Predicting Mortality after Transcatheter Aortic Valve Replacement: External Validation of the TVT Registry Model

Data Supplement

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Supplemental Table 1. TRIPOD Checklist

Section/Topic	Item		Checklist Item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	3
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	4
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	4
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	4
	5b	D;V	Describe eligibility criteria for participants.	4
	5c	D;V	Give details of treatments received, if relevant.	4
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	4-5
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	N.A.
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	4-5
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	N.A.
Sample size	8	D;V	Explain how the study size was arrived at.	N.A.
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	5.
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	N.A.
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	5
	10c	V	For validation, describe how the predictions were calculated.	5
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	5-6
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	N.A.
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	5
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	N.A.
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	6.
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	6
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	N.A.
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	6
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	Supplemental Table 2
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	6
	15b	D	Explain how to the use the prediction model.	10
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	6 and Figure 1 and 2
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	N.A.
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	10
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	9
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	8-10
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	8-10
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	N.A
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	N.A.

Supplemental Table 2. Baseline clinical characteristics of patients in the validation and development cohorts

	SWISS TAVI Registry n= 3491	**STS/ACC TVT Registry n= 13718**
Age (years)	82.1 ± 6.5	82.1 ± 8.3
Male gender (%)	1760 (50%)	6680 (48.7%)

Values are mean ± SD or percentages.

Supplemental Table 3. Type and frequency of transcatheter heart valves in the Swiss TAVI cohort

	All patients n= 3,491	**Survivors** n= 3,390	**Died in hospital** n= 101
Medtronic CoreValve	917 (26%)	892 (26%)	25 (25%)
Edwards Sapien XT	606 (17%)	582 (17%)	24 (24%)
Symetis Acurate	98 (3%)	96 (3%)	2 (2%)
JenaValve	57 (2%)	53 (2%)	4 (4%)
SJM Portico	87 (3%)	85 (3%)	2 (2%)
Medtronic Engager	2 (0%)	1 (0%)	1 (1%)
Direct Flow Medical	34 (1%)	33 (1%)	1 (1%)
Edwards Sapien 3	1163 (33%)	1131 (33%)	32 (32%)
BSC Lotus	186 (5%)	186 (6%)	0 (0%)
Medtronic Evolut R	330 (9%)	321 (9%)	9 (9%)

Supplemental Table 4. Univariable and multivariable predictors of mortality rates from the external validation cohort

	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p value
In-hospital mortality				
Age (5 year intervals)	1.36 (1.13 - 1.63)	0.001	1.41 (1.16 - 1.71)	0.001
GFR (5-U increments)	0.91 (0.87 - 0.95)	<0.001	0.92 (0.87 - 0.98)	0.005
Dialysis	1.77 (0.64 - 4.94)	0.27	1.20 (0.38 - 3.79)	0.76
NYHA class IV	1.60 (0.94 - 2.73)	0.083	1.04 (0.58 - 1.89)	0.89
Severe chronic lung disease	1.20 (0.69 - 2.10)	0.52	1.30 (0.73 - 2.33)	0.37
Non femoral access	2.59 (1.65 - 4.07)	<0.001	2.97 (1.86 - 4.73)	<0.001
Acuity category 2	3.08 (1.39 - 6.85)	0.006	3.25 (1.41 - 7.52)	0.006
Acuity category 4	6.04 (2.29 - 15.93)	<0.001	6.20 (1.90 - 20.24)	0.003
30 day mortality				
Age (5 year intervals)	1.34 (1.14 - 1.58)	<0.001	1.39 (1.17 - 1.64)	<0.001
GFR (5-U increments)	0.89 (0.85 - 0.93)	<0.001	0.90 (0.86 - 0.95)	<0.001
Dialysis	2.08 (0.89 - 4.87)	0.091	1.15 (0.44 - 3.03)	0.78
NYHA class IV	1.39 (0.85 - 2.26)	0.191	0.79 (0.45 - 1.38)	0.40
Severe chronic lung disease	1.31 (0.81 - 2.11)	0.27	1.47 (0.89 - 2.41)	0.13
Non femoral access	2.48 (1.66 - 3.72)	<0.001	2.80 (1.85 - 4.25)	<0.001
Acuity category 2	2.30 (1.04 - 5.07)	0.04	2.45 (1.07 - 5.63)	0.034
Acuity category 4	8.27 (3.67 - 18.64)	<0.001	8.56 (3.06 - 23.89)	<0.001

Refitted coefficients are shown for descriptive purpose only. Original coefficients were used to assess the predictive performance of the TVT Registry model in the external validation cohort. Missing data was imputed using chained equations to generate 20 imputations sets. Estimates were combined using Rubin's rule. No acuity category 3 patients defined. eGFR, Estimated glomerular filtration rate; NYHA, New York Heart Association.

Supplemental Table 5. Performance of the TVT Registry Model across different time periods

	AUC (95% CI)	χ^2*	p value*
November 2011- February 2014 (N = 1317)			
In-hospital death	0.68 (0.59 - 0.76)	11.51	0.174
30 day death	0.68 (0.61 - 0.75)	7.59	0.475
March 2014-February 2016 (N = 2174)			
In-hospital death	0.63 (0.54 -0.71)	4.2	0.839
30 day death	0.66 (0.59 - 0.73)	2.97	0.936

November 2011- February 2014 corresponds to the same time period of the derivation cohort. *Hosmer-Lemeshow test. **Combination of Chi² statistics in MI result in values from an F distribution.

Supplemental Table 6. Model fit statistics after multiple imputation of missing variables

	AUC (95% CI)	p value*
TVT Registry Model		
In-hospital mortality	0.66 (0.60 - 0.71)	0.25
30-day mortality	0.68 (0.63 - 0.73)	0.46
STS-PROM score		
In-hospital mortality	0.61 (0.56 - 0.67)	0.63
30-day mortality	0.64 (0.59 - 0.68)	0.56

Combination of Chi^2 statistics in MI result in values from an F distribution. *Hosmer-Lemeshow test. The following variables were imputed: age(0.26% of cases), estimated glomerular filtration rate (0.43%), dialysis (0.11%), NYHA class 4 (2.21%).