Meta-Analysis of Predictors of All-Cause Mortality After Transcatheter Aortic Valve Implantation.

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Meta-Analysis of Predictors of All-Cause Mortality After Transcatheter Aortic Valve Implantation

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Q4 The aim of this study was to identify predictors of 30-day and midterm mortality after transcatheter aortic valve implantation (TAVI) by means of a systemic review. TAVI was demonstrated to be safe and efficacious in patients with severe aortic stenosis. An accurate estimation of procedural risk of these patients represents an actual challenge. The PubMed and Cochrane Collaboration databases were systematically searched for studies reporting on the incidence and independent predictors of 30-day and midterm mortality. Adverse events were pooled with random effect, whereas independent predictors are reported as odds ratios (ORs) with 95% confidence intervals (CIs). A total of 25 studies with 8,874 patients were included (median age 82.5 – 1.5 years, 54.6% women). At 30 days, 7.5% of patients (n ▮ 663) died. At midterm follow-up (median 365 days, interquartile range 267 to 365 days), the cumulative mortality rate was 21.6% (n ▮ 1,917). Acute kidney injury (AKI) stage ‡2 (OR 18.0, 95% CI 6.3 to 52), preprocedural hospitalization for heart failure (OR 9.4, 95% CI 2.6 to 35), periprocedural acute myocardial infarction (OR 8.5, 95% CI 2.6 to 33.5), and increased proebrain natriuretic peptide (pro-BNP) levels (OR 5.4, 95% CI 1.7 to 16.5) were the most important independent predictors of 30-day mortality. Increased pro-BNP levels (OR 11, 95% CI 1.5 to 81), AKI stage 3 (OR 6.8, 95% CI 2.6 to 15.7), left ventricular ejection fraction <30% (OR 6.7, 95% CI 3.5 to 12.7), and periprocedural acute myocardial infarction (OR 6.5, 95% CI 2.3 to 18.1) represented the predictors of midterm mortality. In conclusion, in this large meta-analysis of patients undergoing TAVI, we found that high pro-BNP levels and postprocedural AKI were the strongest independent predictors of both 30-day and 1-year mortality. These findings may contribute to a better understanding of the risk assessment process of patients undergoing TAVI. (Am J Cardiol 2014;–:–e–)

Despite being one of the most important aspects of transcatheter aortic valve implantation (TAVI) practice, adequate patient selection represents a clinical issue not fully resolved. Allocating transcatheter treatment to the correct patients, reasonably expected to benefit in terms of functionality and survival, is essential to avoid unnecessary high-risk procedures with accompanying costs.[1e4] However, assessment of patient eligibility is often complex because of the extensive co-morbidity encountered in candidates for TAVI, rendering it difficult to estimate whether a beneficial treatment effect can be expected in individual patients, especially because surgical risk scores (EuroSCORE and

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See page 7 for disclosure information.

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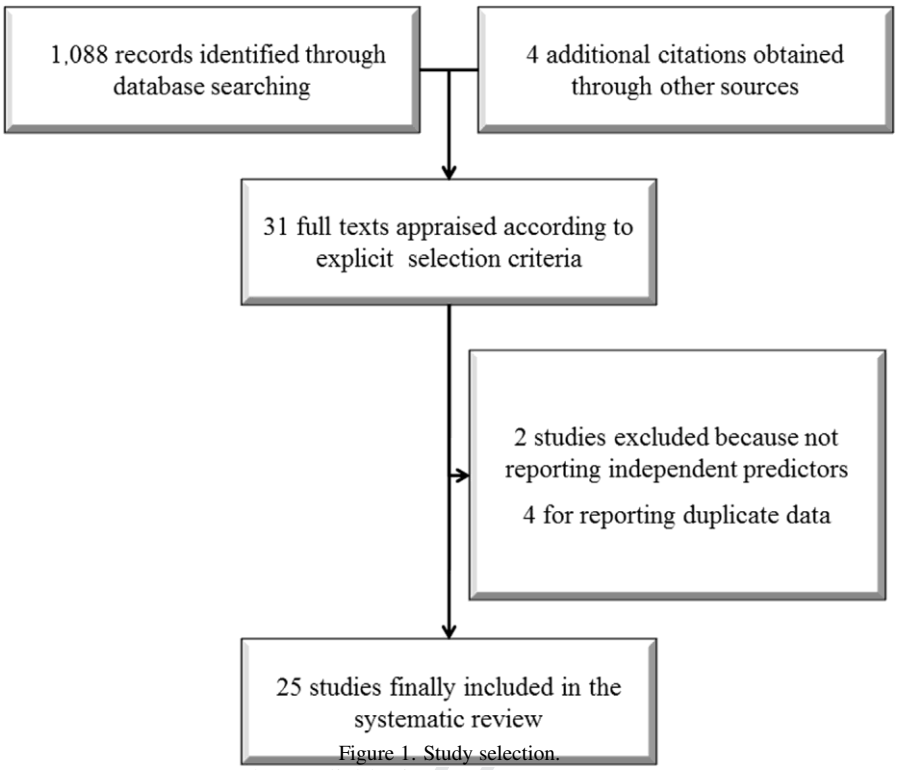

