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ORIGINAL ARTICLE
Valvular heart disease

Marital status, educational level, and mid-term mortality risk in 5924 patients after transcatheter aortic valve implantation

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Aims

There is scarce knowledge about the association between social factors and mid-term outcome in older patients undergoing transaortic valve implantation (TAVI). Our aim in this study is to explore associations between marital status, educational level, and mortality risk in patients after TAVI.

Methods and results

Patients aged ≥65 who underwent TAVI in Sweden during 2014–2020 were identified from the SWEDEHEART registry. Social factors and comorbidities were collected from mandatory national registries. Cox regression models adjusted for baseline comorbidities, age, sex, year of TAVI, social factors, and smoking were used to estimate mortality risk. Median follow-up was 1.9 years (interquartile range: 0.9–3.3). Overall, 5924 patients were included (47.3% women), with a mean age of 82.1 years (standard deviation: 6.1). Of the 1410 (23.8%) deaths during follow-up, 721 (51.2%) were related to cardiovascular causes. Patients with low education (<10 years) had a higher risk of mortality than patients with the highest education level [>12 years; adjusted hazard ratio (aHR): 1.20, 95% confidence interval (CI): 1.03–1.41]. Never being married/cohabiting was associated with an increased risk of mortality in comparison with being married/cohabiting (aHR: 1.32, 95% CI: 1.05–1.65). A separate analysis of men and women showed an increased risk among never-married men (aHR: 1.63, 95% CI: 1.23–2.14) but not among never-married women (aHR: 0.85, 95% CI: 0.56–1.30).

Conclusion

Disadvantage in social factors was associated with an increased mortality risk after TAVI in older patients. These findings emphasize the importance of developing strategies to increase health literacy and social support after TAVI in older patients with unfavourable social factors.

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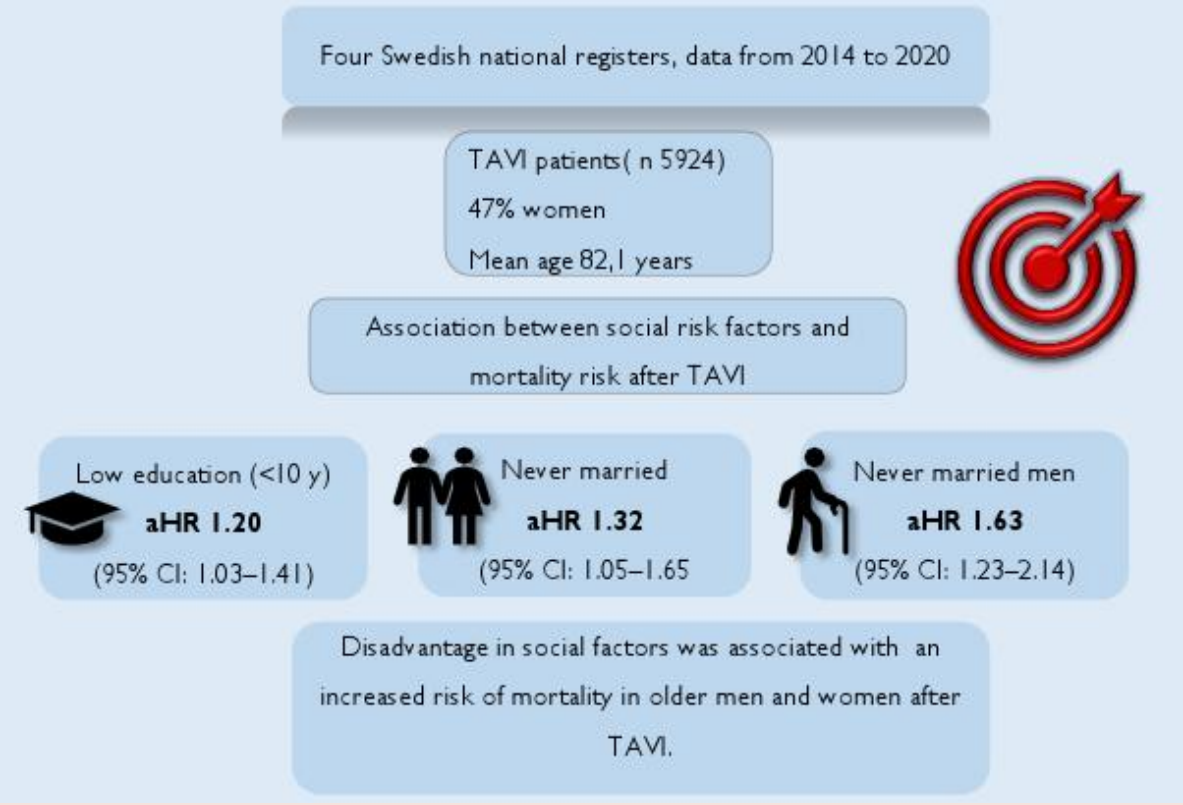
Graphical Abstract



