# Advances in cardiac computed tomography angiography and characterization of cardiac disease

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# PART II

## Characterization of left ventricular remodeling in severe aortic stenosis

# CHAPTER 5

## Sex differences in left ventricular remodeling in patients with severe aortic valve stenosis

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# ABSTRACT

**BACKGROUND:** Women with severe aortic valve stenosis (AS) have better long-term outcome after transcatheter aortic valve implantation (TAVI) but worse survival after surgical aortic valve replacement compared to men. Whether this is related to sex differences in left ventricular (LV) remodeling is unknown. The aim of this study was to examine sex differences in LV remodeling with multidetector row computed tomography (MDCT) and outcome in patients with severe AS undergoing TAVI between 2007 and 2018.

**METHODS:** Patients with severe AS who underwent TAVI between 2007 and 2018 with a pre-procedural MDCT scan were included. LV volumes, mass and function were analyzed with MDCT. Patients were classified into 4 LV remodeling patterns based on LV mass index and LV mass-to-volume ratio: 1) normal geometry, 2) concentric remodeling, 3) concentric hypertrophy and 4) eccentric hypertrophy. The primary endpoint was all-cause mortality after TAVI.

**RESULTS:** A total of 289 patients (age 80±6 years, 54% male) were included. Women showed smaller LV volumes and mass compared to men. Concentric hypertrophy (50%) was the most frequent pattern of LV remodeling followed by eccentric hypertrophy (33%), normal geometry (13%) and concentric remodeling (4%). Men showed more concentric remodeling compared to women (91% vs. 9% respectively, $p=0.011$). However, no sex differences were observed in the remaining LV remodeling patterns. During a median follow-up of 3.8 (IQR 2.2-5.1) years after TAVI, 87 patients died. Women demonstrated better outcome after TAVI compared to men (log-rank $\chi 2=4.29$, $p=0.038$). No association was observed between the interaction of the LV remodeling patterns and sex with outcome.

**CONCLUSION:** LV concentric and eccentric hypertrophy are similarly observed in men and women with severe AS but concentric remodeling was more common in men. Women demonstrated better outcome after TAVI as compared to men. The interaction between the LV remodeling patterns and sex was not associated with survival.

# INTRODUCTION

Aortic stenosis (AS) is the most prevalent valvular heart disease and the incidence is expected to increase due to advanced aging[1-3]. Surgical aortic valve replacement is the treatment of choice while transcatheter aortic valve implantation (TAVI) has emerged as an effective therapy for patients with severe AS who are inoperable or have high operative risk, and showed promising results also among patients at intermediate and low surgical risk[4]. The outcomes of surgical aortic valve replacement and TAVI differ for men and women. While men have better outcome than women when treated with surgical aortic valve replacement, data from numerous studies have shown better long-term survival after TAVI for women versus men (even after correction for higher 30-day complication rates among women)[5-8].

Several factors have been suggested for this sex-related difference in outcomes after aortic valve replacement. One of them may be the different response of the left ventricle to the pressure overload in men versus women[9,10]. Left ventricular (LV) remodeling in response to the pressure overload in AS may result in various remodeling patterns and, depending on when the diagnosis of severe AS is established, can be classified into 4 main patterns (according to the LV mass and the relative wall thickness): normal geometry, concentric remodeling, concentric hypertrophy and eccentric hypertrophy[10,11].



For a similar degree of AS severity, women demonstrate more preserved LV ejection fraction (LVEF), smaller LV cavity size, and LV mass (index) compared to men[12-14]. In addition, based on cardiovascular magnetic resonance analysis, women with severe AS show more frequently normal and concentric LV remodeling patterns whereas men presented more frequently with concentric and eccentric hypertrophy[15]. Whether these findings can be observed in a population with severe AS undergoing TAVI, which consists of older patients with associated comorbidities and longer exposure to AS, remains unknown. In addition, the prognostic implications of the various LV remodeling patterns in men versus women with severe AS undergoing TAVI remain unexplored. Accordingly, the aims of this study were to examine sex differences in LV remodeling in patients with severe AS and to evaluate the potential relation with outcomes after TAVI.

# METHODS

**Study population**

Patients with severe AS undergoing TAVI at the Leiden University Medical Center (Leiden, the Netherlands) between 2007 and 2018 were included in this retrospective analysis.

