recruited. Investigations were performed on the same day once listed for AVR and 6 months following surgery; venous blood samples were drawn, centrifuged within 30 min and frozen at −80°C until assayed. MMP 2, 3 and 9 and TIMPs 1, 2 and 4 and additionally NT-proBNP were measured using similarly designed non-competitive immunoluminometric assays. All samples both pre- and post-operative were thawed and analysed at the same time to ensure consistency of assays. LV geometry, function and remodelling were assessed with transthoracic echocardiography for diastolic function and cardiac magnetic resonance for cardiac mass/volumes and myocardial fibrosis on late gadolinium enhancement.

Results Three patients did not attend follow-up. The remaining 43-paired data-sets were used for analysis. Data that were not normally distributed (including all biomarker data) were log transformed before analysis. Change in biomarker values between pre- and post-op were examined using paired t-tests and results are shown in Abstract 075 table 1. The relationship between baseline biomarkers and functional parameters (both at baseline and the ratio of change; pre/post-operative) were examined using bivariate correlations and are shown in Abstract 075 table 2. There are significant falls in MMP 2 and 9 and TIMPs 1 and 2 despite no significant change in NT-proBNP by six months post AVR.

Abstract 073 Table 1

Log10	Pre-operative	Post-operative	p Value
MMP2	1.56 (0.13)	1.49 (0.12)	<0.001
MMP3	1.43 (0.13)	1.44 (0.13)	0.45
MMP9	2.19 (0.19)	2.11 (0.21)	0.03
TIMP1	2.53 (0.12)	2.50 (0.11)	<0.001
TIMP2	2.20 (0.08)	2.18 (0.07)	0.02
TIMP4	0.72 (0.29)	0.74 (0.29)	0.20
NT-proBNP	2.20 (0.73)	2.23 (0.56)	0.70

Abstract 075 Table 2

	Pre-operative	Ratio of pre-operative/ post-operative
MMP2	Sep E/e' e' r=0.4, p=0.006; RVMI r=0.37, p=0.01	RVMI r=0.46, p=0.003
MMP3	Sep E/e' e' r=0.31, p=0.04	Sep E/e' e' r=0.38, p= 0.01; LAVI r=−0.34, p=0.03; RVMI; r=0.33, p=0.03
MMP9	Nil	Nil
TIMP1	Nil	LAVI r=−0.31, p=0.047
TIMP2	Sep E/e' e' r=0.44, p=0.002; LAVI r=0.3, p=0.047	RVMI r=0.43, p=0.006
TIMP4	Nil	LAVI r=−0.57, p<0.00; RVMI r=0.47, p=0.002
NT-proBNP	Sep E/e' e' r=0.44, p=<0.001; LVMI r=0.44, p=0.002; LVEDVI r=0.32, p=0.03; LAVI r=0.29, p=0.048	LVEF r=−0.35, p=0.03

Discussion NT-proBNP is perhaps unsurprisingly associated with mainly left ventricular geometry. In contrast the MMPs and TIMPs seem to be more closely related to measures of diastolic function, namely septal E/e' (a measure of LVEDP) and left atrial volume along with right ventricular mass. The role of MMPs and TIMPs as biomarkers in aortic stenosis is of interest and warrants study in a larger patient cohort including asymptomatic patients under surveillance.

076 FAILURE OF AORTIC VALVE REPLACEMENT TO IMPROVE OBJECTIVE FUNCTIONAL CAPACITY IN PATIENTS WITH ISOLATED SEVERE AORTIC STENOSIS

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Introduction Aortic stenosis (AS) is the commonest valve disease requiring surgery in the developed world. Development of symptoms is a Class 1 indication for aortic valve replacement (AVR) which reduces mortality. However, regression of left ventricular hypertrophy may be incomplete, myocardial fibrosis and diastolic dysfunction may be irreversible which may limit the functional improvement seen following AVR. We sought to examine the impact of AVR on cardiac remodelling and objective improvements in functional capacity.

Methods 46 patients with isolated severe AS (peak velocity >4 m/s or mean pressure gradient (MPG) >40 mm Hg or aortic valve area (AVA) <1 cm^2) without obstructive coronary artery disease (on angiography) were recruited. Investigations were performed on the same day once listed for AVR and 6 months following surgery; transthoracic echocardiography (TTE) for stenosis severity, diastolic function; cardiac magnetic resonance (CMR) for ventricular geometry, left atrial volumes, myocardial fibrosis on late gadolinium enhancement (LGE), adenosine stress/rest perfusion for absolute quantification of myocardial blood flow and calculation of myocardial perfusion reserve (MPR); cardiopulmonary exercise testing (CPEX) for objective exercise capacity (peak VO_2); venepuncture for NT-proBNP.

