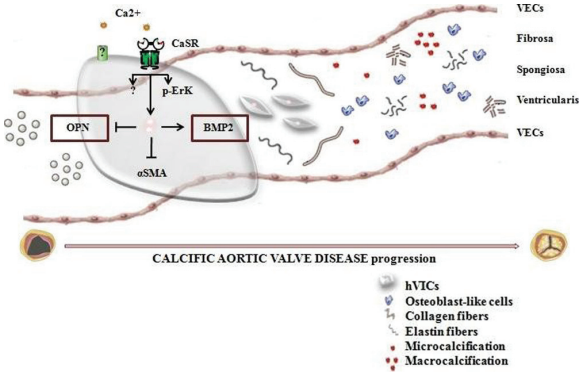
strated, for the first time, that hVICs expressed the CaSR. This receptor is functionally regulating ErK phosphorylation. Its activation with calcium or NPS R-568 and inhibition with NPS R-2143 was associated with a stimulation and an inhibition of VC respectively. We also showed that CaSR activation leads to the phenoype switching of hVICs into an osteoblat-like phenotype characterized by increased osteogenic differentiation factors such as BMP2, OPN, Runx2 and osterix and a decreased alpha SMA. For further validation of CaSR implication in the calcification process, we showed that up-regulation of CaSR expression after plasmid-CaSR transfection activated a BMP2/OPN dependant osteoblastic differentiation process of hVICs, while down-regulation of the receptor expression with a siRNA inhibited the development of VC. More importantly, higher CaSR expression levels were found to be associated with the calcified parts of human aortic valves as opposed to non-calcified parts.



Calcific aortic valve disease

Conclusion: Activation of the CaSR is associated with the hVICs osteoblastic differentiation and calcification most likely via a BMP2/OPN dependant mechanism.
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P5093
Kidney dysfunction is a risk factor for developing aortic stenosis: results from the SCREAM project

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Background: Aortic stenosis (AS) is the most common primary valve disease. Individuals with chronic kidney disease (CKD) have a high prevalence of atherosclerotic risk factors. However, it is unknown whether the presence of CKD is associated to an increased risk of developing AS.
Aim: The aim of this study was to assess whether kidney function is associated with AS incidence in a large Swedish population-based cohort.
Methods: This study utilizes the Stockholm CREAtinine Measurements (SCREAM) cohort, a healthcare-utilization cohort that includes all residents in the region of Stockholm, Sweden, undertaking serum creatinine tests in outpatient or inpatient care between 2006–2011. We included 1,121,875 participants without a prior diagnosis of aortic stenosis from the Stockholm CREAtinine Measurements (SCREAM) project. Estimated glomerular filtration rate (eGFR, ml/min/1.73m^2) was calculated from serum creatinine and follow-up was carried out for the occurrence of aortic stenosis diagnostic codes.
Results: The median age was 50 (interquartile range 36–64) years and 54% were women. Median eGFR was 96 (interquartile range 82–109) and 66,949 (6.0%) participants had eGFR <60 ml/min/1.73m^2 (CKD). During a median follow-up time of 5.1 years (IQR 3.3 - 6.1), there were 5858 (0.5%) participants who developed AS (incidence rate (IR) 1.13 per 1000 person-years). Compared to eGFR>90 (IR 0.34 per 1000 person-years), lower CKD strata were associated with higher multivariable-adjusted hazards of AS (Figure 1): eGFR>60–90 IR 1.88; HR 1.14 (95% CI 1.05–1.25); eGFR>45–59 IR 4.61, HR 1.17 (95% CI 1.05–1.30); eGFR>30–44 IR 6.62; HR 1.22 (95% CI 1.07–1.39) and eGFR<30 IR 8.27; HR 1.56 (95% CI 1.29–1.87). The association between CKD (eGFR <60 ml/min/1.73 m^2) and AS was assessed across various predefined subgroups: females with CKD having a 20% higher risk (HR 1.20, 95% CI 1.11–1.31) of AS compared to those without CKD. The presence of CKD among younger patients was more common and more strongly associated to AS in the absence of comorbid ischemic heart disease, diabetes mellitus, hypertension and heart failure.
Conclusions: This study shows in a region-representative population sample that kidney dysfunction is associated with increased risk of incident AS. In this context, even mild eGFR reductions within the normal range (eGFR 90–60 ml/min/1.73m^2) were associated with increased AS risk (Figure 1).

