Impact of baseline left-ventricular ejection fraction on 30-day and 1-year outcome after transfemoral aortic valve implantation: Interaction with mean gradient across the aortic valve

K. El Chiali, P.C. Patsalis, F. Al-Rashid, H. Hildebrandt, M. Totzek, A. Lind, R.A. Janosi, T. Rassaf, P. Kahliert. University Hospital of Essen, West German Heart and Vascular Center, Department of Cardiology and Vascular Medicine, Essen, Germany

Background: Abnormal left-ventricular ejection fraction (LVEF) is associated with increased mortality after transcatheter aortic valve implantation (TAVI). The cutoff point for outcome prediction remains poorly defined.

Methods: We analyzed data of 505 consecutive single center TAVI patients. LVEF was categorized according to the recommendations of the American Society of Echocardiography.

Results: Baseline LVEF was normal in 280 (55%), mildly abnormal in 121 (24%), moderately abnormal in 74 (15%) and severely abnormal in 30 (6%) patients, respectively. 30-day and 1-year mortality were 8.5% and 22.4%, respectively. Patients with normal and mildly abnormal LVEF had similar outcomes after TAVI, but all-cause mortality was increased in patients with moderately and severely abnormal LVEF. Outcome also depended on the baseline mean pressure gradient across the aortic valve, especially in the latter groups. Patients with moderately/severely abnormal LVEF and a mean transaortic gradient <40 mmHg (LGAS) had double all-cause mortality rate at 1-year (40.3%) compared to any other patient subgroup (Fig. 1). In the multivariate analysis, only the combination of LVEF <40% with LGAS was predictive of an increased 30-day (HR 3.33, 95% CI 1.76 to 6.3) and 1-year morality (HR 2.42, 95% CI 1.57 to 3.72).

Conclusion: Moderately and severely abnormal LVEF at baseline is associated with increased mortality after TAVI, especially when the mean transaortic gradient is less than 40 mmHg, while outcome in patients with normal and mildly abnormal LVEF are comparable regardless the pressure gradient across the aortic valve.

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Increased plasma ACE2 activity is a marker of subclinical LV systolic dysfunction in patients with aortic stenosis

J. Ramchand1, S.K. Patel1, L.G. Kearney1, E. Velkoska1, G. Matalanis2, O. Farouque1, P.M. Srivastava1, L.M. Burrell1, K. El Chilali, P.C. Patsalis, F. Al-Rashid, M. Beer4, S. Gattenloehner2, S. Stoerk1, W. Voelker1, E. Velkoska1, G. Ertl1, S. Kerrmann1, 1University of Melbourne, Department of Medicine, Austin Health, Melbourne, Australia; 2Austen Health Hospital, Department of Cardiac Surgery, Melbourne, Australia

Background: Subclinical left ventricular systolic dysfunction (LVSD) determined by global longitudinal strain (GLS) portends a poor prognosis in patients with aortic stenosis (AS). Angiotensin converting enzyme 2 (ACE2) is a membrane bound protein highly expressed in the human heart and functions to degrade the vasoconstrictor, profibrotic peptide, angiotensin II. Plasma ACE2 levels are elevated in patients with heart failure and ACE2 knockout mice have severe systolic dysfunction. In patients with AS, it is not known if early maladaptive processes within the myocardium are associated with changes in plasma and/or tissue ACE2.

Purpose: To investigate if subclinical LVSD in patients with aortic stenosis is associated with elevated plasma ACE2 activity and/or reduced myocardial ACE2 gene expression.

Methods: Plasma ACE2 activity was measured in 111 patients with AS and normal LV ejection fraction with satisfactory (<15%, n=77) and abnormal (>15%, n=34) GLS. Gene expression of ACE2 was measured in atrial samples collected from a subset of patients during aortic valve replacement (n=20).