Figure 1. Study selection.

Society of Thoracic Surgery score) are less reliable in patients undergoing TAVI.[5e7] The primary challenge to improve patient selection and counseling is hindered by the search for accurate and validated risk factors for mortality after TAVI. The investigation of predictors of mortality may yield helpful tools that could facilitate decision making of the heart team. Contemporary literature falls short in addressing this issue, despite the availability of numerous publications, as the knowledge on predictors of mortality is fragmentary. Meta-analyses have currently been performed only for reporting the incidence of TAVI-related complications or identifying predictors of specific adverse events, for example, paravalvular leak.[8,9] However, a comprehensive analysis of predictors of 30-day and midterm mortality is still lacking. The aim of this study was thus to identify predictors of post-TAVI 30-day and midterm mortality by means of a systemic review of the currently available literature.

Methods

This study was conducted in accordance with the current guidelines, including the recent Preferred Reporting Items for Systematic reviews and Meta-Analyses amendment to the Quality of Reporting of Meta-analyses statement, and recommendations from The Cochrane Collaboration and Meta-analysis Of Observational Studies in Epidemiology (MOOSE).[10]

PubMed and Cochrane databases were searched for reports published in English from January 2002 to June 2013 according to the following highly sensitive strategy, in compliance with established methods and incorporating wildcards (identified by *): (TAVI* OR TAVR OR "transcatheter aortic") AND ("adverse events" OR "30 days events" OR "mid-term prognosis") AND english[lang] AND ("c"[pdat]:"3000"[pdat]) NOT (review[pt] OR editorial[pt] OR letter[pt]).

Retrieved citations were first screened for relevance Q5 independently by 2 reviewers (FG and FDA) at the title and/or abstract level. The reports remaining after the initial screening were appraised in the full text with respect to the following inclusion criteria: (1) human study, (2) investigating patients undergoing TAVI, (3) reporting predictors of mortality at 30 days or at midterm follow-up, and (4) online full-text available publication. All criteria had to be met for inclusion. Exclusion criteria were (1) duplicate reporting and (2) study population <50 patients. The presence of even one of the exclusion criteria sufficed for exclusion. Duplicate reporting was handled by selecting the study reporting on the largest sample of patients undergoing TAVI, or if equal, the study with the largest number of overall patients.

The quality and validity of the included studies were independently assessed by 2 reviewers (FG and FDA). After modifying the MOOSE item list, to ensure compatibility with the included studies, each study was summarized and critically appraised with respect to study design, data source, the statistical methods used for multivariate analysis, and the risk of bias (graded as low, moderate, high, or unknown because incomplete reporting may render it impossible to ascertain the risk of bias).[10] Encountered bias was further subdivided into analytical, selection, adjudication, detection, and attrition bias.

