SUPPLEMENTAL MATERIAL

Data S1. Supplemental Methods

LGE-CMR imaging

Acquisition protocol: Images were obtained with a 3.0 Tesla CMR (Magnetom Prisma Siemens Healthcare, Germany) and a dedicated 32-channel cardiac coil. LGE-CMR scans were acquired 20 min after an intravenous bolus injection of 0.2 mmol/kg gadobutrol (Gadovist, Bayer Hispania) using a free-breathing 3D navigator and ECG-gated inversion-recovery gradient-eco sequence applied in the axial orientation. The voxel size was 1.25x1.25x2.5 mm. Repetition time/echo time was 2.3/1.4 ms; flip angle, 11º; bandwidth, 460 Hz/pixel; inversion time (TI) 280 to 380 ms; and parallel imaging with GRAPPA technique, with reference lines of R=2 and 72. A TI scout sequence was used to nullify the left ventricular myocardial signal and determine optimal TI. Typical scan time for LGE-CMR sequence was 15 minutes (11-18), depending on heart rate and breathing patterns.

Post-processing: RA and LA segmentation was performed using ADAS 3D software (Barcelona, Spain). Atrial contours of the wall were manually drawn by two expert operators in each axial plane of the LGE-CMR, without invading the interatrial common septum, and a tridimensional model was constructed. ADAS automatically builds a 3D shell. Subsequently, pulmonary veins at the ostium level, mitral valve plane and left appendage were excluded in the LA, and the superior and inferior vena cava at the ostium level, tricuspid valve plane and coronary sinus were excluded in the RA.

Signal intensity was internally (within each patient) normalized to blood pool intensity to provide an absolute signal intensity value that would allow comparisons between patients. The LA blood pool was automatically identified by the software. It was chosen both for LA and RA wall normalization because it was found to be less

variable than the RA blood pool. Image Intensity Ratio (IIR) was calculated as the ratio between the signal intensity of each single pixel and the mean blood pool intensity for each patient. Each IIR value was colour-coded as healthy (IIR<1.20), interstitial fibrosis (1.20≤IIR≤1.32) and dense scar (IIR≥1.32) using previously standardized thresholds for the LA.[11] Dense scar threshold was defined as those fibrotic patches that were predicted conduction block in re-do procedures. Interstitial fibrosis was defined as atrial tissue with IIR lying between the normality-fibrosis boundary (average IIR + 2SDs in a healthy volunteer cohort) and the dense scar threshold.[11] Of note, however, formal histological validation is missing.

Sphericity assessment: Sphericity evaluates the variation between the chamber and the sphere that best fitted its shape. The radius of such sphere is calculated as the mean of distances between all points of the atrium wall and the center of mass (average radius-AR). Finally, the coefficient of variation of the sphere (CVS = AR standard deviation/AR) was obtained to define the atrium sphericity [(1- CVS)*100]. A comprehensive technical description of the method is provided in its original description[13] and its Supplemental Methods (https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1111%2Fjce.12116&file=jce12116-sup-0001-S1.doc). The final sphericity number is a unitless value which may potentially be from 0 to 100 (a perfect sphere), but common values in the LA range from 70 to 90.[13] No previous data are available for the RA.

Table S1. Correlation between RA and LA remodeling parameters for total population and by subgroups.

	Overall		Healthy volunteers		Paroxysmal AF		Persistent AF	
RA / LA correlation	**R Pearson**	**P**	**R Pearson**	**P**	**R Pearson**	**P**	**R Pearson**	P
Volume (mL)	0.695	<0.0001	0.457	0.25	0.426	0.001	0.581	<0.0001
Surface (cm^2)	0.725	<0.0001	0.473	0.2	0.600	<0.0001	0.547	<0.0001
Total fibrosis (%)	0.589	<0.0001	0.837	0.005	0.468	<0.0001	0.679	<0.0001
Interstitial fibrosis (%)	0.463	<0.0001	0.713	0.031	0.460	<0.0001	0.450	0.002
Dense scar (%)	0.638	<0.0001	0.67	0.054	0.406	0.002	0.784	<0.0001
Sphericity	-0.010	0.92	0.12	0.75	-0.050	0.72	-0.222	0.14