All patients had undergone a pre-procedural full-cardiac cycle contrast-enhanced multidetector row computed tomography (MDCT) scan to evaluate TAVI eligibility. Patients with bicuspid aortic valves were excluded, as well as patients with significant concomitant mitral valve disease or aortic regurgitation. Patients who underwent transapical TAVI, or in whom the MDCT data were not acquired through the full cardiac cycle were also excluded. Demographic and clinical characteristics were collected from the departmental electronic patient records (EPD-vision, Leiden University Medical Center, Leiden, the Netherlands). The distribution of the different LV remodeling patterns (concentric hypertrophy, concentric remodeling, eccentric hypertrophy and normal) among men versus women were evaluated. The association between gender and the LV remodeling patterns versus survival after TAVI was also evaluated. This retrospective analysis complies with the Declaration of Helsinki and was approved by the institutional review board which waived the need for written informed consent.

**Transcatheter aortic valve implantation**

Eligibility and feasibility of TAVI as well as access route and valve type were decided by the local heart team. Transcatheter heart valve size was selected based on MDCT measurements of the aortic annulus, as previously described[16]. The TAVI procedure was performed according to standard practice[17]. Balloon- and self-expandable valves were used: Edwards SAPIEN, SAPIEN XT, SAPIEN 3 (Edwards Lifesciences, Irvine, CA, USA) and Medtronic CoreValve Evolut (Medtronic, MN, Minnesota, USA).

**Echocardiography**

Transthoracic echocardiographic examinations were performed before TAVI to evaluate AS severity. All echocardiographic examinations were acquired by experienced echocardiographers using Vivid-7 or E9 (General Electric Vingmed, Horten, Norway) ultrasound systems. Echocardiographic image analysis was performed offline (EchoPac version 203; GE Medical Systems). Valvular hemodynamics were reported following current recommendations[18]. Aortic valve function was evaluated by 2-dimensional color, continuous and pulsed wave Doppler from parasternal and apical views. Peak and mean transvalvular gradients were measured from continuous-wave Doppler recordings of the apical 3- or 5-chamber views according to the Bernoulli equation. Aortic valve area (AVA) was calculated using the continuity equation and indexed for body surface area (AVAi). Severe aortic valve stenosis was defined as an AVA <1.0 $cm^2$ or AVAi <0.6 $cm^2/m^2$, mean transvalvular pressure gradient ≥40 mmHg and a peak aortic jet velocity ≥4 m/s[18].

### MDCT data acquisition and analysis

Preprocedural contrast-enhanced MDCT scans were performed using a 64-slice (Aquilion 64, Toshiba Medical Systems, Otawara, Japan) or 320-slice computed tomography scanner (AquilionOne; Toshiba Medical Systems, Tochigi-ken, Japan). Methods for image acquisition have been reported previously[19]. MDCT data were reconstructed in 10% phases of the cardiac cycle and slice thickness of 3 mm. Analysis of the MDCT data sets were performed with feature tracking software (Medis Suite CT® version 3.1.16.22, Medis Medical Imaging Systems, Leiden, the Netherlands). Detailed image analysis has been reported previously[20]. In brief, the 2-, 3- and 4-chamber views of the left ventricle were reconstructed. Subsequently, the contours of the LV endocardium were manually traced in each view at end-diastole and end-systole. The endocardial contours were automatically interpolated to the remaining cardiac phases[20]. The LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), LVEF and LV global longitudinal strain (GLS) were calculated. In accordance with previous studies, patients with a GLS >-14% were considered to have impaired systolic LV function[20,21].

LV mass was quantitively analyzed from the total LV myocardial volume and multiplied by the myocardial specific gravity of 1.05 g/mL[22]. Short-axis reconstructions (slice thickness 6 mm, interslice gap 4 mm) were created to calculate the LV myocardial volume. The contours of the LV endocardium and epicardium were automatically traced in each slice at end-diastole with manual contour adjustments if necessary. Subsequently, the 3-dimensional LV myocardial volume was calculated as the sum of the cross-sectional area of each slice multiplied by the slice thickness. LV mass and cardiac chamber volumes were indexed for body surface area.