Keywords Transcatheter aortic valve implantation • Mortality risk • Survival • Social factors • Marital status • Education

Introduction

Severe aortic stenosis is a life-threatening condition. In patients with severe symptomatic stenosis, the risk of mortality without treatment is ~50% over the 2-year period after diagnosis.[1–3] Transcatheter aortic valve implantation (TAVI) is the recommended treatment option both in older patients with severe stenosis and in patients with high or intermediate surgical risk.[4,5] Since the beginning of the TAVI era, studies have demonstrated improved survival and health after TAVI.[6,7] However, patients may still experience deterioration of health after TAVI due to a high burden of multimorbidity and frailty.[8–10] Among older people, loneliness and social isolation are associated with poorer health-related outcomes.[11,12] The association between loneliness and mortality has been shown to be stronger in older men than in older women.[13,14] The risk of becoming physically frail is higher in older people who experience high levels of loneliness.[15] Living alone at older ages is associated with an increased mortality risk, and older people are especially vulnerable when their marriage arrangement dissolves.[16] Low socio-economic status has a well-known association with both cardiovascular diseases and increased mortality.[17–19] Previous studies have shown an increased long-term risk of mortality after cardiac surgery in patients with low income, patients with low education, and patients who have never married.[20,21] It is not clear whether the same association exists among older patients undergoing TAVI, and few studies have investigated whether there are sex-specific differences in the associations between marital status, education, and mortality after TAVI. The aim of the present study is therefore to explore associations between marital status, education, and mortality risk in older men and women undergoing TAVI due to severe aortic stenosis.

Methods

Study design, study population, and data sources

This nationwide observational population-based cohort study included all patients aged ≥65 who underwent TAVI for aortic stenosis in Sweden during 2014–2020 ($n = 5924$). Mortality status was registered until 31 December 2020. The outcome measure was all-cause mortality. Median follow-up was 1.9 years (interquartile range: 0.9–3.3 years). Patients were identified from the Swedish Transcatheter Cardiac Intervention Registry (SWENTRY), which is part of the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART).[22] The SWENTRY includes all patients undergoing TAVI in Sweden since 2010, with variables regarding patient characteristics, pre-operative information, early complications, and outcome at the 1-year follow-up.[23]

Codes from the 10th revision of the International Classification of Diseases (ICD-10) were used to identify the TAVI procedures (FMD 12 and FMD 96), in combination with the diagnosis code for aortic stenosis (I35.0). Patients who died before discharge from the hospital were excluded ($n = 82$), as were patients who underwent balloon aortic valvuloplasty, without an aortic valve implantation ($n = 169$). A flow chart depicting

included and excluded patients is shown in Supplementary material online, *Figure S1*.