Relevant study data were extracted independently by the reviewers (FG and FDA). The extracted data comprised authors and journal names, year of publication, location of

Table 1
Baseline characteristics

First Author	Recruitment Years	Number	Age	Women	DM	NYHA III	CAD*	Previous AMI	Previous Revascularization (Surgical or Percutaneous)	Previous Cardiac Surgery	COPD	GFR <60 ml/min/m^2
Thomas[17] (2011)	2007e2009	1038	81	576 (56%)	—	146 (14%)	537 (52%)	—	495 (48%)	236 (23%)	286 (28%)	305 (29%)
Kempfert[18] (2011)	2006e2010	299	82	209 (70%)	115 (52%)	252 (84%)	159 (53%)	8 (3%)	—	86 (29%)	129 (43%)	26 (9%)
Parenica[19] (2012)	—	29	82	21 (72%)	3 (10%)	26 (90%)	—	—	—	1 (3%)	5 (17%)	—
Halliday[20] (2012)	2008e2010	101	83 1	52 (51%)	22 (22%)	—	—	—	—	—	—	—
Yong[21] (2012)	2007e2011	119	81 8	72 (61%)	31 (26%)	—	24 (20%)	22 (18%)	41 (34%)	15 (13%)	40 (34%)	—
Barbash[22] (2012)	2007e2011	165	85 6	96 (58%)	53 (32%)	—	92 (56%)	—	81 (49%)	54 (33%)	45 (69%)	128 (78%)
Sinning[23] (2012)	2009e2010	1315	82 6	765 (58%)	462 (35%)	1166 (89%)	791 (60%)	209 (16%)	693 (53%)	289 (22%)	314 (24%)	786 (60%)
Buellesfeld[24] (2012)	2007e2010	353	83	203 (58%)	92 (26%)	263 (75%)	203 (58%)	61 (17%)	151 (43%)	82 (23%)	—	77 (22%)
Humphries[25] (2012)	2005e2011	641	83	329 (5%1)	197 (31%)	554 (86%)	467 (73%)	259 (40%)	328 (51%)	—	170 (27%)	413 (64%)
Tchetche[26] (2012)	2010e2011	134	82 5	53 (40%)	30 (22%)	111 (83%)	56 (42%)	—	56 (42%)	16 (12%)	34 (25%)	37 (28%)
Akin[27] (2012)	2007e2008	45	82 7	27 (60%)	17 (38%)	43 (91%)	—	—	—	3 (6%)	8 (2%)	25 (56%)
Rodes-Cabau[28] (2012)	2005e2009	339	81 8	187 (55%)	79 (23%)	308 (90%)	234 (69%)	173 (51%)	215 (63%)	116 (34%)	100 (30%)	—
Latib[29] (2012)	2003e2011	111	81 7	49 (44%)	21 (19%)	75 (67.6%)	44 (40%)	16 (14%)	..	0	29 (26%)	— Q11
Pilgrim[30] (2012)	2007e2011	389	82 6	224 (58%)	105 (27%)	—	238 (61%)	64 (17%)	166 (43%)	72 (18%)	72 (19%)	268 (69%)
Hayashida[31] (2012)	2006e2011	400	83 6	206 (52%)	92 (23%)	347 (87%)	237 (59%)	—	—	63 (16%)	124 (31%)	249 (63%)
Généreux[32] (2013)	2008e2011	218	85 8	106 (48%)	62 (29%)	—	—	—	177 (80%)	89 (40%)	64 (29%)	18 (8%)
Amabile[33] (2013)	2008e2012	173	84 6	91 (53%)	43 (25%)	—	107 (63%)	—	—	—	46 (27%)	121 (71%)
Van der Boon[34] (2013)	—	940	81 7	434 (46%)	268 (29%)	761 (81%)	425 (45%)	158 (17%)	484 (52%)	207 (22%)	323 (34%)	591 (63%)
Toggweiler[35] (2013)	2005e2007	88	87 7	41 (47%)	22 (25%)	—	63 (72%)	69 (78%)	—	34 (39%)	23 (26%)	47 (53%)
Stortecky[36] (2013)	2007e2011	389	83 6	224 (58%)	105 (27%)	255 (66%)	238 (61%)	64 (16%)	166 (43%)	72 (19%)	—	268 (69%)
Codner[37] (2013)	2008e2012	153	82 6	95 (62%)	45 (29%)	149 (87%)	—	11 (7%)	82 (54%)	38 (25%)	43 (28%)	60 (39%)
Borz[38] (2013)	2006e2011	250	83 7	135 (54%)	64 (26%)	—	87 (35%)	—	—	49 (20%)	—	—
D'Onofrio[39] (2013)	2008e2012	774	81 7	446 (58%)	205 (27%)	621 (80%)	168 (22%)	23 (3%)	226 (29%)	167 (33%)	247 (32%)	80 (10%)
López-Otero[40] (2013)	2008e2011	85	83 5	31 (37%)	20 (24%)	70 (82%)	9 (9%)	—	—	—	20 (24%)	—
Seiffert[41] (2013)	2008e2011	326	81 1	181 (56%)	—	266 (82%)	201 (62%)	65 (20%)	180 (55%)	65 (20%)	87 (27%)	29 (9%)