Left ventricular hypertrophy (LVH) was defined as a LV mass index (LVMi) >65 g/m$^2$ for women and >80 g/m$^2$ for men[22]. The LV mass-to-volume ratio (equivalent of the echocardiography-derived relative wall thickness) was calculated by dividing the LVMi by the LVEDV index. A mass-to-volume ratio ≥1.15 was considered abnormal[23]. Patients with AS were classified into 4 LV geometry patterns defined by presence of LVH and the LV mass-to-volume ratio[11]: normal geometry (absence of LVH and normal mass-to-volume ratio), concentric remodeling (absence of LVH and abnormal mass-to-volume ratio), concentric hypertrophy (LVH and abnormal mass-to-volume ratio) and eccentric hypertrophy (LVH and normal mass-to-volume ratio, Figure 1).

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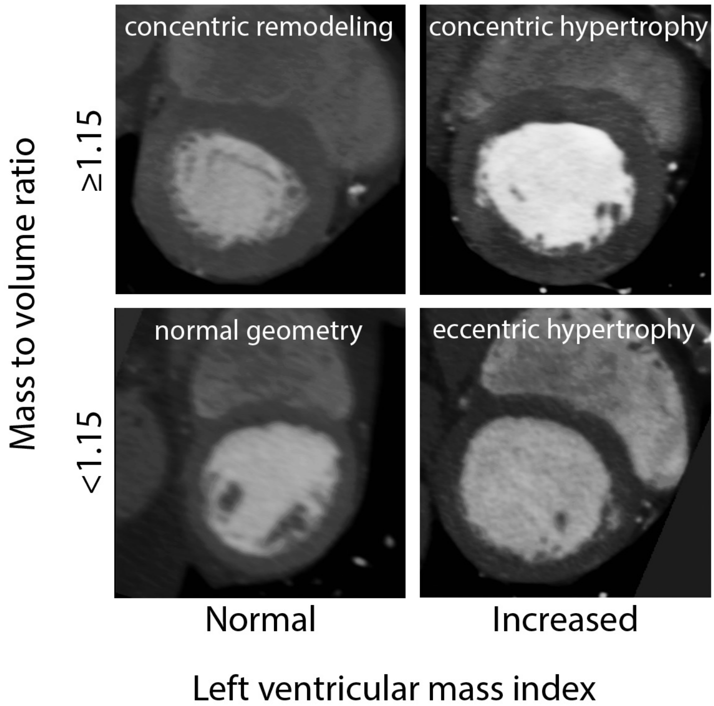


**FIGURE 1.** Short-axis computed tomography images of the left ventricle illustrating the different left ventricular remodeling patterns: normal left ventricular geometry (lower left quadrant), concentric remodeling (upper left quadrant), concentric hypertrophy (upper right quadrant) and eccentric hypertrophy (lower right quadrant).-

### Follow-up

Patients were followed-up for the occurrence of the primary endpoint of all-cause mortality after TAVI. The outcome data were collected from the departmental electronic patient records and civil municipal registries for all patients and was restricted to 8 years.

### Statistical analysis

Continuous variables following a normal distribution are presented as mean ± standard deviation and non-normally distributed variables as median with 25%-75% interquartile range. Distribution of continuous variables was evaluated using histograms and Q-Q plots. To compare the continuous variables between sexes the independent Student t-test or Mann-Whitney U test were used, as appropriate. One-way ANOVA was used to compare the GLS across the remodeling patterns. Post-hoc analysis with Dunn-Bonferroni's test was performed if there was a significant difference between the LV remodeling patterns. Categorical variables are presented as absolute values and percentages and were compared using the $\chi 2$ test or Fisher's exact test as appropriate. The estimated cumulative event-free survival rates for all-cause mortality were generated with the Kaplan-Meier curves and the Log-rank test was used to compare the survival distributions between men and women. Multivariable Cox proportional hazards regression analysis was used to evaluate the association of sex on all-cause mortality. Potential confounders including age, body mass index, hypertension, hypercholesterolemia, diabetes mellitus, coronary artery disease, previous myocardial infarction, previous stroke/transient ischemic attack, chronic obstructive pulmonary disease, peripheral vascular disease, chronic kidney disease (defined as an estimated glomerular filtration rate <60 mL/min/1.73 $m^2$), pre-TAVI LVEF and mean gradient were incorporated in the multivariable Cox proportional hazard model. Multivariable Cox proportional hazard regression models were used to test the association between the LV remodeling patterns and sex (as an interaction term) with outcome. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated and reported. A two-sided p-value <0.05 was considered significant. Data analysis were performed with SPSS version 25.0 (IBM SPSS Statistics, IBM Corporation, Armonk, New York, USA).



