SUPPLEMENTAL MATERIAL

Myocardial Scar and Mortality in Severe Aortic Stenosis:

Data from the BSCMR Valve Consortium

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Overview:

1. **Figure S1: Study Diagram**

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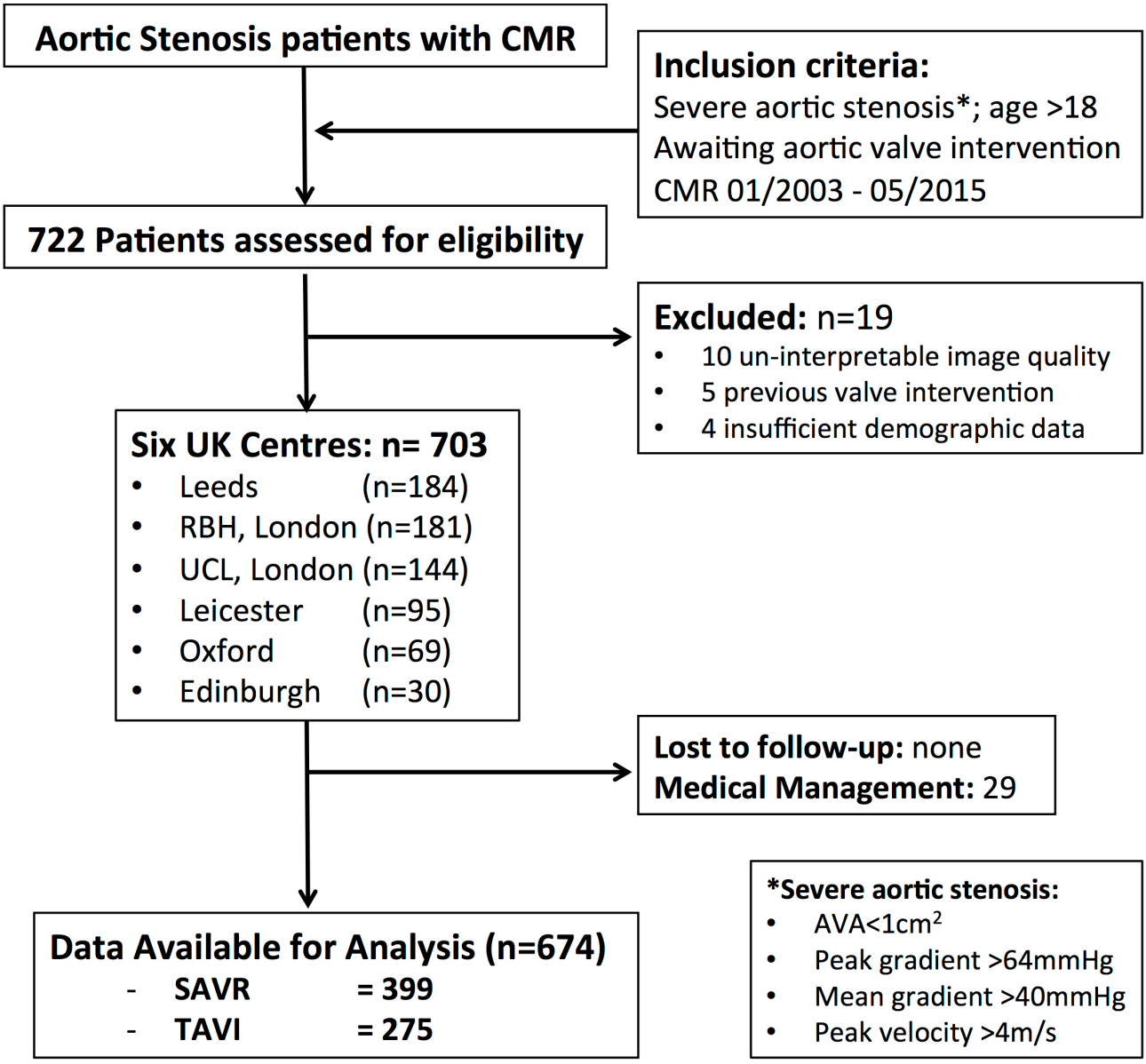
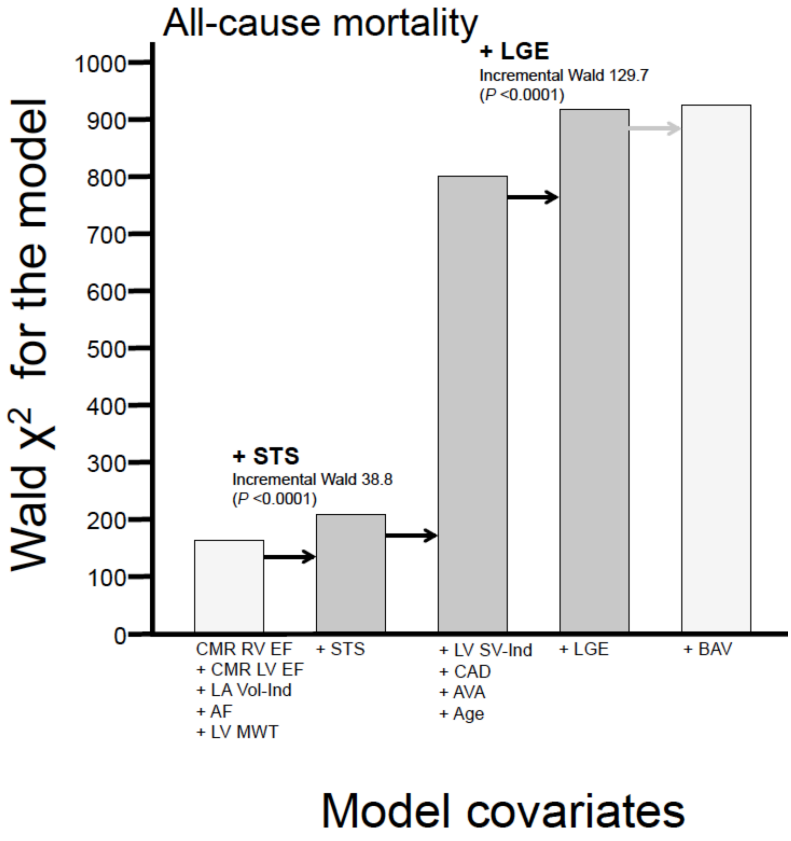


Figure S1: BSCMR AS700 Flow Diagram.
A longitudinal, observational outcome study in patients with severe AS referred to six UK cardiothoracic surgical centres and listed for valve intervention. Between January 2003 and May 2015, patients were prospectively recruited after evaluation by the multi-disciplinary heart team. Inclusion criteria were patients >18 years with severe AS (one of: aortic valve area [AVA]<1cm^2, peak pressure gradient >64mmHg, mean pressure gradient >40mmHg, peak velocity >4m/s) who had undergone CMR imaging for clinical or research purposes.
AVA, aortic valve area; CMR, cardiovascular magnetic resonance; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement; RBH, Royal Brompton Hospital; UCL, University College London.

