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Influence of Left Atrial and Ventricular Volumes on the Relation Between Mitral Valve Annulus and Coronary Sinus

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Abstract

The aim of this study was to evaluate the anatomic relation between the coronary sinus (CS), mitral annulus, and coronary arteries using 64-multislice computed tomography (MSCT) in patients presenting with a wide range of atrial volumes and left ventricular functions to determine the potential clinical use for percutaneous mitral annuloplasty (PMA). The MSCT data of 165 patients (age 63.65 ± 12.89 years, 67.3% men) were evaluated. The following variables were measured: CS length, CS ostium area, area of the section of CS when it becomes great cardiac vein, area between CS and atrioventricular groove assessed in volume-rendered 3-dimensional images, axial angle measured as the angle between CS and mitral annulus assessed in axial section, mitral valve annulus (MVA) area, left atrium volume, and left circumflex artery/marginal branch-CS relation referring to mitral annulus. The correlation was inversed between the reduction of the axial angle and all following variables: enlargement of both left ventricular end-systolic ($r = -0.429$, $p < 0.001$) and end-diastolic ($r = -0.428$, $p < 0.001$) volumes, left atrial volume ($r = -0.361$, $p < 0.001$), and MVA ($r = -0.324$, $p < 0.001$). Similarly, there was inverse correlation between the reduction of the area between CS and atrioventricular groove, and enlargement of both left ventricular end-systolic ($r = -0.376$, $p < 0.001$) and end-diastolic ($r = -0.291$, $p < 0.001$) volumes, left atrial volume ($r = -0.221$, $p = 0.001$), and MVA ($r = -0.155$, $p = 0.019$). Of note, circumflex artery was located between CS and MVA in 77% of the patients, but in patients with severe mitral regurgitation CS crossed circumflex/marginal branch artery more frequently (97% of cases). In conclusion, a close proximity of the CS to the mitral annulus but also to circumflex artery is more likely to occur with left atrial and ventricular enlargement. Thus, MSCT should be considered as part of the selection process of potential candidate to PMA to avoid external compression of circumflex artery/marginal branch by the device.

The increased number of nonpharmacological treatments in heart failure patients such as catheter-based percutaneous mitral annuloplasty (PMA),¹ cardiac resynchronization therapy, and novel pacing or ablation approaches has raised interest in cardiac venous anatomy.^{2–7} Autopsy-based observations in human heart and latest multislice computed tomography (MSCT) findings in patients with normal left ventricular dimensions have recently warned

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about the paradigm of close proximity of the coronary sinus (CS) and mitral valve annulus (MVA). These studies also addressed the potential risk related to compression of the left circumflex coronary artery during PMA.^{8–11} Because of possible use of PMA in patients with heart failure, the spatial relation between CS location and coronary arteries has been investigated at minimum extent.^{8–11} Although previous studies showed a significant variation in coronary venous anatomy,^{8–11} in the majority of patients, the CS courses superiorly to the MVA and the circumflex artery courses between the CS and the MVA. These studies, however, included limited numbers of patients with heart failure and provided limited information about the left atrial and ventricular volumes. Thus, it is unknown whether changes in both left atrial and ventricular volume would impact the CS anatomical course and the relation between CS and circumflex artery/marginal branch. The aim of the present study was to evaluate the spatial relation in CS, MVA, and coronary arteries in patients with varying left atrial and ventricular volumes to determine the potential clinical use for PMA.

Methods

Included in this study were 165 consecutive patients who underwent routine MSCT examination for evaluation of possible coronary artery disease at Fondazione Cardiocentro Ticino, Lugano, Switzerland (n = 97) and Massachusetts General Hospital, Boston, Massachusetts (n = 68). Patients in whom blurring artifacts (due to cardiac, respiratory, or postural motion), “stairstep” artifact beam (due to nonoptimal phase selection), or with limited enhancement of CS were excluded from this analysis. The present study conforms to the principles outlined in the Declaration of Helsinki. The research protocol was approved by the locally appointed ethics committee, and all patients provided oral and written informed consent to the scanning procedure and agreed to the data retrieval and analysis.

