Insight Into the Dynamics of the Coronary Sinus/Great Cardiac Vein and the Mitral Annulus
Implications for Percutaneous Mitral Annuloplasty Techniques

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Background—Implantation of devices into the coronary sinus (CS)/great cardiac vein (GCV) to reshape the mitral annulus (MA) is being investigated, despite these structures not being within the same plane and coronary arteries frequently traversing between them. Furthermore, dynamic changes in their relationship have never been studied. We analyzed the CS/GCV dimensions and its relationship with the MA and the coronary arteries.

Methods and Results—Of 390 consecutive computed tomography angiographies reviewed, 56 met the inclusion criteria. Mean age of the patients was 68.9±13.1 years (26.8% men). The dimensions of the CS/GCV and the distance between this structure and the MA were measured at 10 different spatial points along the CS/GCV trajectory and at 3 different time points along the cardiac cycle (phases 0%, 40%, and 75% of the RR interval) by using curved multiplanar reconstruction technique. The CS/GCV was larger in phase 40% than in phase 75% and was smallest in phase 0% (P<0.001). The distance between the CS/GCV and the MA was longest in phase 40% and shortest in phase 0% (P=0.013). The diameter of the MA was measured in oblique 2- and 4-chamber reconstructions, being largest in phase 0% and smallest in phase 40% (P=0.019). A coronary artery traversed between the CS/GCV and the MA in 85.7% of the patients.

Conclusions—This study demonstrated dynamic changes in the relationship between the CS/GCV and the MA and also that coronary arteries frequently traverse between both structures. Whether these findings are of clinical relevance for patients undergoing percutaneous mitral annuloplasty needs to be prospectively evaluated.

Key Words: mitral valve regurgitation ■ dynamics ■ computed tomography ■ imaging

The ultimate goal of percutaneous indirect mitral annuloplasty techniques is to reduce the mitral annulus (MA) septal-to-lateral distance by exerting force through a device deployed in the coronary sinus (CS)/great cardiac vein (GCV).1–7 Although initial preclinical and clinical studies have shown the feasibility of these techniques,4–7 anatomic studies describing the spatial relations of the CS/GCV have raised concerns regarding their potential clinical efficacy and risk of complications.8

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The effect of these devices will depend on their individual mechanism of action and in the anatomic relation between the CS/GCV and the MA. But more important, this effect may be difficult to predict in each specific case due to the nonplanar, 3D anatomy of the MA and because in a majority of cases the CS does not lie directly on the atrioventricular (AV) groove9–14 (Figure 1). A device deployed in a CS/GCV that is too far from the MA or in an unusual 3D orientation may result in an insufficient alteration of the MA shape and in an insufficient reduction of the degree of mitral regurgitation. Furthermore, it is well known that the MA has rotational and translational motion with changes in its surface area throughout the cardiac cycle.15 However, changes in the spatial-temporal relationship of the CS/GCV and the MA have not been reported. A detailed knowledge of the anatomy and dynamic relationships of the structures involved in these technologies seems therefore essential.

Finally, coronary arteries frequently traverse between the CS/GCV and the MA,9,11–13,16 and there have been reports of extrinsic compression of the coronary arteries by these devices.1,17,18 Multidetector computed tomography angiography (MDCTA) is a noninvasive technique that has clearly demonstrated its utility in the evaluation of the coronary arteries. It has recently been used to evaluate the cardiac venous anatomy,16,19–23 the relationship between the CS/GCV and the nearby arteries, and the relationship between the CS and the MA.9,11,12,24 However,
previous studies have not assessed those relationships in a dynamic fashion throughout the cardiac cycle.

Therefore, the aim of this study is to retrospectively analyze 64 MDCTA data to describe the dynamic anatomy and the relationships of the CS/GCV, including (1) the intrinsic dimensions of the CS/GCV at several spatial points along its trajectory; (2) the distance and relative position between the CS/GCV and the MA at several spatial points along the CS/GCV curvature; (3) the variations in these dimensions and distances at different time intervals along the cardiac cycle; (4) describe the tributary veins and the venous anatomy at the crux cordis; and (5) describe the relationship between the cardiac veins and the coronary arteries.