*Abbreviations: AF: atrial fibrillation; LA: left atrium; RA: right atrium

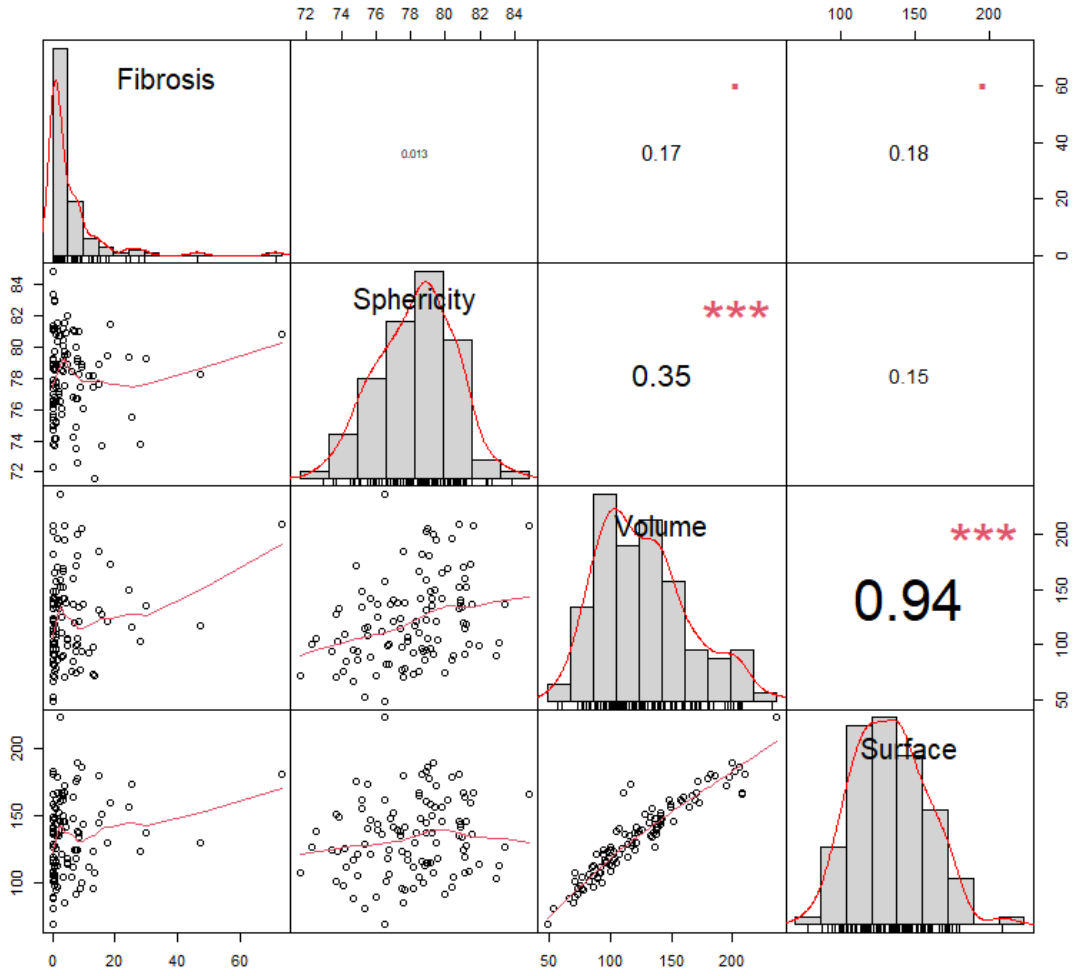
Table S2. Prediction models of RA remodeling - total fibrosis (%), area (cm2) and sphericity- between clinical, electrocardiographic, and echocardiographic parameters, using univariate and multivariate linear regression analysis.

