The impact of education as a marker of socio-economic status on survival of patients after transcatheter aortic valve implantation

Barbora Chabová[1], Petr Hájek[1], Radka Adlová[1], Eva Hansvenclová[1], Monika Pecková[2], Josef Veselka[1]

[1]Department of Cardiology, Motol University Hospital, Prague, Czech Republic

[2]Institute of Applied Mathematics and Information Technologies, Faculty of Science, Charles University, Prague, Czech Republic

Abstract

Introduction: An association exists between low socio-economic status (SES) and increased cardiovascular and all-cause mortality worldwide.

Aim: To evaluate the impact of educational level as a marker of socio-economic status (SES) on the clinical condition of patients before transcatheter aortic valve implantation (TAVI) and survival after TAVI.

Material and methods: We conducted a retrospective observational study involving patients with severe aortic stenosis (AS) who underwent TAVI. We divided patients based on their level of education into lower (LLE) and higher educational level (HLE) groups. We evaluated periprocedural (combined endpoints of device success (DS) and early safety (ES), according to VARC2 criteria) and mid-term outcomes (all-cause and cardiovascular mortality).

Results: Of the 379 study patients, 212 were in the LLE group. The mean follow-up was 2.1 ±1.8 years. Patients with a LLE were younger (77.4 ±7.2 vs. 79.4 ±6.5 years, $p = 0.006$) and more often female (58% vs. 40%, $p < 0.001$). They had higher body mass index (29.5 ±5.7 vs. 28.3 ±4.8, $p = 0.037$), more often type 2 diabetes mellitus (43% vs. 31%, $p = 0.013$) and moderate or severe aortic regurgitation (8% vs. 2%, $p = 0.026$), and some patients' condition required urgent TAVI (5% vs. 0%, $p = 0.003$). There were no differences in combined procedural endpoints. The all-cause mortality during mid-term follow-up was 25% in the LLE group and 24% in the HLE group (log-rank, $p = 0.941$). Cardiovascular mortality was 19% in both groups (log-rank, $p = 0.925$).

Conclusions: Patients with an LLE required TAVI at a younger age, had more comorbidities and had a more risky profile. Level of education did not influence periprocedural and mid-term outcomes.

Key words: aortic stenosis, transcatheter aortic valve implantation, education, socio-economic status.

Summary

An association exists between low socioeconomic status and increased cardiovascular and all-cause mortality worldwide. However, there are no data in patients with aortic stenosis treated with transcatheter aortic valve implantation (TAVI). We found that even though patients in lower and higher educational groups had different baseline characteristics, their periprocedural and mid-term outcomes after TAVI did not differ. The findings of this study underline the importance of early intervention of risk factors in patients with a lower level of education. Once these patients undergo TAVI, their periprocedural and mid-term outcomes are comparable to patients with a higher level of education.

Introduction

An association exists between low socioeconomic status (SES) and increased cardiovascular and all-cause mortality worldwide [1–4]. This relationship has been extensively studied primarily in coronary artery disease (CAD), and many studies have demonstrated increased mortality in acute coronary syndrome (ACS) in patients with low SES [5–9]. Education, rather than wealth, is the socioeconomic indicator most consistently associated with outcomes [4]. Other factors, including income, cardiovascular risk factors, and health behaviors only partially explain this relationship [10].

Corresponding author:

Barbora Chabová MD, Department of Cardiology, Motol University Hospital, Prague, Czech Republic, e-mail: barborachabova@gmail.com

Aortic stenosis (AS) is the most common primary valve disease leading to intervention in Europe and North America, with a growing prevalence due to the ageing population [11]. Aortic stenosis shares several risk factors with atherosclerosis and CAD [12], although therapy differs [13]. Transcatheter aortic valve implantation (TAVI) is now the method of choice for a wider range of patients and has led to fewer untreated patients [14–17].

Aim

We hypothesized that a lower level of education would have similar adverse effects on prognosis of patients with severe AS as seen in CAD. We conducted this study to evaluate the impact of educational level, as an indicator of socio-economic status, on baseline characteristics and periprocedural and mid-term outcomes of patients with severe aortic stenosis after TAVI.