All subjects underwent standard electrocardiogram-gated contrast-enhanced 64-slice cardiac MSCT protocol for computed tomography (CT) coronary angiography per departmental protocol while supine and with all images acquired during an inspiratory breath-hold. Intravenous β blockers for heart rate >65 beats/min and sublingual nitroglycerin were used if not contraindicated. Image acquisition at the 1 site was performed using GE MSCT LightSpeed volume computed tomography (VCT) (General Electric Healthcare, Milwaukee, Wisconsin) with the following parameters: 0.625 mm slice thickness, tube voltage 120 kVp, maximum tube current 850 mAs, gantry rotation time 350 ms. Image acquisition at the other site was performed using Sensation 64 (Siemens Medical Solutions, Forchheim, Germany) with the following parameters: 0.6 mm slice thickness, tube voltage 120 kVp, maximum tube current 850 mAs, gantry rotation time 330 ms. At both sites, pitch was dependent on patient’s heart rate and tube modulation was optional. Iodinate contrast was given at a rate of 5 ml/s followed by saline infusion, with total contrast volume dependent upon scan range.

After the scan, axial multiphase reformats between 10 to 90% (10% interval, total of 9 phases) were constructed using the GE Advantage (General Electric Healthcare, Paris, France) or Leonardo (Siemens Medical Solutions, Forchheim, Germany) workstation. All patient information was de-identified and the multiphase reformats were recorded on a CD and sent to CT Core Lab at Fondazione Cardiocentro Ticino for off-line postprocessing analyses. The scans were evaluated in consensus by 2 experienced observers.

The length of the CS was defined as the distance between the orifice of the CS and the transition of the great cardiac vein in the anterior interventricular vein. The area of the ostium of the CS a half centimeter behind the atrial septal wall and the area of the great cardiac vein right at the take-off were measured using a calibrated internal tool of the workstation. The area between CS and atrioventricular groove was assessed in volume-rendered 3-dimensional images by MSCT. This area is usually curved and is limited medially by the entry of CS into the right

atrium and laterally by the point when the CS enters into the atrioventricular groove (Figure 1). In axial sections, the angle between CS and mitral valve orifice was measured; this angle was defined by the intersection of a line passing through the insertions of anterior and posterior mitral leaflets on the ventricular wall and a line obtained connecting the anterior insertion of the mitral valve on the ventricular septum with the center of CS (Figure 1). Left atrial contours, excluding origin of the pulmonary veins according to Lang et al,¹² but including left atrial appendage were manually traced; atrial volume was then automatically measured by a postprocessing tool. MVA area was calculated according to Ormiston et al.¹³

Standard echocardiography, including Doppler studies, was performed (Vivid 7, General Electric Vingmed Ultrasound, Horten, Norway). Left ventricle dimensions and ejection fraction were measured by 2-dimensional guided M-mode echocardiography according to the guidelines of the American Society of Echocardiography. Mitral valve regurgitation was quantified by visual assessment. All patient information was de-identified and the acquisitions were recorded on a CD and sent to Echocardiography Core Lab at Fondazione Cardiocentro Ticino for off-line postprocessing analyses. The echocardiograms were evaluated in consensus by 2 experienced observers.

Descriptive statistics were computed as mean $\pm$ SD or median and interquartile range for continuous variables and percentages for categorical variables. Patients with none to mild (0 to 2) versus moderate to severe MR (3 to 4) were compared dichotomized. The Mann-Whitney U test or the Fisher's exact test was used when appropriate. General linear regression models were fitted to relate echocardiographic findings with MSCT measurements. All models were adjusted for etiology. Stata 9.2 (Stata Corp., College Station, Texas) was used for computation. A 2-sided p value <0.05 was considered statistically significant.

Results

Table 1 summarizes the demographic and clinical data of the study population, which included some patients who had slow ventricular rate during atrial fibrillation or had a pacemaker. The overall mean left ventricular ejection fraction was slightly reduced and the left ventricular volumes were slightly increased in the total cohort (Table 2).

After correcting for etiology, there was a fair inverse correlation between the reduction of the axial angle and enlargement of both left ventricular end-systolic ($r = -0.429$, $p < 0.001$) and end-diastolic ($r = -0.428$, $p < 0.001$) volumes, left atrial volume ($r = -0.361$, $p < 0.001$), and MVA area ($r = -0.324$, $p < 0.001$; Figures 2 and 3). Independent of etiology, there was a fair inverse correlation between the reduction of the area between CS and atrioventricular groove, and enlargement of both left ventricular end-systolic ($r = -0.376$, $p < 0.001$) and end-diastolic ($r = -0.291$, $p < 0.001$) volumes, left atrial volume ($r = -0.221$, $p < 0.001$), and MVA area ($r = -0.155$, $p = 0.019$; Figures 2 and 3). These findings indicated that CS was located along the left atrial wall in patients with small left ventricular chambers but close to the MVA in those with large left atrium and ventricle. Moreover, CS length increased with enlargement of left atrial ($r = 0.736$, $p < 0.001$) and ventricular volumes (end-systolic: $r = 0.614$, $p < 0.001$; end-diastolic: $r = 0.594$, $p < 0.001$). Of note in 77% of the patients, the left circumflex artery/marginal branch was located between CS and mitral valvular annulus.

