Baseline frailty status and outcomes important for shared decision-making in older adults receiving transcatheter aortic valve implantation, a prospective observational study

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Abstract

Aims The objective of this study was to examine baseline frailty status (including cognitive deficits) and important clinical outcomes, to inform shared decision-making in older adults receiving transcatheter aortic valve implantation (TAVI).

Methods and results We conducted a prospective, observational study of 82 TAVI patients, recruited 2013 to 2015, with 2-year follow-up. Mean age was 83 years (standard deviation (SD) 4.7). Eighteen percent of the patients were frail, as assessed with an 8-item frailty scale. Fifteen patients (18%) had a Mini-Mental Status Examination (MMSE) score below 24 points at baseline, indicating cognitive impairment or dementia and five patients had an MMSE below 20 points. Mean New York Heart Association (NYHA) class at baseline and 6 months was 2.5 (SD 0.6) and 1.4 (SD 0.6), (p < 0.001). There was no change in mean Nottingham Extended Activities of Daily Living (NEADL) scale between baseline and 6 months, 54.2 (SD 11.5) and 54.5 (SD 10.3) points, respectively, mean difference 0.3 (p = 0.7). At 2 years, six patients (7%) had died, four (5%, n = 79) lived in a nursing home, four (5%) suffered from disabling stroke, and six (7%) contracted infective endocarditis.

Conclusions TAVI patients had improvement in symptoms and maintenance of activity of daily living at 6 months. They had low mortality and most patients lived in their own home 2 years after TAVI. Complications like death, stroke, and endocarditis occurred. Some patients had cognitive impairment before the procedure which might influence decision-making. Our findings may be used to develop pre-TAVI decision aids.

Keywords Aortic stenosis · TAVI · Activity of daily living · Shared decision making · Older adults

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Introduction

Transcatheter aortic valve implantation (TAVI) is an established treatment for severe and symptomatic aortic stenosis in patients not eligible for open heart surgery, and it improves symptoms and increase life expectancy [1, 2]. While indication for TAVI has expanded to also include younger and lower risk groups, the majority of TAVI patients are older and have significant comorbidity and frailty that contraindicates surgery. The Valve Academic Research Consortium-2 (VARC 2) consensus document recommends evaluation of independence in activity of daily living before the procedure as risk stratification [3]. However, few studies have focused on independence in activity of daily living as an outcome measure [4, 5].

Among older adults who are seriously ill, death might not be feared as the worse outcome. For many, reduced quality of life and functional or cognitive impairment [6, 7], are relatively greater concerns. Dementia is highly prevalent in older adults [8] and is the leading cause of dependency in older age [9]. Shared decision-making is the favoured model for health care decisions, enhancing treatment choices to reflect patients’ values and preferences [10]. However, the context of cognitive impairment or dementia makes it more difficult for TAVI candidates to participate in the decision-making process [11].

Thus, the aim of this study was to examine baseline frailty status including cognition and outcomes important to decision-making prior to TAVI.

Methods

Study design

This is a single-centre prospective, observational cohort study of 82 elective TAVI patients, with 2-year follow-up. Ninety-four patients were eligible for inclusion, five refused to participate and seven were not included due to logistical reasons. The patients were recruited consecutively from 2013 to 2015.

Participants

Patients ≥ 70 years with symptomatic and severe aortic stenosis accepted for TAVI at Haukeland University Hospital in Western Norway were included. The hospital has a tertiary function for TAVI and serves a population of 1.1 million inhabitants. Severe aortic stenosis was defined by echocardiography according to the European Society of cardiology (ESC) guidelines [1]. Before accepting patients for TAVI, a heart team including interventional cardiologists, cardiac surgeons and imaging specialists, had declined them for surgical aortic valve replacement due to high risk. At the time of the study, there was no screening for frailty preceding the intervention, and the frailty score of the study patients was not known to the treatment team. The number of patients selected for conservative treatment is not known but suspected to be small. Nursing home patients and patients with severe dementia are rarely referred for valve intervention in Norway. Exclusion criteria were inability to understand or speak Norwegian.

