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Multimodality imaging to guide cardiac interventional procedures

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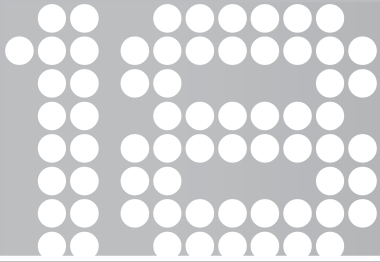
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Non-invasive evaluation of coronary sinus anatomy and its relation to the mitral valve annulus: implications for percutaneous mitral annuloplasty

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ABSTRACT

Background: Percutaneous mitral annuloplasty has been proposed as an alternative to surgical annuloplasty. In this respect, evaluation of the coronary sinus (CS) and its relation with the mitral valve annulus (MVA) and the coronary arteries is relevant. The feasibility of evaluating these issues non-invasively with Multi-slice Computed Tomography (MSCT) was determined.

Methods and Results: In 105 patients (72 men, age 59 ± 11 years), 64-slice MSCT was performed for non-invasive evaluation of coronary artery disease. Thirty-four patients with heart failure and/or severe mitral regurgitation were included. Three-dimensional reconstructions and standard orthogonal planes were used to assess CS anatomy, and its relation with the MVA and circumflex artery. In 71 patients (68%) the circumflex artery coursed between the CS and the MVA, with a minimal distance between the CS and the circumflex artery of 1.3 ± 1.0 mm. The CS was located along the left atrial wall, rather than along the MVA, in the majority of the patients (ranging from 90% at the level of the MVA to 14% at the level of the distal CS). The minimal distance between the CS and MVA was 5.1 ± 2.9 mm. In patients with severe mitral regurgitation, the minimal distance between the CS and the MVA was significantly greater as compared to patients without severe mitral regurgitation (mean 7.3 ± 3.9 mm vs. 4.8 ± 2.5 mm, $p < 0.05$).

Conclusion: In the majority of the patients, the CS courses superior to the MVA. In 68% of the patients, the circumflex artery courses between the CS and the mitral annulus. MSCT may provide useful information in the selection of potential candidates for percutaneous mitral annuloplasty.

INTRODUCTION

Mitral annuloplasty is the most commonly performed surgical procedure for ischemic mitral regurgitation (MR) (1). Recently, a percutaneous approach to mitral annuloplasty has been proposed. Validation studies in animals have shown the feasibility of the percutaneous transvenous mitral annuloplasty (2-5). In addition, preliminary results of the first human experience with percutaneous mitral annuloplasty have been described (6).

However, anatomical studies have demonstrated the variable relationship between the coronary sinus (CS) and the mitral valve annulus (MVA) (7-9). It was noted that the CS may course adjacent to the posterior wall of the left atrium rather than along the MVA. Furthermore, a close relation between the CS and the left circumflex coronary artery (LCX) was detected, potentially limiting the use of percutaneous mitral annuloplasty. However, these anatomical studies were performed in structural normal hearts.

Evaluation of the CS anatomy and its relation with the MVA and the coronary arteries may be of value in patients who are considered for percutaneous mitral annuloplasty. Multi-slice computed tomography (MSCT) can provide an accurate non-invasive evaluation of the anatomy of the CS (10). Recent preliminary data suggest a potential use of MSCT scanning in patients considered for percutaneous mitral annuloplasty (11).

Accordingly, the purpose of the present study was to evaluate the relation between the CS, the MVA and the coronary arteries using 64-slice MSCT in patients with structural normal hearts and in patients with severe MR.

METHODS

Study population

The study population comprised 105 consecutive patients referred for MSCT coronary angiography. The total study population was divided into 3 groups: group I (controls, n=35) included patients without coronary artery disease and without structural heart disease; group II (CAD, n=36) comprised patients with either a history of myocardial infarction / percutaneous transluminal coronary angioplasty / coronary artery bypass grafting, or a significant stenosis in ≥ 1 coronary artery on the MSCT scan; group III (heart failure, n=34) included patients with severe heart failure (left ventricular ejection fraction $\leq 35\%$).