Diagnoses for baseline characteristics and comorbidities were obtained from SWEDEHEART and the Swedish National Patient Register (NPR). Registration in the NPR is mandatory, and the register has complete national coverage from 1987 for all patients hospitalized in Sweden with an overall diagnosis validity of 85–95%.[24] Diagnoses in the NPR are based on ICD codes, with ICD-9 used up to 1997 and ICD-10 thereafter (see Supplementary material online, *Table S1*). Data on marital status and educational level were collected from the Longitudinal Integration Database for Health Insurance and Labor Market Studies (LISA) register. The LISA registry includes all citizens in Sweden aged ≥16 years from 1990 onwards and is updated annually.[25]

Social variables

Marital status was divided into four levels: married/cohabiting, never married/cohabited, divorced, and widowed. Education was stratified into three levels: <10 years (compulsory school only), 10–12 years (upper school), and >12 years (college/university level). No individuals had missing data for marital status, while 62 (1.0%) had missing data regarding education.

Dates of death were obtained from the Swedish Cause of Death register, in which all deaths of Swedish citizens have been registered since 1952.[26] Data from the four national registers were linked together through the personal 10-digit social security number, which is unique for all Swedish citizens.

Statistical methods

Baseline characteristics are presented as frequencies and percentages for categorical variables and as means with standard deviations (SDs) for continuous variables. The follow-up time varied from minimum 1 month to a maximum 6.9 years, since the follow-up time started at the date of discharge from the hospital after TAVI and ended at death or end of study (31 December 2020), whichever occurred first. Incidence rates were estimated as numbers of deaths divided by follow-up time in years and were reported as incidence rate per 100 person-years with 95% confidence intervals (CIs).

Survival probabilities were calculated using Kaplan–Meier survival curves with 95% CI. For all analyses, a *P*-value of <0.05 was considered statistically significant.

Cox proportional hazards regression was used to calculate the crude [hazard ratio (HR)] and adjusted HR (aHR) mortality risk, separately for marital status and education, using married/cohabiting and education >12 years as references. The multivariate models were adjusted for clinically relevant baseline characteristics [age, year of TAVI, body mass index, sex, smoking, myocardial infarction, diabetes, hypertension, heart failure, New York Heart Association (NYHA) class, atrial fibrillation, previous stroke, chronic respiratory disease, peripheral vascular disease, renal insufficiency, history of cancer, depression, dementia, prior cardiac surgery] and for social factors other than the response variable (marital status and education) and interaction with sex. The hazard ratios for mortality risk for all variables are shown in Supplementary material online, *Table S2*.

All statistical analyses were performed using version 4.2.0 of R.

Ethical considerations

The present study was performed in line with the Declaration of Helsinki and was approved by the Swedish Ethical Review Authority (registration number: 2021-00122). All personal identifiers were replaced by codes before analysis to ensure anonymity. The need for individual patient consent was waived by the committee. This article follows the recommendations from the statement of Strengthening the Reporting of Observational Studies In Epidemiology.[27]

Results

General

The study group comprised 5924 TAVI patients (47.3% women) aged ≥65 years (mean age: 82.1, SD: 6.0). At baseline, 84.7% of the total population had a history of hypertension, 45.2% had a history of heart failure, 81.1% had severe symptoms of heart failure corresponding to NYHA functional Class III–IV, 42.8% had atrial fibrillation, 29.7% had diabetes, 21.3% had chronic respiratory disease, and 51.0% had a history of smoking. Diabetes, atrial fibrillation, and a history of smoking were more common among men, while chronic respiratory disease and depression were more common among women (*Table 1*). Baseline characteristics divided by marital status and education are shown in Supplementary material online, *Tables S3 and S4*.

Survival probability and incidence of mortality

Among the 23.8% of the patients who died during the follow-up period, 721 deaths (51.2%) were related to cardiovascular causes (see Supplementary material online, *Table S5*). The overall incidence rate for mortality was 10.57 (95% CI: 10.02–11.13) per 100 person-years. Mortality incidence divided by sex is given in Supplementary material online, *Table S6*.