	Univariate			*Multivariate*		
	Beta	**95% CI**	**p**	**Beta**	**95% CI**	**p**
RA FIBROSIS (%)						
Age	0.05	-0.08 to 0.18	0.45			
Female sex	-0.34	-3.36 to 2.67	0.82			
Bundle branch block	**4.13**	**-0.19 to 8.44**	**0.006**			
QRS	-0.04	-0.10 to 0.03	0.293			
PR	-0.03	-0.08 to 0.01	0.12			
BMI	0.19	-0.05 to 0.42	0.12			
Hypertension	-0.05	-2.81 to 2.70	0.97			
Diabetes	**7.71**	**2.92 to 12.5**	**0.002**	**7.70**	**2.81 to 12.5**	**0.002**
Sleep apnea	1.83	-2.53 to 6.18	0.41			
Atrial Flutter	0.35	-4.02 to 4.72	0.87			
AF pattern	0.08	-2.68 to 2.84	0.96			
LVEF	0.04	-0.15 to 0.22	0.71			
LA diameter	0.16	-0.08 to 0.40	0.19			
TR ≥ moderate	3.52	-0.65 to 7.68	0.10			
RA AREA (cm^2)						
Age	0.01	-0.48 to 0.52	0.96			
Female sex	**-12.57**	**-23.7 to -1.4**	**0.028**	**-14.95**	**-24.9 to -4.94**	**0.004**
Bundle branch block	5.10	-11.6 to -21.8	0.545			
QRS (ms)	-0.01	-0.27 to 0.25	0.92			
PR (ms)	**0.13**	**-0.03 to 0.29**	**0.11**	**0.15**	**0.011 to 0.28**	**0.034**
BMI	0.43	-0.46 to 1.32	0.34			
Hypertension	-3.32	-13.83 to 7.19	0.53			
Diabetes	-3.25	-21.6 to 15.1	0.73			
Sleep apnea	8.57	-8.12 to 25.25	0.31			
Atrial flutter	-3.61	-20.4 to 13.2	0.67			
AF pattern	**27.77**	**18.8 to 36.7**	**<0.0001**	**26.3**	**17.4 to 35.2**	**<0.0001**
LVEF	**-0.801**	**-1.49 to 0.11**	**0.02**			
LA diameter	**1.37**	**0.49 to 2.26**	**0.003**			
TR ≥ moderate	**13.17**	**-2.82 to 29.2**	**0.11**	**12.9**	**-1.11 to 26.9**	**0.07**
RA SPHERICITY						
Age	-0.021	-0.07 to 0.03	0.41			

Female sex	0.534	-0.63 to 1.70	0.36			
Bundle branch block	0.163	-1.53 to 1.86	0.85			
QRS (ms)	-0.003	-0.03 to 0.02	0.85			
PR (ms)	<0.001	-0.02 to 0.02	0.96			
BMI	0.026	-0.07 to 0.12	0.57			
Hypertension	-0.50	-1.56 to 0.57	0.36			
Diabetes	-1.30	-3.15 to 0.55	0.17			
Sleep apnea	-0.14	-1.85 to 1.57	0.87			
Atrial Flutter	0.10	-1.61 to 1.81	0.91			
AF pattern	0.85	-0.21 to 1.92	0.11			
LVEF	-0.05	-0.12 to 0.02	0.17			
LA diameter	-0.03	-0.12 to 0.07	0.59			
TR ≥ moderate	**1.55**	**-0.06 to 3.17**	**0.06**	**1.47**	**-0.17 to 3.10**	**0.08**

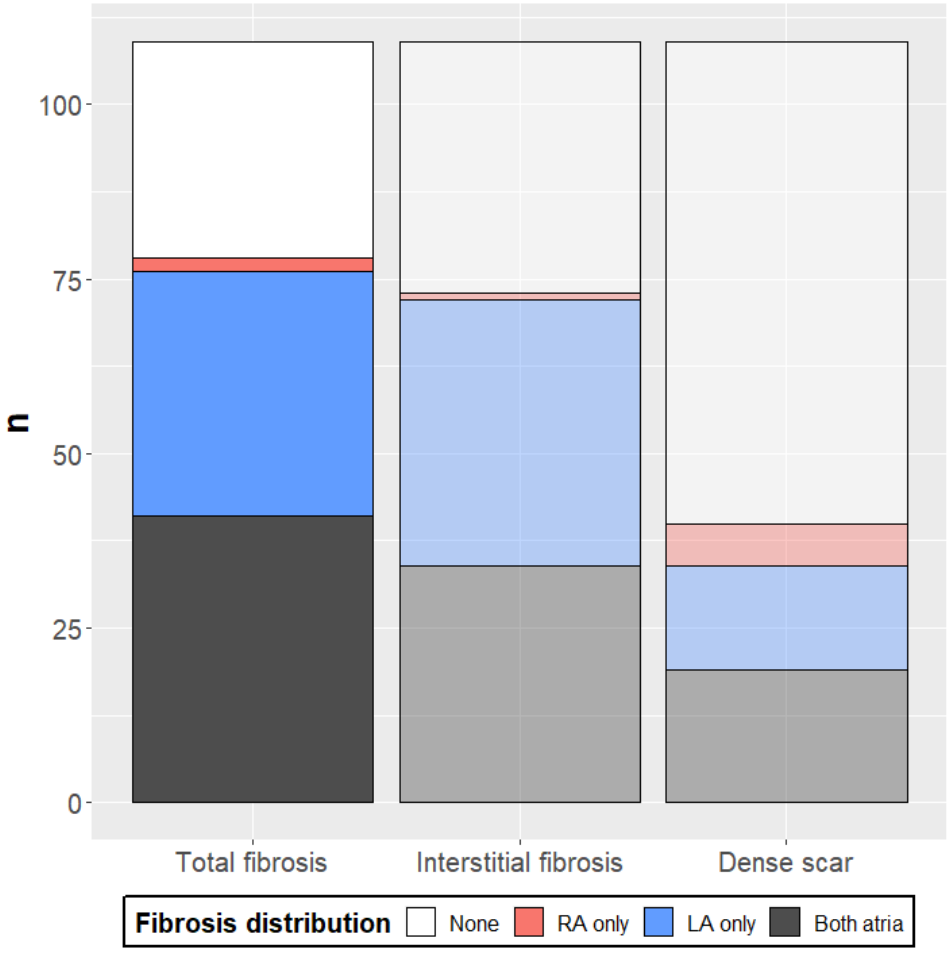
*Abbreviations: AF: atrial fibrillation; BMI: body mass index; LA: left atrium; LVEF: left ventricular ejection fraction; RA: right atrium; TR: tricuspid regurgitation