# RESULTS

### Study population

A total of 289 patients (age 80±7 years, 54% male) with severe AS were included in this analysis. The demographic and clinical characteristics of the overall population and divided according to sex are presented in Table 1. Male patients had more frequently a history of coronary artery disease (67% vs. 52%, p=0.022), myocardial infarction (27% vs. 12%, p=0.002), coronary revascularization (64% vs. 46%, p=0.004) and peripheral vascular disease (21% vs. 12%, p=0.047) as compared to female patients. Hence, men were more frequently using antiplatelet and statin therapy (65% vs. 52%, p=0.034 and 71% vs. 54%, p=0.003, respectively).

**TABLE 1.** Baseline patient demographical and clinical characteristics and the echocardiography-derived aortic valve hemodynamics of the overall population and according to sex.

| Variable | Overall population n=289 | Men n=155 | Women n=134 | p-value |
|---|---|---|---|---|
| Age, years | 80 ± 7 | 80 ± 7 | 81 ± 6 | 0.15 |
| Body surface area, $m^2$ | 1.87 ± 0.20 | 1.98 ± 0.17 | 1.74 ± 0.17 | <0.001 |
| Body mass index, $kg/m^2$ | 27.0 ± 4.7 | 27.0 ± 3.9 | 27.0 ± 5.4 | 0.91 |
| EUROSCORE | 12.3 [8.5-19.2] | 12.4 [8.3-20.1] | 12.1 [9.0-17.8] | 0.79 |
| eGFR (CKD-EPI), mL/min/1.73 $m^2$ | 61± 20 | 61± 21 | 61 ± 19 | 0.96 |
| Hypertension, n (%) | 224 (78) | 118 (76) | 106 (80) | 0.47 |
| Hypercholesterolemia, n (%) | 178 (62) | 103 (67) | 75 (56) | 0.080 |
| Diabetes mellitus, n (%) | 93 (32) | 53 (34) | 40 (30) | 0.43 |
| History of smoking, n (%) | 58 (20) | 37 (24) | 21 (16) | 0.083 |
| CAD, n (%) | 173 (60) | 103 (67) | 70 (52) | 0.014 |
| Prior myocardial infarction, n (%) | 57 (20) | 41 (27) | 16 (12) | 0.002 |
| PCI, n (%) | 96 (33) | 52 (34) | 44 (33) | 0.004 |
| CABG, n (%) | 64 (22) | 46 (30) | 18 (13) | |
| Atrial fibrillation, n (%) | 68 (24) | 40 (26) | 28 (21) | 0.33 |
| Previous stroke/TIA, n (%) | 48 (17) | 30 (20) | 18 (14) | 0.18 |
| Peripheral vascular disease, n (%) | 48 (17) | 32 (21) | 16 (12) | 0.047 |
| NYHA classification, n (%) | | | | |
| I-II | 105 (36) | 62 (40) | 43 (32) | 0.16 |
| III-IV | 184 (64) | 93 (60) | 91 (68) | |
| Chronic obstructive pulmonary disease, n (%) | 59 (21) | 36 (23) | 23 (18) | 0.25 |
| Medication, n (%) | | | | |
| Beta-blocker | 181 (63) | 93 (60) | 88 (66) | 0.28 |
| ACE-I/ARB II | 152 (53) | 79 (51) | 73 (55) | 0.51 |
| Calcium antagonist | 62 (22) | 33 (21) | 29 (22) | 0.92 |
| Diuretics | 148 (51) | 75 (48) | 73 (55) | 0.27 |
| MR antagonist | 24 (8) | 16 (10) | 8 (6) | 0.19 |
| Statins | 182 (63) | 110 (71) | 72 (54) | 0.003 |
| Antiplatelet | 170 (59) | 100 (65) | 70 (52) | 0.034 |
| Anticoagulation | 105 (37) | 62 (40) | 43 (33) | 0.21 |
| Echocardiography | | | | |
| Peak gradient (mmHg) | 67 ± 25 | 65 ± 24 | 70 ± 26 | 0.15 |
| Mean gradient (mmHg) | 42 ± 16 | 41 ± 15 | 42 ± 17 | 0.57 |
| AVA ($cm^2$) | 0.75 ± 0.21 | 0.78 ± 0.21 | 0.73 ± 0.20 | 0.049 |
| AVAi ($cm^2/m^2$) | 0.41 ± 0.11 | 0.39 ± 0.10 | 0.42 ± 0.12 | 0.062 |