Methods
This retrospective study was undertaken following institutional review board approval and a waiver of informed consent.

Study Population
Three hundred and ninety consecutive MDCTA studies performed for coronary artery evaluation between January 1, 2008, and April 30, 2008, were screened. Patients were included in the protocol if they met the following inclusion criteria: age older than 18 years; absence of congenital cardiac anomalies or mitral valve disease; no history of atrial fibrillation; no history of coronary artery bypass surgery; and in each phase, the straight distance between the center of the MA and the CS/GCV was measured (Figure 2). Once the ostium of the CS was identified in the straightened CPR view, the following distances were measured: distance from the CS ostium to the point where the GCV leaves the AV groove, distance from the CS ostium to the distal GCV, and distance from the CS ostium to the first cross-sectional image in which a tributary vein or an arterial intersection was identified (every identified tributary vein was included, independently of its diameter or extension). Cross-sectional images of the CS/GCV were generated at the CS ostium and in 10-mm distance increments from it, until the distal point was reached (Figure 2A and 2B). Areas were carefully drawn and adjusted at each of these cross-sections and average diameters were automatically calculated (Figure 2C).

Distance Between the MA and the CS/GCV in Obligate Reconstructions
The common axis of the 3 crossing planes (Figure 3B) automatically generated in the Functional Analysis module (Comprehensive Cardiac Analysis software, Philips Medical Systems) was initially adjusted to match the LV inflow long axis. Then, these planes were rotated on this axis until oblique reconstructions similar to the 4 chambers (4C) (Figure 3A), 2 chambers (2C) (Figure 3C), and 3 chambers (3C) (Figure 3D) views were generated. In all these views and in each phase, the straight distance between the center of the CS/GCV and the closest point of the MA was measured (Figure 3E). In the 2C and 4C views, the distances between the 2 identifiable points of the MA (“MA diameter”) were also measured (Figure 3E). The absence of myocardium at the mitro-aortic continuity in the 3C view precludes the accurate identification of the mitral plane and therefore, MA diameter was not measured in this view.

Evaluation of the Distance and Relative Position of the CS/GCV and the MA Along the CS/GCV Curvature Using CPR
Images were transferred to an Aquarius Workstation (TeraRecon, Inc, San Mateo, Calif). The centerline of the CS/GCV was built (Figure 2A and 2B), and the CS ostium was identified as previously described. This software allows for the generation of perpendicular
planes to any centerline, in which not only the vessel but also the adjacent structures can be visualized. Therefore, perpendicular planes to the centerline were generated at the CS ostium and in 10-mm distance increments from it; the spatial points at which these cross-sections are generated are marked as green crosses in A and as green horizontal lines in B. In each of these cross-sections, vessel area is drawn (curved green line in C), and the average diameter is automatically calculated. The distance to the closest MA is also measured (green straight line in D), and a basic reconstruction of the relationship between the CS/GCV and the MA is obtained (E, the curved green line represents the CS/GCV centerline, the inner crosses represent the MA position, and the green straight lines between them represent the distance between each CS/GCV position and its corresponding MA position).

Statistical Analysis
A general linear model repeated measures procedure was used. The multiple observations recorded for each patient across the CS/GCV circumference formed the within-subjects factor of the outcome variable (diameter, area, distance between CS and MA, height, and MA diameter). The 3 different phases of the cardiac cycle were conceptualized as the 3 levels of between-subjects factors, which separated the patients into 3 different groups. In summary, we used a mixed model in which the within-subjects factor was the repeated measure and the grouping variable was the cardiac cycle. SPSS version 16.0.2 was used for statistical analysis. P<0.05 was considered to indicate statistical significance.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results
Of 390 studies screened, 56 met the strict study criteria and constitute the study population. The most frequent reason for exclusion was low contrast enhancement in the CS/GCV, especially in phase 0%.

Patient Characteristics
Mean age of the patients was 68.9±13.1 years, 73% were women. Mean ejection fraction was 60.7±11.4%, mean heart rate during the study was 62±9 beats per minute, and 13% of the patients were in atrial fibrillation. Patient characteristics are listed in Table 1.