Tables 2 and 3 summarize the echocardiographic findings and MSCT measurements in patients with and without moderate-severe mitral regurgitation. As expected, the selected patients with moderate-severe mitral regurgitation had significantly larger left atrium and ventricle volumes. In nearly all patients with moderate-severe mitral regurgitation, the axial angle was less than 18° , indicating a near perfect alignment between the CS and the MVA (Figure 4). However,

in this group of patients CS crossed circumflex artery/marginal branch more frequently (97% of cases; Table 3).

Discussion

This is the largest anatomic MSCT-based study to semi-quantitatively investigate the relation between CS and mitral annulus area. Our main findings are that (1) CS is shifted toward the posterior part of the MVA when the left cardiac chambers and mitral annulus dilate; (2) CS remodels are longer in patients with enlarged left atrium and ventricle; and (3) the circumflex artery or marginal branch frequently is crossed by the CS, and in selected patients with moderate-severe mitral regurgitation this cross is observed in nearly all cases.

CS and cardiac veins are increasingly becoming target of both interventional and electrophysiological procedures. Catheter-based methods for the treatment of mitral regurgitation and implantation of pacing leads for delivery of cardiac resynchronization therapy require access of the CS and coronary veins, thus good anatomical and morphological understanding of the cardiac venous system is important. PMA aims to a gradual change in septolateral distance of the mitral annulus and to increase leaflet coaption, which contributes to mitral regurgitation reduction. To achieve that, a device is delivered into the CS based upon the assumption of proximity and running parallel to the CS to mitral annulus. Recent autopsy data have questioned this assumption; indeed, Maselli et al⁹ showed that the CS in normal human heart lies higher than the mitral annulus with a mean distance of 9.7 mm at the level of P2 scallops of the mitral valve. Similar values have been reported previously by other investigators.^{14,15} Our data are consistent with Maselli et al⁹ and showed that in vivo and in a large group of patients with normal ventricular function CS lies always behind the posterior wall of the left atrium at a significant distance from mitral valvular annulus. In patients with normal dimension of left chambers, we also observed a large variability in the distance between CS and mitral annulus. This distance was quantified by the angle in axial section and by the area between the CS and MVA. The anatomical position of the CS behind the left atrial wall in patients with normal left chambers volume is not a rare finding. Indeed, the anatomical position of CS behind the left atrial wall may be indicative of anatomical reserve of CS. The plasticity of the CS we are hypothesizing is substantiated by the observed high correlation between elongation of the CS and volumetric changes of left ventricular chambers. This novel observation is also concordant with remodelling of MVA area.

Our study is the first to report the changes in position of the CS in relation to left atrial size and left ventricular volumes. We demonstrate that a gradual but progressive shift of CS toward the mitral annulus occurs when left chambers enlarge, as evident by changes in both angular and planimetric measures. However, due to the strong mutually dependence of left atrial size and left ventricular size, it was not possible to discriminate the main determinant (atrial or ventricular dimension) of this relation. The gradual and progressive shift of the CS toward the mitral annulus was equally evident in patients with coronary artery disease or idiopathic cardiomyopathy. Patients with moderate to severe mitral insufficiency frequently present with larger left atrial and ventricular volumes,¹⁶ as also shown in our series. These patients may particularly benefit from the PMA due to the closer proximity of CS to the mitral annulus. However, Choure et al⁸ showed in a study of 36 patients that the CS to mitral annulus distance increases in patients with severe mitral regurgitation and annular dilation, mainly in the posterolateral location. In contrast to their measurements, we assessed the distance from mitral annulus plane in the axial section; in our opinion, this is as relevant as the changes in the anteroposterior plane calculated by Choure et al. Finally in both Choure et al and our series, the left circumflex artery was frequently located between CS and mitral valvular annulus. This frequency increased up to 96% of cases when severe mitral regurgitation was present. Both

our and the findings of Choure et al raise significant concerns about efficacy and safety when treatment of mitral regurgitation by PMA is applied.