Data are presented as mean ± SD, median (IQR) and n (%). ACE-I = angiotensin-converting enzyme, ARB II = angiotensin-II receptor blocker, AVA = aortic valve area, AVAi = aortic valve area indexed to body surface area, CABG = coronary artery bypass grafting, CAD = coronary artery disease, CKD-EPI = chronic kidney disease epidemiology collaboration, eGFR = estimated glomerular filtration rate, MR = mineralocorticoid receptor, NYHA = New York Heart Association, PCI = percutaneous coronary intervention, TIA = transient ischemic attack.

### Echocardiographic and MDCT parameters

The transvalvular gradients were comparable between male and female patients before TAVI. Men showed a trend towards lower AVAi compared to women (0.39±0.10 $cm^2/m^2$ vs. 0.42±0.12 $cm^2/m^2$, p=0.062, Table 1). Women presented with smaller LVEDV index and LVESV index as compared to men (69 [60-81] $mL/m^2$ vs. 80 [65-99] $mL/m^2$ and 31 [26-42] $mL/m^2$ vs. 39 [29-55] $mL/m^2$ respectively, p<0.001 for both; see Table 2). In addition, LVMi was significantly smaller in female patients as compared to male patients (86±22 $g/m^2$ vs. 97±22 $g/m^2$, respectively; p<0.001). Yet, the prevalence of LVH was higher in women (88% vs. 79%, respectively, p=0.047). There were no differences in LVEF and LV GLS in women versus men.

**TABLE 2.** Computed tomography-derived left ventricular parameters for the overall population and according to sex.

| | Overall population n= 289 | Men n=155 | Women n=134 | p-value |
|---|---|---|---|---|
| LVEDV, mL | 141 [113-175] | 159 [133-189] | 120 [102-143] | <0.001 |
| LVESV, mL | 68 [48-93] | 80 [59-106] | 54 [43-74] | <0.001 |
| LVEDV index, $mL/m^2$ | 75 [62-93] | 80 [65-99] | 69 [60-81] | <0.001 |
| LVESV index, $mL/m^2$ | 35 [27-50] | 39 [29-55] | 31 [26-42] | <0.001 |
| LVEF, % | 50 ± 11 | 49 ± 10 | 51 ± 11 | 0.073 |
| LV GLS, % | -15.2 ± 4.5 | -15.1 ± 4.4 | -15.4 ± 4.5 | 0.52 |
| LV mass, g | 172 ± 46 | 191 ± 43 | 150 ± 38 | <0.001 |
| LV mass index, $g/m^2$ | 92 ± 23 | 97 ± 22 | 86 ± 22 | <0.001 |
| LV mass/volume | 1.21 ± 0.30 | 1.22 ± 0.32 | 1.21 ± 0.27 | 0.67 |
| LV GLS >-14%, n (%) | 105 (36) | 60 (39) | 45 (34) | 0.37 |
| LVH | 241 (83) | 123 (79) | 118 (88) | 0.047 |

Data are presented as mean ± SD, median (IQR) and n (%). GLS = global longitudinal strain, LV = left ventricular, LVEDV = left ventricular end-diastolic volume, LVEF = left ventricular ejection fraction, LVESV = left ventricular end-systolic volume, LVH = left ventricular hypertrophy.

### Sex differences in LV remodeling patterns

The distribution of the LV remodeling patterns as assessed with MDCT and the differences between sexes are shown in Figure 2. In the overall population, the majority of patients developed concentric hypertrophy (n=145, 50%) followed by eccentric hypertrophy (n=96,

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33%), normal geometry (n=37, 13%) and concentric remodeling (n=11, 4%). Concentric remodeling was more prevalent among male patients (91% vs. 9%, p=0.011). However, no significant differences were observed between sexes for the remaining patterns of LV remodeling. The mean LV GLS was significantly different across the LV remodeling patterns. In both sexes, the LV GLS was significantly more impaired in patients with concentric and eccentric hypertrophy compared to those with a normal LV geometry (Figure 3).

