CARDIOVASCULAR MEDICINE

Left ventricular myocardial mass determination by contrast enhanced colour Doppler compared with magnetic resonance imaging

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Objective: To assess the feasibility of using contrast enhanced colour Doppler echocardiography to determine left ventricular (LV) mass and to compare its accuracy with LV mass obtained by magnetic resonance imaging (MRI).
Methods: Images were acquired in the short axis plane of the heart, derived from coronal and sagittal scout views and double oblique angulation. The LV mass was calculated by two methods: Simpson's rule and the area–length method. Levovist (Schering AG, Berlin, Germany) 2.5 g was given by slow intravenous bolus or infusion over about 45 seconds for contrast imaging. LV images were captured in the apical two chamber, four chamber, and three chamber views. Each contrast harmonic colour Doppler image was converted to a cavity-only image by simple image mathematics.
Results: 27 (77.1%) of the patients (mean (SD) age 66.2 (8.9) years) were men. There was a mean (SD) interval of 6.6 (8.6) days (range 0–27 days) between echocardiography and MRI. The mean (SD) LV mass determined by MRI Simpson's rule method was 171.0 (52.4) g (range 105.1–318.7 g). The mean LV mass (SD) determined by the echocardiographic Simpson's rule method was 178.2 (47.0) g (range 112.6–307.6 g). The mean (SD) MRI area–length LV mass was 187.3 (64.5) g (range 109.0–393.6 g). The linear regression correlation between LV mass determined by MRI Simpson's and echocardiographic Simpson's methods was excellent ($y = 1.022x$, $R^2 = 0.986$) with a mean (SD) difference of 7.20 (20.9) g. The linear regression correlation between the MRI area–length LV mass and MRI Simpson's LV mass was excellent ($y = 1.101x$, $R^2 = 0.989$) with a mean (SD) difference of 16.3 (22.3) g.
Conclusions: LV mass may be obtained reliably by contrast enhanced colour Doppler and two dimensional echocardiography. The contrast Doppler method accurately determines LV mass with excellent agreement with the MRI technique.

I t is well known that patients with left ventricular (LV) hypertrophy have an increased incidence of cardiac events, including mortality, and that their treatment options are different from those for patients without this risk factor.[1–3] Echocardiographic imaging with single dimensional (M mode) and two dimensional techniques is the most widely available clinical tool to detect LV hypertrophy, as determined by the calculated LV mass. Echocardiographic techniques have the advantage of being widely available, non-invasive, and relatively inexpensive. However, echocardiography is limited by imaging artefacts and by the planar nature of the imaging technique when the LV cavity is misshapen.

The area–length method by two dimensional echocardiography has been reported to be more accurate than M mode when the shape of the ventricle is abnormal. This method has been validated in comparison with magnetic resonance imaging (MRI) and with postmortem determination.[4–6] Despite this, the accuracy and reproducibility of LV mass measurement by echocardiographic techniques are still controversial.[7 8]

MRI is considered the ideal method for the determination of LV mass because of its high spatial resolution, generally good image quality, and ability to reconstruct the heart's shape in three dimensions.[9–11] However, it is not widely used clinically because of higher cost, reduced availability, and limited access for critically ill patients or patients with implanted electronic devices (for example, pacemakers and defibrillators). Like echocardiography, MRI can also have artefacts that limit image quality, especially in severely obese patients. Unlike echocardiography, the usefulness of MRI is limited in patients with irregular heart rhythms.

Recent improvements in transthoracic echocardiographic techniques suggest that echocardiography may also be able to reconstruct the three dimensional shape of the heart with high spatial resolution in almost all patients. These advances include the availability of second harmonic technique, ultrasound contrast, and digital echocardiography. When combined with multiplane harmonic Doppler imaging, the contrast echocardiographic technique also allows identification of endocardial borders and a semi-three dimensional LV shape determination.[12–14]

The aim of this study was to assess the feasibility of using a contrast enhanced colour Doppler echocardiography technique to determine LV mass. Results were compared with MRI derived LV mass as the yardstick.

