Abstract

Transcatheter aortic valve implantation (TAVI) is a tremendous therapeutic advance for patients with severe aortic stenosis and high-surgical risk. Since TAVI-treated patients are elderly with multiple co-existing conditions, limited life expectancy and disproportionate health-care expenditures, the aspect of the health-related quality of life (HRQoL) benefits becomes of fundamental importance. Based on recent evidence, TAVI appears to improve significantly HRQoL measures compared with optimal standard care, which are restored to age-adjusted population norms over time.

Keywords: quality of life, transcatheter aortic valve implantation, older people

Introduction

As population is ageing, aortic stenosis (AS) creates a major health problem both for the individual and the society [1]. Advancing age is not only associated with reduced responsiveness to medical therapy for AS, such as beta-blockers, but could also be considered a contraindication in some cases [2]. On the other hand, conventional aortic valve replacement (AVR) is associated with higher morbidity and mortality rates in the elderly compared with younger patients [3]. Transcatheter aortic valve implantation (TAVI) is a therapeutic alternative for high-risk elderly patients with severe symptomatic AS [1, 4]. The clinical results of TAVI are promising, with over 90% procedural success rates and superior 1-year survival, when compared with medical treatment but with similar rates, when compared with surgery [1, 4]. Sustained favourable outcomes have recently been reported at 2- and 3-year post-TAVI from large national registries and randomised trials [5, 6]. Appropriate pre-procedural selection of patients and careful planning strategy for TAVI is crucial to optimise procedural success and ultimate outcome [6]. The impact of any new medical intervention on the health-related quality of life (HRQoL) should also be taken into serious consideration in the decision-making process, particularly if this is associated with high complication risks and costs [7].

It would be a great challenge to achieve a consensus on ideal HRQoL assessment or interpretation in elderly patients with AS undergoing TAVI for several reasons. First, old age is an independent prognostic indicator of high mortality and morbidity [3]. Secondly, TAVI population is a heterogeneous group with different lifespans, co-morbidities and disabilities, which complicate risk stratification and further management [1, 4–6]. Thirdly, previous clinical trials have excluded elderly patients, limiting the available evidence to guide treatment in this population [3]. So far, 12 studies assessed the HRQoL outcome after TAVI compared with baseline in patients with the same disease status (i.e. symptomatic severe AS needed treatment) [8–19]. Only one was a randomised, multi-centre study of TAVI versus optimal standard care (PARTNER trial Cohort B) or versus surgical valve replacement (PARTNER trial Cohort A) [1, 4].

HRQoL evaluation instruments for patients with TAVI

Currently, there is no comprehensive and standardised HRQoL instrument specific for patients with AS undergoing TAVI. Such instrument should have the ability to serve four goals: evaluation, discrimination, quantification and prediction. A proper evaluation of the overall burden,
Table 1. Baseline characteristics of patients undergoing transcatheter aortic valve implantation