Figure S1. Correlation between RA remodeling parameters.



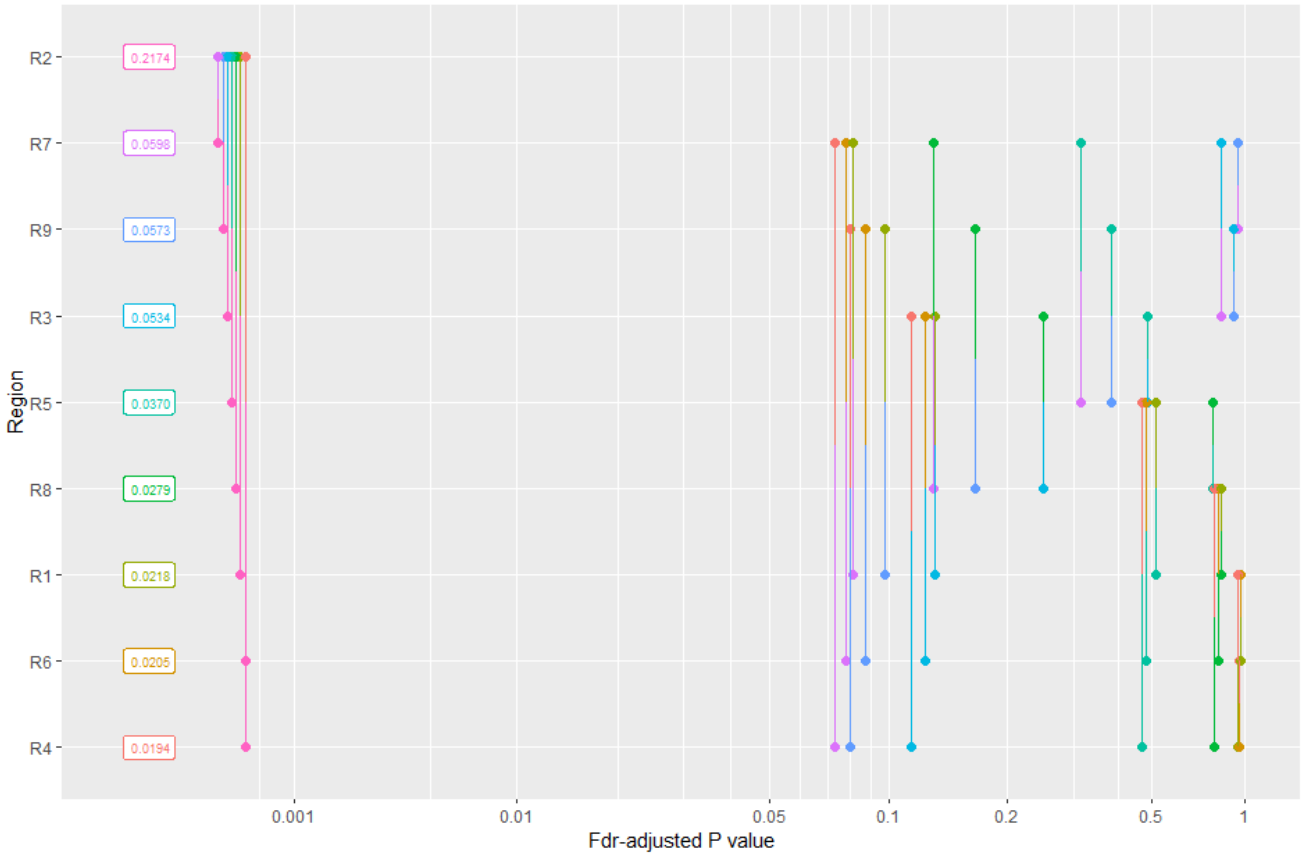
The diagonal cells show the distribution of each fibrosis, sphericity, volume, and surface. In the lower-left corner, their bivariate scatter plot is shown in the intersection cell. In the upper-right corner, the magnitude of their correlation (Pearson coefficient) is shown in number, and the significance in asterisks (***p<0.001; • 0.10<p<0.05; no sign means p>0.1).

