RATES AND PREDICTORS OF HOSPITAL READMISSION AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION

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SUPPLEMENTAL MATERIAL

Supplemental Methods

Study procedure

The decision to perform TAVI was based on the Heart Team evaluation. The procedure was performed according to standardized protocols. Post-procedural care consisted of heart rhythm monitoring for at least 48 hours after intervention, laboratory tests and 12-lead electrocardiogram on daily basis, and echocardiography before discharge.

Data collection

In-hospital complications were closely monitored until discharge. Active follow-up was scheduled at 30 days and 12 months. Patients were questioned about their health status, medication and the occurrence of adverse events. In case of hospital readmission (with a length stay of at least 1 day), patients were requested to provide medical documents including discharge letters, interventional and blood laboratory reports. In case detailed information was required, a formal query to the primary care physician was sent. A dedicated clinical event committee, involving cardiologists and cardiac surgeons, evaluated and adjudicated all suspected events according to the Valve Academic Research Consortium (VARC-2) criteria. All data were entered into a dedicated web-based database held at the Clinical Trials Unit Bern (Bern University Hospital, Switzerland).

Supplemental Table 1. Procedural characteristics

	All patients alive at discharge	Hospital readmission within one year		p-value
		None	Once or more	
	N = 868	N = 647	N = 221	
Procedure time (min)	68.3 ± 33.0	68.5 ± 33.7	67.7 ± 31.0	0.76
Amount of contrast (ml)	226.3 ± 96.3	224.9 ± 96.6	230.4 ± 95.4	0.47
General anesthesia, n(%)	286 (32.9%)	220(34.0%)	66(29.9%)	0.28
Access Route				0.78
Femoral, n(%)	708(81.6%)	527(81.5%)	181(81.9%)	0.92
Apical, n(%)	148(17.1%)	112(17.3%)	36(16.3%)	0.76
Subclavian, n(%)	12(1.4%)	8(1.2%)	4(1.8%)	0.51
Valve Type				0.99
Medtronic CoreValve, n(%)	405(47.5%)	298(46.9%)	107(49.1%)	0.58
Edwards Sapien Valve XT, n(%)	351(41.1%)	264(41.6%)	87(39.9%)	0.69
Symetis Acurate Valve, n(%)	37(4.3%)	28(4.4%)	9(4.1%)	1.00
SJM Portico, n(%)	3(0.4%)	2(0.3%)	1(0.5%)	1.00
Edwards Sapien Valve 3, n(%)	48(5.6%)	36(5.7%)	12(5.5%)	1.00
BSC Lotus, n(%)	9(1.1%)	7(1.1%)	2(0.9%)	1.00
Procedural Specifications				
Coronary Revascularization, n(%)	132(15.2%)	104(16.1%)	28(12.7%)	0.24
Balloon valvuloplasty, n(%)	786(90.8%)	584(90.5%)	202(91.4%)	0.79
Post TAVI - Aortic Regurgitation 2 or 3	91(10.6%)	67(10.5%)	24(10.9%)	0.90
Valve in series, n(%)	14(1.6%)	10(1.5%)	4(1.8%)	0.76
Need for Permanent Pacemaker ≤ 30 Days, n(%)	190(21.9%)	136(21.0%)	54(24.4%)	0.30

Depicted are means ± SD with p-values from t-tests, or counts (%) with p-values from Fisher's or chi-square tests.

Supplemental Table 2. Characteristics of hospital stay at the index procedure and in-hospital events