METHODS
Patient population
Consecutive unselected patients scheduled for routine cardiac MRI for clinical reasons were asked to participate in a study, which required the addition of only a resting contrast enhanced transthoracic echocardiogram. All enrolled patients were imaged in the Department of Internal Medicine of the University of Genoa. The standard exclusion criteria for cardiac MRI were used (atrial fibrillation, ventricular arrhythmias, clinically unstable patients, and patients with general contraindications to MRI[15]). The protocol was

reviewed by the human subject review committee and completed according to their guidelines. The enrolment criteria for contrast echocardiography were that the patients be eligible to receive intravenous echo contrast injections (pregnancy was the only exclusion criteria) and that they consent to the procedures. Patients scheduled for an immediate coronary intervention before the contrast echocardiography were also excluded. All the enrolled patients were in stable clinical conditions without changes in the medical treatment. None had any acute myocardial infarction or acute coronary syndromes in the six months preceding both ultrasound and MRI examinations.

LV mass calculation
LV mass was calculated from the product of the myocardial volume and specific gravity of heart muscle (1.05 g/ml). The myocardial volume was determined from the difference between the epicardial and endocardial LV volumes by a semi-three dimensional data set for both MR and echocardiographic techniques (see below).

MRI protocol
A superconducting 1.5 T MRI unit was used (Vision, Siemens Medical Systems, Erlangen, Germany) with 25 mT/m gradients and 0.6 ms rise time and ECG gating. Images were acquired in the short axis plane of the heart, derived from coronal and sagittal scout views with double oblique angulation.

Cine MRI was performed with a segmented ECG gated breath hold cine gradient echocardiographic sequence to acquire 6–11 short axis contiguous 10 mm slices covering the entire length of the LV cavity. The repetition time was set at 100 ms, the echo time at 6.1 ms, the flip angle at 25° with one excitation, and a 126×126 matrix, 56%, and a pixel dimension of 2.43×1.37 mm. The averages of seven and 14 cardiac phases were acquired depending on the R–R interval. No delay time was used so as to obtain the first image related to the R wave as an end diastolic frame. Total examination time was less than 10 minutes.

Calculation of myocardial volume by MRI
Myocardial volume was calculated by standard MRI software and all images were stored on magnetic tape. The window settings were standardised with the high level set just below the pericardial fat signal intensity and the low level set slightly over the interventricular signal intensity (noise). A series of LV end diastolic short axis images was created starting at the mitral annulus and advancing through the ventricle to the apex at 10 mm intervals. The LV myocardial volume was calculated by two methods: Simpson's rule and the area–length method. Simpson's rule states that the volume of a three dimensional structure can be determined by dividing the structure into a sequence of two dimensional slices and then summing the product of the slice cross sectional area and thickness.[10][16] The area–length method states that the ventricular volume may be calculated from the product of the short axis area and the LV length (fig 1).[17][18]

Ultrasound imaging protocol
The echocardiograms were obtained with 1.75/3.5 MHz harmonic two dimensional imaging and 1.75/3.5 MHz harmonic colour Doppler imaging (Acuson C256 Sequoia, Siemens Ultrasound, Malvern, Pennsylvania, USA). The imaging protocol started with the capture of non-contrast parasternal M mode images for measurement of LV wall thickness. Levovist (Schering AG, Berlin, Germany) 2.5 g was then delivered by slow intravenous bolus over about 45 seconds. Contrast enhanced harmonic colour Doppler imaging of the LV was then obtained by techniques previously described.[13] Briefly, the study technique requires ECG triggering to digitally capture successive end diastolic and end systolic LV images. The harmonic colour Doppler is adjusted for maximum colour filling of the LV cavity by using the maximum ultrasound output power setting (this destroys bubbles, thus creating the Doppler illusion of motion) and a lower than normal Nyquist limit (about 20 cm/s, to maximise endocardial border delineation). The result is a colour Doppler image with well defined endocardial border resolution (due to the 3.5 MHz harmonic Doppler) and a series of images representing the end diastolic and end systolic cavity silhouettes. LV images were captured in the standard apical two chamber, four chamber, and three chamber views.