Material and methods

Design

We conducted a single-center, retrospective observational study comparing outcomes of adult patients with severe AS who underwent TAVI based on their SES. We used educational status rather than wealth as a socio-economic indicator, because of its stronger association with outcomes [4]. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients and procedures

A total of 379 consecutive patients with severe AS who underwent TAVI between 2010 and 2020 were enrolled in this study. Patients were first admitted either as hemodynamically stable for planned diagnostic evaluation or admitted acutely with decompensated heart failure. Diagnosis of severe AS was made according to echocardiographic criteria. The indication for TAVI was established by a consensus of members of the Heart Team. All TAVI procedures were performed by highly experienced interventional cardiologists at a single tertiary center. Clinical, demographic, and echocardiographic data were recorded at baseline and during follow-up. Patients had a clinical and echocardiographic examination 5 days after TAVI, 30 days after TAVI, and 1 year after TAVI. Information on education was obtained on admission or through phone calls. Information on specific events was obtained from follow-up visits and from the National Institute of Health Information and Statistics.

Patients were divided into two groups based on their educational level. The group with a lower level of education (LLE) had a primary school education, and/or vocational school education as a form of secondary education; overall, this group had a total of 12 years of school attendance or less. The group with a higher level of education (HLE) had secondary school education other than vocational and tertiary education; overall, this group had 13 or more years of school attendance.

Outcomes

Primary outcomes were mid-term (I) all-cause mortality and (II) cardiovascular mortality. Secondary outcomes included device success (DS) and early safety (ES) defined according to the "Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium (VARC2)" [18]. Device success was defined as the absence of procedural mortality, correct positioning of a single prosthetic heart valve, as well as the intended performance of the prosthetic heart valve. Early safety was defined as a composite endpoint at 30 days including all-cause mortality, all stroke, life-threatening bleeding, acute kidney injury stage 2 or 3, coronary artery obstruction requiring intervention, major vascular complication, and valve-related dysfunction requiring a repeated procedure [18].

Statistical analysis

Data are presented as means ± standard deviations (SD) for normally distributed variables and median ± interquartile range for variables with non-normal distribution. Continuous variables of the LLE and the HLE groups were compared using the Welch two-sample *t* test for the normally distributed variables and by the two-sample Wilcoxon test for the variables with some outliers. Categorical variables were compared using Pearson's χ^2 test of independence or Fisher's exact test (in the case of small, expected counts).

The log rank test was used to compare survival times between groups; Kaplan-Meier estimates of the survival curves are presented. A Cox proportional hazards model was used to identify predictors of all-cause mortality and cardiovascular mortality. A multivariate Cox model was built with all potential predictors of survival identified in univariate analysis. The model was used to test the differences between the LLE and HLE groups and to adjust for potential baseline differences between the groups. All analyses were performed using the statistical program R. A *p*-value < 0.050 was considered statistically significant.

Results

Baseline characteristics

A total of 439 patients with severe AS underwent TAVI at a single tertiary cardiology center between 2010 and 2020. After excluding 46 patients who had missing data on education, and 14 who underwent TAVI for aortic regurgitation or valve-in-valve procedures, 379 were included in the analysis. Mean follow-up was 2.1 ±1.8 years.

We identified 212 patients with LLE and 167 patients with HLE. Baseline clinical and echocardiographic characteristics of the study population are summarized in

Table I. Patients with LLE were significantly younger (*p* = 0.006), more frequently female (*p* < 0.001), had a higher body mass index (BMI; *p* = 0.037), a higher prevalence of type 2 diabetes mellitus (*p* = 0.013), and moderate or severe aortic regurgitation (*p* = 0.026) compared with patients with HLE. Ten patients, all in the LLE group, required urgent TAVI (*p* = 0.003).