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<tbody>
<tr>
<td>Age, years</td>
<td>79.1 ± 7</td>
<td>81 ± 6</td>
<td>81.7 ± 4.7</td>
<td>86 ± 2.9</td>
<td>82 ± 8</td>
<td>80.5 ± 5.9</td>
<td>78 ± 6.6</td>
<td>81 ± 4.6</td>
<td>83 ± 9</td>
<td>84 ± 7</td>
<td>80 ± 6</td>
<td>80.8 ± 6.8</td>
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<td>Log Euroscore or STS score (%)</td>
<td>18.3 ± 12.4</td>
<td>20</td>
<td>25.3 ± 8.1</td>
<td>24 ± 15.1</td>
<td>19.3 ± 9.9</td>
<td>29.7 ± 13.7</td>
<td>19.6 ± 11.3</td>
<td>23.4 ± 14.7</td>
<td>18.3 ± 10.2</td>
<td>11.2 ± 5.8</td>
<td>11.8 ± 1.4</td>
<td>6.5 ± 6</td>
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<tr>
<td>Prior MI, n (%)</td>
<td>15 (34)</td>
<td>8 (8.1)</td>
<td>10 (33)</td>
<td>0 (0)</td>
<td>8 (23.5)</td>
<td>12 (36)</td>
<td>0 (0)</td>
<td>11 (29.7)</td>
<td>23 (16)</td>
<td>23 (27.4)</td>
<td>88 (26.8)</td>
<td>9 (9)</td>
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<td>Prior PCI/CABG, n (%)</td>
<td>25 (57)</td>
<td>21 (21.2)</td>
<td>20 (67)</td>
<td>29 (36)</td>
<td>25 (33.8)</td>
<td>25 (69.4)</td>
<td>25 (56)</td>
<td>56 (39)</td>
<td>140 (42.7)</td>
<td>140 (42.7)</td>
<td>28 (28)</td>
<td>27 (15)</td>
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<td>CVD, n (%)</td>
<td>11 (11.1)</td>
<td>3 (10)</td>
<td>11 (14)</td>
<td>7 (19.4)</td>
<td>12 (36)</td>
<td>8 (23.5)</td>
<td>12 (36)</td>
<td>8 (23.5)</td>
<td>49 (27.4)</td>
<td>88 (26.8)</td>
<td>30 (9.1)</td>
<td>23 (27.4)</td>
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<td>COPD, n (%)</td>
<td>17 (39)</td>
<td>17 (17.2)</td>
<td>17 (17)</td>
<td>23 (29.3)</td>
<td>30 (40.5)</td>
<td>15 (41.7)</td>
<td>19 (37)</td>
<td>31 (21.7)</td>
<td>38 (21.2)</td>
<td>30 (9.1)</td>
<td>23 (27.4)</td>
<td>37 (20)</td>
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<td>Chronic renal insufficiency, n (%)</td>
<td>24 (55)</td>
<td>18 (18.4)</td>
<td>14 (47)</td>
<td>9 (11)</td>
<td>22 (29.7)</td>
<td>6 (17.1)</td>
<td>33 (65)</td>
<td>32 (22.4)</td>
<td>10 (5.6)</td>
<td>9 (9)</td>
<td>33 (18)</td>
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STS score, society of thoracic surgeon; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; CVD, cerebrovascular disease; COPD, chronic obstructive pulmonary disease; chronic renal insufficiency-serum creatinine >1.8 g/dl.
severely limited compared with age-matched healthy population before TAVI, there are contradictory results regarding the mental component [10, 13]. Differences in study population characteristics (i.e. sex composition, specific cognitive disorders) or even regional differences may affect the perceived mental faculties.

Short-term HRQoL after TAVI

Elderly patients with severe symptomatic AS, who are treated with TAVI, report a significant improvement in HRQoL even in 1 month after the procedure (Table 2) [8, 18]. The immediacy of HRQoL improvement after TAVI has also been demonstrated as early as 1 month in the landmark PARTNER trial. Cohort B randomised 358 patients with severe ‘inoperable’ AS to receive either TAVI or standard therapy (including balloon valvuloplasty in approximately 80%). The largest effect sizes were observed in the KCCQ social limitation and QoL components not only within the TAVI group compared with baseline (mean difference, 26 points, 95% CI: 18.6–33.5, P < 0.001 and 31.4, 95% CI: 26.5–36.4, P < 0.001, respectively), but also between the two study arms at 1 month (mean difference, 16.1 points, 95% CI: 8.1–24.1, P < 0.001 and 14.8, 95% CI: 8.6–21, P < 0.001, respectively) [16]. The elderly patients undergoing TAVI seem to perceive the impact of their disease on their general health and interpersonal relations much more seriously than physical health. The SF-12 physical health was substantially enhanced between and within-groups at 1 month but with a marked change in mental health seen only within the TAVI group at 1 month and between groups at 6 months [16].