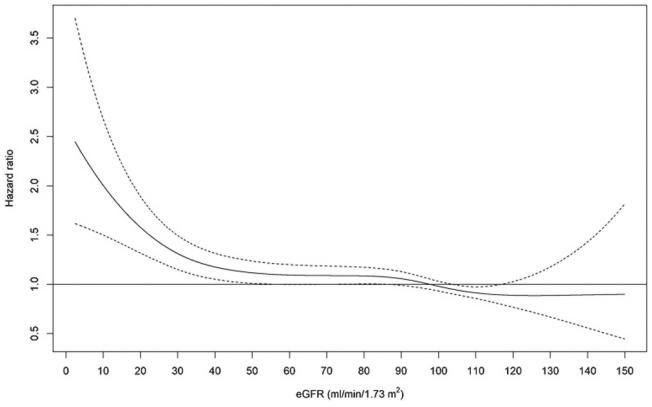

Figure 1

P5094
Combined predictability of cardiac valvular calcification, protein-energy wasting and inflammation status for cardiovascular mortality in incident haemodialysis patients

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Background: Cardiac valvular calcification, frequently seen in end-stage renal disease (ESRD) patients, potentially reflects systemic atherosclerosis. Malnutrition and chronic inflammation status are also prevalent, and associated with increasing cardiovascular (CV) risk in this population. We investigated the combined predictability of valvular calcification, geriatric nutritional risk index (GNRI) and C-reactive protein (CRP) for CV mortality in ESRD patients at starting haemodialysis (HD) therapy.
Methods: A total of 1,351 ESRD patients who electively started HD therapy were screened by echocardiography. Valvular calcification was defined as bright echoes >1mm on one or more cusps of the aortic and/or mitral valve. Patients were followed-up for 10 years. The improvement of predictability for mortality was accessed using C-index, net reclassification improvement (NRI) and integrated discrimination improvement (IDI).
Results: During follow-up period (median of 63 months), 322 patients (23.8%) died including 141 (10.1%) CV cause. Cox multivariate analysis revealed that valvular calcification [hazard ratio (HR) 1.31, 95% CI 1.04–1.67, p=0.021], GNRI<92.0 as a median value (HR 1.65, 95% CI 1.31–2.09, p<0.0001) and CRP>1.9 mg/l as a median value (HR 1.73, 95% CI 1.37–2.19, p<0.0001) were independent predictors for CV mortality. When patients were divided into groups according to number of these three risk factors, patients with any 1, any 2 and all risk factors had 1.58-fold (95% CI 0.97–2.72), 2.41-fold (95% CI 1.50–4.12) and 3.86-fold (95% CI 2.38–6.63) higher risk for mortality compared to those without any risk factor, respectively (p<0.0001 for trend) after adjustment for other confounders. Furthermore, the addition of these 3 factors to a prediction model based on established risk factors improved the C-index (0.688 to 0.761, p<0.0001), NRI (0.647, P<0.0001) and IDI (0.031, P<0.0001) greater than that of each individual factor alone (Table).

Table 1

	C-index (95% CI)	P value	NRI	P value	IDI	P value
Basic model	0.688 (0.628–0.748)	Reference		Reference		Reference
+ Valvular calc.	0.740 (0.667–0.793)	0.011	0.483	<0.0001	0.025	<0.0001
+ GNRI	0.710 (0.651–0.769)	0.027	0.287	0.0087	0.006	0.023
+ CRP	0.700 (0.640–0.761)	0.030	0.411	0.0003	0.006	0.010
+ All factors	0.761 (0.709–0.813)	<0.0001	0.647	<0.0001	0.031	<0.0001

Conclusions: Combination of valvular calcification, GNRI and CRP were additively associated with increasing risk of both CV mortality, and contribute to improve the predictability in ESRD patients just starting HD therapy.

P5095
CT valvular calcification in severe aortic stenosis - Which parameter better predicts prognosis?

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Introduction and aim: The prognostic value of aortic valve calcification measured by CT is well established in patients with aortic stenosis. However, the best way to report it, either by absolute value (calcium score) or indexed to left ventricular outflow tract (LVOT) dimensions (calcium density), remains uncertain. The