Periprocedural outcomes

During TAVI, Acurate (Boston Scientific, USA) valves were implanted more often in the LLE group (*p* = 0.007), and Evolut R (Medtronic, USA) valves were more often implanted in the HLE group (*p* = 0.001). After TAVI, it was necessary to implant a permanent pacemaker more often in the HLE group (*p* = 0.030). All other procedural and postprocedural parameters were comparable between the two groups (Table II).

Mid-term outcomes

A total of 92 deaths occurred during 796 patient-years, which translates to 11.7 and 11.4 deaths per 100 patient-years in the LLE and HLE group, respectively. Periprocedural, 30-day, first year and all-cause mortality during follow-up were 4/379 (1.1%), 12/379 (3.2%), 44/379 (11.6%), and 92/379 (24.3%), respectively. Cardiovascular mortality rates after the first year and during follow-up were 33/379 (8.7%) and 71/379 (18.7%), respectively. Between study groups, we did not find any difference in mortality evaluated in various time periods (Table III, Figures 1, 2). Relative risk of all-cause mortality for the LLE group compared with the HLE group was 0.984 (95% CI: 0.651–1.489), and relative risk of cardiovascular mortality was 0.978 (95% CI: 0.610–1.566).

Subanalysis

In a univariate analysis, all-cause mortality was associated with NYHA ≥ III, atrial fibrillation, and increase in creatinine levels after the procedure (Table IV). Similar results were also seen for cardiovascular mortality with the exception of increase in creatinine levels (Table IV). *P*-values were < 0.050 for all above – mentioned variables.

We also studied the association between all-cause and cardiovascular mortality and continuous variables.

Table I. Baseline characteristics*

Parameter	Educational status		*P*-value
	Low (*n* = 212)	High (*n* = 167)	
Age [years]	77.4 ±7.2	79.4 ±6.5	0.006
Male, *n* (%)	88 (42)	100 (60)	< 0.001
Follow-up [years]	2.1 ±1.8	2.1 ±1.8	0.997
Body mass index	29.5 ±5.7	28.3 ±4.8	0.037
NYHA class†	3.0 ±1.0	2.5 ±1.0	0.113
NYHA class ≥ III, *n* (%)	112 (53)	74 (44)	0.061
Diabetes mellitus, *n* (%)	91 (43)	51 (31)	0.013
Arterial hypertension, *n* (%)	170 (80)	136 (81)	0.760
Atrial fibrillation, *n* (%)	64 (30)	65 (39)	0.075
Coronary artery disease, *n* (%)	93 (44)	76 (46)	0.750
Creatinine [μmol/l]†	87.0 ±34.5	89.0 ±35.0	0.246
Hemoglobin [g/l]	125.4 ±17.1	124.9 ±17.0	0.752
Platelets [× 10^9/l]	209.1 ±70.0	188.0 ±60.6	0.002
Pacemaker, *n* (%)	23 (11)	23 (14)	0.387
STS score†	2.6 ±2.6	2.3 ±2.1	0.273
Acute procedure, *n* (%)	10 (5)	0 (0)	0.003
Agatston score†	2428 ±1418	2994 ±2058	0.054
Peak velocity [m/s]	4.1 ±2.2	4.2 ±2.3	0.290
Mean gradient [mm Hg]	41.0 ±13.6	43.1 ±14.3	0.149
Aortic valve area [cm²]	0.7 ± 0.2	0.7 ±0.2	0.741
Aortic regurgitation grade ≥ 3, *n* (%)	16 (8)	4 (2)	0.026
LVEF (%)†	57.5 ±13.3	60.0 ±13.3	0.360
Septal wall thickness [mm]	12.6 ±2.2	12.7 ±1.8	0.612
Posterior wall thickness [mm]	11.9 ±1.7	11.9 ±1.5	0.917
Mitral regurgitation grade ≥ 3, *n* (%)	20 (9)	14 (8)	0.857
Bicuspid aortic valve, *n* (%)	30 (14.2)	23 (13.8)	1.000

Plus-minus values are mean ± SD. †Plus-minus values are median ± interquartile range (IQ range).