Multi-slice Computed Tomography

MSCT was performed using a Toshiba Multi-slice Aquilion 64 system (Toshiba Medical Systems, Tokyo, Japan) with a collimation of 64 x 0.5 mm and a rotation time of 400 – 500 ms, depending on the heart rate. The tube current was 300 mA, at 120 kV. Non-ionic contrast material (Iomeron 400, Bracco, Altana Pharma, Konstanz, Germany) was administered in the antecubital vein, with

an amount of 80 to 110 ml depending on the total scan time, and a flow rate of 5.0 ml/sec. Automated peak enhancement detection in the descending aorta was used for timing of the contrast bolus. After the threshold level of +100 Hounsfield units was reached, data acquisition was automatically initiated. Data acquisition was performed during an inspiratory breathhold of approximately 8 to 10 seconds, while the ECG was recorded simultaneously to allow retrospective gating of the data. The data set was reconstructed at 75% of the RR interval, with a slice thickness of 0.5 mm and a reconstruction interval of 0.3 mm.

Data analysis

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Data analysis was performed on a remote post-processing workstation (Vitrea 2, Vital Images, Plymouth, Minnesota). Three-dimensional volume rendered reconstructions and standard orthogonal planes were used to assess the anatomy and the course of the CS and its tributaries. Furthermore, the course of the coronary arteries and the coronary artery dominance (right, left, or balanced) was assessed. In particular, the course of the LCX in relation to the CS (inferior or superior) was determined (Figure 1). The axial slices were studied to assess the minimal distance between the LCX and the CS.

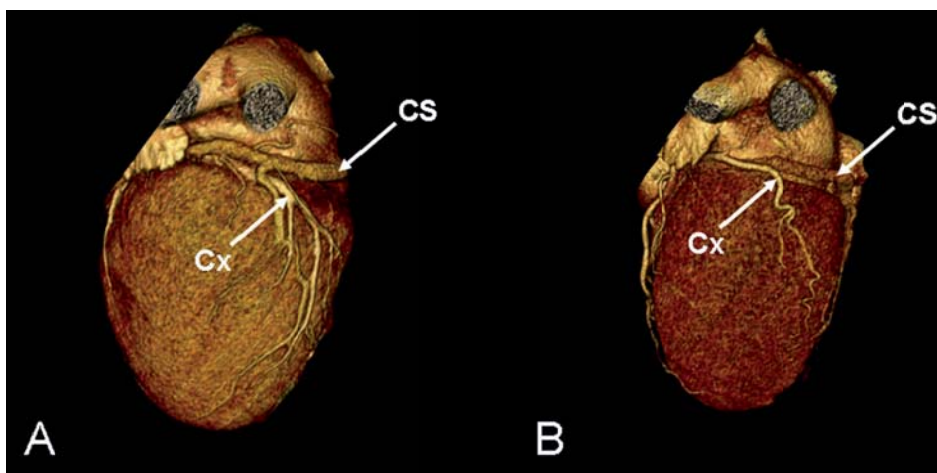


Figure 1. Volume-rendered reconstructions showing the relation between the coronary sinus (CS) and the left circumflex coronary artery (Cx). In panel A, the Cx courses deeper than the CS, and lies between the CS and the mitral valve annulus. In panel B, the Cx courses superior to the CS.

With the use of reconstructed long-axis two- and four-chamber views and volume-rendered three-dimensional reconstructions, the relation between the CS and the MVA was assessed (Figure 2). The position of the CS in relation to the MVA (superior/inferior/same level), and the minimal distance between the CS and the MVA was determined (Figure 3). The anatomical and quantitative data were assessed at three different levels: at the proximal CS, the distal CS, and at the level of the MVA. The proximal CS was defined as the site where the CS makes an angle with the right atrium. The distal CS was defined as the site where the CS makes a sharp angle

anteriorly and continues as the anterior interventricular vein (12). The level of the MVA was reconstructed using the long-axis two- and four-chamber views.

Furthermore, the diameter of the MVA was derived from the long-axis two- and four-chamber views (Figures 2A and 2B); the perimeter of the MVA was assessed on the reconstructed level of the MVA (Figure 2C). In addition, the anterior-posterior diameter and the superior-inferior diameter of the proximal and distal CS were determined, as previously described (10). The analyses of the anatomical relations and the quantitative data were performed by two independent observers, blinded to the clinical data of the patients.