AMI ¼ acute myocardial infarction; CAD ¼ coronary artery disease; COPD ¼ chronic obstructive pulmonary disease; DM ¼ diabetes mellitus; GFR ¼ glomerular filtration rate; NYHA ¼ New York Heart Association.
* Defined as coronary stenosis >50%.

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Table 2
Echocardiographic and procedural features

First Author	LVEF	Aortic Valve MG	MR >2þ	Pulmonary Hypertension	TF	TA	TS	TAo	EDW	CV	Log ES	STS Score
Thomas[17] (2011)	—	—	257 (25%)	—	463 (45%)	575 (55%)	0	0	1038 (100%)	0	28	—
Kempfert[18] (2011)	55 13	—	3 (1%)	81 (27%)	0	299 (100%)	—	—	299 (100%)	0	31 16	13 8
Parenica[19] (2012)	57	50	—	11 (38%)	14 (25%)	15 (26%)	—	—	29 (100%)	0	24	—
Halliday[20] (2012)	—	—	—	—	45 (45%)	56 (55%)	0	0	—	—	22 0.9	—
Yong[21] (2012)	—	49 16	10 (8%)	—	119 (100%)	0	0	0	0	119 (100%)	19 13	6 5
Barbash[22] (2012)	51 15	—	—	—	117 (71%)	48 (29%)	0	—	—	—	—	12 4
Sinning[23] (2012)	52 15	—	—	—	1143 (87%)	121 (9%)	41 (3%)	10 (1%)	—	—	21 14	—
Buellesfeld[24] (2012)	50	44	—	88 (25%)	353 (100%)	0	0	0	34 (10%)	319 (90%)	26	—
Humphries[25] (2012)	—	41	166 (26%)	—	351 (55%)	290 (45%)	0	0	622 (97%)	19 (3%)	—	8
Tchetche[26] (2012)	47 13	48 15	0	—	125 (93%)	0	9 (7%)	0	0	134 (100%)	24 10	—
Akin[27] (2012)	48	57	41 (85%)	—	45 (100%)	—	—	—	45 (100%)	—	21	—
Rodes-Cabau[28] (2012)	55 14	—	27 (8%)	84 (25%)	163 (48%)	176 (52%)	0	0	339 (100%)	0	—	10 6
Latib[29] (2012)	54 13	—	—	—	111 (100%)	0	0	0	70 (63%)	41 (37%)	23 15	4.6 2.3
Pilgrim[30] (2012)	52 15	44 17	—	111 (31%)	308 (80%)	76 (20%)	5 (1%)	0	164 (42%)	225 (58%)	24 14	6.8 5.3
Hayashida[31] (2012)	—	—	—	—	—	—	—	—	347 (87%)	53 (13%)	22	8
Généreux[32] (2013)	48 16	45 15	—	—	140 (64%)	78 (36%)	0	0	218 (100%)	0	—	12 5
Amabile[33] (2013)	55 15	49 18	—	—	139 (81%)	32 (19%)	0	0	132 (77%)	39 (23%)	22 12	—
Van der Boon[34] (2013)	—	—	—	—	79 (84%)	89 (10%)	57 (6%)	4 (0.4%)	435 (46%)	505 (54%)	21	—
Toggweiler[35] (2013)	60	46 18	—	17 (19%)	64 (73%)	24 (27%)	0	0	88 (100%)	0	—	9
Stortecky[36] (2013)	52 15	44 17	—	—	308 (79%)	76 (20%)	5 (1%)	0	165 (42%)	224 (58%)	24 14	7 5
Codner[37] (2013)	—	51 15	52 (33%)	—	112 (73%)	27 (18%)	13 (9%)	1 (1%)	62 (41%)	91 (60%)	23 13	9 5
Borz[38] (2013)	—	45 17	—	—	190 (76%)	60 (24%)	0	0	250 (100%)	0	23 13	—
D'Onofrio[39] (2013)	53 13	50 15	173 (22%)	87 (11%)	0	774 (100%)	0	0	774 (100%)	0	26 16	10 8
López-Otero[40] (2013)	—	—	—	—	—	0	—	0	0	85 (100%)	29 8	—
Seiffert[41] (2013)	—	37 2	30 (9%)	48 (19%)	149 (45%)	177 (51%)	0	0	281 (81%)	45 (13%)	23 2	8 1