Results: Median [25th, 75th quartile] plasma ACE2 activity was significantly higher in patients with abnormal versus normal GLS (29.0 [18.5, 45.25] vs. 20.8 [12.8, 35.04] pmol/ml/min; P=0.03). Myocardial ACE2 gene expression was significantly reduced (0.5-fold, P<0.01) in those with abnormal GLS (n=10) compared to normal GLS (n=10). Plasma ACE2 activity correlated negatively with ACE2 messenger RNA (R2 – 0.45, P=0.047).

Conclusions: In patients with aortic stenosis, elevated plasma ACE2 activity is associated with subclinical LVSD and reduced myocardial ACE2 gene expression. Approaches to enhance cardiac ACE2 may have a role in preventing progression to overt LV dysfunction in AS.

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Impact of myocardial fibrosis on 10-year outcome in patients undergoing aortic valve replacement

B. Fries1, F. Weidemann2, D. Liu3, K. Hu1, J. Strotmann3, P. Nordbeck1, M. Beer4, S. Gattenloehner2, S. Stoerk1, W. Voelker1, E. Ertl1, S. Herrmann1, 1University Hospital Würzburg, Department of Cardiology, Würzburg, Germany; 2Städtisches Krankenhaus Kiel, Department of Cardiology, Kiel, Germany; 4University Hospital Ulm, Department of Radiology, Ulm, Germany

Introduction: In extension to earlier published data from 2009, we performed a 10-year follow-up of patients who underwent conventional aortic valve replacement (AVR) due to symptomatic severe aortic valve stenosis (AS).

Purpose: To assess the impact of myocardial replacement fibrosis (MF) on long-term outcome.

Methods: In this prospective study, endomyocardial biopsy specimens were acquired in 58 consecutive patients during AVR between May 2004 and March 2007. MF was graded using the calculated percentage area of fibrosis. Patients were grouped according to the amount of MF: severe MF (n=21), mild MF (n=15) and no MF (n=22). Biomarkers including NT-pro-BNP were obtained, Echocardiography including Strain imaging, as well as cMRI gadolinium late enhancement were performed at baseline, 1 year and 10 years after AVR. Survival status was ascertainment during clinical visits or telephone interview.

Results: The median survival time in the whole cohort was 9.18 years (interquartile range: 3.92 years). Death of any cause occurred in 21 patients (38.9%); 3 (14.3%) in the group without MF, 6 (42.9%) in the mild MF group and 12 (63.2%) in the severe MF group (p=0.006), resulting in the lowest cumulative survival for patients with severe MF (log rank p=0.003, figure A). Regarding cardiovascular mortality, patients with severe fibrosis had the lowest cumulative survival of the stochastic radio-induced events. More than 10% of patients received a global exposure greater than 100 mSv, associated with a lifetime cancer risk of 1/100.

All-cause (A) and CV mortality (B)
three groups (log rank p=0.026, figure B): Cardiovascular death occurred in 3 patients (21.4%) with mild MF and 5 patients (28.3%) with severe MF. Of the patients without MF, none died of cardiovascular cause. Although the presence of fibrosis was associated with a poor prognosis, the total amount of MF correlated poorly with the survival time (r = 0.403, p=0.003). Conversely, no difference in cardiovascular mortality could be noted in the direct comparison between patients with mild MF and patients with severe MF.

**Conclusion:** The present data show the severe impact of MF on mortality in patients with AS. Even 10 years after AVR, significant differences in all cause mortality, as well as cardiovascular mortality could be noted. Of note, the total amount of MF made no difference in the long-term outcome. Therefore, care should be taken to avoid unnecessary delays in AVR, especially when myocardial fibrosis is not yet present.

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Sudden death in primarily asymptomatic patients with aortic valve stenosis

J. Minners1, A. Rossebo2, A. Gren3, S. Ray4, K. Boman5, C. Gohike-Baewol5, F.J. Neumann1, K. Wachtholz2, N. Jander1, 1University Heart Center Freiburg- Bad Krozingen, Bad Krozingen, Germany; 2University of Oslo, Oslo, Norway; 3Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark; 4University Hospital of South Manchester NHS Foundation Trust, Manchester, United Kingdom; 5Umea University Hospital, Umea, Sweden

**Background:** The risk of sudden cardiac death (SCD) in patients with asymptomatic aortic stenosis (AS) is thought to be relatively low (1%) and mostly dependent on AS severity. We retrospectively analyzed outcome data from the Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) study with the aim to assess the incidence and potential risk factors of SCD in this prospectively followed cohort of asymptomatic patients.