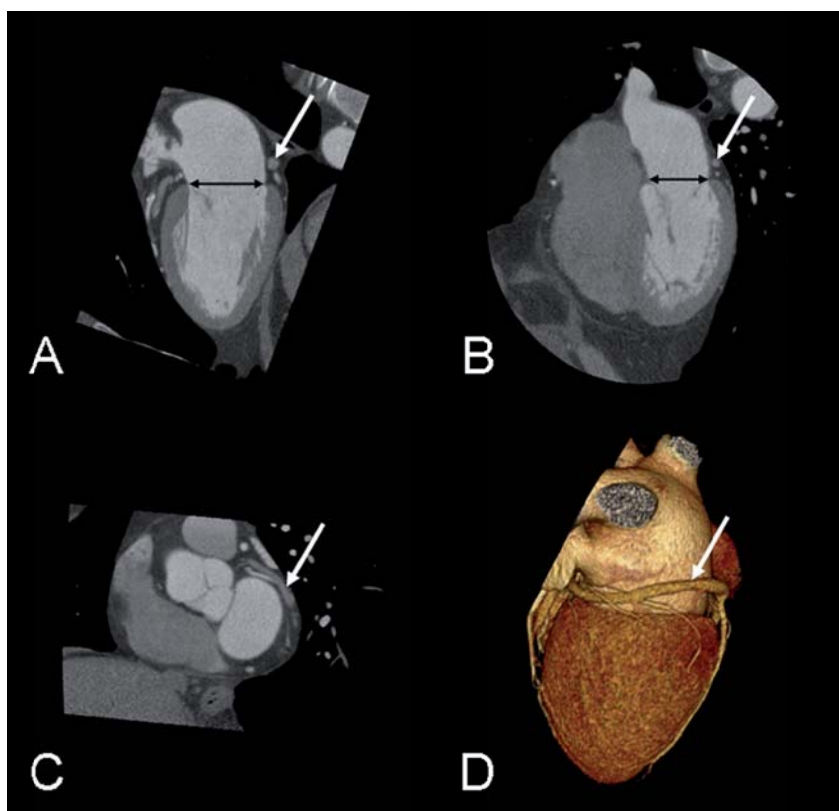


Figure 2. Long-axis 2-chamber (panel A) and 4-chamber (panel B) views were used to assess the course of the coronary sinus (CS) (white arrow) in relation to the mitral valve annulus (MVA), and the diameter of the MVA (black arrow). Furthermore, at the reconstructed level of the MVA (panel C), the CS location and the MVA perimeter were determined. Panel D shows a three-dimensional volume-rendered reconstruction demonstrating the course of the CS and its relation to the MVA and the left circumflex coronary artery.

Echocardiography

Standard two-dimensional echocardiograms were obtained with patients in the left lateral decubitus position using a commercially available system (Vingmed Vivid 7, General Electric-Vingmed, Milwaukee, Wisconsin, USA). Images were obtained using a 3.5-MHz transducer at a depth of 16 cm in the parasternal (long- and short-axis) and apical (two- and four-chamber)