Overall, regardless of marital status or educational level, the cumulative survival rates after TAVI in men were 83% (95% CI: 81.8–84.8) at 2 years, 52% (95% CI: 49.0–55.5) at 5 years, and 16% (95% CI: 4.0–66.0) at the end of follow-up. The corresponding results for women were 86% (95% CI: 84.3–87.2) at 2 years, 56% (95% CI: 52.3–59.0) at 5 years, and 36% (95% CI: 28.9–46.1) at the end of follow-up ($P = 0.0018$; *Figure 1A*).

Cumulative survival rates 5 years after TAVI were 48% (95% CI: 38.9–59.4) in never-married patients, compared with 56% (95% CI: 52.6–59.2) in those who were married/cohabiting. The corresponding figures at the end of follow-up were 34% (95% CI: 20.3–57.0) and 37% (95% CI: 31.1–44.3; $P = 0.55$; *Figure 1B*). Five years after TAVI, the survival rate in patients with the most education (>12 years) was 58% (95% CI: 53.1–63.9), and the survival rate in those with the least education (<10 years) was 51% (95% CI: 47.8–54.7). At the end of follow-up, the corresponding figures were 40% (95% CI: 28.1–55.5) and 30% (95% CI: 22.1–40.8; $P = 0.0015$; *Figure 1C*).

Marital status and risk of mortality

In total, 47.9% of the patients were married or cohabiting (63.0% of the men and 31.0% of the women), while 46.9% of the women and 16.0% of the men were widowed (*Table 1*). Hazard ratios adjusted for age and year of TAVI showed no increased risk for mortality in never-married or cohabiting patients, compared with married/cohabiting patients (HR: 1.23, CI: 0.99–1.53), but after adjustment for sex, comorbidities, year of TAVI and education, an increased risk was observed (aHR: 1.32, 95% CI: 1.05–1.65; *Table 2*). A separate analysis for men and women showed that never-married men had an increased risk of mortality compared with married men (aHR: 1.63, 95% CI: 1.23–2.14). No increased risk was observed in never-married women compared with married women (aHR: 0.85, 95% CI: 0.56–1.30; see Supplementary material online, *Table S7*). Compared with married patients, no increased mortality risk was observed among either divorced patients (aHR: 0.94, 95% CI: 0.79–1.11) or widowed patients (aHR: 0.95, 95% CI: 0.82–1.09; *Table 2*). In the separate analysis of men and women, widowed women had a lower risk of mortality (aHR: 0.81, 95% CI: 0.66–0.99) compared with married women. No difference in mortality risk was observed between widowed men and married men (aHR: 1.05, 95% CI: 0.85–1.29; see Supplementary material online, *Table S7*).

Education and risk of mortality

Overall, 42.1% of the patients had compulsory school education only (<10 years), while 37.0% had 10–12 years of education, and 20.9% had >12 years of education (*Table 1*). In the unadjusted model, patients with <10 and 10–12 years of education had an increased mortality risk

Table 1 Comorbidities at baseline in 5924 patients aged ≥65 years who underwent transcatheter aortic valve implantation