Figure S2. Bar chart representing percentage of AF patients with fibrosis in RA and LA (total fibrosis and breakdown by type of fibrosis).



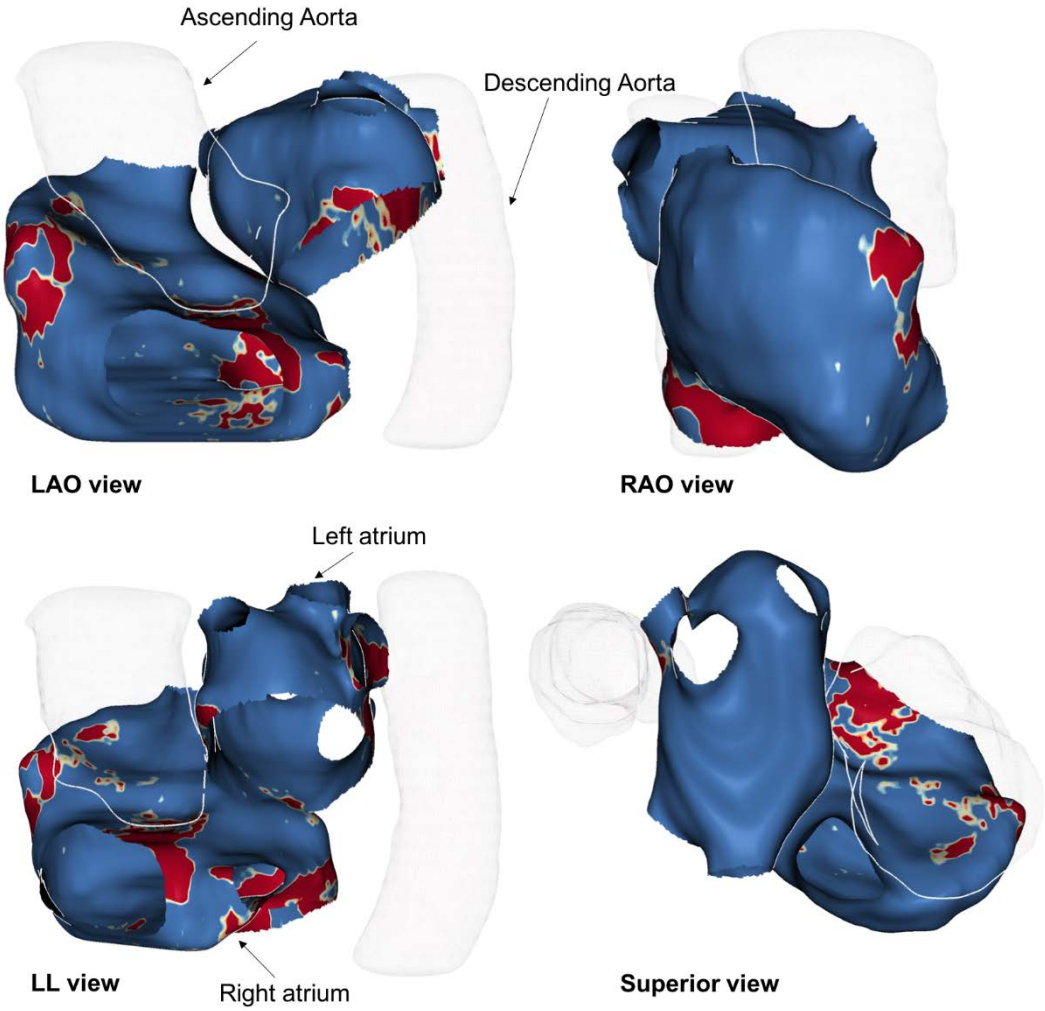
*LA: left atrium; RA: right atrium

Figure S3. Pairwise comparisons of atrial fibrosis burden for each of the RA regions.



Each region is plotted in the Y-axis (top to low: higher to lower fibrosis burden, labels). Segments linking two regions are plotted in the X-axis value corresponding to the fdr-adjusted p-value of their pairwise comparison.

Figure S4. Anatomical relationship between right and left atria and ascending and descending aorta.



3D shells postprocessed together.

*LAO: left anterior oblique; LL: left lateral; RAO: right anterior oblique