At 3-month follow-up, Krane et al. reported a significant increase in a SF-36 physical health summarised score after TAVI consistent with high patient’s degree of independence [9, 19]. Of interest, there was no change in a SF-36 mental health score, mainly due to a remarkable reduction in role emotional and social functioning. The inclusion of patients referred to trans-apical TAVI may have led to this negative result. Further, the SF-36 may not be sufficiently effective

<table>
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<th>Table 2. Summary of studies assessing health-related quality of life in patients undergoing transcatheter aortic valve implantation</th>
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<td>Author</td>
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<td><strong>Short-term</strong></td>
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<tr>
<td>Gotzmann et al. [8]</td>
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<td>Krane et al. [9]</td>
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<td>Ussia et al. [10]</td>
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<td>Belereldjian et al. [11]</td>
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<td>Gonçalves et al. [12]</td>
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<td><strong>Mid-term</strong></td>
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<td>Georgiadou et al. [13]</td>
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<td>Gotzmann et al. [14]</td>
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<td>Ussia et al. [15]</td>
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<td>Reynolds et al. [16]</td>
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<td>Fairbairn et al. [17]</td>
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<td>Krane et al. [19]</td>
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**Pts**, patients; y, years; F, French; MLHFQ, Minnesota Living with Heart Failure Questionnaire; SF, Short Form; KCCQ, Kansas City Cardiomyopathy Questionnaire.
in detecting changes in individuals after TAVI over short periods of time. The use of such generic measure is more suitable for large-study populations or studies comparing patients with AS and healthy persons [21].

The benefits of physical functioning are not only sustained but further improved at 5 and 6 months after TAVI. In a patient population of the most advanced age, Bekeredjian et al. observed a significant improvement of all SF-36 health components, with the greatest gain observed in physical functioning 6 months after the procedure [11]. These findings were consistent with those reported by Ussia et al. [10]. Fairbairn et al. observed the greatest change in physical component to be obtained at 30 days but with further significant improvement to 6 months [18]. Gonçalves et al. also suggested the presence of significant peripheral vascular disease as a significant determinant of lower improvement in HRQoL [12]. Likewise, Reynolds et al. showed a higher positive impact on SF-12 physical summary scores at 6 months within the TAVI group. Regarding KCCQ, the extent of improvement was greater after TAVI compared with controls at 6 months than that at 1 month (mean between-group difference 21 versus 13 points). The KCCQ social limitation and QoL components were still the major contributors to these changes [16].

**Mid-term HRQoL after TAVI**

Seven studies, so far, have showed a substantial enhancement in HRQoL at 1 year after TAVI compared with baseline [13–19]. The physical health scores declined insignificantly between 6 months and 1 year in all surveys, reflecting worsening health, which could gradually become significant over longer follow-up periods (Table 2), (Figure 1). Conflicting results exist regarding the 1-year mental evaluation component. Reports suggesting mental health improvement have also shown the lowest benefit in this domain (Figure 1). In the PARTNER trial Cohort B, TAVI therapy has persistent beneficial effects on a global KCCQ summary score by 20–25 points at 1 year, corresponding to an average improvement of two levels of New York Heart Association class [16]. One-year post-procedural SF-12 physical and mental health scores were favourable with mean differences of 5.7 and 6.4 points ($P < 0.001$), compared with the standard care (Figure 1), [16]. The physical improvement was suggested to be roughly comparable with a 10-year reduction in effective age.

The 1-year health of TAVI population has been consistently shown to become similar to age-matched general population norms; except from Greek patients who scored higher compared with the anticipated of the standard population, indicating the relative higher perception of their health probably due to lower expectations [13,15,18,19]. Among patient- and procedural-related characteristics assessed, the male sex and the operator experience have been identified as independents predictors of post-procedural HRQoL improvement [18].