2. Figure S2: Incremental Risk Stratification

To demonstrate the sequence in which information becomes clinically available for risk stratification, the global Wald χ^2 are shown for separate Cox regression models predicting all-cause death, showing how the successive addition of volumetric indices, clinical variables, STS score and LGE significantly increase the global Wald χ^2 (probability values attributable to the addition of the new variable are also shown accounting for the variables already present in the model).



AF, atrial fibrillation; AVA, aortic valve area; BAV, bicuspid aortic valve; CAD, coronary artery disease; CMR, cardiovascular magnetic resonance; EF, ejection fraction; LGE, late gadolinium enhancement; LA, left atrium; LV, left ventricle; MWT, maximal wall thickness; STS, Society of Thoracic Surgery score; SV, stroke volume; Vol, volume.

3. Pre-specified Standard Operating Procedure for Data Analysis

Data analysis was pre-specified in a standard operating procedure document (SOP). This SOP ensured a consistent approach in respect of image analysis across the six sites. The analysis was performed in a distributed core-lab approach. All patients were uploaded as anonymised scans to a central repository. Each centre analysed a specific domain across the whole cohort (Figures in this section are not referred to in the main manuscript).

Standard Operating Procedure – BSCMR Valve Consortium

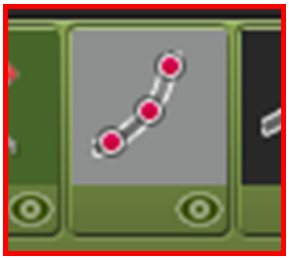
3.1 Circle Cardiovascular Imaging cvi42: Housekeeping

1) The same version of the CVI42 is utilised across the 6 sites (Version 5.1.2, Calgary, Canada). This, in particular, is important for those sites designated LV and RV chamber quantification. There are obvious differences in dashboard aesthetics and "smoothness" of contouring tools and it would be optimal for analysis to be performed on the same software.

2) To use a pre-specified zoom '%' of x2.0 or x2.7 for the workspace prior to contouring.

3) To use the pre-defined cvi windowing setting of 3 (although custom windowing should obviously be used if this setting is of suboptimal image quality)

4) Manual contouring of the LV and RV is performed using the bezier tool ('click-draw' icon displayed, see below).



5) To employ the following cvi42-specific SOP for standardising backend contour settings:

SubPixel Matrix size = 4X4
Signal Intensity SD = use subpixel weighted SD (and not biased SD)
Contour detection = check contour detection connect to view
Rounded SAX endocardial contour = leave inactive
Papillary muscle detection = check this
SAX chord generation = uncheck this

6) The contours drawn are saved locally

- "save workspace DICOM" via workspace option on task bar
- return to patient list view
- and choose "extended view" option at bottom left of screen
- select patient under study
- scroll down to end of sequence list and select the saved DICOM workspace
- right click on this and "export series"
- save in a designated folder on local drive

- upload contour workspace straight into the research participant's REDCap module using 'File Upload' option

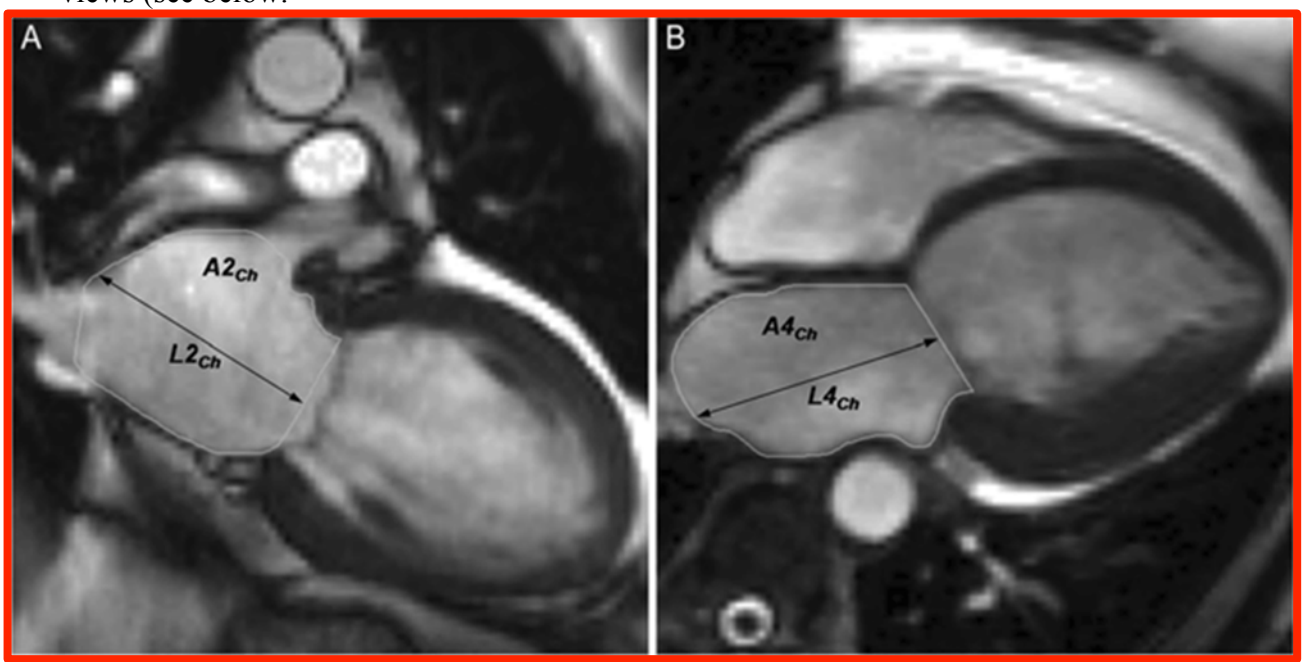
7) Similarly, that derived values (e.g. absolute LVEDV, LV mass etc) are manually entered into the CMR variables section of the BSCMR project in RedCAP under the patient being studied.