Calculation of myocardial volume by ultrasound
The contrast enhanced harmonic colour Doppler images vividly enhance the LV cavity with clear delineation of the endocardial borders (fig 2, left). To aid in the machine interpretation of the endocardial borders, each contrast harmonic colour Doppler image was converted to a cavity-only image by simple image mathematics to subtract all grey scale information from the image, leaving an image that contains only the colour content of the original image (fig 2, right). Custom software was then used to detect automatically the endocardial border according to intensity criteria and to create an estimated epicardial border based on the M mode measured LV wall thickness. The custom software then calculated the endocardial and epicardial LV volumes according to the modified Simpson's rule, an algorithm common to all available commercial echocardiographic instruments. Endocardial and epicardial volumes were measured from multiple cardiac cycles and in as many apical views as possible (usually three cycles in each of the three apical views), the averages of which were used to create a single semi-three dimensional end diastolic LV volume. The LV myocardial volume and mass were then calculated by the same techniques described above for MRI.

Statistical analysis
The patients' characteristics and the MRI data were analysed by a one way analysis of variance. All values are reported as mean (SD). In each case the null hypothesis was rejected if $p < 0.05$. LV masses calculated by different geometrical assumptions and methods were compared by linear regression analysis (no intercept model) and by assessment of the agreement between the different sets of measurements (Bland-Altman).[19]

To evaluate intraobserver agreement,[20] a single operator measured myocardial mass by the MRI manual contouring method at an interval of three weeks. All the area measurements were transformed to an equivalent percentage scale of the intraobserver agreement through the following formula:

$$\text{Intra-observer agreement} = 1 - \frac{|X_{1st} - X_{2nd}|}{(X_{1st} + X_{2nd})/2}$$

in which X_{1st} and X_{2nd} are the area measurements obtained in a twice repeated evaluation made by the same observer using the same method.

To evaluate the interobserver agreement, the myocardial mass determined by MRI was calculated by two independent observers (one cardiologist and one MRI radiologist). The myocardial area of the same image obtained by the two observers was transformed to an equivalent percentage scale of the interobserver agreement through the following formula:
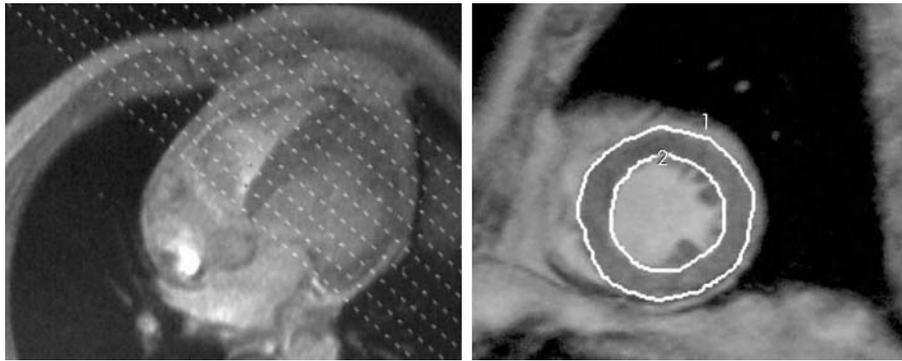
Figure 1 Illustration of the method used to select the left ventricular short axis plane. (Left) Initial long axis scout plane from which the single short axis slices are derived. (Right) Gradient echocardiogram short axis with manual contours shown as lines (one epicardial and two endocardial).

$$\text{Inter-observer agreement} = 1 - \frac{|X_a - X_b|}{(X_a + X_b)/2}$$

in which X_a and X_b are the same myocardial area evaluated by the two observers using the same method.

In the case of the ultrasound images, the primary variability is in the acquisition of images and to a lesser extent in their analysis. Once the grey scale information is subtracted from the image, the primary variability is in the assessment of myocardial wall thickness. The variability of M mode thickness measurement has been previously documented.[21] [22] To reduce variability the myocardial thickness used was an average of the interventricular septum and posterior wall. Two standard deviations of the intraobserver and interobserver agreement indices were used to assess the variance in reproducibility.

RESULTS
Patients' characteristics
The study population consisted of 35 patients with a diverse combination of ventricular shape and function (table 1). Mean (SD) age was 66.2 (8.9) years and 27 (77.1%) of the patients were men. The mean (SD) interval between echocardiography and MRI scan was 6.6 (8.6) days (range 0–27 days). All patients were in sinus rhythm and were in New York Heart Association functional class I or II with stable resting haemodynamic parameters (no significant changes in blood pressure and heart rate between examinations). According to the study protocol, no therapeutic or interventional procedures were performed in the time between the echocardiography and MRI scan. The mean (SD) ejection fraction derived from MRI was 53.5 (13.5)% (range 15.9–71.8%).