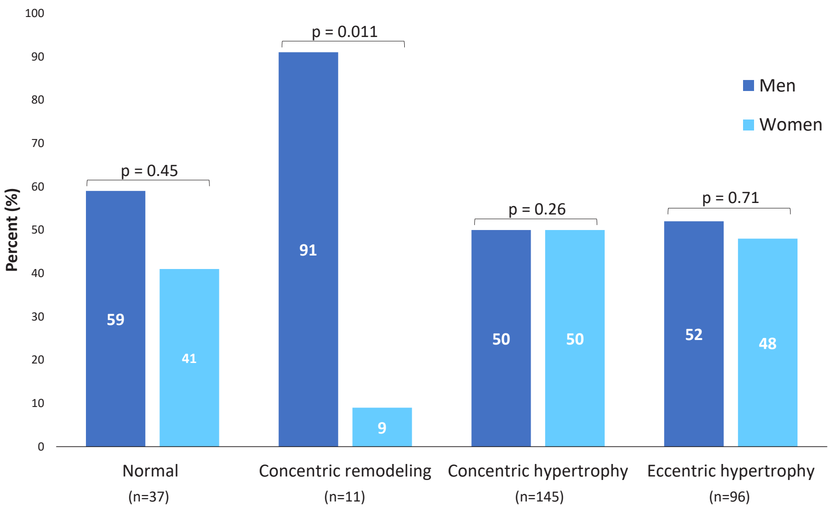



**FIGURE 2.** Bar chart demonstrating the frequency of the left ventricular remodeling patterns and the distribution according to sex.

## Follow-up

During a median follow-up of 3.8 [2.2-5.1] years after TAVI, 87 patients (30%) died. In the overall population, the Kaplan-Meier analysis demonstrated significantly higher all-cause mortality in men versus women (log-rank $\chi^2$=4.29, p=0.038, Figure 4). Moreover, multivariable Cox regression analysis demonstrated that male sex was independently associated with all-cause mortality (adjusted HR: 1.65 (95% CI: 1.03-2.63), p=0.037). When dividing the population according to the LV remodeling patterns, female patients with concentric hypertrophy showed better outcome after TAVI compared to their male counterparts (log-rank $\chi^2$=4.91, p=0.027). In contrast, the Kaplan-Meier survival curves were comparable between sexes in the group of patients with eccentric hypertrophy (log-rank $\chi^2$=1.10, p=0.29, Figure 5). In addition, there was no significant association between the LV remodeling patterns and sex, as interaction term, with outcome (normal geometry p=0.055, concentric remodeling p=0.96, concentric hypertrophy p=0.25 and eccentric hypertrophy p=0.81).

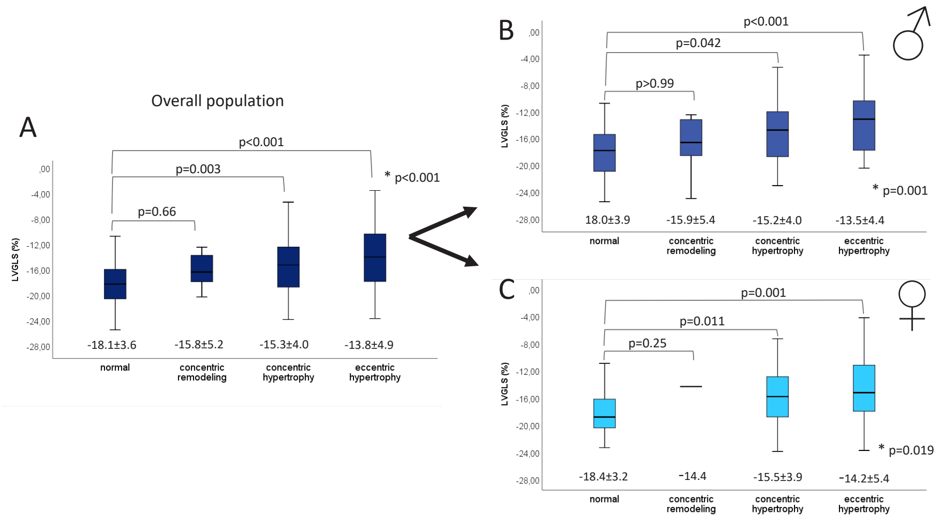
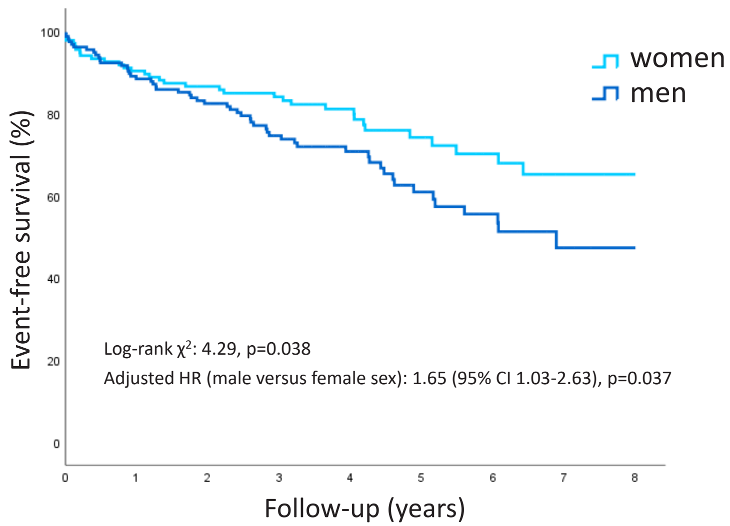