	TAVI patients *n* (%)	Men *n* (%)	Women *n* (%)	*P*-value
Number of patients	5924	3123 (52.7)	2801 (47.3)	
Mean age (SD)	82.1 (6.0)	81.5 (6.1)	82.8 (5.9)	<0.001
Comorbidities				
BMI (SD)	26.7 (5.1)	26.7 (4.6)	26.7 (5.6)	0.906
Ever smoked	2759 (51.0)	1795 (61.8)	964 (38.5)	<0.001
Myocardial infarction	1292 (21.8)	834 (26.7)	458 (16.4)	<0.001
Diabetes	1758 (29.7)	1039 (33.3)	719 (25.7)	<0.001
Hypertension	5020 (84.7)	2647 (84.8)	2373 (84.7)	0.996
Heart failure	2679 (45.2)	1486 (47.6)	1193 (42.6)	<0.001
NYHA Class III–IV	4804 (81.1)	2517 (80.6)	2287 (81.6)	0.093
Atrial fibrillation	2536 (42.8)	1425 (45.6)	1111 (39.7)	<0.001
Hyperlipidaemia	2284 (38.6)	1344 (43.0)	940 (33.6)	<0.001
Previous stroke	918 (15.5)	527 (16.9)	391 (14.0)	0.002
Chronic respiratory disease	1262 (21.3)	597 (19.1)	665 (23.7)	<0.001
Peripheral vascular disease	951 (16.1)	580 (18.6)	371 (13.2)	<0.001
Renal insufficiency	1037 (17.5)	681 (21.8)	356 (12.7)	<0.001
History of cancer	2165 (36.5)	1228 (39.3)	937 (33.5)	<0.001
History of depression	298 (5.0)	133 (4.3)	165 (5.9)	0.005
Dementia	55 (0.9)	33 (1.1)	22 (0.8)	0.342
Prior cardiac surgery	1019 (17.2)	754 (24.2)	265 (9.5)	<0.001
Marital status				
Married/cohabiting	2836 (47.9)	1967 (63.0)	869 (31.0)	<0.001
Not married	381 (6.4)	224 (7.2)	157 (5.6)	
Divorced	893 (15.1)	433 (13.9)	460 (16.4)	
Widowed	1814 (30.6)	499 (16.0)	1315 (46.9)	
Education				0.001
<10 years	2495 (42.1)	1255 (40.2)	1240 (44.3)	
10–12 years	2191 (37.0)	1164 (37.3)	1027 (36.7)	
>12 years	1238 (20.9)	704 (22.5)	534 (19.1)	

BMI, body mass index; NYHA class, New York Heart Association functional classification of heart failure symptoms; TAVI, transcatheter aortic valve implantation.

compared with patients with >12 years of education (HR: 1.27, 95% CI: 1.10–1.47 and HR: 1.17, 95% CI: 1.00–1.36, respectively; *Table 2*). The increased mortality risk persisted in patients with <10 years of education (aHR: 1.20, 95% CI: 1.03–1.41) in the multi-adjusted analysis but not in patients with 10–12 years of education (aHR: 1.11, 95% CI: 0.94–1.30; *Table 2*).

Sex-specific analyses are presented in Supplementary material online, *Table S7*. Compared with men with >12 years of education, no increased mortality risk was observed either in men with <10 years (aHR: 1.18, 95% CI: 0.96–1.45) or in those with 10–12 years of education (aHR: 1.08, 95% CI: 0.88–1.33). Similar results were found in women, in whom neither 10–12 years of education nor <10 years of education were associated with an increased mortality risk (aHR: 1.15, 95% CI: 0.89–1.48 and aHR: 1.18, 95% CI: 0.92–1.51, respectively).

Discussion

In this national observational cohort study, including 5924 TAVI patients with a mean age of 82 years, the main finding was that never being married/cohabiting was associated with an increased risk of mortality after TAVI, with a marked association in men. Moreover, an overall increased mortality risk was observed among patients with compulsory school education only. Five years after TAVI, the survival rate was >50% among both men and women. There is a well-known association between comorbidities and outcome after TAVI.[28,29] The present study involved older patients, with a mean age of 82 years and a high burden of cardiovascular and non-cardiovascular comorbidities at baseline. However, 2 years after TAVI, >80% of the patients were alive, which is a survival rate in line with those of previous reports.[30,31]