Table 1 Patient demographic data and clinical characteristics

	Mean (SD)	Range
Patients (number)	35	
Men	27 (77.1%)	
Age (years)	66.2 (8.9)	49.0–83.0
Weight (kg)	75.6 (11.6)	60.0–102.0
Height (cm)	168.7 (7.5)	154.0–186.0
BMI (kg/m^2)	26.5 (3.6)	20.7–36.0
NYHA class (number)		
I	27	
II	8	
MRI LVEF (%)	53.5 (13.5)	15.9–71.8
MRI–US interval (days)	6.6 (8.6)	0–27
Diagnosis (number)		
Post-ischaemic LV dysfunction	10	
Hypertension	13	
Congestive heart failure	6	
Aortic stenosis	5	
Pulmonary embolism	1	

Data are mean (SD) unless otherwise indicated.
BMI, body mass index; LV, left ventricular; LVEF, left ventricular ejection fraction; MRI, magnetic resonance imaging; NYHA, New York Heart Association; US, ultrasound.

LV mass
Table 2 shows the LV mass parameters. The mean (SD) LV mass from MRI by Simpson's rule was 171.0 (52.4) g (range 105.1–318.7 g). The mean (SD) LV mass from echocardiography by Simpson's rule was 178.2 (46.0) g (range 112.6–307.6 g). The mean (SD) LV mass from MRI by the area–length method was 187.3 (64.5) g (range 109.0–393.6 g) (fig 3).

The linear regression correlation of LV mass determined by MRI Simpson's and echocardiographic Simpson's methods
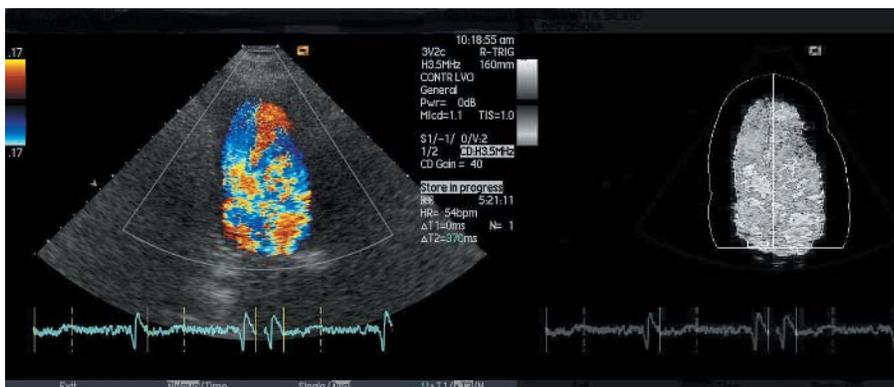

Figure 2 (Left) A contrast harmonic colour Doppler apical two chamber image is shown after the grey scale information has been subtracted and (right) the endocardial and epicardial contours have been auto traced by custom software.

Table 2 Main parameters obtained by Simpson's rule and the area–length method with contrast Doppler computer interpreted analysis and with MRI

Method	OD (cm)	ID (cm)	Thickness (cm)	LV mass (g)	
				Simpson's rule	Area–length method
MRI					
Mean (SD)	7.76 (0.85)	5.46 (0.76)	1.15 (0.19)	171.0 (52.4)	187.3 (64.5)
Range	6.35–9.97	3.57–6.71	0.84–1.67	105.1–318.7	109.0–393.6
Contrast Doppler computer interpreted analysis					
Mean (SD)	6.93 (0.71)	4.73 (0.54)	1.10 (0.16)	178.2 (46.0)	NA
Range	6.03–8.72	3.96–6.43	0.89–1.49	112.6 (307.6)	NA

ID, internal diameter; NA, not applicable; OD, epicardial diameter.

was excellent (y = 1.022x, R^2 = 0.986) with a mean (SD) difference of 7.20 (20.9) g (fig 4).