Results 46 patients were studied pre-AVR. Baseline characteristics; mean age 66±9 years, 74% male, peak velocity 4.4±0.57 m/s, MPG 49±14 mm Hg and AVA 0.86±0.22 cm^2. 43 patients returned for follow-up, of these 2 did not have CMR due to permanent pacemaker implantation and three had CMR without gadolinium (renal impairment/refused/extravasation). Non-normal data were log-transformed before analysis, paired t-tests were used for continuous variables, χ^2/McNemar tests for categorical. 42/43 had a biological prosthesis. Comparison between pre- and post-operative values; Abstract 076 tables 1 and 2. There were significant improvements in symptomatic status and reductions in LVMI, LVEDVI and left atrial volume index (LAVI) but this was not associated with improvement in objective exercise capacity (or NT-proBNP), significant reduction in E/e' or increase in MPR.

Discussion The majority of patients had minimal or no symptoms at the time of AVR. As expected there is a significant fall in LV mass and volumes by 6 months. The fall in left atrial volumes likely reflects the fall in left atrial pressure (and LVEDP consistent with a reduced, albeit not significantly, E/e'). Despite an improvement in NYHA Class there is no significant improvement in objective exercise capacity (peak VO_2) at 6 months. Over half the patients have

Abstract 076 Table 1

	Pre-operative	Post-operative	p Value
Septal E/e'	13.7 [11.1−18.6]	12.5 [10.6−17.1]	0.76
LVMI (g/m^2)	71.5 (17.5)	60.5 (16.1)	<0.001*
LVEDVI (ml/m^2)	97.4 (15.2)	80.6 (13.3)	<0.001*
LVEF (%)	56.4 (6.2)	57.8 (5.6)	0.15
LAVI (ml/m^2)	59.6 [49.2−66.4]	51.5 [45.6−59.9]	<0.001*
RVEDVI (ml/m^2)	80.1 (10.8)	79.6 (15.7)	0.79
RVEF (%)	61.6 (6.8)	57.7 (7.5)	<0.001*
LGE present	26 (57%)	24 (63%)	0.62
MPR	2.05 (0.51)	2.29 (0.60)	0.06

evidence of myocardial fibrosis (LGE) by the time of AVR, which does not regress post-operatively. Equally there is a failure of myocardial perfusion reserve to improve. This suggests that although significant LV remodelling occurs it is likely that irreversible fibrosis limits improvement in functional capacity.

Abstract 076 Table 2

	Pre-operative	Post-operative	p Value
VO2 (ml/kg)	15.4 (4.1)	16.0 (5.0)	0.24
Respiratory exchange ratio (RER)	1.1 (0.1)	1.1 (0.1)	0.62
Heart rate (% predicted)	85 (12)	88 (12)	0.08
O_2 pulse	9.8 (2.6)	9.9 (2.7)	0.77
VE/VCO_2 slope	29.2 (3.7)	29.7 (3.7)	0.38
NYHA	I=9; II=32; III=5	I=35; II=7; III=1	0.03*
NT-proBNP (Log fmol/ml)	2.20 (0.73)	2.23 (0.56)	0.70

077 OSTEOPOROSIS AND BISPHOSPHONATE'S USE ASSOCIATED WITH REDUCED PROGRESSION OF CALCIFIC AORTIC STENOSIS: RETROSPECTIVE OBSERVATIONAL SINGLE CENTRE STUDY

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Purpose Progression of Aortic Stenosis (AS) has been subject of much debate in the recent past with studies evaluating effects of statin therapy. Little is known about the factors that affect progression of AS. Recently there is a growing interest in the field of Bone modifiers reducing progression of AS. In this study we aim to study the effects of osteoporosis and bisphosphonate on progression of calcific AS.