CS and GCV Anatomy and Dimensions
The mean distances from the CS ostium to the point where the GCV leaves the AV groove and to the distal GCV (measured at phase 75%) were 102.3±12.4 mm and 124.7±16.4 mm, respectively. Mean length of the path of the GCV on the free wall of the left ventricle (calculated as the subtraction of these 2 measurements) was 22.4±10.6 mm.

Area and Diameter
A consistent anatomic profile was found (Figure 4A and 4B), with the maximum diameter and area measured at the CS ostium in the 3 phases evaluated, and with a progressive and significant decrease in the measured dimensions along the CS/GCV trajectory (P<0.001). However, great variability between patients was found for each of the spatial points evaluated along the CS/GCV trajectory, and some patients were found to be frequent outliers (extreme measurements observed for these patients at several spatial points). Statistically significant differences were found among the 3 phases of the cardiac cycle, with the largest diameter and area observed at phase 0% (P<0.001).

Distance Between the CS/GCV and the MA
Curvilinear Profile
When the distance between the CS/GCV and the MA was analyzed, a consistent spatial profile was found in the 3
phases of the RR evaluated. This distance progressively increased over the first 4 to 5 cm of the CS/GCV trajectory (Figure 4C) and decreased afterward, being this variation statistically significant ($P < 0.001$). When dynamic changes were analyzed, distances observed in phase 40% were consistently larger than the distances observed in phase 0%, with average differences between these phases of 2 to 3 mm ($P < 0.013$).

### Oblique Reconstructions

The analysis of oblique reconstructions showed a similar profile (Figure 4D), with the distance between the CS/GCV and the MA significantly increasing from the posterior CS (2C view) to the inferolateral portion of the CS/GCV (3C view) and decreasing in the lateral GCV (4C view) ($P < 0.001$). Statistically significant differences in the distance between the CS/GCV and the MA were also found along the cardiac cycle, with largest distances found in phase 40% and smallest in phase 0% ($P = 0.003$).

### CS/GCV Position in Relation to the AV Groove

A bimodal curve was observed in the relationship between the CS/GCV and the AV groove. The ostium of the CS was located at the level of the AV groove in only 54.5% (in phase 40%) to 62% (in phase 75%) of the patients, and in the rest it was located above it (Figure 4E). This percentage dramatically decreased within the first centimeters of the CS trajectory; and at 40 mm from the ostium, the CS/GCV was at the level of the AV groove in $<10\%$ of the patients. From this point, the percentage of patients in which the CS was located at the level of the AV groove progressively increased. Toward the end of the trajectory, some of the GCV were identified below the AV groove.

### MA Diameter

The superior-to-inferior MA distance (as represented in the 2C view) was consistently larger than the septal-to-lateral distance (as represented in the 4C view) in all the studied phases ($P < 0.001$). Statistically significant variations occurred throughout the cardiac cycle, with maximum distances found in phase 0% and minimal distances found in phase 40% ($P < 0.019$; Figure 4F).

### Coronary Arteries and Relation to CS/GCV

Right coronary artery dominance was observed in 51 patients (91%) and left and balanced dominance in 2 (4%) and 3 (5%) patients, respectively. The CS/GCV crossed an artery once in
Figure 4. The x axis represents the spatial point analyzed (either in absolute distance from the CS ostium or in the oblique reconstructions). The y axis represents the mean value and the SE obtained for each variable at each spatial point in every phase (except in E, in which it represents the percentage of patients). A and B, Consistent profile is evident in the dimensions of the CS/GCV, which are maximum at the ostium and progressively decrease along the vessel trajectory, showing significant differences among phases. C and D, Distance between the CS/GCV and the MA is not constant along the vessel trajectory, being biggest at 4 to 5 cm from the CS ostium (or in the inferolateral segment in the oblique reconstructions). This distance is dependant on the phase of the cardiac cycle, and it is largest at phase 40% and smallest at phase 0%. E, Area above the superior lines represents the percentage of patients in which the CS/GCV is located above the AV groove. The area below the inferior lines represents the percentage of patients in which the CS/GCV is below the AV groove. In between, those patients in which the CS/GCV is located on the AV groove. F, MA diameter is bigger in the anteroposterior dimension than in the medial-to-lateral dimension, with maximum average distances observed in phase 0% and minimum in phase 40%.
Discussion