3.2 Left Atrial Volume Quantification

- Measurement of left atrial (LA) volume is by the biplane area–length method.
- Images are analysed in the viewer module of cvi42 with a dual panel display selected to permit synchronisation of HLA and VLA by phase.
- All measurements are taken from the two-chamber (A) and four-chamber (B) views at end-ventricular systole, ensuring maximal LA size.
- The atrial endocardial border is traced to determine LA area with exclusion of the pulmonary veins, LA appendage, and mitral valve recess.
- LA length is measured from the midpoint of the mitral annulus plane to the posterior aspect of the left atrium. Left atrial volume (LAV) was calculated using the formula:

$$LAV = 8(A2Ch)(A4Ch) / 3\pi L$$

- where A2Ch and A4Ch refer to the LA area in the two-chamber and four-chamber views, respectively, and L is the shorter of the two LA length measurements (L2Ch, L4Ch) from these views (see below.



(Adapted from Gulati et al. 2013. European Journal of Heart Failure; 15(6); 660-670).

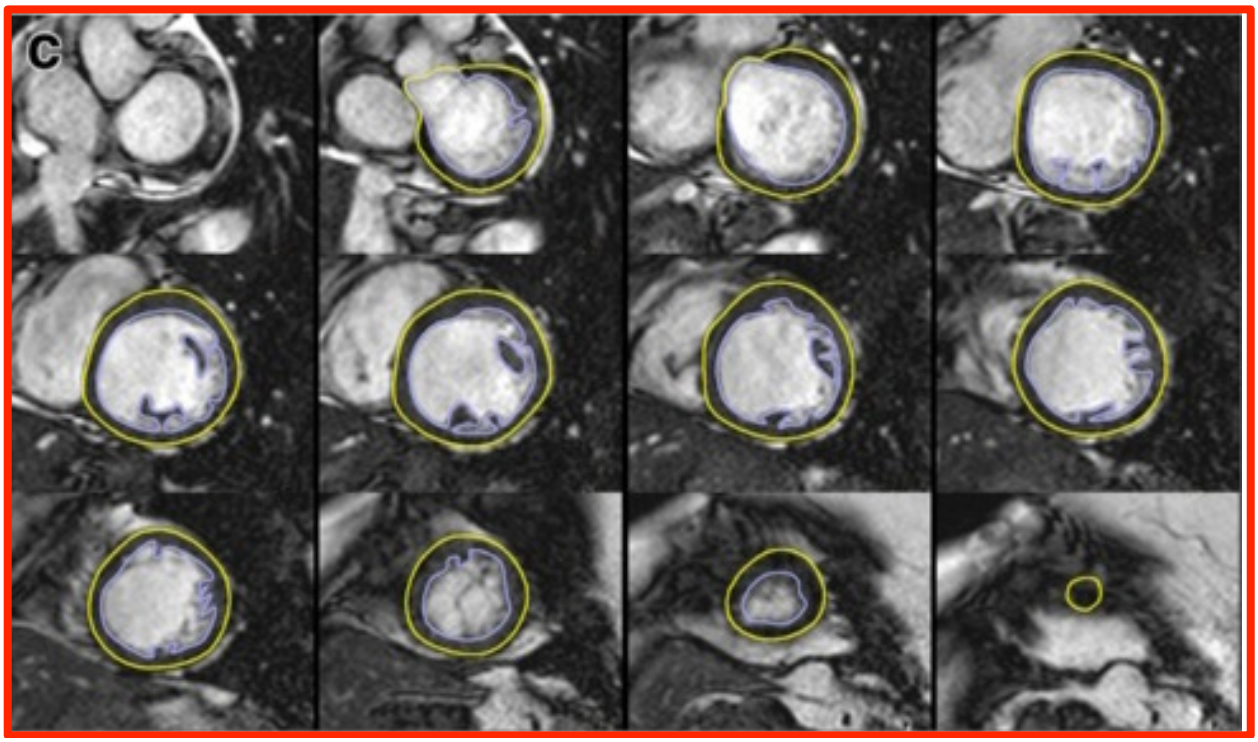
3.3 Left and Right Ventricular Volume and Mass Quantification

(adapted from Schulz-Menger et al. Journal of Cardiovascular Magnetic Resonance 2013, 15:35)

- For each study, LV and RV volumes and LV mass are to be contoured by the same one individual.
- If no intra- or extracardiac shunts are present, the RV and LV stroke volumes should be nearly equal (small differences are seen as a result of bronchial artery supply). Since the LV stroke volume is more reliably determined than the RV stroke volume, the LV data can be used to validate RV data.
- The dedicated LV short axis cine stack is to be contoured for both LV AND RV quantification.
- Manual contouring performed in cvi42 using the Bezier tool is the suggested method of analysis; the fully automated contour detection option is to be avoided.
- For the purposes of facilitating consistency of standards across different sites, a control sample of 5 cases will all be analysed by each of the three readers quantifying LV and RV parameters. These will then be surveyed by the PI to help provide feedback on technique and assist in answering any outstanding queries.