**FIGURE 3.** Boxplot showing the mean left ventricular global longitudinal strain (LV GLS) of the different left ventricular remodeling patterns for the overall population (Panel A), men (Panel B) and women (Panel C). * shows p-value for comparing the mean LV GLS between the left ventricular remodeling patterns with One-way ANOVA.




Number at risk

| | | | | | |
|---|---|---|---|---|---|
| Women | 134 | 106 | 65 | 31 | 12 |
| Men | 155 | 116 | 59 | 26 | 9 |

**FIGURE 4.** Kaplan-Meier curves for men and women demonstrating the estimated event-free survival from all-cause mortality of the overall population after transcatheter aortic valve implantation.

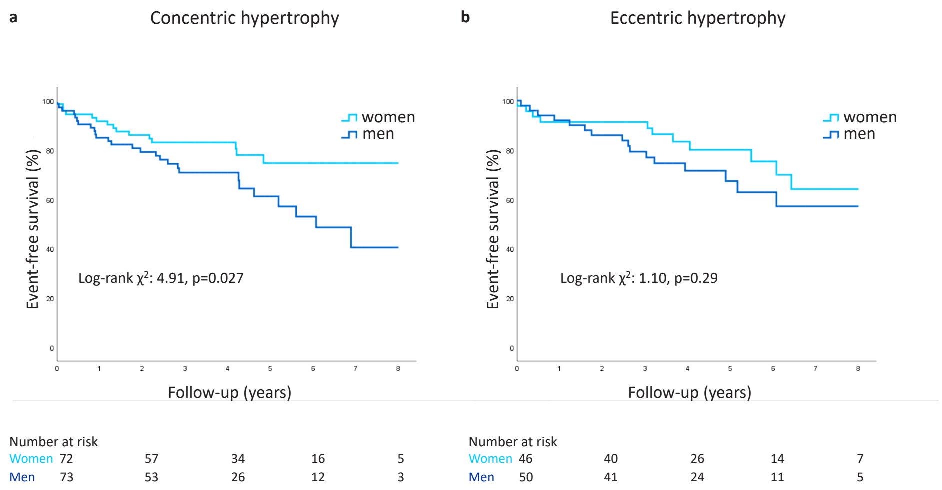



**FIGURE 5.** Kaplan-Meier curves demonstrating the estimated event-free survival from all-cause mortality after transcatheter aortic valve implantation for men and women in subjects with concentric hypertrophy (Panel A) and eccentric hypertrophy (Panel B).

# DISCUSSION

In patients with severe AS, women had smaller LV cavity size and LV mass compared to men but the frequency of concentric and eccentric hypertrophy was comparable between both sexes. Concentric remodeling was more common in men but represents a minority in remodeling patterns. Moreover, women demonstrated more favorable outcome after TAVI, which was mainly present in the group of patients with concentric hypertrophy. No association was noted between the interaction of the LV remodeling patterns and sex with outcome.

### Sex differences in LV remodeling in severe aortic stenosis

LV remodeling is considered to be an adaptive physiological response in patients with AS. The hypertrophic response of the LV myocardium counteracts the chronic pressure overload imposed by the stenotic valve in order to normalize wall stress and maintain cardiac output[9,10].