The linear regression correlation between the MRI area–length LV mass and MRI Simpson's LV mass was excellent (y = 1.101x, R^2 = 0.989) with a mean (SD) difference of 16.3 (22.3) g (fig 5).

Assessment of variability

The variability in LV mass determination by MRI was good based on intraobserver (6.38%) and interobserver (7.29%) analyses. The intraobserver (5.10%) and interobserver (5.63%) variability for M mode measurement of LV wall thickness was also good.

DISCUSSION

The aim of this study was to show, as a proof of principle, that a new contrast enhanced echocardiographic technique may compare favourably with the current ideal for the measurement of myocardial mass in a patient population with diverse cardiac disease. To the best of our knowledge, only healthy control subjects or patients with limited regional contraction heterogeneity were examined in most of the published studies. In the case of MRI, many of the published studies used explanted hearts, which are free of movement, respiratory, and other artefacts commonly associated with in vivo preparations. Therefore, for this study we chose evaluation methods that use both a geometric model (Simpson's rule) and a semi-three dimensional data set to take into account regional LV shape deformities. Further, a patient population rich in cardiac disease was chosen to
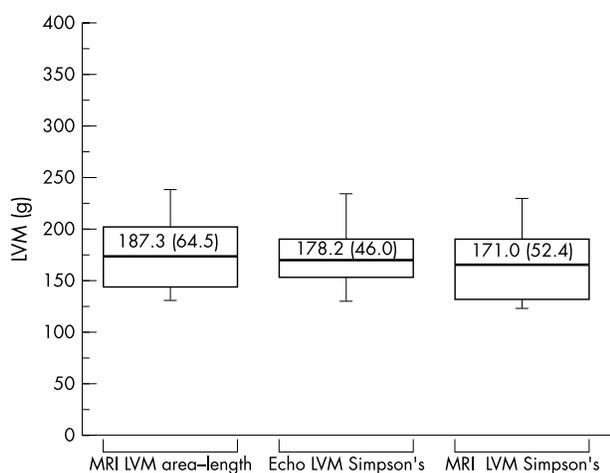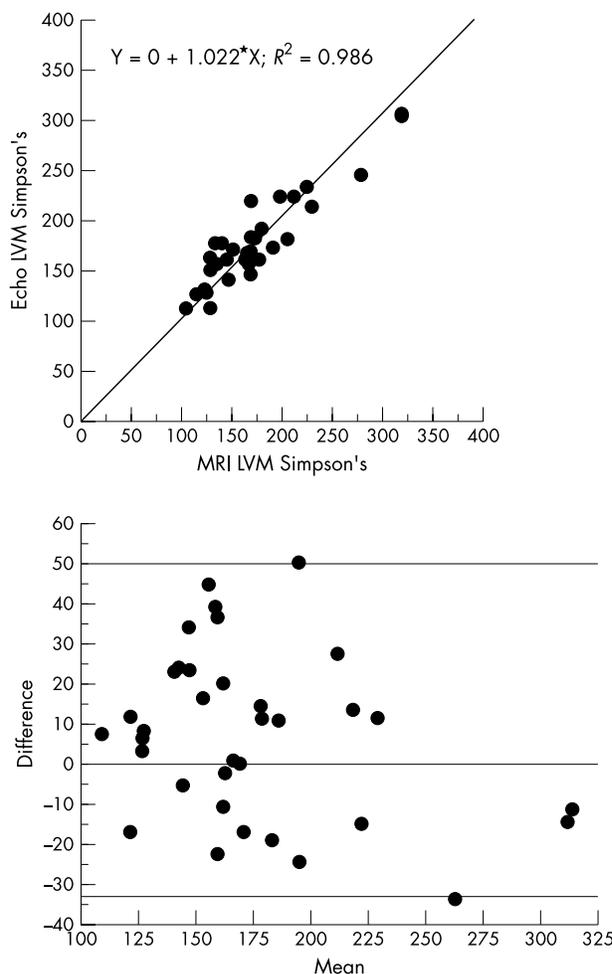

Figure 4 (Top) Linear regression analysis of LVM derived by contrast colour Doppler computer interpretation and by MRI. (Bottom) Bland-Altman plot shows the mean difference and ±2SD confidence intervals.

include patients with dilated misshapen ventricles as well as those with small hypertrophic cavities.

