

## Supplementary materials

### Causes of Death in Patients with Severe Aortic Stenosis:

#### An Observational study

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## **Supplementary Tables**

**Supplementary Table 1.** Classifications of causes of death into cardiac and non-cardiac categories

**Supplementary Table 2.** Baseline clinical and echocardiographic characteristics

**Supplemental Table 1. Classifications of causes of death into cardiac and non-cardiac categories**

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**Cardiac death**

Any of the following criteria

Death due to acute myocardial infarction, heart failure, and other cardiac cause (e.g. tamponade)

All aortic valve procedure-related death, including directly related to the procedure or complications during hospitalization after AVR/TAVI

Sudden or unwitnessed death

Death of unknown cause in which cardiac cause could not be excluded

**Non-cardiac death**

Death caused by non-coronary vascular disease such as cerebrovascular disease, peripheral arterial disease, dissecting aneurysm, or other vascular disease

Other non-cardiac deaths were sub-classified into the following categories: malignancy, accidental, infection/sepsis, respiratory failure, renal failure, hepatic failure, or other (e.g. senility, hemorrhage, suicide)

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AVR=aortic valve replacement, TAVI=transcatheter aortic valve implantation

**Supplementary Table 2. Baseline clinical and echocardiographic characteristics**

<b>Variable</b>	<b>All patients (N=3815)</b>
<b>Clinical characteristics</b>	
Age, mean (SD), years *	77.8 (9.8)
Age ≥80 years, No. (%)	1729 (45)
Male, No. (%) *	1443 (38)
BMI, mean (SD)	21.8 (3.8)
BMI <22, No. (%),    *	2326 (61)
BSA, mean (SD), m <sup>2</sup>	1.46 (0.18)
Initial AVR cohort, No. (%)	1197 (31)
Hypertension, No. (%) *	2667 (70)
Current smoking, No. (%) *	196 (5.1)
History of smoking, No. (%)	830 (22)
Dyslipidemia, No. (%), †	1327 (35)
On statin therapy, No. (%)	970 (25)
Diabetes mellitus, No. (%)	897 (24)
On insulin therapy, No. (%) *	188 (4.9)
Coronary artery disease, No. (%) *	1144 (30)
Prior myocardial infarction, No. (%) *	323 (8.5)
Prior PCI, No. (%)	502 (13)
Prior CABG, No. (%)	199 (5.2)
Prior symptomatic stroke, No. (%) *	503 (13)
Atrial fibrillation or flutter, No. (%) *	828 (22)
Aortic/peripheral vascular disease, No. (%) *	282 (7.4)
Serum creatinine, median (IQR), mg/dL *	0.9 (0.7-1.26)
Dialysis *	405 (11)
Anemia, No. (%),§ *	2117 (55)
Hemoglobin (IQR), g/dl	11.6 (10.2-13)
Liver cirrhosis (Child–Pugh B or C), No. (%) *	38 (1.0)
Malignancy, No. (%)	517 (14)
Malignancy currently under treatment *	149 (3.9)
Recurrence of malignancy, No. (%)	58 (1.5)
Chest wall irradiation, No. (%)	25 (0.7)
Immunosuppressive therapy, No. (%)	131 (3.4)
Chronic lung disease, No. (%)	400 (10)
Chronic lung disease (moderate or severe) *	112 (2.9)

Logistic EuroSCORE, median (IQR), %	9.7 (5.8-16.7)
EuroSCORE II, median (IQR), %	2.9 (1.62-4.82)
STS score (PROM), median (IQR), %	3.8 (2.2-6.5)
Symptoms at index echocardiography, No. (%)	2005 (53)
Chest pain	498 (13)
Syncope	198 (5.2)
Chronic exertional dyspnea	1603 (42)
Admission for heart failure at index echocardiography, No. (%)*	790 (21)
Etiology of aortic stenosis, No. (%)	
Degenerative	3379 (89)
Congenital (Unicuspid, Bicuspid, or Quadricuspid)	258 (6.8)
Rheumatic	150 (3.9)
Infective endocarditis	7 (0.2)
Others	21 (0.6)
<b>Echocardiographic variables</b>	
V <sub>max</sub> , mean (SD), m/s	4.1 (0.9)
V <sub>max</sub> ≥4m/s, No. (%) *	2185 (57)
Peak aortic PG, mean (SD), mmHg	71.8 (31.6)
Mean aortic PG, mean (SD), mmHg	40.8 (19.7)
AVA (equation of continuity), mean (SD), cm <sup>2</sup>	0.72 (0.18)
AVA index, mean (SD), cm <sup>2</sup> /m <sup>2</sup>	0.50 (0.13)
LV end-diastolic diameter, mean (SD), mm	45.9 (7.0)
LV end-systolic diameter, mean (SD), mm	30.2 (7.9)
LVEF, mean (SD), %	62.8 (13.5)
LVEF <68%, No. (%) *	2242 (59)
IVST in diastole, mean (SD), mm	11.3 (2.3)
PWT in diastole, mean (SD), mm	11.0 (2.0)
ny combined valvular disease (moderate or severe), No. (%) *	1558 (41)
Moderate or severe AR	791 (21)
Moderate or severe MS	133 (3.5)
Moderate or severe MR	763 (20)
Moderate or severe TR	628 (16)
TR pressure gradient ≥40 mmHg, No. (%) *	606 (16)

\* Variables selected for cause-specific Cox proportional hazard models.

|| Body mass index was calculated as weight in kilograms divided by height in meters squared.