Table II. Procedural and postprocedural characteristics*

Variable	Educational status		*P*-value
	Low (*n* = 212)	High (*n* = 167)	
Device, *n* (%):			
Acurate	84 (40)	44 (26)	0.007
CoreValve	25 (12)	17 (10)	0.620
Evolut	57 (27)	71 (43)	0.001
Lotus	46 (22)	35 (21)	0.862
Balloon valvuloplasty, *n* (%)	83 (40)	69 (41)	0.724
Open surgical access, *n* (%)	100 (47)	92 (55)	0.126
Contrast dye [ml]†	120 ±60	120 ±70	0.806
Troponin in 24 h [ng/l]†	511.9 ±886.9	504.0 ±743.2	0.733
Creatinine [μmol/l]†	77.8 ±38.8	77.0 ±43.5	0.394
Hemoglobin [g/l]	113.5 ±18.4	111.9 ±17.1	0.390
Platelets [× 10⁹/l]	138.5 ±57.7	127.8 ±48.6	0.052
AVB requiring PM implantation, *n* (%)	35 (17)	43 (26)	0.030
Length of hospital stay after TAVI [days]	6 ±3	6 ±3	0.858

Plus-minus values are mean ± SD. †Plus-minus values are median ± interquartile range (IQ range). AVB – atrioventricular block, PM – pacemaker.

Table III. Clinical outcomes and echocardiographic characteristics after TAVI*

Variable	Educational status		*P*-value
	Low (*n* = 212)	High (*n* = 167)	
All-cause mortality at 72 h, *n* (%)	3 (1)	1 (1)	0.634
Incorrect positioning of a valve, *n* (%)	6 (3)	6 (4)	0.674
Myocardial infarction at 72 h, *n* (%)	0 (0)	1 (1)	0.442
All-cause mortality at 30 days, *n* (%)	6 (3)	6 (4)	0.674
Major stroke at 30 days, *n* (%)	4 (2)	3 (2)	1.000
Life-threatening bleeding at 30 days, *n* (%)	7 (3)	3 (2)	0.523
Acute kidney injury – stage 2 or 3, *n* (%)	1 (1)	2 (1)	0.586
Major vascular complications at 30 days, *n* (%)	9 (4)	7 (4)	0.979
Device success, *n* (%)	200 (94)	159 (95)	0.707
Early safety, *n* (%)	197 (93)	154 (92)	0.805
All-cause mortality during follow-up, *n* (%)	52 (25)	40 (24)	0.941
Cardiovascular mortality during follow-up, *n* (%)	40 (19)	31 (19)	0.925
Peak velocity before discharge [m/s]	2.2 ±1.4	2.1 ±1.4	0.242
Mean gradient before discharge [mm Hg]	10.2 ±4.9	9.6 ±4.4	0.198
Aortic regurgitation grade ≥ 3 before discharge, *n* (%)	2 (1)	3 (2)	0.659
Peak velocity at 1 year [m/s]	2.2 ±1.3	2.1 ±1.4	0.532
Mean gradient at 1 year [mm Hg]	9.7 ±3.7	9.6 ±4.4	0.921
Aortic regurgitation grade ≥ 3 at 1 year, *n* (%)	1 (1)	0 (0)	1.000
LVEF at 1 year (%)†	60.0 ±5.0	60.0 ±5.0	0.702

Plus-minus values are mean ± SD. †Plus-minus values are median ± interquartile range (IQ range).

We observed a significant association between all-cause mortality and increased age, lower BMI, higher creatinine levels before and after TAVI, lower hemoglobin level before and after TAVI, higher STS score and higher wall thickness (Table IV). Similar results were also seen for cardiovascular mortality with the exception of BMI (Table IV). *P*-values were < 0.050 for all above - mentioned variables.