CV ¼ CoreValve; EDW ¼ Edwards Sapien; ES ¼ EuroSCORE; LVEF ¼ left ventricular ejection fraction; MR ¼ mitral regurgitation; STS ¼ Society of Thoracic Surgery; TA ¼ transapical; Tao ¼ transaortic; TF ¼ transfemoral; TS ¼ trans-subclavian.

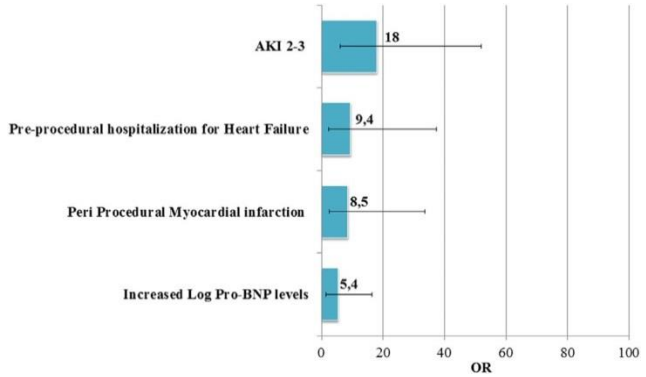

Figure 2. Independent predictors of 30-day mortality at 1 year with OR >5.

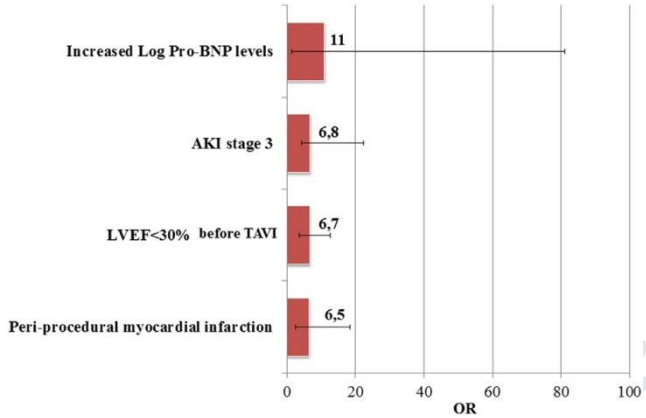

Figure 3. Independent predictors of all-cause mortality at midterm follow-up with OR >5.

Table 3
Meta-regression of baseline features on all-cause death at follow-up

	Beta	LCI	UCI	p
Age	0.16	0.24	0.32	0.09
Female gender	0.001	0.37	0.45	0.90
Diabetes mellitus	0.004	0.006	0.004	0.61
NYHA class more than III	0.01	0.005	0.02	0.04
Coronary artery disease	0.03	0.04	0.06	0.89
COPD	0.06	0.08	0.10	0.75
Reduced renal function	0.10	0.01	0.12	0.88

COPD ¼ chronic obstructive pulmonary disease; LCI ¼ low confidence interval; NYHA ¼ New York Heart Association; UCI ¼ upper confidence interval.

the study group, baseline patient characteristics, procedural features, and multivariate predictors of all-cause mortality (estimator, point summary estimate of risk, 95% confidence intervals [CIs]). End points of interest for the present review were the incidence of TAVI-related complications and 30-day and midterm all-cause mortality. Multivariate predictors with an odds ratio (OR) >5 reported in at least 3 studies were reported. Meta-regression analysis was performed for midterm all-cause mortality for baseline clinical variables.