† Dyslipidemia was defined as total cholesterol levels ≥240 mg/dL, high-density lipoprotein

cholesterol levels <40 g/dL, or the use of statin

§ Anemia was defined by the World Health Organization criteria (hemoglobin <12.0 g/dL in women and <13.0 g/dL in men).

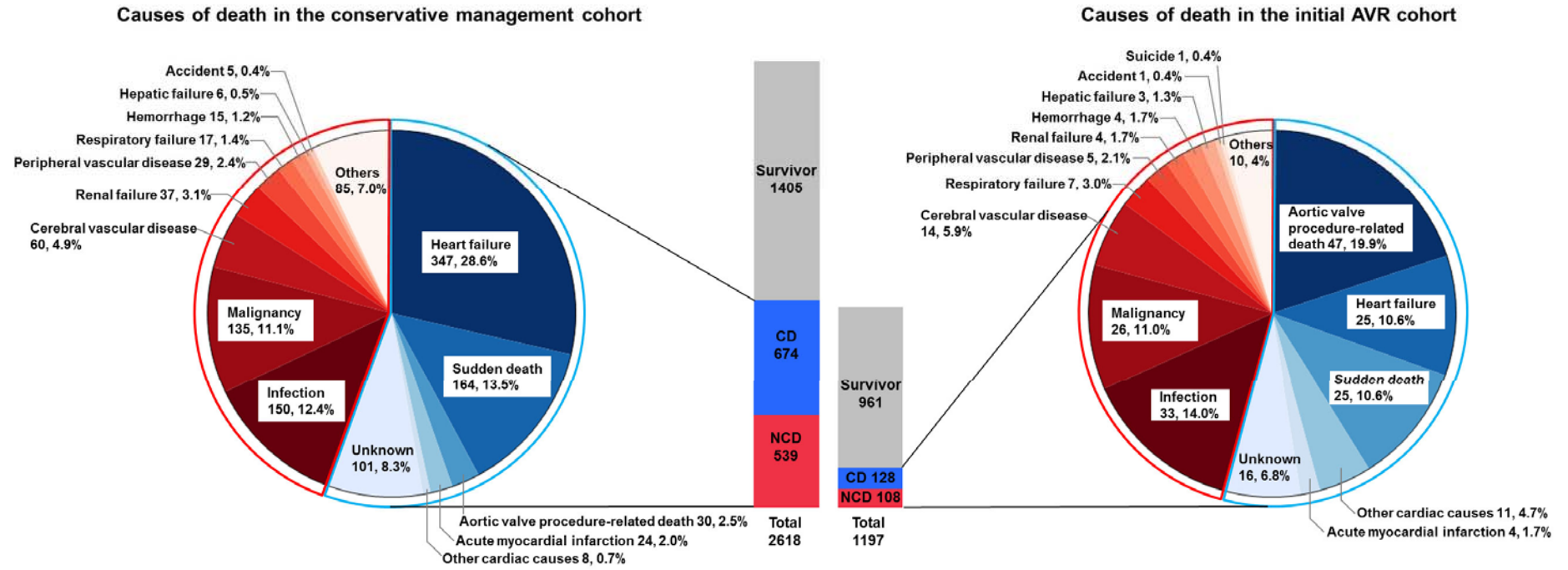
AR=aortic regurgitation, AVA=aortic valve area, AVR=aortic valve replacement, BMI=body mass index, BSA=body surface area, CABG=coronary artery bypass grafting, ESRD=end-stage renal disease, IQR=interquartile range, IVST=interventricular septal wall thickness, LV=left ventricular, LVEF=left ventricular ejection fraction, MR=mitral regurgitation, MS=mitral stenosis, PCI=percutaneous coronary intervention, PG=pressure gradient, PROM=predicted risk of mortality, PWT=posterior wall thickness, SD=standard deviation, and STS=Society of Thoracic Surgeons, TR=tricuspid regurgitation, and Vmax=peak aortic jet velocity

**Supplementary figure legend****Supplementary Figure 1.** Causes of death according to management strategy

AVR=aortic valve replacement, CD=cardiac death, and NCD=non-cardiac death



Supplementary Figure 1.



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