Multivariate analysis, using variables identified as significantly associated with mortality in univariate analysis (Table IV), revealed that lower BMI, lower hemoglobin before TAVI, higher STS score, higher inferior wall thickness, higher creatinine after TAVI, and atrial fibrillation were independently associated with mortality risk. Similar results were also seen for cardiovascular mortality, with addition of NYHA ≥ III. *P*-values were < 0.050 for all above-mentioned variables. Addition of educational level into this model that controls all studied characteristics shows no significant effect
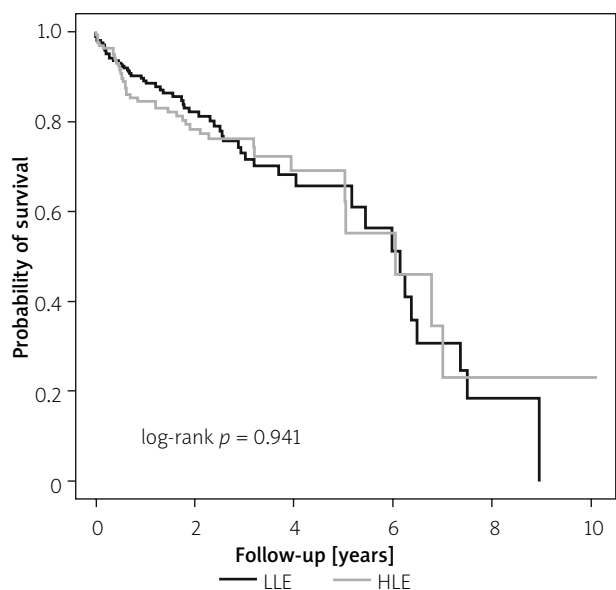
Figure 1. All-cause mortality and education
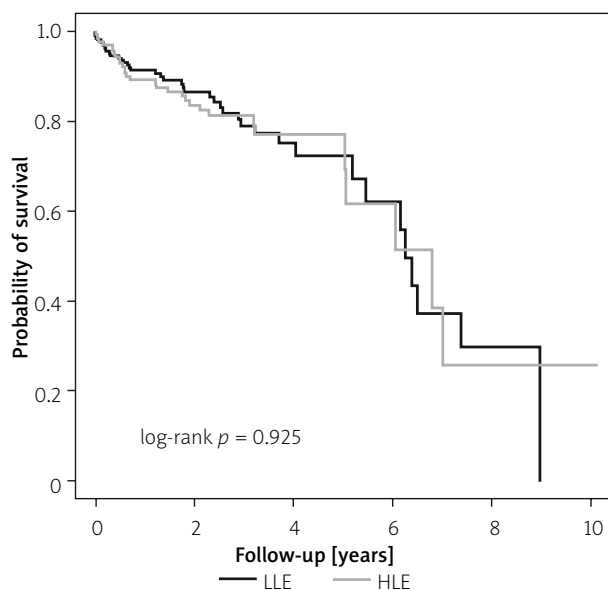
Figure 2. Cardiovascular mortality and education

on all-cause or cardiovascular mortality ($p = 0.462$ and $p = 0.716$).

Discussion

To the best of our knowledge, this is the first study evaluating the association between educational level and outcomes in patients with aortic stenosis who underwent TAVI. Here, we report essential findings: (I) patients with a lower educational level were more often females, required a TAVI procedure at a younger age, and had higher BMI, a higher prevalence of type 2 diabetes mellitus, and concomitant aortic regurgitation; (II) all urgent TAVI procedures were performed in patients with a lower educational level; (III) early safety and device success were comparable in both groups; (IV) there were no significant differences between patients in the low and high level of education groups in all-cause and cardiovascular mortality after TAVI during mid-term follow-up.

Education and risk factors

Even though SES is a multidimensional construct related to both adequate financial resources and educational attainment, education is the most widely used measure of SES in epidemiology studies [19]. In our study we considered only educational attainment as it represents a parameter with less variability throughout a person's life and has a proven association with the outcomes from previously published studies. Lower levels of education are associated with a higher prevalence of CV risk factors, higher incidence of CV events, and higher CV mortality, independent of other sociodemographic factors [1, 4].