3.3.1 The Left Ventricle

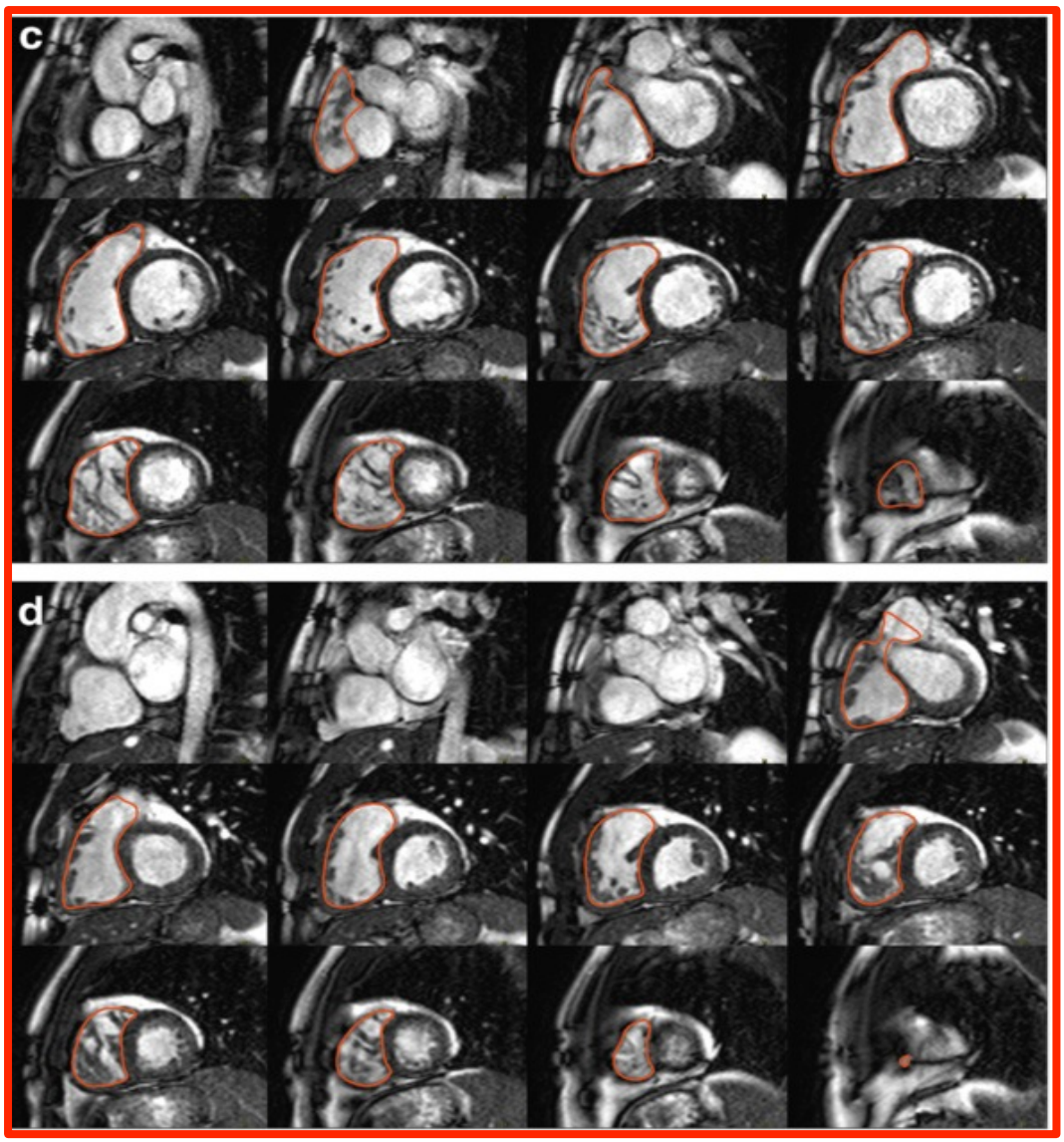
- The LV end-diastolic and end-systolic image should be chosen as the images with the largest and smallest LV blood volumes respectively. (For their identification, the full image stack should be evaluated)
- Deviations may occur and extra care should be taken in the setting of LV dyssynchrony or severe mitral regurgitation. Aortic valve closure defines end-systole.
- If a slice is uninterpretable (e.g. degraded by triggering/breathing artefact) it should be excluded from systolic and diastolic measurements of both the LV and RV.
- The LV outflow tract is included as part of the LV blood volume. When aortic valve cusps are identified on the basal slice(s) the contour is drawn to include the outflow tract to the level of the aortic valve cusps.
- Care must be taken with the one or two most basal slices. A slice that contains blood volume at end-diastole may include only left atrium (LA) without LV blood volume at end-systole. The LA can be identified when less than 50% of the blood volume is surrounded by myocardium and the blood volume cavity is seen to be expanding during systole.
- Papillary muscles are to be EXCLUDED from the LV cavity for the purpose of analysis and included within the LV mass (thus DO require specific delineation).
- Epicardial borders should be drawn on the middle of the chemical shift artifact line (when present).
- Absolute LV mass is derived from diastolic epicardial and endocardial delineation; systolic epicardial contours are NOT required.
- Maximal LV Wall Thickness is measured as the thickest portion of the interventricular septum in short axis at end diastole (mm)
- When the most basal slice contains only a small crescent of basal lateral myocardium and no discernible ventricular blood pool, an epicardial contour for the visible myocardium is included for LV mass only.
- Similarly, when the most apical slice contains only a circle of myocardium without cavitary blood pool, an epicardial contour without an endocardial contour should be drawn for LV mass calculations



Left ventricular (LV) chamber quantification. For LV chamber quantification, the endocardial (blue) and epicardial (yellow) contours are delineated in diastole in a stack of short axis slices that cover the whole left ventricle. c) illustrates the approach with EXclusion of the papillary muscles as part of the LV volume.

3.3.2 The Right Ventricle

- As for the LV, it may be necessary to review all image slices in the stack to define end-diastole and end-systole for the RV.
- Trabeculations of the RV are ignored and a smooth endocardial border is drawn to improve reader reproducibility (RV trabeculae and papillary muscles are typically included in RV volumes).
- Again, if no intra- or extracardiac shunts are present, the RV and LV stroke volumes should be nearly equal (small differences are seen as a result of bronchial artery supply).
- Since the LV stroke volume is more reliably determined than the RV stroke volume, the LV data can be used to validate RV data.
- The pulmonary valve may be visualized, and contours are included just up to, but not superior to this level.