Procedural characteristics

TAVI was delivered by different routes, seventy five (92%) trans-femoral, five trans-subclavian and two with direct aortic access. Two different valves were used, the Medtronic Core Valve in 52 (63%) and Boston Scientific LOTUS Valve in 30 (37%) patients.

Measurements

Baseline

Mini-Mental Status Examination (MMSE) assesses cognition as a scale that ranges from 0 to 30, with higher scores indicating better cognition [12]. The cut-off for normal cognitive function is usually set at 24, with a sensitivity of 0.85 and a specificity of 0.90 for identifying anyone with dementia [13].

The research team developed an 8-item frailty scale [14]. The total score is calculated by adding different domain scores: cognition (MMSE ≥ 7 = 0 points, MMSE 20–26 = 1 point, MMSE ≤ 19 = 2 points), instrumental activity of daily living (NEADL ≤ 43 = 1 point), nutrition (BMI < 20.5 = 1 point), modified SOF (low energy = 1 point, weight loss (reported, not measured weight loss; therefore, modified) = 1 point, chair stand, not able = 1 point) [15], Charlson Comorbidity Index (≥ 3 = 1 point) [16], and psychological factors (HADS ≥ 15 = 1 point) [17]. The score range from 0 to 9, were 9 represents the frailest patients. Patients were classified frail if they scored ≥ 4 points. This cut-off had a specificity of 80% and sensitivity of 60% at predicting 2-year mortality for this population. In a receiver operating curve, the area under the curve was 0.81 (95% confidence interval 0.71–0.90) [14].
Baseline and 6 months:

*Nottingham Extended Activity of Daily living scale* (NEADL) is a scale originally developed to assess activities of daily living (ADL) for stroke patients discharged to home, yet frequently used in non-stroke populations [18, 19]. The scale measures extended activities of daily living using a 22-item questionnaire, evaluating four different sections: mobility, kitchen, domestic and leisure. Patients are asked whether they perform the different activities, and the response categories are 0 = not at all, 1 = with help, 2 = on my own with difficulty, 3 = on my own. The different scores sums into a total score of 0 to 66 points, with higher scores indicating greater independence. A score ≤ 43 indicates dependence [19]. One study of stroke patients reported a valid and reliable change if the NEADL improved or deteriorated by 4.9 points or more, and clinically important if the mean change score was in the range from 2.4 to 6.1 points after treatment [20].

*The New York Heart Association (NYHA)* classification describes patients’ symptoms of heart failure [21] and has been applied to TAVI patients [3]. NYHA class I represents no symptoms of heart failure and no limitation of physical activity, while NYHA class IV represents symptoms of heart failure at rest. Despite limitations it’s widely used both in research and clinical practice.

Follow-up measurements

Baseline NEADL and NYHA were assessed and then repeated at 6 months. Due to some patients living far from the hospital, we performed telephone interviews at 6 months, and MMSE and frailty testing were, therefore, not conducted. For the first 2 years, we recorded composite endpoints as recommended by the Valve Academic Research Consortium-2 (VARC-2) consensus document. We collected data of admission to long-term nursing homes for the first 2 years.

Statistical analyses

We present the data as means and standard deviations (SD), counts and percentages. Changes from baseline to 6 months are analysed using paired *t*-tests. There were little missing data so we have used complete case analysis and report the number of observations each analysis is based on. Statistical analysis was carried out in IBM SPSS Statistic 24 and R version 3.6.0 [22]. *p* values < 0.05 were considered statistically significant.

Results

Baseline data

General characteristics

We examined 82 patients with severe and symptomatic aortic stenosis, 39 (48%) women. Mean age was 83 years (SD 4.7), two patients were over 90 years, the oldest 95 years old, and there were six patients under 75 years. Most patients (62%) lived with their spouse. A majority (55%) had only primary school, while 20% had a university degree.

Geriatric characteristics

Fifteen patients (18%) had an MMSE score < 24, suggesting they were cognitively impaired. One fifth of the patients had a low NEADL score (≤ 43), implying dependence in at least one instrumental activity of daily living. As expected, NEADL and MMSE was correlated (Spearman’s rho = 0.47, *p* < 0.001). Eleven patients had a low BMI, however, 27 (33%) reported weight loss last year. Charlson comorbidity index was ≥ 3 in 36 (44%) of the patients, demonstrating a high burden of comorbidity. Six (7%) patients had a score ≥ 15 on the Hospital Anxiety and Depression Scale; i.e., few patients had severe anxiety or depression. For 80 patients, baseline 8-item frailty scale was calculated, and 14 patients (18%) were defined as frail.

