giant corporate operation. The goal was to capture as large segments as possible of the well-defined "high risk/no option" AS market, and then, to move into the lower-risk AS market. However, it is notable that both Edwards Lifesciences and Medtronic have maintained dual roles as both incumbents and entrants, because these companies have also dominated the bio-prosthetic surgical valves market. Thus, for these companies, the so-called worst case scenario of a disruptive innovation could actually become beneficial. A potential shift in the paradigm of valve utilization from the SAVR to the TAVR approach for treating AS would pose no major threat to their major core businesses. In fact, for these companies, expanding demands and increased market opportunities are about to materialize. It is even more interesting that, in the current phase of TAVR development, its adoption is

expanding and moving upmarket, which is the prerequisite for a true innovation disruption. This is where we currently stand within the field of TAVR.

The trajectory of TAVR

Recent data have indicated that, with the most contemporary valve devices, TAVR is showing non-inferior clinical outcomes compared to SAVR. Being the less invasive approach for AS therapeutics and based on these recent data, the FDA has expanded the Sapien S3 TAVR indication to include patients with AS at intermediate risk of a surgical outcome, and the Evolut R obtained a CE mark of approval for a similar group of patients, with an imminent FDA approval, following favorable results from the SURgical replacement and Transcatheter Aortic Valve Implantation (SURTAVI) trial.[6] Moreover, ongoing studies aim to explore the non-inferiority of TAVR compared to SAVR among patients with AS that are at low risk of a poor surgical outcome; those results are expected to be published in the next few years. Thus, the trajectory of disruption has already shifted towards expanded utilization, and it is beginning to capture the mainstream demand; i.e. patients with AS at relatively low risk of poor surgical outcome, which were traditionally treated with SAVR. However, it should be noted that, according to AHA/ACC and ESC guidelines, surgery remains the default approach for AS management in eligible patients that are deemed suitable for surgery.[16,17] Thus, the question at hand is whether innovative disruption has already occurred or does it remain imminent?

The impact of TAVR on overall clinical practice in relation to SAVR was recently assessed in Germany with a national survey conducted from 2007 to 2013.[18] In Germany, common practices regarding AS treatment do not necessarily match or synchronize with those of the US or other countries. The adoption of TAVR was much more expedient in Germany compared to the US. In many centers, adoption was predominant among cardiac surgeons, but some years ago, it had begun to shift toward providing TAVR to patients at low risk of poor surgical outcome. Thus, the German example could provide predictive insight into what might occur soon in the US and in other countries around the world. The reimbursement system in Germany played a major role in the fast adoption of TAVR. In this country, 32,581 TAVR and 55,992 SAVR procedures were performed during the survey period. The number of TAVR procedures increased from 144 in 2007 to 9147 in 2013, and the number of SAVR decreased slightly, from 8622 to 7048, during the same period. Patients that underwent TAVR were older than those that underwent SAVR (mean age, 81.0 vs. 70.2 years) and the former group was at higher preoperative risk. The estimated logistic European System for Cardiac Operative Risk Evaluations (EuroSCOREs) were 22.4% for the TAVR group and 6.3% for the SAVR group. The EuroSCORE is rated on a scale of 0–100%, with higher scores indicating greater risk. Between 2007 and 2013, in-hospital mortality decreased from 13.2% to 5.4% for the TAVR group and from 3.8% to 2.2% for the SAVR group. The incidences of stroke, bleeding, and pacemaker implantation also declined in both groups. Similar trends, albeit less profound, were reported by additional investigators in other countries. Thus, it seems that, although SAVR utilization has started to decline, the surgical domain has remained sustainable. Thus, although the TAVR trajectory has moved towards patients with AS at low risk of poor surgical outcome, presently, significant ground remains to be traversed before innovation disruption against SAVR has been accomplished (Figure 1).

Remaining milestones

To reach the stage of full innovative disruption, several milestones must be accomplished. First, TAVR must meet the SAVR benchmark, in terms of the quality of valve replacement. Specifically, para-valvular leakage, which represents the Achilles-heel of TAVR, must be eliminated, negligible, or at least comparable to that observed with SAVR. Second, it remains unclear which specific TAVR technology will set the highest standard for clinical performance over the short- and long-term. Indeed, it is uncertain which technique is superior, the balloon-expandable or the self-expandable valve, or whether these methods are equivalent or even complementary, each with their own specific indications. Currently, there is a paucity of truly comparative data for assessing the various, most contemporary TAVR devices; thus, it is not possible to define the highest available technical and clinical performances. Moreover, the matched propensity type of analysis and/or a comparison between TAVR-treated and historical SAVR-treated cohorts have not been sufficiently qualified for defining the best clinical practice. Thus, we have not established new therapeutic thresholds for evaluating the best interventional medical practice among patients with AS. Defining a new benchmark for TAVR performance is of the outmost importance in endeavors to meet current clinical needs and to advance the TAVR trajectory to capture most