Result analysis of the studies was registered on dedicated electronic forms. The forms were piloted over the first 5

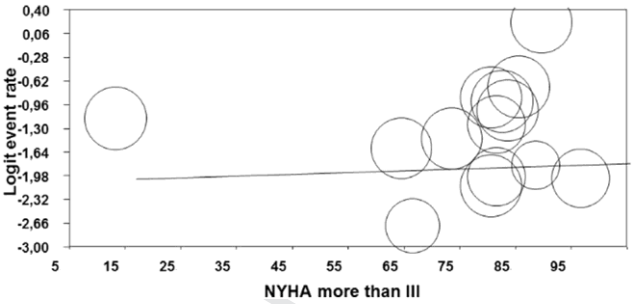

Figure 4. Regression of NYHA class >III on logistic event rate.

cases for consistency and discrimination. Any divergence in opinion between the reviewers at any stage of the review process was resolved by consensus discussion.

Continuous variables are reported as mean SD or median and range. Categorical variables are expressed as counts and percentages. Independent predictors of TAVI-related complications and 30-day and midterm all-cause mortality were appraised and ordered according to their measure of risk (either OR or hazard ratio) with Review Manager (RevMan), version 5.2, freeware package (The Cochrane Collaboration, The Nordic Cochrane Center, Copenhagen, Denmark) and Comprehensive Meta-Analysis. Small study bias was appraised by graphical inspection of funnel plots. Hypothesis testing for superiority was set at the 2-tailed 0.05 level. Hypothesis testing for statistical homogeneity was set at the 2-tailed 0.10 level and based on the Cochran Q test, with I^2 values of 25%, 50%, and 75% representing, respectively, mild, moderate, and extensive statistical inconsistency.

Results

The search strategy yielded 1,088 reports. Four reports derived from congresses were added, resulting in a total of 1,092 citations. All citations were first screened at title and abstract level; the 31 remaining reports were subsequently screened full text. Of the full-text analyzed citations, 4 were excluded because of reporting duplicate data[11e14] and 2 because of the absence of data on independent predictors for adverse events.[15,16] Twenty-five studies were finally included in this systemic review (Figure 1).[17e41]

The 25 included studies reported on a total of 8,874 patients treated with TAVI for symptomatic severe aortic stenosis (AS). Approximately 1/2 of the patients were women (54.6%); median age was 82.5 1.5 years. Mean logistic EuroSCORE-I was 23.4 3.1% and was above 20% in all studies, except for one (19 13%).[21] In those studies (n ¼ 5) in which reporting results was exclusively done using the Society of Thoracic Surgery score,[22,25,28,32,35] the mean risk of perioperative mortality was >5%. Diabetes mellitus was present in 24% (n ¼ 2,153) of patients, renal insufficiency in 48% (n ¼ 4,264), and a history of previous revascularization (either surgical or percutaneous) in 40% (n ¼ 3,541). Left ventricular ejection fraction (LVEF) was in general preserved, except for 3 studies in which mean LVEF was mildly compromised (range of mean LVEF 47% to 60%).[26,27,32] The most important baseline characteristics are reported in Table 1.

A small majority of patients were treated by the transfemoral approach (51.1%), followed by the transapical approach (33.7%), and only few patients received a direct aortic or trans-subclavian procedure (1.5% and 0.2%, respectively). In 60.8% (n ¼ 5,392) of patients, an Edwards SAPIEN or SAPIEN XT balloon-expandable valve (both Edwards Lifesciences, Irvine, California) was implanted, and in 21.4% (n ¼ 1,899) of patients, the self-expandable third-generation Medtronic CoreValve (Medtronic Inc., Minneapolis, Minnesota) prostheses were used, whereas 3 studies (comprising 15.8% of patients, n ¼ 1,583) did not specify the type of valve implanted.[20,22,23] Because of the infrequent reporting of conversion to surgery and intraprocedural death, no reliable incidence could be reported for these events. Table 2 summarizes procedural TAVI characteristics in the various studies.