Cardiovascular characteristics

Logistic EuroSCORE [23] was below 10 (predicting low surgical risk) in 20 (24%) and over 20 (high surgical risk) in 19 (23%) of the patients. Almost half (48%) of the patients had NYHA ≥ 3 at baseline, indicating a significant burden of symptoms. Few patients (11%) had a pacemaker before TAVI, and 26 (32%) had atrial fibrillation at baseline (Table 1).

Follow-up

One patient was lost to follow-up at the telephone interview and three had died. For three patients, information was missing on whether they lived at home or in nursing home at 2-year follow-up. VARC 2 composite endpoint is presented in Table 2, and endocarditis is separately presented in Table 3 with complementary data.

Mortality and morbidity

Two patients (2%) died early (< 30 days), and one had a disabling stroke. At 1 year, four patients (5%) had died and
Six patients (7%) had a disabling stroke. After 2 years, 6 (7%) patients had died, five of cardiovascular and one of non-cardiovascular cause. Four patients lived in nursing homes. There were no new disabling stroke from one to 2 years. Six patients (7%) had endocarditis during the first 2 years. Thirty-two patients (39%) got a new pacemaker perioperative (during the hospital stay).

**Patient-reported outcome measures at 6 months**

**NEADL**

The NEADL score was available in 78 patients at 6 months. All patients were reached in person except for one, where the spouse provided information. For one patient, only NEADL at 6 months was available. There was no change in mean NEADL ($n = 77$) at baseline and 6 months with 54.2 (SD 11.5) and 54.5 (SD 10.3), respectively, mean difference 0.3 ($p = 0.7$). Even so, 13 patients (17%) improved 5 points or more at the NEADL from baseline to 6 months, and 14 patients (18%) deteriorated 5 points or more. We did not find an association between frailty status and deterioration in NEADL score. For example, the proportion of patients who deteriorated in NEADL score was similar in the frail and the non-frail group (42% and 55%, respectively, $p = 0.53$, Fisher’s exact test).

**NYHA class**

After 6 months, the majority was in NYHA I (68%), about a quarter were in NYHA II (27%) and a few in NYHA III (5%). No patients were in NYHA IV. Mean NYHA ($n = 78$) at baseline and 6 months was 2.5 (SD 0.6) and 1.4 (SD 0.6), respectively, a significant improvement ($p < 0.001$). Four patients had missing NYHA class at 6 months (three dead, one lost to follow-up) (Fig. 1).
Discussion

This prospective observational study of 82 patients documents symptom improvement and maintenance of activities of daily living 6 months after TAVI. They had low mortality and most patients lived in their own home 2 years after TAVI. At baseline, 18% had an MMSE score, indicating cognitive impairment or dementia. We found a higher frequency of endocarditis than expected. According to the basic principles of shared decisions-making, balanced information regarding risks and benefits, and exploring patients’ values and goals are important. Physicians should be aware that patients’ cognitive impairment or dementia might affect the ability to participate in the decision-making process and give an informed consent.

Mortality at one (5%) and 2 years (7%) after TAVI was low in this cohort, where mean age is over 80 years and there is a substantial burden of comorbidity and frailty. We found a substantial improvement in NYHA class from baseline to 6 months. Based on the improvement of symptoms we expected to find an improvement in NEADL. However, we found no change in mean NEADL. There was a variation on an individual level. Some patients improved their independence and others deteriorated, although for most patients, the