	Patients alive at discharge	Patients with 1-year readmission		p-value
	n=868	None n=647	Once or more n=221	
Any PRBC transfusion	201(23.2)	149(23)	52(23.5)	0.93
Length of hospital stay (days)	7.7±4.5	7.5±4.0	8.4±5.9	0.019
Length of ICU stay (days)	0.4±1.5	0.3±1.0	0.5±2.3	0.16
Length of IMC stay (days)	2.9±2.2	2.8±2.1	3.2±2.6	0.040
Cerebrovascular Events	29(3.3)	18(2.8)	11(5)	0.13
Disabling Stroke	21(2.4)	12(1.9)	9(4.1)	0.076
Myocardial infarction	4(0.5)	2(0.3)	2(0.9)	0.27
Bleeding	266(30.6)	199(30.8)	67(30.3)	0.93
Life-threatening	75(8.6)	52(8)	23(10.4)	0.27
Major	149(17.2)	115(17.8)	34(15.4)	0.47
Acute Kidney Injury	102(11.8)	65(10.0)	37(16.7)	0.011
Access Site Complications	166(19.1)	133(20.6)	33(14.9)	0.074
Major	76(8.8)	60(9.3)	16(7.2)	0.41
Minor	86(9.9)	71(11.0)	15(6.8)	0.089
Peak Troponin(µg/l)	0.79±7.70	0.54±5.22	1.53±12.3	0.064
Peak Creatinine(µmol/l)	124.6±85.1	118.1±76.3	143.9±104.7	<0.001
BNP(pg/ml)	488.3±865.1	473.7±914.1	533.0±694.1	0.012
Discharge medication				0.002
ASA	23(2.7)	17(2.6)	6(2.7)	1.00
Clopidogrel	14(1.6)	12(1.9)	2(0.9)	0.54
OAC/NOAC	44(5.1)	25(3.9)	19(8.6)	0.012
DAPT	556(64.1)	433(67)	123(55.7)	0.003

Depicted are means ± SD with p-values from t-tests, or counts (%) with p-values from Fisher's or chi-square tests.
ASA, Acetylsalicylic acid; DAPT, Dual antiplatelet therapy; ICU, Intensive care unit; IMC, Intermediate care unit; NOAC, non-vitamin K antagonist oral anticoagulant; OAC, oral anticoagulant; PRBC, Packed red blood cells.

Supplemental Table 3. Reasons for hospital readmission within one year after TAVI

	All readmissions	Temporal sequence of readmissions				p-value
		1st	2nd	3rd	4th to 8th	
	N = 308	N = 221	N = 55	N = 18	N = 14	
Reasons for Hospital Readmission						0.40
Cardiovascular causes	142(46%)	101(46%)	26(47%)	10(56%)	5(36%)	
Cancer	15(5%)	12(5%)	2(4%)	1(6%)	0(0%)	
Surgery	36(12%)	23(10%)	6(11%)	2(11%)	5(36%)	
Infectious Disease	12(4%)	8(4%)	1(2%)	1(6%)	2(14%)	
Gastrointestinal Disease	30(10%)	22(10%)	7(13%)	0(0%)	1(7%)	
Respiratory Disease	14(5%)	9 (4%)	3(5%)	2(11%)	0(0%)	
Kidney Disease	8(3%)	6 (3%)	1(2%)	1(6%)	0(0%)	
Other	51(17%)	40(18%)	9(16%)	1(6%)	1 (7%)	

Depicted are counts (% of all reasons; p-value from Chi-square tests).

Supplemental Table 4. Causes of hospital readmission classified as "Others"	
Cause	**N. of readmissions**
Fall with/without related injury	11
Immunological disorders	6
Chronic pain	5
Hyponatremia	5
Depression or psicosis	4
Percutaneous LAA closure	3
Hyperglicemia	3
Pre-syncope	3
Neurological disease (Parkinson)	2
Pressure ulcers	2
Obstructive sleep apnea	2
Hypertensive emergency	1
Cataract treatment	1
Fever of unknown origin	1
Rhabdomyolysis	1
Overdose of oral anticoagulants	1

Supplemental Table 5. Time to first hospital readmission since hospital discharge after TAVI

	Days from Discharge to Readmission		
	n	Mean ± SD	Median (25%-75% IQR)
Total	221	117.9 ± 109.5	70 (23-204)
Cardiovascular causes	101	105.4 ± 104.2	59 (25-190)
Cancer	12	105.8 ± 111.2	79 (4-167.5)
Surgery	23	180.7 ± 106.4	154 (86-279)
Infectious disease	8	101.4 ± 110.8	58.5 (10.5-201)
Gastrointestinal disease	22	104.1 ± 109.0	66.5 (15-171)
Respiratory disease	9	80.1 ± 104.8	38 (13-94)
Kidney disease	6	171.7 ± 96.5	169.5 (96-202)
Other	40	128.4 ± 118.6	68 (22-231.5)

Depicted are sample sizes and means with standard deviations, medians with interquartile range IQR for the first rehospitalization.