Right ventricular (RV) chamber quantification. For RV volume quantification, the endocardial (red) contours are delineated in diastole (top) and systole (bottom) or short-axis (c and d) slices that cover the whole RV.

3.4 Aortic Valve haemodynamic assessment from quantification of VENC images

(adapted from Schulz-Menger et al. Journal of Cardiovascular Magnetic Resonance 2013, 15:35)

- Phase and magnitude images are analysed in the Flow module of cvi42 software.
- The dedicated aortic valve short axis cine (typically 8 slices) is viewed in the viewer module to determine the anatomic aortic valve orifice by 2D valve planimetry in peak systole when the opening of the aortic valve is widest. This is done by manually tracing the inner leaflet edges of the aortic valve cusps at the time of maximal opening; recording the average of three consecutive AVA measurements.
- Images are windowed to the appropriate brightness and contrast so that the borders of the ROI are sharp.

- Through-plane phase contrast images are examined to ensure the quality is sufficient and that the VENC chosen was appropriate.
- The borders of the vessel of interest are traced on each phase and magnitude image so that only the cavity of the vessel is included ensuring noise outside the vessel is not included
- Checks are made that this is performed correctly on the magnitude images (as always the phase images contain the encoded information)
- Where a number of phase contrast sequences have been acquired, the highest value for peak flow velocity and forward flow volumes should be recorded. Regurgitant fraction should be derived from non breath held images.

Pitfalls:
- On the phase images, the area of flow may be slightly larger than the area of the magnitude images.
- If aliased the sequence should be disregarded and another analysed.
- The use of software correction to analyse aliased images is to be avoided.
- In general, the area that exceeds the VENC in the ROI is in the centre of the vessel and not at the edges; if at the edges, it is usually (but not always) outside the vessel.

3.5 Late Gadolinium Enhancement Quantification

- All images are to be quantified using CVI 42.
- Manual epi and epdocardial quantification are performed from the dedicated LV volume short axis cine stack in end diastole in order to quantify LV mass (papillary muscles were excluded).
- The short axis LV stack acquired 10-15 minutes following Gadolinium (Doteram 0.2mmol/kg) contrast administration is used for the purposes of late gadolinium quantification.
- Each slice is visually inspected by 2 doctors experienced in MRI analysis for the presence or absence of gadolinium enhancement.
- Phase swap and other geometry images were used in order to assist in decision making where required.
- In only those slices deemed to have LGE present, epi and endocardial contours were manually drawn, with care take to exclude artefact, blood pool, fat and pericardium.
- The auto-identification tool was then applied and an area of normal remote myocardium defined alongside identification of areas with increased signal intensity.
- Any hyperintense regions felt to be related to artefact are manually excluded.
- The 2SD, 5SD and full width half max techniques are used to determined LGE mass.

NB: There was no significant difference in association of the different LGE quantification techniques. Previous reports showed that the FWHM technique was the most reproducible for infarct and non-infarct LGE (Flett et al. Circulation Cardiovascular Imaging 2011), thus we chose this *a priori* as the technique for our analysis.

4. Supplementary Tables:

4.1 TABLE S1: FOLLOW-UP AND MORTALITY

	All patients (n = 674)	All TAVR (n=275)	All SAVR (n=399)	P VALUE
Follow-up				
Follow-up duration post CMR date (days)	1515 ± 847	1190 ± 692	1740 ± 872	**<0.0001**
Mortality				
30-day mortality post intervention (%)	12 (1.8)	7 (2.6)	5 (1.3)	0.570
1-year mortality post intervention (%)	42 (6.2)	30 (10.9)	12 (3.0)	**<0.0001**
All – Cause Death, No. post CMR (%)	145 (21.5)	93 (33.8)	52 (13.0)	**<0.0001**
CV Death, No. post CMR (%)	70 (10.4)	51 (18.5)	19 (4.8)	**<0.0001**