Risk factors for development of AS are similar to those for atherosclerosis [12]. Yan *et al.* [20] reported that arterial hypertension, diabetes mellitus, and dyslipidemia have independent associations with the incidence of AS in an unselected population of individuals older than 65 years and together accounted for approximately one-third of the incidence of severe AS. A positive dose-response relationship between the number and duration of cardiac risk factors and risk of AS has been observed [20]. Genetically increased body mass index was causally associated with higher risk of aortic valve stenosis and replacement [21].

The above-mentioned findings are consistent with the results of our study. Patients with an LLE, although younger, had significantly higher BMI and a higher prevalence of type 2 diabetes mellitus (Table I). These findings could explain the earlier occurrence of AS in the LLE group observed in this study.

The results of our study showed there was no significant difference between the groups in terms of prevalence of arterial hypertension, atrial fibrillation, or CAD. Comparing our findings to previously published studies that included the general population as well as patients with the first clinical manifestation of CAD, the overall prevalence of arterial hypertension, atrial fibrillation, and CAD was higher in our study [4, 22]. We hypothesize that these findings might be explained by the higher mean age of patients in our study.

Education and awareness

Some recent studies have explained that lower educational level might directly impair an individual's abili-

Table IV. Univariate analysis of all-cause and cardiovascular mortality and its association with categorical and continuous variables*

Variable	All-cause mortality		Cardiovascular mortality	
	RR (95% CI)	*P*-value	RR (95% CI)	*P*-value
Categorical variables:				
Male gender	1.339 (0.880–2.036)	0.171	1.224 (0.758–1.976)	0.408
NYHA ≥ III before TAVI	1.605 (1.022–2.520)	0.038	2.203 (1.276–3.802)	0.004
Diabetes mellitus	1.357 (0.897–2.054)	0.147	1.362 (0.849–2.184)	0.198
Arterial hypertension	0.877 (0.523–1.472)	0.619	0.951 (0.520–1.739)	0.870
Atrial fibrillation	2.108 (1.395–3.188)	< 0.001	1.901 (1.185–3.050)	0.007
Coronary artery disease	1.329 (0.879–2.010)	0.176	1.284 (0.802–2.056)	0.297
Pacemaker before TAVI	1.243 (0.714–2.164)	0.441	1.279 (0.688–2.381)	0.436
Pacemaker after TAVI	0.994 (0.598–1.651)	0.980	0.771 (0.429–1.385)	0.730
Balloon valvuloplasty during TAVI	0.844 (0.537–1.327)	0.463	0.974 (0.584–1.625)	0.920
Open surgical access	1.329 (0.837–2.111)	0.226	1.344 (0.794–2.276)	0.270
Creatinine worsening after the procedure	1.606 (1.042–2.473)	0.030	1.572 (0.959–2.578)	0.071
Continuous variables:				
Age	1.050 (1.011–1.090)	0.011	1.049 (1.005–1.095)	0.028
Body mass index	0.942 (0.903–0.982)	0.005	0.958 (0.915–1.002)	0.063
Creatinine before TAVI†	1.029 (1.012 - 1.047)	0.001	1.029 (1.008–1.050)	0.006
Creatinine after TAVI†	1.029 (1.015–1.045)	< 0.001	1.030 (1.013–1.047)	< 0.001
Hemoglobin before TAVI†	0.759 (0.669–0.861)	< 0.001	0.750 (0.650–0.867)	< 0.001
Hemoglobin after TAVI†	0.826 (0.722–0.945)	0.005	0.818 (0.701–0.956)	0.011
Platelets before TAVI†	1.007 (0.977–1.040)	0.643	1.007 (0.972–1.044)	0.699
Platelets after TAVI†	1.003 (0.961–1.045)	0.902	0.984 (0.935–1.036)	0.543
Troponin after TAVI‡	1.000 (0.995–1.006)	0.874	1.001 (0.996–1.007)	0.564
Agatston score‡	1.000 (0.978–1.022)	0.980	1.002 (0.971–1.026)	0.901
STS score	1.047 (1.022–1.073)	< 0.001	1.047 (1.020–1.075)	< 0.001
Mean aortic valve gradient before TAVI	1.001 (0.986–1.017)	0.901	1.002 (0.984–1.020)	0.843
Mean aortic valve gradient after TAVI	1.012 (0.967–1.060)	0.600	0.999 (0.946–1.055)	0.967
Aortic valve area before TAVI	1.523 (0.492–4.172)	0.466	1.085 (0.297–3.973)	0.901
Left ventricle ejection fraction	0.991 (0.976–1.006)	0.222	0.991 (0.974–1.008)	0.297
Septal wall thickness	1.091 (0.989–1.204)	0.081	1.115 (1.000–1.244)	0.050
Inferior wall thickness	1.185 (1.047–1.342)	0.007	1.253 (1.088–1.442)	0.002