Methods Retrospective electronic case notes of patients who had diagnosis of AS with at least two echocardiogram between 2005 and 2009 were studied. Exclusion criteria includes diagnosis of Rheumatic heart disease, bicuspid aortic valve and other significant valvular pathology. Demographics, AS severity, statin use. Peak velocity, Mean gradient, Left ventricular function were recorded. Rate of change of mean gradient (mm Hg/year) and Peak velocity (m/s/year) were then calculated from this data. Previous studies evaluating natural history of progression of AS shown that on average the rate of progression of Peak velocity across aortic valve is 0.24 m/s/year (m/s/yr). We have used this value as cut-off to identify patients in which AS has progressed. Electronic case notes were reviewed to identify osteoporotic patients on bisphosphonate during the study period.

Results N 103 Male 13 Mean Age 79.89 SD ±10.29. Patient are then divided into two groups based on diagnosis of osteoporosis (Bisphosphonate group) and Control (Non-bisphosphonate). No statistically significant differences was found in between groups in terms of demographics. Please refer to Abstract 077 table 1. Differences in rate of change of Peak velocity (m/s/yr) and mean gradient (mm Hg/yr) between the bisphosphonate and non-bisphosphonate groups were assessed using linear regression with statin status and left ventricular function included as covariates. Differences in rate of change of velocity of 0.13 m/s/year (95% CI 0.01 to 0.26), p=0.034 and in mean gradient of 2.59 m/s/year (95% CI 0.75 to 4.45), p=0.006 were demonstrated. Patient group, statin status, severity of AS and left ventricular function were included as independent variables in a logistic regression model used to discriminate between "progressors" (defined as a rate of change of velocity of >0.24 m/s/year) and "non-progressors" (≤0.24 m/s/year). The OR associated with being a progressor (Non-bisphosphonate/bisphonate group) was 4.83 (95% CI 1.63 to 14.32), p=0.006 or equivalently the RR was 2.96 (if the patient is not treated with bisphosphonates).

Abstract 077 Table 1

	Group A (patients on bisphosphonate)	Group B (control)
Total number	52	51
Male	7 (13%)	6 (12%)
Age	80.55 SD 6.89	78.89 SD 7.09
Average duration of treatment with bisphosphonate	40 months (3.33 years)	
Time interval between echo scans	25 SD 10	27 SD 9

Conclusion Our study has shown that Osteoporotic patients on Bisphosphonate have significantly decreased progression of AS. Whether this result was due to bone metabolism associated with either osteoporosis and/or bisphosphonate use needs to be clarified further in randomised control trials.

078 A RANDOMISED STUDY OF THE EFFECTS OF BI-LEAFLET PROSTHESIS ORIENTATION ON AORTIC HAEMODYNAMICS AND CORONARY FLOW VELOCITY PROFILES

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Objectives The orientation of curved bi-leaflet mechanical prosthesis has been shown to significantly affect the development of aortic sinus flow in the in vitro study. However, its clinical implication for trans-aortic pressure gradient or coronary flow dynamics remains to be defined. The present study was aimed to characterise these two haemodynamic aspects by randomising the orientation of MIRA aortic prosthesis in patients undergoing aortic valve replacement (AVR).

Methods 45 patients (58±12 years, 36 males) undergoing AVR with a MIRA prostheses were randomised to anatomic (leaflets parallel to left coronary) or anti-anatomic (leaflets perpendicular to left coronary) orientation. Echocardiography was performed at 1 week and 12 months after AVR to assess prosthesis pressure gradient, LV mass and LAD flow velocity profiles.

Results Aortic prosthesis and coronary LAD haemodynamics were analysed with respect to follow-up time and orientation by twoway ANOVA. In valve size >23 mm, prosthesis orientation did not affect valve haemodynamics, LAD flow profiles or LV mass index (all p>0.05). In valve size ≤23 mm, anti-anatomic orientation group had higher mean prosthesis pressure gradient (8.1±0.5 vs 6.3±0.5, mm Hg, p=0.023), but also a greater LAD systolic flow velocity (17.5±1.1 vs 13.8±1.4, cm/s, p=0.048) and longer LAD systolic flow duration (235±7 vs 208±9, ms, p=0.030) than those of anatomic orientation. LAD diastolic flow velocity and LV mass index did not differ between the two orientations (p>0.05).

Conclusions Anti-anatomic orientation of MIRA aortic prosthesis appears to produce more physiological LAD systolic flow profiles, which can be explained by a stronger aortic sinus vortices flow demonstrated by previous in vitro study. A greater pressure gradient in the same orientation, however, suggests the possibility of fluid dynamics across its central orifice may be insulated by the vortices flow in aortic sinus, implying a complex 3D velocity profile produced by the curved bi-leaflets prosthesis.