This is the first study to show that, using an MDCTA postprocessing protocol that allows for the assessment of these anatomic relationships at any desired point along the vessel trajectory, dynamic changes in the CS/GCV intrinsic dimensions and in the distance between the CS/GCV and the MA do occur throughout the cardiac cycle. We also confirmed that in the majority of patients a coronary artery traverses between the CS/GCV and the MA. The findings in this group of patients may indicate that only a limited number of patients with mitral regurgitation might qualify for techniques to reshape the MA using the CS approach, and therefore a detailed evaluation of the individual anatomy might help in the selection of the most appropriate candidates.

Given the similar density of the fibrous MA to the adjacent structures, none of the currently available imaging modalities is able to directly identify it and surrogates for the MA must be used. In previous echocardiography, MRI, and MDCTA studies, it was identified as the point of insertion of the mitral leaflets in the cardiac wall. In our study, we used the point immediately below this insertion, because contrast enhancement in the left ventricle is easily differentiated. Furthermore, due to its complex saddle shape, the 3D profile of the MA and its relationship with the CS/GCV is difficult to assess using 2D imaging techniques. This characterization is enhanced by any 3D volume rendering imaging technique. MRI and computed tomography have been lately used to assess the relationship between the CS and the MA and to evaluate the cardiac veins (with 2 small series showing good correlation with balloon occlusion angiography).

Nevertheless, previous studies have methodological limitations: CS dimensions and distance to MA were only measured in 1 cardiac phase and in 2 or 3 axial or oblique reconstructions to measure the distance from the CS to the AV groove (Figure 1). In this type of reconstructions, the angulation of the plane where the measures are performed cannot be standardized and therefore this methodology is very operator dependent, which results in similar methodological errors. This study uses a different postprocessing protocol, based mainly on a CPR technique. This allows for the generation of strictly perpendicular cross-sections of the CS/GCV at any desired point along its centerline. In these cross-sections, diameter and area can be measured minimizing angulation errors, and the distance from the CS/GCV to the closest MA position can also be easily assessed. We have repeated these measurements at 3 different time points throughout the cardiac cycle to analyze temporal variations in dimensions and relationships.

We found a consistent profile of dynamic changes in the distance between the center of the CS and the MA throughout the cardiac cycle, with the largest distances observed in phase 40% and the smallest in phase 0%. Although differences between average values were in the range of 2 to 3 mm, individual variations may be higher, and therefore whether this is of clinical relevance in the specific patient undergoing indirect mitral annuloplasty techniques should probably be prospectively evaluated. The CS/GCV was mostly located above the AV groove, as previous necropsy studies and...
MDCTA\textsuperscript{11,12} reports showed. The distance between the CS/GCV was larger in the inferolateral segments (3C) than in the posterior segments (2C) and was smallest in the lateral segments (4C), in accordance with previous findings\textsuperscript{12,13}. Nevertheless, the CPR reconstruction allowed us for more detailed information of the relationship between these structures, and we showed that distance between the CS and the MA smoothly increased over the first 4 cm of the CS/GCV trajectory and decreased afterward (bimodal relationship).

When the MA was analyzed, the superior-to-inferior MA distance was longer than the septal-to-lateral distance in all phases, which is consistent with the saddle shape of the MA. Interestingly, differences in diameter were found throughout the cardiac cycle, with maximum diameters measured in phase 0\% and minimal diameters in phase 40\%. This correlates with human studies using MRI showing a maximum mitral area in late diastole, with a decrease in early systole and a minimum in mid-to-late systole,\textsuperscript{26} and this reduction in the MA area may partially explain the increase in the distance to the CS/GCV in phase 40\%. Nevertheless, the methodology commonly used to assess MA dimensions (distance measurements between opposite points of leaflets insertion in the echocardiography-like views) is a very limited approximation to the complex shape of the MA, and further validation of this methodology and improvements in software are essential to assess dynamic 3D structures.