To our knowledge, no previous study has examined the association between education, marital status, and risk of mortality after TAVI in a national cohort of older patients. Two previous meta-analyses demonstrated that loneliness and a small social network were associated with increased mortality in older people.[32,33] Jensen *et al.*[34] showed that living alone was a significant predictor of mortality in men among the general population, and that those with a lower socio-economic position were more likely to be socially isolated and at particular risk for death. A recent systematic review and meta-analysis by Zhu *et al.*[35] showed that following a myocardial infarction, married and cohabitated

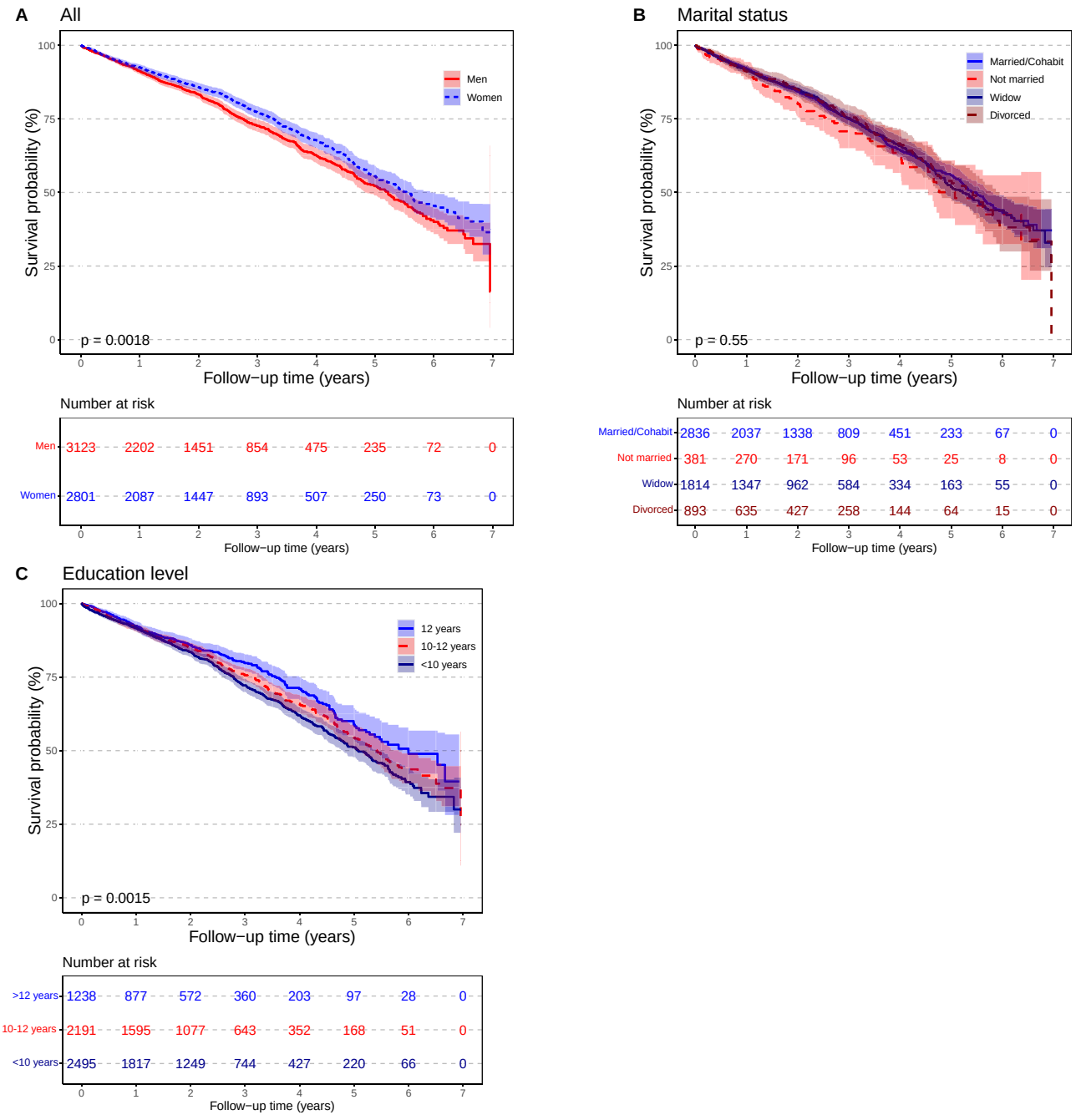


Figure 1 (*A*) Cumulative survival probability in men and women after transcatheter aortic valve implantation, divided by (*B*) marital status and (*C*) education level.