The correlation that was shown in this study between the echocardiographic and MRI techniques is excellent (regression slope 1.022), with only a modest degree of scatter (mean (SD) difference 7.20 (20.9) g). This result compares favourably with other studies of MRI with directly measured LV mass[23][24] and suggests that with second harmonic and contrast echocardiographic techniques the accuracy and reproducibility may be sufficient for use in clinical trials where change in LV mass is the outcome variable.[25–27]

Figure 3 Mean (SD) left ventricular mass (LVM) derived by Simpson's rule by both echocardiographic and magnetic resonance imaging (MRI) determination and the area–length by MRI determination.

$$Y = 0 + 1.101 \text{*} X; R^2 = 0.989$$

respirations. The large range of LV ejection fraction reported in the present study indicates the presence of contraction abnormalities and abnormally shaped ventricles. This type of information is critical to the interpretation of data scatter in the LV mass measurements. In addition, there are no published data on the reproducibility of either the echocardiography or MRI techniques in large patient populations.

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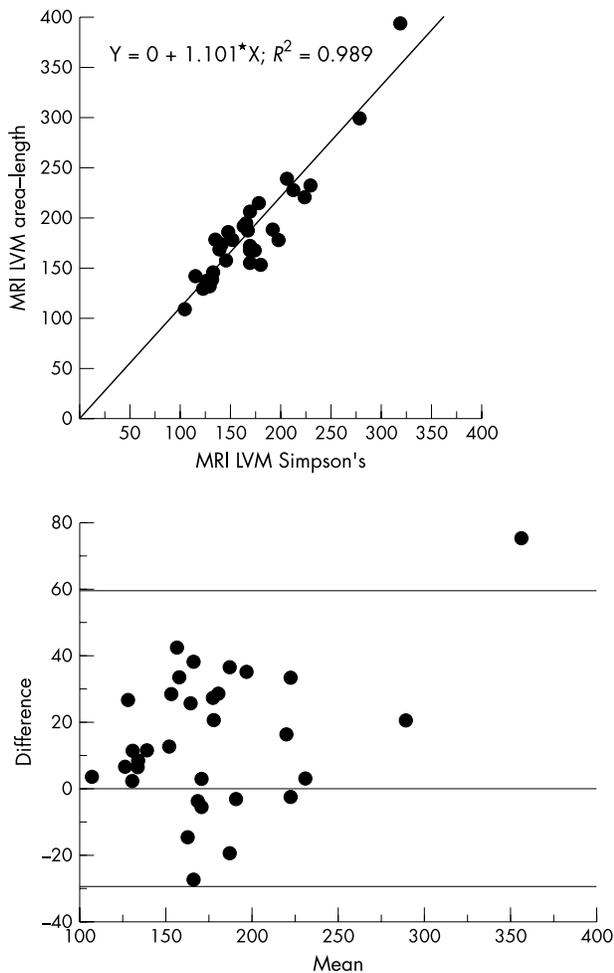
Figure 5   (Top) Linear regression analysis of LVM calculated by the area–length method and by Simpson's rule from MRI. (Bottom) Bland-Altman plot shows the mean difference and ±2SD confidence intervals.

No test is error-free. The use of MRI as the ideal has never been tested in living patients against LV weight measured after death in large study samples. Therefore, LV mass data scatter with the MRI technique is unknown and may be responsible for at least a portion of the scatter seen in the echocardiography–MRI correlation analysis. To address this issue, we compared the MRI area–length LV mass with the Simpson's LV mass. This analysis showed good agreement and a similar degree of data scatter to that obtained with the echocardiographic method (regression slope 1.101, mean (SD) difference 16.3 (22.3) g). Therefore, at least part of the data scatter seen in the echocardiography–MRI correlation is probably caused by scatter in the yardstick technique itself.

In conclusion, our results indicate that the contrast Doppler method produces an accurate determination of LV mass with an excellent agreement with the MRI technique.

Limitations

Larger sample sizes are needed for both the new echocardiographic technique and the MRI method, and ideally with pathological correlation. These type of data are very difficult to obtain because of the obvious difficulties of having high quality imaging data soon before a death so that pathological LV mass can be determined. Published data on pathologically measured and imaging measured LV mass of explanted hearts is helpful but only partially relevant to clinical imaging studies on beating hearts in a chest that is also moving due to

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IMAGES IN CARDIOLOGY ....