Supplemental Table 6. Days spent in hospital readmission within one year after TAVI

		Number of days	
Readmissions	**N**	**Average Days (±SD)**	**Median Days (25-75% IQR)**
Readmission average	308	10.1 ± 11.0	7 (3-13)
First	221	10.5 ± 12.0	7 (3-14)
Second	55	8.8 ± 8.2	6 (3-11)
Third	18	8.1 ± 6.8	6.5 (2-12)
Fourth	6	11.7 ± 7.3	11 (6-18)
Fifth	3	13.7 ± 11.0	19 (1-21)
Sixth	2	10.0 ± 2.8	10 (8-12)
Seventh	2	5.0 ± 2.8	5 (3-7)
Eight	1	23	23
Cumulative during 1 Year	221	14.1 ± 15.5	9 (4-19)

Depicted are average in-hospital times with standard deviations (days) and median days in-hospital times with 25% to 75% interquartile range. Discharged on the same day as re-admission counted as a in-hospital time of 0 days.

Supplemental Table 7. Predictors of hospital readmission adding echocardiographic parameters measured after the procedure

	Multivariate competing risk regression	
	SHR (95% CI)	p-value
Any readmission*		
Mean transprosthetic gradient	0.98 (0.95-1.02)	0.325
Indexed aortic valve area	1.01 (0.34-2.98)	0.989
Left ventricular ejection fraction	1.00 (0.98-1.01)	0.490
Any aortic regurgitation	1.10 (0.71-1.68)	0.671
Moderate/severe mitral regurgitation	1.14 (0.69-1.89)	0.598
Cardiovascular readmission**		
Mean transprosthetic gradient	0.99 (0.94-1.04)	0.626
Indexed aortic valve area	0.61 (0.13-2.97)	0.544
Left ventricular ejection fraction	0.98 (0.97-1.00)	0.026
Any aortic regurgitation	1.15 (0.73-1.81)	0.557
Moderate/severe mitral regurgitation	0.98 (0.47-2.01)	0.948

Supplemental Table 8. Clinical outcomes according to time of hospital readmission after TAVI

	Not readmitted within 30 days after TAVI		Readmitted within 30 days after TAVI		Hazard Ratio (95% CI)	p-value
	At risk	Events (%)	At risk	Events (%)		
Mortality	801	84 (10.6)	45	11 (24.4)	2.62 (1.40-4.91)	0,003
Cardiac mortality	801	53 (6.8)	45	8 (18.5)	3.00 (1.43-6.31)	0,004
Cerebrovascular accident	785	12 (1.6)	40	0 (0.0)	0.78 (0.05-12.94)	1,000
Major stroke	792	6 (0.8)	41	0 (0.0)	1.47 (0.08-25.65)	1,000
Minor stroke	795	1 (0.1)	45	0 (0.0)	5.83 (0.24-141.13)	1,000
Transient ischemic attack	800	5 (0.7)	44	0 (0.0)	1.64 (0.09-29.19)	1,000
Myocardial infarction	798	10 (1.3)	44	0 (0.0)	0.85 (0.05-14.27)	1,000
Periprocedural myocardial infarction	798	0 (0.0)	45	0 (0.0)	-	
Spontaneous myocardial infarction	801	10 (1.3)	44	0 (0.0)	0.86 (0.05-14.44)	1,000
Acute kidney injury	709	0 (0.0)	39	1 (2.6)	53.89 (2.23-1301.76)	0,052
Stage 3	779	0 (0.0)	42	1 (2.4)	55.02 (2.28-1330.59)	0,051
Bleeding	557	22 (4.2)	24	0 (0.0)	0.51 (0.03-8.16)	1,000
Life threatening bleeding	733	13 (1.9)	37	0 (0.0)	0.72 (0.04-11.88)	1,000
Major bleeding	664	8 (1.3)	35	0 (0.0)	1.10 (0.06-18.68)	1,000
Minor bleeding	748	9 (1.3)	41	0 (0.0)	0.95 (0.06-16.04)	1,000
Structural valve deterioration	800	3 (0.4)	44	0 (0.0)	2.57 (0.13-48.99)	1,000
Repeat unplanned iIntervention	796	7 (0.9)	44	0 (0.0)	1.19 (0.07-20.51)	1,000
Pacemaker implantation	632	14 (2.4)	28	1 (3.8)	1.64 (0.22-12.47)	0,633

Depicted are patients still at risk (at risk) for the specified event at 30 days and nr of events afterwards (% from life-table estimates) with p-values from Cox's Regressions (landmark at 30 days).
Clinical outcomes only first event of each type counted per patient. (continuity corrected Risk ratios and Fisher's tests in case of zero events).

Supplemental Figure 1

Flow chart of patients included in the study