patients reported a higher health-related quality of life than unpartnered patients, but a sex-specific association between marital status and health-related outcomes was less clear. However, loneliness has been found to have a stronger association with mortality among older men than among older women in the general population.[13,14] This emphasizes the results in the present study, where we observed a markedly increased mortality risk among never married/cohabiting men but not in their female counterparts. On the other hand, Newell *et al.*[36] found that married women had an increased risk of mortality 1 year after TAVI, which could suggest that the support given from spouses to older women after TAVI may not always be sufficient. In line with Newell, we observed a lower risk of mortality among widowed women but not among widowed men, which may reflect a lower marital satisfaction among these women, which also has been described in previous studies.[14,37] This could be of importance for healthcare professionals to be aware of when planning for discharge from hospital after TAVI.

Impaired mobility, loneliness, and depression are more prevalent in older people who live alone, and these factors have been shown to contribute to a higher mortality risk.[16] These aspects may also be part of

Table 2 Incidence rates and hazard ratios with 95% confidence intervals in 5924 patients, aged ≥65 years who underwent transcatheter aortic valve implantation

	Total number of patients	Number of events	Person time (years)	IR per 100 person-years (95% CI)	HR[a] (95% CI)	aHR[b] (95% CI)	*P*-value for interaction with sex
Marital status							
Married/cohabitated	2836	651	6265	10.39 (9.61–11.22)	Ref.	Ref.	
Never married	381	96	804	11.94 (9.67–14.58)	1.23 (0.99–1.53)	1.32 (1.05–1.65)	0.001
Divorced	893	203	1955	10.38 (9.00–11.91)	1.03 (0.88–1.21)	0.94 (0.79–1.11)	0.77
Widowed	1814	460	4320	10.65 (9.70–11.67)	0.92 (0.81–1.04)	0.95 (0.82–1.09)	0.69
Education							
>12 years	1238	241	2720	8.86 (7.78–10.05)	Ref.	Ref.	
10–12 years	2191	505	4908	10.29 (9.41–11.23)	1.17 (1.00–1.36)	1.11 (0.94–1.30)	0.43
<10 years	2495	664	5716	11.62 (10.75–12.53)	1.27 (1.10–1.47)	1.20 (1.03–1.41)	0.07

aHR, adjusted hazard ratio (multivariable model); CI, confidence interval; HR, hazard ratio.
[a]Model adjusted for age and year of TAVI.
[b]Multivariable model adjusted for age, sex, year of TAVI, marital status, education, and baseline comorbidities: ever-smoking, body mass index, myocardial infarction, hypertension, diabetes, heart failure, New York Heart Association functional classification of heart failure symptoms, atrial fibrillation, stroke, renal failure, chronic respiratory disease, peripheral vascular disease, history of cancer, hyperlipidaemia, depression, dementia, prior cardiac surgery, and social factors.

the increased mortality observed in never-married patients in the present study.