One-unit increase, †ten-unit increase, ‡hundred-unit increase.

ty to obtain effective care in several ways, including low awareness of the importance of seeking timely care or reduced access to information on how and where to obtain it [4]. Despite the prognostic significance of severe AS, awareness and concern is very limited in the general population. Research shows that people are most concerned about non-cardiac diseases such as cancer or neurological entities (and among heart conditions, the concern is 5 times higher with heart attack). This is despite the fact that mortality of untreated AS is considerably higher than that of most malignancies [23]. We assumed that once patients are well aware of their condition they will actively participate in their healthcare and therefore optimal timing of TAVI can be planned. In this study, patients in the LLE group were more often admitted in a severe condition requiring urgent procedures (Table I), whereas patients in the HLE group were all admitted for diagnostic hospitalization, indicated by an outpatient specialist, who made a diagnosis through screening or at annual visits.

Socioeconomic status and outcomes of TAVI

The interaction between outcomes following TAVI and SES has not been studied in detail thus far. Mohee *et al.* [24] studied the association of low SES with outcomes following TAVI in 387 patients. In contrast to our study, they evaluated SES mainly by income and concluded that social deprivation was not associated with adverse outcomes. In the present study, during 2 years of follow-up, mortality was not affected by education compared with BMI, creatinine, hemoglobin, STS score, wall thickness and atrial fibrillation, which were identified as independent prognostic factors. Our study suggests that TAVI had a positive effect in attenuating worse baseline clinical conditions.

Limitations

This study has several limitations. First, the retrospective, observational, single-center design has its own inherent limitations that should be considered before generalization of the results. A second limitation is the unequal gender representation between groups. This reflects the historical situation in the Czech Republic and unequal availability of education in the past favoring men [25].

We found a significant difference between implanted valves in HLE and LLE groups (Table III). We believe this is an accidental finding, because valve choice was based on patient's anatomy and the availability of the valve. Currently, we are not aware of any evidence that would suggest that valve type affects mortality.

It is not known how many patients with severe AS were sent for surgery or were discouraged from TAVI, and therefore we cannot evaluate our selection bias. Although we had patients referred from different locations and almost all districts of the country, our cohort is rather small and can potentially give biased results. On the other hand, data on outcomes after TAVI based on SES or education are rather scarce [24], and therefore we believe that our current data carry considerable weight.

Conclusions

Patients with lower educational level and severe AS were indicated for TAVI at a younger age, had more comorbidities and had a more risky profile compared with patients with a higher educational level. After TAVI, there were no significant differences in all-cause and cardiovascular mortality during mid-term follow-up.

Acknowledgments

Conflict of interest

The authors declare no conflict of interest.