Radiofrequency ablation of a posteroseptal atrioventricular accessory pathway in a patient with mechanical mitral valve

A 32 year old woman presented with nine years of paroxysmal palpitation which became more frequent recently. The baseline 12 lead ECG showed normal sinus rhythm with no pre-excitation. ECG during palpitation documented supraventricular tachycardia. She had a history of mitral valve replacement with a bileaflet prosthetic mechanical valve nine months previously for severe rheumatic mitral stenosis and regurgitation.

Electrophysiologic study suggested a concealed left posteroseptal atrioventricular accessory pathway associated with the tachycardia. As ablation above the mitral annulus by the transseptal approach was unlikely to succeed, and mapping in the coronary sinus demonstrated no ideal target site, we decided to ablate beneath the annulus by the transaortic approach. To avoid damaging the mechanical valve with the ablation catheter during the procedure, the ablation catheter tip was not advanced with a curve when it reached the aortic valve. When the catheter tip entered the left ventricle, it was kept on the side of left ventricle under careful fluoroscopic monitoring. Then the catheter was manipulated to below the mitral annulus. The earliest atrium activation site during ventricular pacing was mapped at the annulus below the posterior cusp of the mitral valve in the posteroseptum region (1.5 cm from the coronary sinus ostium) (panel A). The inscription of the atrial electrogram in the terminal ventricular electrogram was targeted. Atrioventricular morphology was not affected by the rheumatic lesion. Radiofrequency application at 60℃ was attempted during ventricular pacing. Retrograde pathway function was lost (panel B). Tachycardia could no longer be induced.

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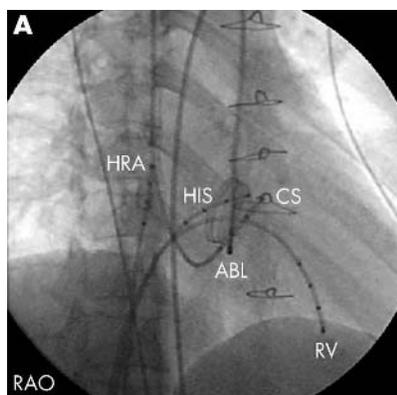
Right anterior oblique view during ablation. HRA, HIS, CS, RV, and ABL represent catheters for high right atrium, His bundle, coronary sinus, right ventricular electrograms, and ablation, respectively.
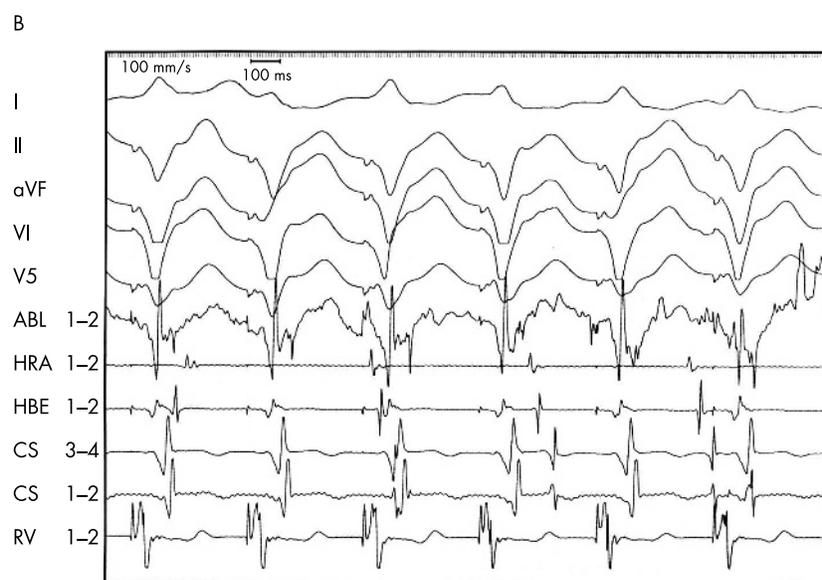
Surface ECG and intracardiac electrograms during radiofrequency energy delivery.