Dynamic changes in CS/GCV dimensions were also evident. Diameter and area were largest in phase 40\% and smallest in 0\%, with phase 75\% somewhere in between. An increase in phase 0\% dimensions was appreciated at the end of the trajectory, that we explain due to (a) the lower accuracy of the measurements in this phase because of the highest velocity of motion (and increased motion artifacts) of the vascular structures when compared with 40\% and 75\%, and (b) due to the difficulty in identifying the contours of the vessel when it is surrounded by highly enhanced structures (LCX and left atrial appendage). The improvement in temporal resolution of the new scanners not only depends on the number of detectors but also on the rotational speed and number of x-ray tubes, and therefore they will ameliorate this limitation.

Finally, in 86\% of the patients at least 1 coronary artery lay between the CS/GCV and the MA, being the LCX the most common, in accordance with previous reports showing that the LCX lies between the CS/GCV and the MA in 63\% to 80\% of patients.\textsuperscript{8,11–13,16} This artery was considered of clinical relevance in 66\% of the patients. This certainly may be a major handicap, as clinically relevant coronary ischemia associated with the deployment of CS devices has already been reported.\textsuperscript{1,17,18}

MDCTA provides us with detailed information on the individual anatomy and the relationships of the structures involved, and therefore it may be of help in the selection of patients eligible for these new techniques aimed to reshape the MA.

**Study Limitations**

Although 390 studies were evaluated for inclusion in the study, the final sample size is small. This is mainly due to low contrast enhancement and motion artifacts in the CS/GCV, particularly in phase 0\%, and emphasizes the need for dedicated venous acquisition protocols in these patients and for a better temporal resolution, if the phases of fast heart movement are to be analyzed. Temporal-resolution limitations of 64 slices MDCT did not allow us for the evaluation of systolic phases, and therefore, changes in distance and dimensions may be larger than those reported. In addition, it is not possible to confirm that the exact same points along the CS/GCV were analyzed in the 3 phases evaluated, although no more than minimal differences are to be expected due to the nature of the protocol used. Future software should be implemented to overcome this limitation. Finally, this study evaluated patients in which a normal relation between the CS/GCV and the MA was expected and excluded those with known mitral valve disease, which are the focus of these techniques. Therefore, future studies should evaluate whether CS/GCV relationship and dynamics differ from those reported here, to implement percutaneous mitral repair techniques.

**Conclusions**

This study suggests that the distance between the CS/GCV and the MA significantly varies along the cardiac cycle. Furthermore, we found that a coronary artery lies between the CS/GCV and the MA in 86\% of the patients. As these factors may influence outcomes, individual evaluation of the relationship between the CS/GCV and the MA and coronary arteries should probably be mandatory before direct annuloplasty techniques. Whether these dynamic changes and anatomic characteristics are of clinical relevance for the specific patient undergoing mitral annuloplasty techniques should be evaluated in well-designed, prospective studies.

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**Disclosures**

None.

**References**

The current gold standard treatment for patients with severe mitral regurgitation requiring intervention is surgical repair or replacement, which can be performed with excellent procedural and long-term results in a majority of patients. The transcatheter approach to mitral valve repair is an exciting and innovative concept that fosters new technologies, which currently are in their infancy and with only few of them in clinical testing. Indirect annuloplasty through reshaping of the coronary sinus is an attractive approach used by different technological concepts. Despite proof-of-concept and technical feasibility, establishing clinical safety and efficacy for this approach may be more difficult than previously anticipated. In many instances, a definite implant could not be accomplished for anatomical reasons and furthermore, mitral regurgitation may be responsible for these poor outcomes, and therefore this underlines the importance of defining the functional anatomy of the mitral valve apparatus and surrounding structures. The aim of this study is to shed some light in the complex area of the dynamic anatomy of the mitral valve complex. Prospective studies should further evaluate whether these and other anatomic characteristics may be of help in selecting patients with mitral regurgitation that might benefit from these techniques.
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