| Table 2 Composite endpoints according to VARC 2 criteria |
|----------------------------------------------------------|
| **Device success**                                       |
| Absence of immediate procedural mortalityb               |
| Correct positioning                                      |
| Intended performance of the prosthetic heart valvec      |
| No moderate or severe prosthetic valve regurgitationd     |
| **Early safety (at 30 days)**                           |
| All-cause mortality                                      |
| All stroke(disabling or non-disabling) in hospitale       |
| Life-threatening or disabling bleeding                    |
| Acute kidney injury-stage 2 or 3f                       |
| Coronary artery obstruction requiring intervention       |
| Major vascular complication                              |
| Valve-related dysfunction requiring intervention         |
| **Clinical efficacy (30 days–2 years)**                  |
| All-cause mortality                                      |
| All stroke(disabling or non-disabling)                    |
| Requiring hospitalizations for valve-related symptoms or worsening congestive heart failure |
| NYHA class III or IV                                     |
| **Time-related valve safety**                           |
| Structural valve deterioration                           |
| Valve-related dysfunction (mean aortic valve gradient ≥20 mmHg) and/ or moderate or severe prosthetic valve regurgitationb |
| Requiring repeat procedure (TAVI or SAVR)                |
| Prosthetic valve endocarditisf                          |
| Trombo-embolic events (eg stroke)                       |
| VARC bleeding (life threatening/disabling bleeding or major bleeding), unless clearly unrelated to valve therapy (e.g. trauma) |

SAVR Surgical aortic valve replacement, TAVI transcatheter aortic valve implantation, NYHA New York Heart Association

*The Valve Academic Research Consortium (VARC)-2 consensus document (see references)

bImmediate or consequent death ≤ 72 h post-procedure

cNo prosthesis-patient mismatch. Mean aortic valve gradient < 20 mmHg or peak velocity < 3 m/s

dAfter TAVI procedure at index hospitalization

eAssessment of stroke at index. All strokes verified by CT/MRI

fEvaluation of acute kidney injury is based on serum creatinine, we miss data on urine output

gNYHA at 6 months

hFour patients had new paravalvular leak or vegetation on the aortic valve
change in NEADL was minor. Other factors, like frailty and dementia, probably have more impact on the level of independence than the aortic stenosis per se [4], and 6 months follow-up is probably too short to establish deterioration due to other causes. There was no difference between the frail and robust patients regarding change in NEADL from baseline to 6 months.

At baseline, 15 patients had an MMSE below 24, indicating possible cognitive impairment or dementia [13]. Five patients had an MMSE less than 20, which increases the probability of incapacity, and likely reduces their power of judgement during the decision-making processes before TAVI [11]. Several studies have suggested that a low MMSE score at baseline predicts poor outcomes after TAVI [4, 24]. However, there are also studies demonstrating cognitive improvement after TAVI when impairment is caused by the aortic stenosis itself [25]. For patients with established dementia, surviving to end stage dementia might not be what the patient would choose autonomously. These are difficult issues to discuss with patients with dementia and their families, both due to patients’ anosognosia (a physiological damage to the brain, where patients have no awareness of their disease) [26], and also health care professionals’ fear of patients losing hope when focusing on the deterioration and increased dependence expected after a diagnosis of dementia [27]. It is important to point out that an MMSE < 24 is not diagnostic of dementia, and sensitivity and specificity for MMSE cut-offs in a TAVI population, might be different than in the general population. Suspicion of dementia should, therefore, lead to further investigations.

**Table 3** Infective endocarditis first 2 years after TAVI

| TAVI valve | Age at TAVI and gender | Days after TAVI | Bacteria (4/4 blood cultures) | Dukes criteria<sup>b</sup> | Outcome two year | TTE and TEE | Pacemaker device |
|------------|------------------------|-----------------|-------------------------------|-------------------------|----------------|-------------|-----------------|
| Lotus 27 mm | 86 y, F | 49 | *Staphylococcus aureus* | 1 Major + 3 minor | Dead<sup>c</sup> | No vegetation or PVL | PM, 1 day after TAVI |
| Core valve 31 mm | 77 y, M | 190 | *Streptococcus salivarius* | 2 Major + 2 minor | Alive | Aortic valve vegetation | CRT-D, 3 months before TAVI |
| Core valve 31 mm | 80 y, M | 380 | *Enterococcus faecalis* | 1 Major + 3 minor | Alive | New aortic PVL | CRT-P, 2 months after TAVI |
| Core valve 29 mm | 79 y, M | 407 | *Streptococcus sanguinis* | 1 Major + 3 minor | Alive | New aortic PVL | No |
| Core valve 31 mm | 77 y, M | 448 | *Staphylococcus aureus* | 2 Major + 4 minor | Dead<sup>d</sup> | Aortic valve vegetation | CRT-P, 1 year before TAVI |
| Core valve 31 mm | 80 y, M | 528 | *Streptococcus oralis* | 1 Major + 1 minor | Alive | No vegetation or PVL | PM, 1 day after TAVI |