In terms of health economic benefit of TAVI, a health-utility analysis has recently been published based on the PARTNER trial. By projecting survival data and costs beyond the trial period in the cohort of inoperable patients, the cost-effectiveness analysis for TAVI suggested an
incremental cost-effectiveness ratio below of $62,000 per quality-adjusted life years gained, which is well within the accepted values for typically used cardiovascular technologies [25]. Although follow-up costs were lower with TAVI versus standard care—mainly due to reduced cardiovascular hospitalisations—the overall 1-year costs remained substantially higher with TAVI because of the high index admission costs [25, 26]. A recent report from Belgium supported that this economic benefit is restricted only to the anatomic inoperable patients and not to those inoperable for medical reasons [27].

**HRQoL assessment after TAVI versus surgical AVR**

Surgical AVR has been shown to improve HRQoL scores, comparable with those of general population, even among octogenarians at 1 year after surgery [28]. However, surgical candidates included in these studies were in a less compromised preoperative status than TAVI patients. In the only available randomised PARTNER trial Cohort A, high-risk patients with severe AS were assigned to TAVI (n = 348, 84 ± 7 years) performed via transfemoral (n = 244) or transapical approach (n = 104) or AVR (n = 300, 84 ± 6 years). Over 1-year follow-up, all patients experienced a marked improvement in HRQoL assessed by KCCQ, SF-12 and EQ-5D questionnaires. Transfemoral TAVI resulted in substantial HRQoL improvement over 1-year follow-up with TA VI. These advantages of TAVI but only via a transfemoral approach occur at 1 month compared with conventional surgery and are diminished at later time points. The advantage of TAVI will depend on careful selection of patients who are not surgical candidates, and yet do not have extreme co-morbidities that overwhelm the benefits of TAVI.

**Conclusion**

Along with the positive performance and durability data, TAVI appears to maximise both symptom reduction and HRQoL for elderly ‘inoperable’ patients. This aspect becomes of paramount importance in the context of the high risks and costs involved in this procedure. TAVI yields early substantial HRQoL benefits compared with baseline or standard treatment, which accrue for at least a year. These advantages of TAVI but only via a transfemoral approach occur at 1 month compared with conventional surgery and are diminished at later time points. The ultimate value of TAVI will depend on careful selection of patients who are not surgical candidates, and yet do not have extreme co-morbidities that overwhelm the benefits of TAVI.

**Key points**

- General and disease-specific HRQoL are improved with TAVI over standard care among inoperable patients at 1, 6 and 12 months.
- A substantial enhancement in physical functioning has been unanimously reported, comparable with a 10-year reduction in effective age.
- Both surgical and transcatheter AVR resulted in marked improvement in HRQoL over 1-year follow-up with greater benefits at earlier time points in the transfemoral TAVI group.
- No significant benefit was observed in HRQoL after transapical TAVI over surgical AVR at any time point.
- The penetration of this technology in the broad group of elderly patients with multiple co-morbidities and severe AS will depend on the optimal patient selection and the continuing evolution of the technology.

**Shortcomings and future perspectives**

Except from the PARTNER trial, all the other were single-centre studies with small sample sizes. In design, all these studies were biased due to deaths or patients who failed to complete the questionnaires at the follow-up period, which may result in a study cohort, largely composed by patients who benefited from TAVI. Further, the studies comparing HRQoL changes between TAVI and surgical AVR were unblinded and therefore, a placebo-like effect cannot be excluded; a blinded study would be more informative but this would require a broadened indication of TAVI for patients with lower surgical risk.

It is important to use quantitative methods to complement standardised HRQoL instruments in order to adequately capture the totality of survivor’s experience. The development of an optimal set of HRQoL measures, the identification of specific predictors of future HRQoL, a longer-term follow-up and further refinements regarding the access sites would provide more comprehensive understanding of TAVI patient’s journey.

**Conflicts of interest**

None declared.
Funding

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References

17. Cohen DJ; on behalf of PARTNER Investigators. Health-related quality of life after transcatheter vs. surgical aortic valve replacement in high-risk patients with severe aortic stenosis results from The PARTNER Trial (Cohort A). Transcatheter Cardiovascular Therapeutics Conference. November 7, 2011; San Francisco, USA.