At 30 days, 7.5% (n ¼ 663) of patients died. Acute kidney injury (AKI) occurred in 8.02% (n ¼ 712), lifethreatening and major bleeding in 13.8% (n ¼ 1,224), major vascular complications in 8.8% (n ¼ 782), periprocedural acute myocardial infarction (AMI) in 0.6% (n ¼ 51), and pacemaker implantation in 12.5% (n ¼ 1,106) of patients. At midterm follow-up (median 365 days, interquartile range 267 to 365), 21.6% (n ¼ 1,917) of patients had died. The strongest predictors of 30-day mortality were AKI stage 2 (OR 18.0, 95% CI 6.25 to 52), preprocedural hospitalization for at least 1 week (OR 9.36, 95% CI 2.55 to 35), periprocedural AMI (OR 8.54, 95% CI 2.57 to 33.52), and preprocedural increased pro‐brain natriuretic peptide (pro-BNP) levels (OR 5.35, 95% CI 1.74 to 16.5; Figure 2). The most important predictors for cumulative midterm mortality were increased pro-BNP levels (OR 11, 95% CI 1.51 to 81), AKI stage 3 (OR 6.80, 95% CI 2.55 to 15.66), LVEF <30% (OR 6.67, 95% CI 3.5 to 12.76), and periprocedural AMI (OR 6.52, 95% CI 2.34 to 18.14; Figure 3).

At meta-regression analysis, similarly, NYHA class >III was related to all-cause midterm mortality (Table 3 and Figure 4).

Discussion

Profound understanding of factors determining patient survival after TAVI is of paramount importance in clinical practice not only to enable to accurately select patients, that is, only those in whom treatment benefit outweighs the risk, but also to take appropriate measures to prevent complications in high-risk subjects, especially considering that the commonly used logistic EuroSCORE falls short in predicting mortality, as it does not take account of periprocedural events, and it is known to overestimate operative risk in patients undergoing TAVI.[7]

This is the largest systematic review to assess predictors of periprocedural and long-term mortality in high-risk and highly symptomatic patients with severe AS from all over the world, undergoing TAVI treatment from 2003 to 2012, and thus represents a wide range of TAVI experience. The 30-day and midterm mortality rates in this large group of patients were 7.5% and 21.6%, respectively, signifying that nearly 30% of deaths occurred within the first 30 days after TAVI, well in line with data previously reported by several real-world registries and 1 meta-analysis.[42,43]

Based on Valvular Academic Research Consortium 1 criteria, the strongest predictor for 30-day mortality was stage 2 AKI, whereas stage 3 AKI was an important determinant of midterm mortality. The reported incidence of AKI after percutaneous valve implantation varies from 8% to 28%,[32,44–47] mainly because of differences in AKI definition, which is considerably lower than that observed after cardiac surgery.[48] Many patients actually demonstrate an improvement of renal function after TAVI rather than kidney injury, as abolishment of the valvular obstruction leads to improved renal hemodynamics.[44] Several factors are believed to be involved in the undesired development of AKI. Intraprocedural episodes of hypotension and emboli generated by catheter manipulations, balloon valvuloplasty and/or prosthesis deployment, and postprocedural bleedings might result in tubular ischemia and consequential decrease in kidney function.[46,47] Moreover, the occurrence of paravalvular aortic regurgitation produces acute volume overload with a subsequent increase in left ventricular end-diastolic pressure, ultimately leading to a reduction in diastolic renal blood flow and impairment of renal function.[46] The fact that AKI is most strongly associated with short-term mortality, also shown in the present review, supports this hypothesis.