Nearly 5% of the patients in our study had a previous diagnosis of depression at baseline, which was more prevalent among those patients who had never married or were divorced, but information regarding impaired mobility or perceived loneliness was not available. The group of never-married patients had a higher mortality risk after TAVI, compared with their married counterparts. There were also higher proportions of heart failure, diabetes, and a history of smoking among never-married patients, compared with married patients. These findings stress that a satisfying social network and social support play a crucial role in healthy ageing.[38]

Diabetes, hypertension, heart failure, chronic respiratory disease, and renal insufficiency were more prevalent among patients with <10 years of education and with 10–12 years of education, and our results showed that patients with <10 years of education had an increased risk of mortality. This result is in line with a recently published study from our research group where we found an increased risk of mortality in patients with low educational level (<10 years) who underwent surgical aortic valve replacement.[20] Low education is a strong predictor of cardiovascular mortality in general.[39] Health-related knowledge and behaviours affect health-related outcomes, and low education has been shown to be the most important determinant of health literacy.[40,41] Health literacy can be defined as a person's capacity both to acquire treatment and care and to obtain and understand health information in order to make appropriate health decisions.[41] Older people with limited health literacy have poorer overall health status and higher mortality, due to an less healthy lifestyle, limited physical function, or difficulty interpreting healthcare information.[42] This could explain the association between increased mortality and low education observed in the present study.

Low education could also imply a less-well-paid occupation and hence an unfavourable economic situation throughout life, including in advanced age.[43] This could also affect the possibility of making appropriate health decisions, especially for older men.[44] A prior study highlighted the importance of identifying patients with a disadvantageous socio-economic status before TAVI.[45] Patient-centred approaches may lead to increased motivation and health-related knowledge in the patient,[46] but health literacy could also decline due to cognitive ageing.[47] When planning follow-up for TAVI patients, it is therefore important to evaluate different aspects of patients' social factors in order to develop effective support for individual older patients after TAVI.

The results from the present study add important knowledge about the impact of social factors on outcome after TAVI in older men and women. Our findings emphasize the importance of assessing what support TAVI patients will need after discharge from hospital, in order to develop strategies for appropriate support. Providing such support in patients' daily lives could be challenging, due to the short length of in-patient specialist care at the TAVI centres. It is therefore important to broaden the competence of primary healthcare professionals regarding the needs of TAVI patients. It is not yet clear how sufficient support after TAVI should be provided in a primary healthcare setting, which motivates further studies.

This study has strengths, but also limitations. Strengths of the study include the large population-based cohort, high-quality registry data including comorbidities and social factors, and no patient lost to follow-up. However, we did not include the patients' income level as a part of their social status since the large majority of patients were retired. Social status includes multiple components, and we did not have information regarding living area, information of ethnicity, diet, and physical activity or use of medication during the follow-up period. Furthermore, there was a high proportion of missing values regarding surgical risk evaluation (EuroScore II) and ejection fraction. Another limitation is that the retrospective study design carries an inherent risk of selection bias and additional unmeasured confounders, accordingly, not adjusted for in the statistical models.

Conclusions

Disadvantage in social factors was associated with an increased risk of mortality in older men and women after TAVI. These findings emphasize the importance of assessing what support TAVI patients will need after discharge from hospital and ensuring sufficient social support for patients with unfavourable social factors, in order to increase health literacy.

Lead author biography

Maria Lachonius is a registered nurse, MSc, and a PhD student at Department of Molecular and Clinical Medicine, Institute of Medicine, University of Gothenburg. She works in the Department of Cardiology at Sahlgrenska University Hospital, Gothenburg, Sweden. She has a special interest in aortic valve replacement and different aspects of health, well-being, morbidity, and mortality, focusing on socio-economic aspects and frailty in older patients undergoing TAVI.

Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

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Conflict of interest: A.J. has received fees for consultancy and/or lectures from AstraZeneca, Werfen, Novo Nordisk, Bayer, Boehringer Ingelheim, and LFB Biotechnologies outside the present work. P.P. has received lectures fees from Medtronic and is a proctor for Abbott. O.A. has received lecture fees from Medtronic and is a proctor for Abbott and Meril. None of the other authors have anything to disclose.

Data availability

Data will be shared on reasonable request to the corresponding author if permissions are obtained from SWEDEHEART and the Swedish National Board of Health and Welfare.

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