<sup>a</sup>y years, <sup>M</sup> male, <sup>F</sup> female

<sup>b</sup>All meet criteria for definite infective endocarditis (IE) except the last patient who has a possible IE. All patients had trans-femoral access for TAVI

<sup>c</sup>Died five months after diagnosed with IE

<sup>d</sup>Died one month after diagnosed with IE

**TTE** transthoracic echocardiography, **TEE** trans-oesophageal echocardiography, **PVL** para valvular leak, **PM** pacemaker, **CRT-P/D** coronary resynchronisation therapy with cardiac defibrillator (D) or pacemaker (P)

**Fig. 1** Individual changes in NYHA class from baseline (<i>n</i> = 82) to 6 months (<i>n</i> = 78). The height of each bar is proportional to the number of patients with the corresponding NYHA class, and the width of the ends of each flow line is proportional to the number of patients with the given pattern of change of NYHA class
We found a higher frequency of infective endocarditis (IE) than expected. In a recent meta-analysis with a mean follow-up at 3.4 years, the overall incidence of IE in TAVI was 2.0% [28]. In the present study, five of six patients with IE had a pacemaker or an ICD, which might be associated with an increased risk of IE [29]. Several single-centre studies finding higher incidences suggests that IE is underreported in large studies and registries [30, 31]. Diagnosing endocarditis is challenging, and the presentation might be uncharacteristic since the patients are old with comorbidities [28]. As endocarditis can occur later on, longer follow-up than 1 year seems important. Antibiotic prophylaxis during the TAVI procedure were administered to all patients. General practitioners were informed routinely on discharge about the risk of endocarditis and indications for prophylaxis.

Prior to TAVI, patients need to be informed of expected NYHA class improvement, survival benefit and maintenance of activities of daily living. Rare and severe complications, like death, stroke and infectuous endocarditis, should also be part of the pre-TAVI discussion with the patient. Old patients with substantial comorbidity need to be informed that TAVI will not solve all their health problems. After the study period, written information about the procedure and risks and benefits was developed and administered to patients as part of the decision-making process. Our findings may be used when developing and improving decision aids for this treatment in older adults.

**Strengths of the study**

All hospitals in Western Norway use the same electronic medical records and VARC-2 endpoints are complete with no patients lost to follow-up. All deaths are automatically registered in the patients’ electronic journal. The same investigator (ES) performed the assessment at baseline and 6 months, increasing reliability.

**Limitations of the study**

This is a single centre study performed in the early era of TAVI and some of the results might not be transferable due to improvement of equipment, better patient selection and training of the interventional cardiologists performing the procedure. Most patients were independent before TAVI, and minor (nevertheless important to patients) improvements might not be revealed by the NEADL questionnaire. Due to the small sample size, it was not possible to analyse whether specific subgroups improved or deteriorated in NEADL. We performed only telephone interviews at 6 months, preventing us from assessing MMSE and frailty at follow-up. We assume that living in their own home 2 years after TAVI reflects independence of activities of daily living, however, we cannot exclude that some patients living at home were in need of extended care.

**Conclusion**

TAVI patients had symptom improvement and maintenance of activity of daily living at 6 months. They had low mortality, and most patients lived in their own home 2 years after TAVI. Severe complications, like death, stroke and endocarditis, occurred. Balanced information regarding these risks and benefits is needed to ensure informed consent prior to the procedure, and our findings may be used to develop and improve decision aids assisting this process. Clinicians should be aware that some patients have cognitive impairment before TAVI that might affect their power of judgement and decision-making.

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**Compliance with ethical standards**

**Conflict of interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

**Human and animal rights statement** All procedures performed in the study were in accordance with the ethical standards of the institution and the national research committee and with the 1964 Helsinki declaration and its later amendments. The regional Committee for medical research ethics approved the study (REK 2013/1310).

**Informed consent** Written, informed consent was obtained from all participants.

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