**Methods:** Of the 1873 patients included in the trial, 1204 (64%) with mild to moderate aortic stenosis (jet velocity 2.5–4.0 m/s), complete clinical, echocardiographic, and follow up data remained event-free (except for sudden death) throughout the study period.

**Results:** SCD occurred in 19 patients during a mean follow-up of 26.6±13.2 months (0.7%/year). Patients with SCD were older (p=0.01), had a higher left ventricular (LV) mass (p<0.001), tended to be female (p=0.11) and leaner (p=0.06) than surviving asymptomatic patients. None of the echocardiographic parameters of stenosis severity (or their development over time) were associated with SCD (e.g. jet velocity 3.1±0.4 vs. 2.9±0.5 m/s, p=0.33). Cox regression analysis identified age (HR 1.077, 95% CI 1.012–1.145 per year), LV mass (HR 1.013, 95% CI 1.007–1.018 per gram and BMI (HR 0.836, CI 0.721–0.968 per kg/m²) as independent risk factors of SCD (all p<0.05).

**Conclusion:** Sudden cardiac death in asymptomatic patients with aortic stenosis is rare and strongly related to left ventricular mass but not stenosis severity.

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Causes of death in patients with severe aortic stenosis: a report from the CURRENT AS registry

E. Minamino1, T.K. Katoh1, T.M. Morimoto2, T.T. Taniguchi1, H.S. Shimoi1, K.K. Nakamura1, M.I. Inoko3, S.S. Shirai3, T.K. Kitat3, C.I. Izuami3, T.I. Inada3, K.I. Ishii1, N.S. Saito1, K.M. Minatoya1, T.K. Kimura1 on behalf of the CURRENT AS registry Investigators. 1Kyoto University Graduate School of Medicine, Department of Cardiovascular Medicine, Kyoto, Japan; 2Hyogo College of Medicine, Department of Clinical Epidemiology, Nishinomiya, Hyogo, Japan; 3The Tazuke Kofukai Medical Research Institute, Kitano Hospital, Cardiovascular Center, Osaka, Japan; 4Kokura Memorial Hospital, Department of Cardiology, Kokura, Japan; 5Kobe City Medical Center General Hospital, Department of Cardiovascular Medicine, Kobe, Japan; 6Tenni Hospital, Department of Cardiology, Tenni, Japan; 7Osaka Red Cross Hospital, Department of Cardiovascular Center, Osaka, Japan; 8Kansai Electric Power Hospital, Department of Cardiology, Osaka, Japan; 9Kyoto University Graduate School of Medicine, Department of Cardiovascular Surgery, Kyoto, Japan

**Background:** The prevalence of aortic stenosis (AS) is increasing due to the aging population. The cause of death in patients with AS is not yet clear.

**Purpose:** To know if the patients with AS die from AS-related causes or not.

**Methods and results:** We used data from a Japanese multicenter registry, the CURRENT AS Registry, which enrolled 3,815 consecutive patients (female: 62%, and mean age: 78±10 years) with severe AS (peak aortic jet velocity [Vmax] >4.0 m/s, mean aortic pressure gradient ≤40 mm Hg, or aortic valve area <1.0 cm²). The median follow-up period was 1176 (interquartile range: 733–1618) days, with a 93% follow-up rate at 2-year. Of 1449 deaths observed, 802 (55.3%) were from cardiac causes and 647 (44.7%) were from non-cardiac causes. Heart failure (32.5%) and sudden death (10.1%) caused the majority of cardiac deaths, whereas infection (12.6%) and malignancy (11.1%) were the main causes of non-cardiac deaths. In the initial aortic valve replacement stratum (N=1197), procedure-related death was the leading cause of cardiac death followed by HF and cardiac arrest, while in the conservative stratum (N=2618), HF was the leading cause of cardiac death, followed by sudden death. In a cause-specific Cox proportional hazards model, both non-cardiac factors (age, male, body mass index >22, diabetes, prior history of stroke, aortic/periappendicular artery disease, anemia, malignancy under treatment) and cardiac factors (atrial fibrillation, ejection fraction <68%, and low Vmax) were associated with non-cardiac death.