References

1. Havranek EP, Mujahid MS, Barr DA, et al. Social determinant of risk and outcomes for cardiovascular disease: a scientific statement from the American Heart Association. Circulation 2015; 132: 873-98.
2. Veronesi G, Tunstall-Pedoe H, Ferrario MM, et al. Combined effect of educational status and cardiovascular risk factors on the incidence of coronary heart disease and stroke in European cohorts: Implications for prevention. Eur J Prev Cardiol 2017; 24: 437-45.
3. Stringhini S, Carmeli C, Jokela M, et al. Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1.7 million men and women. Lancet 2017; 389: 1229-37.
4. Rosengren A, Smyth A, Rangarajan S, et al. Socioeconomic status and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study. Lancet Global Health 2019; 7: e748-60.
5. Stirbu I, Looman C, Nijhof GJ, et al. Income inequalities in case death of ischaemic heart disease in the Netherlands: a national record-linked study. J Epidemiol Community Health 2012; 66: 1159-66.
6. Gerber Y, Weston SA, Killian JM, et al. Neighborhood income and individual education: effect on survival after myocardial infarction. Mayo Clin Pro 2008; 83: 663-9.
7. Rosengren A, Subramanian SV, Islam S, et al. Education and risk for acute myocardial infarction in 52 high, middle and low-income countries: INTERHEART case-control study. Heart 2009; 95: 2014-22.
8. Mehta RH, O'Shea JC, Stebbins AL. Association of mortality with years of education in patients with ST-segment elevation myocardial infarction treated with fibrinolysis. J Am Coll Cardiol 2011; 57: 138-46.
9. Gerber Y, Goldbourt U, Drory Y. Interaction between income and education in predicting long-term survival after acute myocardial infarction. Eur J Cardiovasc Prev Rehabil 2008; 15: 526-32.
10. Kaplan RM, Howard VJ, Safford MM, et al. Educational attainment and longevity: results from the REGARDS U.S. national cohort study of blacks and whites. Ann Epidemiol 2015; 25: 323-8.
11. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J 2017; 38: 2739-91.
12. Kanwar A, Thaden JJ, Nkomo VT. Management of patients with aortic valve stenosis. Mayo Clin Proc 2018; 93: 488-508.
13. Afshar M, Kamstrup PR, Williams K, et al. Estimating the population impact of Lp(a) lowering on the incidence of myocardial infarction and aortic stenosis – brief report. Arterioscler Thromb Vasc Biol 2016; 36: 2421-3.
14. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010; 363: 1597-607.
15. Makkar RR, Thourani VH, Mack MJ. Five-year outcomes of transcatheter or surgical aortic-valve replacement. N Engl J Med 2020; 382: 799-809.
16. Mack MJ, Leon MB, Thourani VH. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019; 380: 1695-705.
17. Möllmann H, Bestehorn K, Bestehorn M, et al. In-hospital outcome of transcatheter vs. surgical aortic valve replacement in patients with aortic valve stenosis: complete dataset of patients treated in 2013 in Germany. Clin Res Cardiol 2016; 105: 553-9.
18. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. Eur Heart J 2012; 33: 2403-18.
19. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. Circulation 1993; 88: 1973-98.
20. Yan AT, Koh M, Chan KK, et al. Association between cardiovascular risk factors and aortic stenosis: the CANHEART Aortic Stenosis Study. J Am Coll Cardiol 2017; 69: 1523-32.
21. Kaltoft M, Langsted A, Nordestgaard BG. Obesity as a causal risk factor for aortic valve stenosis. J Am Coll Cardiol 2020; 75: 163-76.
22. Notara V, Panagiotakos DB, Kogias Y, et al. The impact of educational status on 10-year (2004–2014) cardiovascular disease

prognosis and all-cause mortality among acute coronary syndrome patients in the Greek Acute Coronary Syndrome (GREECS) Longitudinal Study. J Prev Med Public Health 2016; 49: 220-9.

23. Gaede L, Di Bartolomeo R, van der Kley F, et al. Aortic valve stenosis: what do people know? A heart valve disease awareness survey of over 8,800 people aged 60 or over. EuroIntervention 2016; 12: 883-9.

24. Mohee K, Protty MB, Whiffen T, et al. Impact of social deprivation on outcome following transcatheter aortic valve implantation (TAVI). Open Heart 2019; 6: e001089.

25. https://www.czso.cz/csu/czso/uroven-vzdelani-obyvatelstva-podle-vysledku-scitani-lidu-2011-xllg5xjb8q