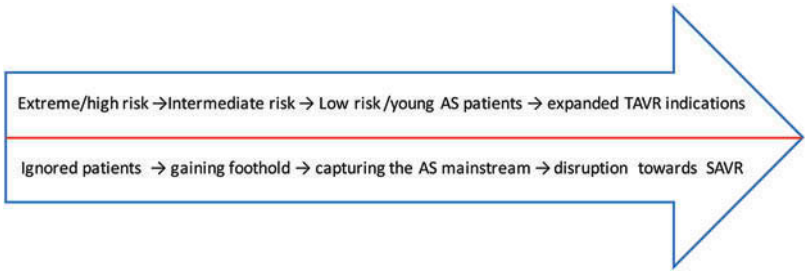

Figure 1. TAVR trajectory of disruptive innovation.

parts of the population with AS. Thus, we await additional, long-term data on TAVR performance among patients with AS at low surgical risk, before we can confirm the legitimacy of TAVR for treating relatively healthy, younger patients with AS. A primary issue for treating the relatively low-risk, young population of patients with AS is that a significant proportion has bicuspid aortic valve (BAV) stenosis.[19] BAV pathology poses a unique challenge for TAVR optimization, and it is a current focus of intense clinical investigation. Presently, the question of whether TAVR valves exhibit sufficient longevity and durability remains to be explored. Hopefully, this question will be resolved before an overwhelmingly swift move towards TAVR utilization, particularly among relatively young patients with AS that are at low surgical risk, because this group has a prolonged life expectancy. In addition, the newly discovered problem of subclinical leaflet thickening/thrombosis in patients who have received a bioprosthetic valve may temper the enthusiasm towards more generalized adoption of TAVR among "all comers" population with severe AS in need for valve replacement.[20] Finally, patient expectations and desires will play a pivotal role in TAVR adoption, because, from the patient's perspective, it is natural to prefer the least traumatic mode of treatment, assuming a favorable medical outcome.

Conclusions

In conclusion, based on the track record of TAVR adoption to date, TAVR appears to have followed the path of disruptive innovation in the field of AS therapeutics (Table 1). Nevertheless, although the trajectory of disruption is certainly heading towards growth and expansion, TAVR continues to lag behind SAVR treatments, because the majority of patients with AS are currently treated with SAVR in most parts of the world. The TAVR strategy of high-end disruption is evolving, but it has encountered a medical and economic barrier to much larger expansion, particularly in countries with limited healthcare resources. Moreover, additional data are needed to support a shift in paradigm to the "all comers" utilization of TAVR over SAVR among the large population of patients with AS. Some unique subgroups of patients represent a specific therapeutic goal, such as patients with BAV and those with predominantly aortic regurgitation. Indeed, TAVR results have been less favorable in patients with BAV compared to results in patients with the conventional tri-leaflet AS pathology. To become more inclusive, TAVR development should address AS pathology under more extreme conditions to maximize its role as a comprehensive, disruptive innovation protagonist. Patient expectations will certainly play a pivotal role in determining the dynamics and pace of TAVR adoption over SAVR, because patients tend to select the least invasive and least painful therapeutic solutions. The future will tell whether the current trajectory of TAVR will lead to a true innovative disruption, or alternatively, what shape the market will take with the new balance and/or market partitioning between TAVR and SAVR therapeutic techniques for AS management.

Table 1. TAVR and disruptive innovation summary.

What is the theory?	The TAVR trajectory	Future outlook
The theory of disruptive innovation has proven to be a powerful tool for thinking about innovation-driven growth. The question on hand is whether Transcatheter aortic valve replacement (TAVR) follows the classic path of disruptive innovation?	TAVR is a procedure initially aimed at treating high risk patients with severe symptomatic aortic stenosis (AS) and now it is geared towards lower risk AS patients and/or expanded valvular indications. In many respects, it follows the model of disruptive innovation and in reference to the surgical aortic valve replacement (SAVR) procedure. The paper assesses the current trajectory of TAVR utilization, pointing to a paradigm shift in the management of severe symptomatic AS.	Certain technical hurdles and unanswered clinical questions still confronts TAVR on its path to become a true disruptive innovation, e.g., the default technique for AS management in place of SAVR in the majority of AS patients and regardless of the surgical risk.

Disclosure statement

The author reports no conflict of interest. The author alone is responsible for the writing and content of this article.

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