4.2 TABLE S2: UNIVARIATE PARAMETERS – Surgical Aortic Valve Replacement.

Parameter	ALL SAVR (n=399)				ALL SAVR (n=399)			
	All Cause Mortality (n=52)				Cardiovascular Mortality (n=19)			
	HR	Z	P value	95% CI	HR	Z	P value	95% CI
Baseline Demographics								
Age	1.60	3.22	**0.001**	1.20 – 2.14	1.64	2.01	**0.044**	1.01 – 2.64
Male gender	0.99	-0.04	0.966	0.54 - 1.80	0.55	-1.27	0.205	0.22 – 1.38
BMI	1.02	0.76	0.447	0.97 - 1.08	1.07	1.40	0.163	0.97 – 1.17
Atrial Fibrillation	2.38	2.24	**0.025**	1.11 - 5.09	5.03	3.06	**0.002**	1.79 – 14.15
Diabetes Mellitus	1.61	1.59	0.112	0.89 - 2.91	2.22	1.67	0.095	0.87 – 5.64
Hypertension	1.73	1.81	0.070	0.96 - 3.12	1.10	0.20	0.846	0.44 – 2.74
Bicuspid AoV	0.51	-2.00	**0.046**	0.27 - 0.99	0.63	-0.90	0.369	0.23 – 1.74
Previous CAD	1.69	1.71	0.088	0.93 - 3.09	1.89	1.29	0.197	0.72 - 4.98
Previous PCI or CABG	0.71	-0.66	0.510	0.25 - 1.99	/	/	0.998	0 >inf
Previous MI	0.77	-0.50	0.616	0.28 - 2.15	1.23	0.20	0.842	1.16 – 9.25
Baseline Medications								
ACE inhibitor or ARB	1.41	1.22	0.223	0.81 - 2.46	1.61	1.03	0.304	0.65 - 3.95
β-blocker	0.85	-0.53	0.594	0.46 - 1.55	1.48	0.84	0.400	0.59 - 3.69
Aldosterone Antagonist	0.75	-0.40	0.692	0.17 - 3.19	1.04	0.04	0.971	0.13 - 8.28
Statin	1.47	1.20	0.231	0.78 - 2.75	2.32	1.49	0.138	0.76 – 7.06
STS score	1.15	1.74	0.083	0.98 - 1.34	1.19	1.57	0.115	0.96 – 1.48
Euroscore	1.03	0.57	0.569	0.93 - 1.13	1.04	0.44	0.662	0.88 – 1.22
Echo Data								
Mean AoV gradient	1.00	-0.12	0.908	0.98 - 1.02	0.99	-0.59	0.553	0.95 – 1.03
Peak AoV gradient	1.00	0.001	0.999	0.99 - 1.01	0.99	-0.41	0.682	0.97 – 1.02
AoV area	0.74	-0.45	0.654	0.20 - 2.79	0.26	-1.16	0.247	0.03 – 2.57
AoV area Indexed to BSA	0.66	-0.32	0.751	0.05 - 8.25	0.08	-1.11	0.269	0.001 - 6.81
Estimated PA pressure								
Moderate	1.42	0.70	0.487	0.53 - 3.78	1.94	0.81	0.417	0.39 – 9.63
Severe	5.27	2.67	**0.007**	1.55 - 17.88	12.8	3.06	**0.002**	2.50 – 65.90
CMR data								
LV end diastolic volume index	1.00	-0.28	0.780	0.99 - 1.01	1.00	-0.39	0.696	0.98 – 1.02
Indexed LV Stroke Volume	0.98	-1.48	0.140	0.96 - 1.01	0.96	-1.96	0.051	0.92 – 1.00
LV Ejection Fraction	0.99	-1.11	0.267	0.97 - 1.01	0.98	-1.27	0.205	0.95 – 1.01
Maximal LV wall thickness	0.99	-0.12	0.902	0.90 - 1.09	1.05	0.61	0.539	0.90 – 1.23
Indexed LV mass	1.00	-0.15	0.878	0.99 - 1.01	1.00	-0.15	0.883	0.98 – 1.02
RV end diastolic volume index	0.98	-2.20	**0.028**	0.96 - 1.00	0.96	-2.21	**0.027**	0.93 – 1.00
RV Ejection Fraction	1.00	-0.03	0.973	0.97 - 1.03	1.01	0.35	0.728	0.96 – 1.06
Indexed LA volume	1.01	1.38	0.167	1.00 - 1.03	1.02	1.92	0.056	1.00 – 1.04
CMR AoV regurgitant fraction	0.97	-1.84	0.066	0.93 - 1.00	0.96	-1.19	0.233	0.90 – 1.03
Valvulo-Arterial Impedance	1.04	0.23	0.817	0.77 - 1.40	0.98	-0.08	0.938	0.58 – 1.65
Late gadolinium enhacement (LGE)								
LGE presence / absence	2.05	2.25	**0.025**	1.09 - 3.84	2.42	1.68	0.093	0.86 – 6.80
LGE pattern								
Non-infarct pattern	2.11	2.22	**0.027**	1.08 - 4.06	2.03	1.24	0.214	0.66 – 6.21
Infarct pattern	1.90	1.45	0.147	0.80 - 4.54	3.52	1.99	**0.047**	1.02 – 12.15
LGE mass, per 1% increase	1.05	1.21	0.226	0.97 - 1.13	1.07	1.24	0.214	0.96 – 1.18

Abbreviations: SAVR, surgical aortic valve replacement; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; MI, myocardial infarction; ARB, angiotensin receptor blocker; AVA, aortic valve area; PASP, pulmonary artery systolic pressure, LV, left ventricle; RV, right ventricle; LGE, late gadolinium enhancement.

3.3 TABLE S3: UNIVARIATE PARAMETERS – Transcatheter Aortic Valve Replacement.

Parameter	TAVR (n=275)				TAVR (n=275)			
	All Cause Mortality (n=93)				Cardiovascular Mortality (n=51)			
	HR	Z	P value	95% CI	HR	Z	P value	95% CI
Baseline Demographics								
Age*	1.43	2.55	**0.011**	1.09 – 1.89	1.65	2.54	**0.011**	1.12 – 2.42
Male Gender	0.94	-0.32	0.751	0.62 – 1.41	0.83	-0.65	0.513	0.48 – 1.44
BMI	0.97	-1.55	0.122	0.93 – 1.01	0.96	-1.59	0.113	0.91 – 1.01
Atrial Fibrillation	1.47	1.61	0.107	0.92 – 2.35	1.68	1.67	0.096	0.91 – 3.07
Diabetes Mellitus	1.07	0.27	0.785	0.67 – 1.70	1.53	1.46	0.144	0.86 – 2.73
Hypertension	1.20	0.87	0.386	0.80 – 1.81	1.34	1.04	0.301	0.77 – 2.32
Bicuspid AoV	0.30	-1.70	0.089	0.07 – 1.20	0.24	-1.43	0.154	0.03 – 1.72
Previous CAD	1.10	0.43	0.671	0.72 – 1.66	1.25	0.77	0.442	0.71 - 2.18
Previous PCI or CABG	1.01	0.04	0.968	0.65 - 1.58	1.19	0.59	0.558	0.67 – 2.11
Previous MI	1.10	0.33	0.745	0.61 – 1.99	0.89	-0.31	0.758	0.42 – 1.89
Baseline Medications								
ACE inhibitor or ARB	1.06	0.24	0.810	0.67 - 1.66	1.01	0.031	0.975	0.56 - 1.82
β-blocker	1.24	1.01	0.311	0.82 - 1.86	1.27	0.85	0.394	0.73 - 2.21
Aldosterone Antagonist	0.60	-1.11	0.266	0.24 - 1.48	0.99	-0.03	0.980	0.39 - 2.50
Statin	0.90	-0.49	0.621	0.59 - 1.38	0.90	-0.36	0.719	0.51 - 1.60
STS score	1.10	3.36	**<0.001**	1.04 – 1.16	1.12	3.37	**<0.001**	1.05 – 1.20
Euroscore	1.04	1.67	0.095	0.99 – 1.10	1.07	2.23	**0.026**	1.01 – 1.13
Echo Data								
Mean AoV gradient	1.00	0.00	1.000	0.98 – 1.01	0.99	-0.98	0.329	0.96 – 1.01
Peak AoV gradient	1.00	-0.53	0.595	0.99 – 1.01	0.99	-1.23	0.218	0.97 – 1.01
AoV area	0.99	-0.01	0.988	0.25 – 3.97	1.34	0.31	0.754	0.21 – 8.60
AoV area Indexed to BSA	1.94	0.52	0.600	0.16- 23.35	5.93	1.08	0.282	0.23 - 151.6
Estimated PA pressure								
Moderate	1.74	1.64	0.102	0.90 – 3.38	1.91	1.41	0.160	0.77 – 4.72
Severe	2.40	1.95	**0.052**	0.99 – 5.77	2.98	1.94	**0.053**	0.99 – 9.00
CMR data								
LV end diastolic volume index	1.00	-0.02	0.983	0.99 – 1.01	1.00	0.05	0.961	0.99 – 1.01
Indexed LV Stroke Volume	0.97	-3.52	**<0.001**	0.95 – 0.98	0.96	-2.97	**0.003**	0.94 – 0.99
LV Ejection Fraction	0.98	-3.03	**0.002**	0.97 – 0.99	0.97	-3.32	**<0.001**	0.95 – 0.99
Maximal LV wall thickness	0.97	-0.70	0.485	0.91 – 1.05	0.96	-0.76	0.446	0.87 – 1.06
Indexed LV mass	1.00	0.57	0.567	0.99 – 1.01	1.00	0.75	0.456	0.99 – 1.02
RV end diastolic volume index	1.00	-0.30	0.764	0.99 _ 1.01	1.00	0.17	0.867	0.99 – 1.02
RV Ejection Fraction	0.97	-3.29	**<0.001**	0.96 – 0.99	0.96	-3.52	**<0.001**	0.94 – 0.98
Indexed LA volume	1.00	0.95	0.341	1.00 – 1.01	1.01	1.23	0.218	1.00 – 1.02
CMR AoV regurgitant fraction	1.00	-0.37	0.709	0.98 – 1.02	0.98	-1.09	0.277	0.96 – 1.01
Valvulo-Arterial Impedance	1.08	0.74	0.457	0.89 – 1.31	1.11	0.77	0.440	0.85 – 1.45
Late gadolinium enhancement (LGE)								
LGE presence / absence	2.21	3.09	**0.002**	1.34 – 3.66	3.45	3.17	**0.001**	1.60 – 7.40
LGE pattern								
Non-infarct pattern	2.37	3.04	**0.002**	1.36 – 4.13	3.46	2.96	**0.003**	1.52 – 7.88
Infarct pattern	2.05	2.44	**0.015**	1.15 – 3.66	3.43	2.89	**0.004**	1.49 – 7.90
LGE mass, per 1% increase	1.07	3.36	**<0.001**	1.03 – 1.11	1.07	2.89	**0.004**	1.02 – 1.12