Our findings have several clinical implications. MSCT is an extremely valuable technique for precisely assessing morphological and anatomical changes of CS and its relation to coronary arteries in patients with heart failure undergoing nonpharmacological device-based therapies delivered via the CS. PMA in an ovine model determined a significant reduction in mitral anteroposterior diameter, which led to a significant reduction in mitral regurgitation jet area. Although no animal data on the effect of PMA on left atrial and ventricular size are available, it is conceivable that a process of reverse remodelling may take place; such reverse remodelling process may also occur at the level of CS and potentially create a safety and efficacy issue. Devices for PMA are still investigational^{17–19} and short-term safety data are not available yet. However, prevalence of coronary venous abnormalities (e.g., angulation of CS, hypoplasia of the CS, narrowing of the proximal portion of CS, or fistula between left persistent superior vena cava and CS) is reported to be up to 3%.²⁰

A possible limitation of our study is that the 64-MSCT scans were tailored for optimal visualization of coronary arteries. This could have caused a suboptimal enhancement of the CS. In addition, the magnitude of the territory served by circumflex artery was not determined. Thus, the hemodynamic relevance of the potential impingement of circumflex artery remains to be explored.

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Figure 1.

Axial angle in a normal ventricle (A) compared with a dilated ventricle (B). Area between CS and atrioventricular (AV) groove in a normal ventricle (C) compared with a dilated ventricle (D).

Figure 2.

Linear regression between left ventricular end-diastolic volume and axial angle (A), left ventricular end-systolic volume and axial angle (B), left ventricular end-diastolic volume and the area between CS and atrioventricular (AV) groove (C), left ventricular end-systolic volume and the area between CS and AV groove (D). Patients with moderate to severe mitral regurgitation are represented in blue and the remaining patients in red. The unadjusted correlation is reported.

Figure 3.

Linear regression between left atrial volume and axial angle (A), MVA area and axial angle (B), left atrial volume and the area between CS and atrioventricular (AV) groove (C), MVA area and the area between CS and AV groove (D). Patients with moderate to severe mitral regurgitation are represented in blue, and the remaining patients in red. The unadjusted correlation is reported.

Figure 4.

Location of circumflex coronary artery and/or marginal branch in the sulcus atrioventricularis and their crossover (*A and B*) the CS in 1 patient without mitral regurgitation (*A*) and with moderate-severe mitral regurgitation (*B*); 2 CS abnormalities are shown: narrowing of the proximal and mid portion of CS (*C*) and a hypoplastic and duplicated CS (*D*).

Table 1

Clinical and echocardiographic characteristics of the 165 patients included in the study

Clinical Characteristics	All patients
Age (yrs)	64 ± 13
Men	67%
Body surface area (m ²)	1.71 ± 0.53
New York Heart Association Functional Class III–IV	28%
Moderate-severe mitral regurgitation	18%
Hypertension	63%
Diabetes mellitus	19%
Coronary artery disease	55%
Atrial fibrillation	7%
Pacemaker	20%

All values are given as mean value ± SD unless indicated otherwise.

Table 2

Echocardiographic findings in patients with and without moderate-severe mitral regurgitation

Variable	All Patients	Moderate-Severe Mitral Regurgitation		p Value
		Yes	No	
Left ventricular end-diastolic diameter (mm)	53 (48–61)	61 (55–65)	51 (47–59)	<0.001
Left ventricular end-systolic diameter (mm)	40 (30–51)	50 (44–57)	35 (28–48)	<0.001
Left ventricular end-diastolic volume (ml)	53 (48–61)	149 (117–218)	98 (83–122)	<0.001
Left ventricular end-systolic volume (ml)	40 (30–51)	111 (81–138)	35 (30–81)	<0.001
Left ventricular ejection fraction (%)	41 (28–61)	28 (22–37)	54 (33–63)	<0.001
Mean pulmonary arterial pressure (mm Hg)	30 (25–40)	46 (32–59)	28 (25–35)	<0.001

All values are given as median value (twenty-fifth to seventy-fifth percentile) unless indicated otherwise.

Table 3

MSCT findings in patients with and without moderate-severe mitral regurgitation

Variable	All Patients	Moderate-Severe Mitral Regurgitation		p Value
		Yes	No	
Left atrial volume (mm ³)	97 (73–136)	140 (110–198)	89 (71–126)	<0.001
Mitral valve area (mm ²)	1,047 (692–1246)	1,129 (1,003–1,433)	1,000 (870–1,196)	0.006
Axial angle (degrees)	18 (14–23)	14 (12–17)	19 (14–25)	<0.001
CS length (mm)	12 (11–14)	14 (13–15)	11 (10–13)	<0.001
CS ostium area (mm ²)	109 (75–155)	141 (95–264)	105 (70–143)	0.009
Great cardiac vein area (mm ²)	16 (12–22)	21 (15–35)	15 (12–20)	0.001
Area between CS and atrioventricular groove (mm ²)	246 (143–332)	150 (61–239)	260 (184–344)	<0.001
Circumflex artery-CS crossover (%)	77	97	73	0.006

All values are given as median value (twenty-fifth to seventy-fifth percentile) unless indicated otherwise.