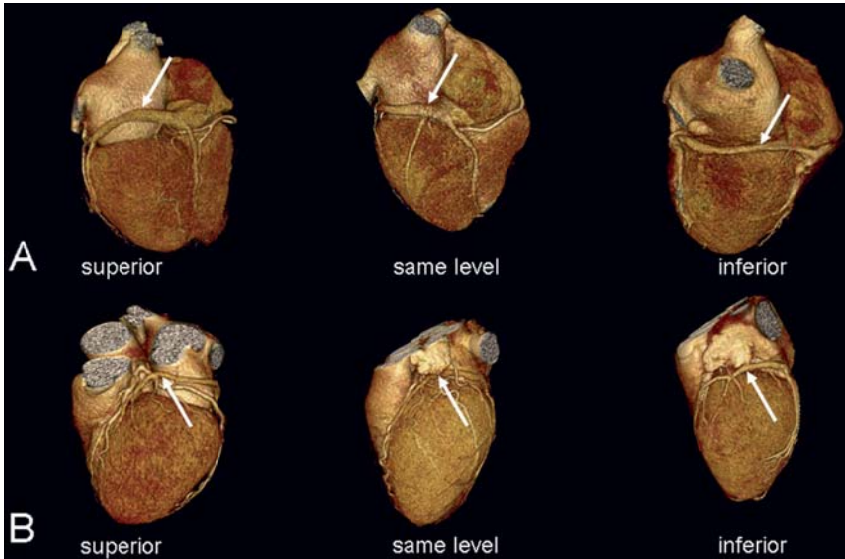


Figure 3. Three-dimensional volume-rendered reconstructions were used to assess the position of the coronary sinus (CS)(white arrow) in relation to the mitral valve annulus. At the proximal CS (panel A) and at the distal CS (panel B), the relative position (super / same level / inferior) of the CS was determined.

views. Standard two-dimensional images and color Doppler data triggered to the QRS complex were digitally stored in cine-loop format. Left ventricular ejection fraction was calculated from apical two- and four-chamber images using the biplane Simpson's rule (13). The severity of MR was graded semi-quantitatively using color-flow Doppler in the conventional parasternal long-axis and apical four-chamber images (14). MR was characterized as: minimal = 1+ (jet area/left atrial area <10%), moderate = 2+ (jet area/left atrial area 10-20%), moderate-severe = 3+ (jet area/left atrial area 20-45%), or severe = 4+ (jet area/left atrial area >45%) (14).

Statistical analysis

Continuous data are presented as mean values \pm standard deviation (SD); categorical data are presented as frequencies and percentages. Differences between the three groups were compared using one-way Analysis of Variance (ANOVA) with Scheffé post-hoc testing for continuous variables, and Chi-square tests for dichotomous variables. Differences between patients with and without severe MR were evaluated using Mann-Whitney U test (continuous variables), or Fisher's Exact tests (dichotomous variables). All statistical analyses were performed using SPSS software (version 12.0, SPSS Inc. Chicago, Illinois, USA). All statistical tests were two-sided, whereas a p-value <0.05 was considered statistically significant.

RESULTS

Study population

A total of 105 patients (age 59 ± 11 years, 72 men) were studied. The study population was divided in 3 groups: controls (n=35), patients with coronary artery disease (n=36), and patients with severe heart failure (n=34, 19 (56%) ischemic cardiomyopathy, 15 (44%) idiopathic cardiomyopathy). The baseline characteristics of the patients are listed in Table 1.

Table 1. Baseline characteristics of the three patient groups

	Controls (n=35)	CAD (n=36)	HF (n=34)
Age, years	54 ± 11	61 ± 10 *	63 ± 11 *
Gender, M/F	21 / 14	25 / 11	26 / 8
LVEF, %	62 ± 5	61 ± 9	27 ± 7 † ‡
Previous MI, n (%)	0	9 (25%)	19 (56%)
Risk factors, n (%)			
Diabetes mellitus	12 (34%)	14 (39%)	6 (18%)
Hypertension	15 (43%)	17 (47%)	14 (41%)
Hypercholesterolemia	14 (40%)	22 (61%)	17 (50%)
Smoking	5 (14%)	15 (42%)	17 (50%)
Positive family history	11 (31%)	10 (28%)	11 (32%)

* $p < 0.05$ vs. controls, † $p < 0.001$ vs. controls, ‡ $p < 0.001$ vs. CAD; CAD = coronary artery disease; HF = heart failure; LVEF = left ventricular ejection fraction; MI = myocardial infarction

Anatomical observations

Coronary arteries and relation with coronary sinus Right coronary artery dominance was observed in 91 patients (87%), left coronary dominance in 13 (12%) and balanced in 1 patient (1%). In 71 patients (68%) the LCX coursed inferior to the CS; thus between the CS and the mitral annulus. In 34 patients (32%) the LCX coursed superior to the CS (Figure 1). The minimal distance between the CS and the LCX was 1.3 ± 1.0 mm. The mean number of marginal branches was 1.2 ± 0.6 ; there were no differences in number of marginal branches between the three groups, or between the patients with right or left coronary dominance.