*Using age variable scaled by epochs of 10.

Abbreviations: TAVR, transcatheter aortic valve replacement; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; MI, myocardial infarction; ARB, angiotensin receptor blocker; AVA, aortic valve area; PASP, pulmonary artery systolic pressure, LV, left ventricle; RV, right ventricle; LGE, late gadolinium enhancement.

3.4 TABLE S4: MULTI-VARIABLE MODEL – all cause mortality (SAVR Patients).

MULTIVARIABLE ANALYSIS TABLE FOR SAVR PATIENTS (LGE Present/Absent)

	ALL SAVR n=399					ALL SAVR n=399			
	ALL CAUSE MORTALITY (n = 52)					Cardiovascular MORTALITY (n = 19)			
Parameter	**HR**	**Z**	**P value**	**95% CI**	**Parameter**	**HR**	**Z**	**P value**	**95% CI**
Baseline Age*	1.53	2.48	**0.013**	1.09 - 2.14	Baseline Age	1.26	0.88	0.377	0.75 - 2.11
Atrial Fibrillation	2.79	2.36	**0.019**	1.19 - 6.57	Atrial Fibrillation	5.60	2.91	**0.004**	1.75 - 17.91
Indexed RV EDV	0.99	-0.79	0.428	0.97 - 1.01	Indexed RV EDV	0.98	-1.12	0.261	0.94 - 1.02
LGE Presence	2.14	2.25	**0.025**	1.10 - 4.15	LGE Presence	1.97	1.24	0.215	0.67 - 5.78

*Using age variable scaled by epochs of 10.

Abbreviations: EDV, end-diastolic volume; LGE, late gadolinium enhancement; RV, right ventricle; SAVR, surgical aortic valve replacement.

3.5 TABLE S5: MULTI-VARIABLE MODEL – All Cause Mortality (TAVR Patients).

MULTIVARIABLE ANALYSIS TABLE FOR TAVR PATIENTS (LGE Present/Absent)

	TAVR n=275					TAVR n=275			
	ALL CAUSE MORTALITY (n = 93)					Cardiovascular MORTALITY (n = 51)			
Parameter	**HR**	**Z**	**P value**	**95% CI**	**Parameter**	**HR**	**Z**	**P value**	**95% CI**
Baseline Age*	1.76	3.61	**<0.001**	1.29 - 2.38	Baseline Age	2.09	3.55	**<0.001**	1.39 - 3.15
CMR LV EF	1.00	-0.20	0.842	0.98 - 1.02	CMR LV EF	0.99	-0.78	0.437	0.97 - 1.02
CMR RV EF	0.98	-1.63	0.103	0.96 - 1.00	CMR RV EF	0.98	-1.49	0.136	0.95 - 1.01
LGE Presence	2.38	3.18	**0.001**	1.40 - 4.06	LGE Presence	3.47	3.09	**0.002**	1.58 - 7.65

*Using age variable scaled by epochs of 10.

Abbreviations: LGE, late gadolinium enhancement; LV, left ventricle; RV, right ventricle; TAVR, transcatheter aortic valve replacement.