Preprocedural elevated pro-BNP levels (measured 24 hours before TAVI) were also a strong independent predictor of both 30-day and midterm mortality. The prognostic value of natriuretic peptides was previously recognized in interventions on the aortic valve.[49,50] Likewise, baseline BNP and pro-BNP levels have been identified as independent predictors of 30-day and long-term mortality in TAVI, respectively.[49–52] The unfavorable outcome of valve interventions in patients with high BNP levels is believed to be related to the presence of impaired systolic and/or diastolic left ventricular function, as both types of myocardial dysfunction are associated with elevated BNP levels.[49] Patients with high preprocedural BNP might benefit from optimization of their hemodynamic status by bridging therapy (optimization of medical therapy or balloon valvuloplasty) before proceeding to TAVI, although further research is warranted to confirm this.

Not surprisingly, preprocedural hospitalization (mainly for decompensated AS) and preprocedural LVEF 30% were among the strongest predictors of 30-day and midterm mortality, respectively. This finding reflects, on one hand, the severity of AS disease and, on the other hand, a poorer functional status, characterizing the more frail patients. Moreover, recent research revealed that clinically inoperable patients, a designation often based on frailty, have worse survival compared with technically inoperable patients.[52]

Finally, periprocedural myocardial injury and infarction were among the strongest predictors of post-TAVI mortality in this analysis. TAVI is systematically associated with Q6 myocardial injury, as an increase in the troponin level above the URL is observed in nearly all patients.[21,53,54] A single study demonstrated a strong association between biomarker-determined myocardial injury (defined as peak values of cardiac troponin T and/or creatine kinase-MB >5 times the URL, not fulfilling the criteria for myocardial infarction) and 30-day and 1-year survival rates.[54] Myocardial injury during TAVI is most likely caused by global myocardial

ischemia, resulting from a mismatch in myocardial oxygen supply and demand. The diffuse nature of myocardial injury makes it unlikely to cause left ventricular dysfunction with subsequent heart failure or myocardial scarring prone to ventricular arrhythmia. Therefore, it was hypothesized that myocardial injury is a marker for more extensive (vascular) disease, which may increase the risk for postprocedural adverse events.[21] Periprocedural myocardial infarction, defined by the additional development of new Q waves and/or wall motion abnormalities according to the Valvular Academic Research Consortium criteria, is a rare finding estimated to occur in approximately 1% of TAVI cases.[21,53–55] In this review, it was identified as one of the strongest predictors of midterm mortality.

There was a great deal of overlap between the strongest predictors of 30-day and cumulative midterm mortality in the present work. This might origin from true shared predictors of both events, or it might reflect an overwhelming effect of 30-day mortality on the analysis of predictors for cumulative midterm death rates. The most powerful preprocedural predictors (elevated BNP, preprocedural hospitalization, and reduced LVEF) of mortality were predominantly related to AS disease severity, suggesting that timely reference for TAVI might be vital to increase the odds of postprocedural survival. All the postprocedural predictors (AKI and AMI) were associated with TAVI complications, emphasizing the importance of preventing these events.[56,57]

In this systematic review, the strongest independent predictors of 30-day and cumulative midterm mortality were identified by means of their measured effect size (expressed by their OR or hazard ratio). The reporting of predictors was therefore entirely determined by an arbitrarily set OR threshold of 5.0, meaning that less-influential predictors were not presented. These include predictors that might be of clinical importance based on their prevalence in the population with TAVI, rather than their effect size. The results of this study should be interpreted in the light of this notion.

Furthermore, the literature referred to in this review represents a considerable range of TAVI experience, institutional routines, follow-up durations, and complication definitions. The present analysis did not take into account this heterogeneity of the included studies, potentially hampering the generalizability of the results. Moreover, the validity of the multivariate analyses that yielded the independent predictors heavily depends on whether all potential predictors were measured and included in the model, as multivariate analysis does not consider unmeasured variables. Finally, the present review is a not patient level–based analysis, consequently limiting methodological relevance of the present work. The assessment of external and internal validity of the separate studies was solely used to select the studies; the reported results were not weighed accordingly.

Disclosures

The authors have no conflicts of interest to disclose.

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