Anatomical relation between the coronary sinus and mitral valve annulus At the level of the MVA, the CS was located more superiorly in 95 patients (90%), more inferiorly in 1 patient (1%), and at the same level in 9 patients (9%). The minimal distance from the CS to the MVA was 5.1 ± 2.9 mm (range 1.4 to 16.8 mm). Also, the relation of the CS and the MVA was determined at the proximal and the distal CS. At the proximal CS, the CS was located more superior to the MVA in 57 patients (54%), more inferiorly in 7 patients (7%), and at the same level in 41 patients (39%). The minimal distance between the CS and the MVA at the proximal CS was 8.3 ± 2.3 mm (range 2.2 to 15.3 mm). At the distal CS, the CS was located more superiorly to the MVA in 15 patients (14%), more inferiorly in 31 patients (30%), and at the same level in 59 patients (56%).

The minimal distance between the CS and the MVA at the distal CS was 8.8 ± 3.4 mm (range 2.6 to 18.6 mm).

There were no statistical differences between the 3 groups, with regard to the location of the CS in relation to the MVA at any level. In contrast, the minimal distance between the CS and the MVA was significantly greater in the heart failure patients, compared with the control patients and the patients with coronary artery disease (Table 2).

Table 2. Quantitative analyses of the coronary sinus and the mitral valve annulus in the three patient groups

	Controls (n=35)	CAD (n=36)	HF (n=34)	p value *
Minimal distance between CS and MVA				
at MVA level	4.4 ± 2.2	4.9 ± 2.7	6.2 ± 3.4 †	0.019
at proximal CS	7.6 ± 1.6	7.9 ± 2.1	9.3 ± 2.8 †	0.006
at distal CS	7.3 ± 3.3	8.5 ± 3.2	10.7 ± 3.0 ‡ §	<0.001
CS diameter at proximal CS				
AP diameter	10.5 ± 2.7	9.7 ± 2.3	9.9 ± 3.3	0.5
SI diameter	15.0 ± 3.2	14.0 ± 3.0	14.2 ± 3.0	0.3
CS diameter at distal CS				
AP diameter	3.9 ± 0.7	3.9 ± 0.6	4.0 ± 0.7	0.7
SI diameter	4.1 ± 0.9	3.9 ± 0.7	4.0 ± 0.9	0.7
Total CS length	108 ± 12	106 ± 14	126 ± 19 ‡	<0.001

* Assessed by analysis of variance with Scheffé post-hoc testing. † $p < 0.05$ vs. controls; ‡ $p < 0.001$ vs. controls; § $p < 0.05$ vs. CAD; || $p < 0.001$ vs. CAD; AP = anterior-posterior; CAD = coronary artery disease; CS = coronary sinus; HF = heart failure; MVA = mitral valve annulus; SI = superior-inferior

Coronary sinus and mitral valve annulus: quantitative observations The mean diameter of the MVA at the two-chamber view was 40.8 ± 4.7 mm, the mean diameter at the four-chamber view was 36.4 ± 4.6 mm. The mean perimeter of the MVA was 119.4 ± 13.3 mm.

The mean diameter of the CS at the proximal part was 10.0 ± 2.8 mm in the anterior-posterior direction, and 14.4 ± 3.1 mm in the superior-inferior direction. The diameter of the CS at the distal part was 3.9 ± 0.7 mm in the anterior-posterior direction, and 4.0 ± 0.9 mm in the superior-inferior direction. No significant differences in diameter of the CS were observed between the 3 groups (Table 2). With the use of multi-planar reformatted images, the total length of the CS was calculated. The mean length was 113 ± 18 mm (range 76 to 170 mm). The mean CS length was significant larger in the heart failure patients, compared with the controls and the patients with coronary artery disease (Table 2).

Mitral regurgitation

In the total study population 50 patients (48%) had no MR, 30 (29%) patients had MR grade 1+ and 10 patients (9%) had MR grade 2+; whereas MR was characterized as 3+ in 13 patients (12%), and 4+ in 2 patients (2%). To detect differences in the anatomical and quantitative data between patients with and without severe MR, the study population was divided in two groups: patients with MR grade $\leq 2+$ ($n=90$) and patients with MR grade 3+ or 4+ ($n=15$).