**Conclusions:** Death from non-cardiac causes, including infection and malignancy, is an important contributor to the overall mortality in patients with severe AS.

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**P2622 | BEDSIDE**

Socioeconomic status, neighborhood deprivation and cardiovascular disease: a large scale population based study

P. Andell1, X. Lu1, C. Andersson2, A. Martinsson1, B. Zoller3, J.G. Smith1, K. Rentzos1, 1Lund University Hospital, Department of Cardiology, Lund, Sweden; 2Center for Primary Health Care Research, Lund University, Malmo, Sweden; 3Gentofte University Hospital, Copenhagen, Denmark

**Background:** Low socioeconomic status (SES) is associated with atherosclerotic vascular disease, such as myocardial infarction (MI) and stroke. Less is known about the association between SES and valvular heart disease, including aortic stenosis (AS).

**Purpose:** To study if low SES, estimated by high neighborhood deprivation, is associated with increased incidence of AS.

**Methods:** We studied the Swedish population with nationwide registers during the study period of 1997–2010. A neighborhood deprivation index (NDI) was calculated based on four items: low educational level (<10 years of formal education), low income, unemployment, and receipt of social welfare. NDI was categorized into low (<1 standard deviation [SD] below the mean), moderate (mean ± 1 SD) and high (>1 SD above the mean) NDI, respectively. Birth year, family income, marital status, urban vs. rural residency, education and country of origin were included as individual sociodemographic covariates. The outcome was AS, defined by an ICD-10 diagnosis code of I15.0 or I15.2. Multivariable (hierarchical) logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals. Analyses were stratified by sex. A sensitivity analysis studied MI as the outcome variable.

**Results:** The total study population (=n=6 411 905) was divided into individuals living in neighborhoods with low (n=1 608 815 [24%]), moderate (n=3 857 387 [58%]) and high (n=1 175 723 [18%]) NDI, respectively. 63 227 incident aortic stenosis cases occurred. After adjustment for individual sociodemographic variables, high NDI compared to low NDI was associated with a slightly greater risk of AS (OR in men: 1.09 [1.05–1.14], in women: 1.10 [1.05–1.15]). The corresponding risk increase was more than doubled for MI (OR in men: 1.23 [1.21–1.25], OR in women: 1.28 [1.26–1.30]).

**Conclusions:** In this nationwide study of the Swedish population, living in a comparatively highly deprived neighborhood was only modestly associated with an increased risk of incident AS. The association was stronger for MI, indicating that AS may be less influenced by traditional socioeconomic risk factors.

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**P2623 | BEDSIDE**

Combined aortic valve replacement and coronary artery bypass grafting: the impact of incomplete revascularization in long term survival


**Introduction:** Combined aortic valve replacement (AVR) and coronary artery bypass grafting (CABG) is associated with a greater risk of operative mortality and a worse late survival than isolated AVR or CABG. We aimed at evaluating the perioperative results, long-term outcomes and time free from major cardio and cerebrovascular events (MACCEs) of patients submitted to AVR plus CABG, and the impact of incomplete revascularization (ICR) in this setting.

**Methods:** From January 2003 to August 2015, 564 consecutive patients underwent combined AVR and CABG, and constituted the study population. Patients with other associated valvular surgeries were excluded. The anatomical conditional definition of complete revascularization (CR) was adopted, defined as a revascularization of all main-branch vessels. Mean follow-up was 4.8±2.9 years and 100% and 94.3% complete for survival and MACCEs, respectively. Cox proportional hazards models were used to analyze risk factors for late mortality and MACCE incidence. Kaplan-Meier methods were used to plot sur-

**Cause of death by treatment strategies**