3.6 Table S6: MULTI-VARIABLE MODEL – ALL CAUSE MORTALITY: incorporating Pulmonary Artery Systolic Pressure (PASP).

	ALL PATIENTS (n=674)			
	ALL CAUSE MORTALITY (n= 145)			
Parameter	**HR**	**Z**	**P value**	**95% CI**
Age*	2.00	4.60	**<0.0001**	1.49 - 2.70
LGE Presence	1.92	2.20	**0.028**	1.07 - 3.43
LV ejection fraction	0.99	-0.75	0.451	0.97 - 1.01
Atrial fibrillation	1.31	0.74	0.457	0.65 - 2.65
CAD	0.81	-0.71	0.481	0.45 - 1.45
AVA (by echo)	1.00	0.001	0.999	0.31 - 3.24
LV maximal wall thickness	0.96	-0.84	0.398	0.88 - 1.05
RV ejection fraction	1.02	1.15	0.250	0.99 - 1.05
Estimated PA pressure				
Moderate	1.77	1.77	0.077	0.94 - 3.32
Severe	2.73	2.42	**0.016**	1.21 - 6.17

*Using age variable scaled by epochs of 10.
Abbreviations: AVA, aortic valve area; CAD, coronary artery disease; LGE, late gadolinium enhancement; LV, left ventricle.

3.7 Table S7: MULTI-VARIABLE MODEL – ALL CAUSE MORTALITY: incorporating coronary revascularization (previous CABG/PCI) instead of CAD.

	ALL PATIENTS (n=674)			
	ALL CAUSE MORTALITY (n= 145)			
Parameter	**HR**	**Z**	**P value**	**95% CI**
Age*	1.91	5,16	**<0.0001**	1.49 - 2.44
LGE Presence	2.30	3.16	**<0.002**	1.37 - 3.86
LV ejection fraction	0.99	-0.80	0.425	0.98 - 1.01
Atrial fibrillation	1.29	0.86	0.391	0.72 - 2.29
Prior PCI/CABG	1.17	0.63	0.529	0.71 - 1.92
AVA (by echo)	0.89	-0.24	0.814	0.33 - 2.41
LV maximal wall thickness	0.93	-1.83	0.068	0.86 - 1.01
RV ejection fraction	1.00	-0.21	0.833	0.98 - 1.02

*Using age variable scaled by epochs of 10.
Abbreviations: AVA, aortic valve area; CAD, coronary artery disease; LGE, late gadolinium enhancement; LV, left ventricle.

3.8 TABLE S8: MULTI-VARIABLE MODEL – percentage scar (All Patients).

MULTIVARIABLE ANALYSIS TABLE FOR ALL PATIENTS (LGE %)

	ALL PATIENTS (n=674)					ALL PATIENTS (n=674)			
	ALL CAUSE MORTALITY (n= 145)					Cardiovascular MORTALITY (n=70)			
Parameter	**HR**	**Z**	**P value**	**95% CI**	**Parameter**	**HR**	**Z**	**P value**	**95% CI**
Age*	2.06	5.56	**<0.0001**	1.60 – 2.66	Age*	2.04	4.56	**<0.0001**	1.05 - 1.13
Atrial Fibrillation	1.38	1.10	0.272	0.78 – 2.42	Male Gender	0.53	-2.42	**0.016**	0.24 - 0.76
Previous CAD	1.20	0.81	0.419	0.77 - 1.89	Atrial Fibrillation	1.57	1.52	0.129	0.46 - 1.94
CMR LV EF	0.99	-0.72	0.474	0.98 - 1.01	Previous CAD	1.48	1.47	0.141	0.86 - 2.83
Echo AVA	1.06	0.11	0.910	0.39 – 2.88	CMR LV EF	0.98	-2.86	0.004	0.96 - 1.00
CMR RV EF	1.00	-0.43	0.670	0.97 - 1.02	LGE mass, per 1% increase	1.08	3.20	**0.001**	1.01 - 1.17
CMR LV maximal wall thickness	0.94	-1.58	0.113	0.87 – 1.01					
LGE mass, per 1% increase	1.11	3.80	**<0.001**	1.05 - 1.17					

*Using age variable scaled by epochs of 10.
Abbreviations: AVA, aortic valve area; CAD, coronary artery disease; EF, ejection fraction; LGE, late gadolinium enhancement; LV, left ventricle; RV, right ventricle.

3.9 Table S9: MULTI-VARIABLE MODEL – ALL CAUSE MORTALITY: excluding the 12 patients with 30-day post intervention mortality.

	ALL PATIENTS (n=662)			
	ALL CAUSE MORTALITY (n= 133)			
Parameter	**HR**	**Z**	**P value**	**95% CI**
Age*	1.95	5.13	**<0.0001**	1.51 - 2.57
LGE Presence	2.46	3.22	**0.013**	1.42 - 4.27
LV ejection fraction	0.99	-0.88	0.378	0.98 - 1.01
Atrial fibrillation	1.19	0.56	0.573	0.65 - 2.20
CAD	1.15	0.59	0.553	0.72 - 1.86
AVA (by echo)	0.81	-0.39	0.699	0.28 - 2.33
LV maximal wall thickness	0.94	-1.56	0.119	0.86 - 1.02
RV ejection fraction	1.00	-0.27	0.788	0.97 - 1.02

*Using age variable scaled by epochs of 10.
Abbreviations: AVA, aortic valve area; CAD, coronary artery disease; LGE, late gadolinium enhancement; LV, left ventricle.

3.10 Table S10: MULTI-VARIABLE MODEL – ALL CAUSE MORTALITY: changing index date to time of intervention.

	ALL PATIENTS (n=662)			
	ALL CAUSE MORTALITY (n= 133)			
Parameter	**HR**	**Z**	**P value**	**95% CI**
Age*	1.93	5.28	**<0.0001**	1.51 - 2.47
LGE Presence	2.16	2.95	**0.003**	1.30 - 3.61
LV ejection fraction	0.99	-0.92	0.358	0.98 - 1.01
Atrial fibrillation	1.33	0.97	0.330	0.75 - 2.36
CAD	1.19	0.74	0.459	0.74 - 1.87
AVA (by echo)	1.01	0.02	0.988	0.37 - 2.72
LV maximal wall thickness	0.93	-1.90	0.058	0.86 - 1.01
RV ejection fraction	1.00	0.01	0.989	0.98 - 1.02

*Using age variable scaled by epochs of 10.
Abbreviations: AVA, aortic valve area; CAD, coronary artery disease; LGE, late gadolinium enhancement; LV, left ventricle.