There were no differences between the two groups in the anatomical relation between the CS and MVA at any level. Furthermore, no significant differences in diameters of the CS were

noted. However, the minimal distance between the CS and the MVA at all levels was significant greater in the patients with severe MR, compared to the patients without severe MR (Table 3). In addition, the diameters of the MVA and the total length of the CS were significantly larger in the patients with severe MR (Table 3).

Table 3. Quantitative analyses of the coronary sinus and the mitral valve annulus in patients with and without severe mitral regurgitation

	Patients without severe MR (n=90)	Patients with severe MR (n=15)	p value *
Minimal distance between CS and MVA			
at MVA level	4.8 ± 2.5	7.3 ± 3.9	0.005
at proximal CS	8.1 ± 2.4	9.3 ± 1.9	0.019
at distal CS	8.3 ± 3.1	12.1 ± 3.6	<0.001
MVA diameter (two-chamber view)	40.2 ± 4.7	44.3 ± 3.3	0.001
MVA diameter (four-chamber view)	35.8 ± 4.4	39.9 ± 4.4	0.002
MVA perimeter	118.1 ± 12.6	127.6 ± 14.7	0.020
Total CS length	110.1 ± 16.6	128.6 ± 14.6	<0.001

* As assessed with Mann-Whitney U test.

DISCUSSION

In the present study, the relation between the CS, the MVA and the coronary arteries was evaluated non-invasively using MSCT. The major findings of the study are as follows: In 68% of the patients, the LCX courses between the CS and the MVA. In the majority of the patients, the CS courses superior to the MVA. In addition, the minimal distance between the CS and the MVA is greater in patients with heart failure and severe MR. The findings of the present study have important implications for percutaneous mitral annuloplasty.

Anatomical observations

Coronary sinus and coronary arteries A close relation between the CS and the LCX may limit the use of a percutaneous mitral annuloplasty. Circumflex artery compression has been reported as a serious complication in one of the first animal studies on the percutaneous mitral annuloplasty (4). Previous anatomical studies have reported the relation between the CS, the coronary arteries and the MVA (8,9). Maselli et al (9) demonstrated that the LCX coursed between the CS and the MVA in 63.9% of the 61 studied human hearts. Of note, when the LCX coursed inferior to the CS, the number of marginal branches of the LCX was larger. However, no data on the minimal distance between the CS and the LCX were provided.

These anatomical observations have previously been confirmed with electron beam computed tomography (15,16). Mao et al (15) reported that in 80.8% of the studied patients, the LCX coursed inferiorly to the CS. Furthermore, it was demonstrated that the overlapping segment of the CS and the LCX was longer than 30 mm in 17.8% of the cases. However, again no data on the minimal distance between the CS and the LCX were provided.

In the present study, the LCX coursed inferiorly to the CS in 68% of the patients, with a minimal distance between the CS and the LCX of 1.3 ± 1.0 mm. The close relation between the CS and the LCX may limit the use of percutaneous mitral valve annuloplasty, in particular when the LCX courses inferior to the CS over a large distance (Figure 4).

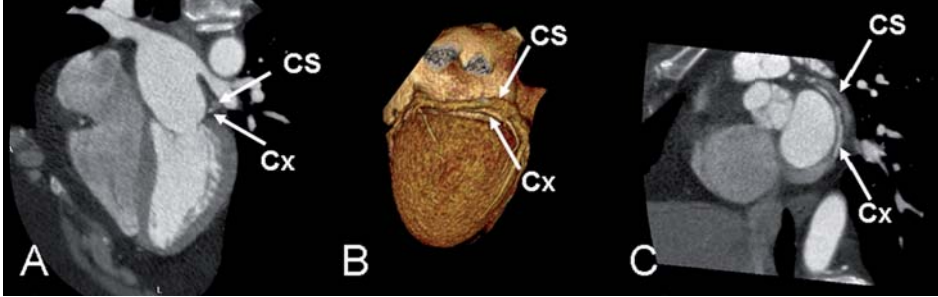


Figure 4. In this patient, the left circumflex coronary artery (Cx) courses between the coronary sinus (CS) and the mitral valve annulus (panel A, four-chamber view). The volume rendered reconstruction (panel B) and the reconstructed mitral valve annulus level (panel C) show that the Cx courses inferior to the CS over a large distance. Performing percutaneous mitral annuloplasty may result in compression of the Cx.