In the current study, the majority of patients with severe AS showed LVH. More specifically, concentric hypertrophy was the most frequently observed LV remodeling pattern followed by eccentric hypertrophy; normal geometry and concentric remodeling were noted in a smaller number of patients. Differences between men and women were observed with regards to LV remodeling: smaller LV mass and LV volumes were observed in women, even after considering body surface area. These results are in line with previous data from echocardiography and CMR imaging studies[13,24-26], but have not been reported previously with MDCT, which was used in the current study. Moreover, concentric remodeling was more prevalent in men, while no differences between sexes were observed in the remaining LV remodeling patterns (normal geometry, concentric and eccentric hypertrophy).

Treibel et al.[15] evaluated sex differences in LV remodeling in patients with severe AS (waiting for surgical aortic valve replacement) using echocardiography and CMR. Normal geometry and concentric remodeling were more commonly observed in women, while concentric hypertrophy and eccentric hypertrophy were more frequently observed in men. However, these sex differences in LV remodeling patterns were only observed with CMR, but not with echocardiography.

Various issues may explain this discrepancy. First, the study populations of the 2 studies were different. The patients included in the present study were being referred for TAVI (instead of surgical aortic valve replacement), were older, and had more comorbidities compared to the population studied by Treibel et al.[15]. Therefore, patients may have been exposed to severe AS for a longer time period, with potentially more profound LV remodeling. The greater distribution of LVH in the current study (83% vs. 56%) might support this hypothesis. Second, the study by Treibel et al.[15] reported lower mass-to-volume ratios in women, whereas in the current study the mass-to-volume ratio was similar between sexes.



**Sex differences in outcome after TAVI and association with LV remodeling patterns**

This study demonstrated better long-term outcome for all-cause mortality in women with severe AS treated with TAVI as compared to men. These results are in agreement with the current evidence reporting a survival benefit in women after TAVI[7,8,27]. Sex differences in LV remodeling in AS have been suggested to influence outcome following TAVI. Previous research evaluating the LV remodeling patterns with echocardiography and associating the various patterns of LV remodeling with outcome in patients with AS and preserved LVEF reported that concentric hypertrophy was independently associated with increased risk of mortality in women, but not in men[28].

In the present study, no significant interaction was observed between outcome and the LV remodeling patterns and sex. Interestingly, the survival benefit in women was solely observed in the group of patients with concentric hypertrophy; the long-term all-cause mortality was similar in men and women with eccentric hypertrophy.

Whereas concentric hypertrophy is associated with an increased wall thickness of the left ventricle and initial preservation of LV cavity size and LVEF, eccentric hypertrophy is characterized by chamber dilatation and impaired systolic function[9,29]. In line, our results showed more impaired LV GLS among patients with eccentric hypertrophy, indicating more reduced LV systolic function compared to patients with normal geometry. Accordingly, eccentric hypertrophy is considered as the end-stage of the LV remodeling process and has been associated with increased mortality risk compared to concentric hypertrophy[30-32]. The association of the eccentric LV remodeling pattern with poor outcomes was similar between sexes in the present study. This finding might suggest that once the LV response to the pressure overload has been exhausted, the benefits of TAVI are not different between the sexes. In men, the LV remodeling response can be exhausted earlier than in women since men with LV concentric hypertrophy had worse outcome than women after TAVI.

### Limitations

Several limitations should be acknowledged. First, this is a retrospective analysis with subsequent limitations related to the study design. Second, only patients with severe AS undergoing TAVI were included. Therefore, these data may not be representative for patients with mild aortic valve disease or undergoing surgical treatment. Third, other determinants besides AS severity are considered to affect the pattern and magnitude of LV remodeling including myocardial fibrosis, co-existent arterial hypertension, and aortic regurgitation or mitral valve disease[15,26,28,31]. Although patients with significant mitral valve disease or aortic regurgitation were excluded, arterial hypertension remained a highly prevalent comorbidity. Since myocardial fibrosis was not assessed from MDCT, this study could not account for the presence and extent of myocardial fibrosis.

## CONCLUSION

LV concentric and eccentric hypertrophy were similarly observed in men and women with severe AS. Concentric remodeling was more common in men but represented a minority in remodeling patterns. Women demonstrated better long-term outcome after TAVI as compared to men, particularly among those with LV concentric hypertrophy. However, the outcome benefit of women after TAVI seems not to be related to sex differences in LV remodeling.

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