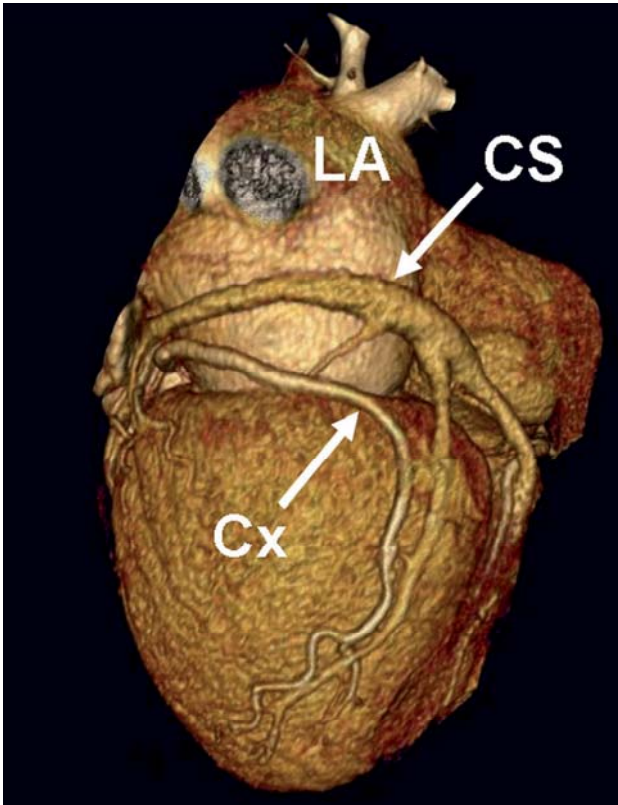


Figure 5. In this patient, the coronary sinus (CS) courses along the left atrial (LA) posterior wall, rather than along the mitral valve annulus. Cx = left circumflex coronary artery.

Coronary sinus and mitral valve annulus Several anatomical studies have addressed the relation between the CS and the MVA (7-9). Shinbane et al (7) studied 10 normal adult cadaver hearts, and reported variable distances between the CS and the MVA along the course of the CS. Mean distances between the CS and the MVA were 14.1 ± 3.1 mm, 10.2 ± 4.9 mm and 10.7 ± 3.5 mm, at 20, 40 and 60 mm distance from the ostium of the CS, respectively. El-Maasarany et al (8) studied the distances between the CS and the MVA in 32 normal cadaver hearts. Distances were assessed in 6 separate regions along the course of the CS. Mean distance was highly variable for the 6 regions; the shortest distance (5.8 mm) was observed at the anterolateral commissure of the MVA. Unfortunately, no data were provided regarding the position of the CS in relation to the MVA (superior/deeper/same level). In the largest anatomical study reported, Maselli et al (9) also noted variable distances between the CS and the MVA. At the level of the P2 and P3 scallops of the mitral valve, mean distances between the CS and the MVA of 5.7 ± 3.3 mm and 9.7 ± 3.2 mm were reported.

In the present study, the highly variable relation between the CS and the MVA was assessed non-invasively with MSCT. The CS was located more superior to the MVA in the majority of the patients (ranging from 90% at the level of the MVA to 14% at the level of the distal CS). Furthermore, minimal distances between the CS and the MVA were assessed at the proximal and the distal CS, and appeared to be highly variable (Table 2). Although this confirms the previous anatomical studies, the use of different reference points makes a direct comparison between the present study and previous *in vitro* studies difficult. Importantly, in patients with severe MR, the minimal distance between the CS and the MVA may increase significantly. In particular, in patients where the CS courses along the left atrial wall the use of percutaneous mitral annuloplasty may be not feasible (Figure 5).

It should be noted however, that in the present study images were routinely reconstructed at 75% of the RR interval. However, the diameter and the distance between the CS and the MVA may vary during the cardiac cycle. Nevertheless, the present study shows that MSCT can accurately depict CS anatomy and its relation with the MVA, thereby providing important information in patients who are considered for percutaneous mitral annuloplasty.

Implications for percutaneous mitral annuloplasty

The present study shows the feasibility of the non-invasive evaluation of the CS anatomy and its relation with the MVA and the coronary arteries. In previous *in vitro* (7-9) and *in vivo* (15,16) studies, the relation between the CS, the MVA and the coronary arteries has been investigated. However, in none of these studies, patients with severe MR were studied. The present study emphasizes the variability in the relation between the CS and MVA. More importantly, it demonstrates that in patients with severe MR, the minimal distance between the CS and the MVA is larger than in control patients (Table 3).

The close relation between the CS and the LCX, and the variable distance between the CS and the MVA may hamper the clinical use of the percutaneous mitral annuloplasty in selected

patients (4). MSCT may identify the patients in whom percutaneous transvenous mitral annuloplasty may not be feasible. In 68% of the patients, the LCX courses between the CS and the MVA (Figure 4), with a potential risk of compression of the LCX when applying percutaneous mitral annuloplasty. Furthermore, in a large number of patients, the CS courses along the left atrial posterior wall, rather than along the MVA (Figure 5). In addition, in patients with severe calcifications of the MVA (Figure 6), a surgical approach may be preferred over a percutaneous approach.

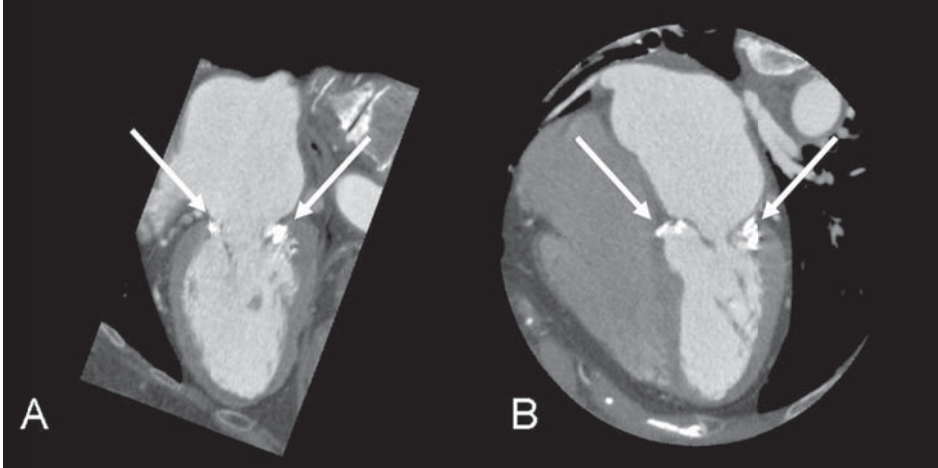


Figure 6. Long-axis two-chamber (panel A) and four-chamber (panel B) views demonstrating a patient with a heavily calcified mitral valve (white arrows).

Our findings are in good relation with recent data demonstrating the feasibility of non-invasive evaluation of the CS anatomy in relation to the MVA using MSCT (11). Similar to the present study, a large variability in the distance between the CS and the MVA was noted (11). Novelities of the present study include the use of a 64-slice MSCT scanner, whereas in the previous study a 16-slice CT scanner (with a collimation of 4 x 1 mm) was used. In addition, in the present study patients with heart failure and patients with severe LV dilatation and subsequent functional MR were included. Therefore, a substantial part of the present study population consisted of potential candidates for percutaneous mitral annuloplasty. Both studies show that MSCT can accurately depict CS anatomy and its relation with the MVA, thereby providing important information in patients who are considered for percutaneous mitral annuloplasty.

CONCLUSIONS

The relation between the CS, the MVA and the LCX can be evaluated non-invasively with MSCT. In 68% of the patients, the LCX coursed between the CS and the mitral annulus. Furthermore, at

the level of the MVA, the CS was located more superiorly in 90% of the patients. In the patients with severe MR, the minimal distance between the CS and the MVA was significantly greater at all levels, compared to the patients without severe MR. MSCT may provide useful information in the selection of potential candidates for percutaneous mitral annuloplasty.

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