Percutaneous Mitral Annuloplasty
An Anatomic Study of Human Coronary Sinus and Its Relation With Mitral Valve Annulus and Coronary Arteries
Daniele Maselli, MD; Fabio Guarracino, MD; Francesca Chiaramonti, MD; Federica Mangia, MD; Gabriele Borelli, MD; Gaetano Minzioni, MD

Background—To allow performance of “stand-alone” mitral annuloplasty with minimal invasiveness, percutaneous techniques consisting of delivery into the coronary sinus (CS) of devices intended to shrink the mitral valve annulus have recently been tested in animal models. These techniques exploit the anatomic proximity of the CS and mitral valve annulus in ovine or dogs. Knowledge of a detailed anatomic relationship between the CS, coronary arteries, and mitral valve annulus in humans is essential to define the safety and efficacy of percutaneous techniques in clinical practice. We sought to determine the qualitative and quantitative anatomic relationships between CS and surrounding structures in human hearts.

Methods and Results—The distance from the CS to the mitral valve annulus and the relationship between the CS and surrounding structures were studied in 61 excised cadaveric human hearts. Maximal distance from the CS to the mitral valve annulus was found to be up to 19 mm (mean, 9.7 ± 3.2 mm). A diagonal or ramus branch, main circumflex artery, or its branches were located between anterior interventricular vein/CS and the mitral valve annulus in 16.4% and 63.9% of cases, respectively.

Conclusions—Surgical anatomy suggests that in humans the CS is located behind the left atrial wall at a significant distance from the mitral valve annulus. Percutaneous mitral annuloplasty devices probably shrink the mitral valve annulus only by an indirect traction mediated by the left atrial wall; a theoretical risk of compressing coronary artery branches exists. Chronic studies are needed to address this problem and to determine long-term efficacy of such methods. (Circulation. 2006;114:377-380.)

Key Words: catheters ■ coronary sinus anatomy ■ mitral valve ■ regurgitation ■ percutaneous annuloplasty

Functional mitral regurgitation (MR) is a common finding among patients with advanced heart failure (HF). An increased cardiovascular mortality has been reported for patients affected by MR of ischemic origin1 or resulting from dilated cardiomyopathy.2–4 Surgical mitral annuloplasty (SMA) has been proposed for treatment of MR in cardiomyopathy to improve symptomatic status and survival.5 Actuarial survival rates at 1, 2, and 5 years of 82%, 71%, and 52%, respectively, and a durable and stable improvement in functional status have been reported with SMA.6–8 Mortality and morbidity of SMA, however, remain significant in this high-risk population.

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Percutaneous catheter-based approaches to mitral annuloplasty (PMA) have recently been developed and tested in animal models.9–12 PMA methods exploit the anatomic proximity of the coronary sinus (CS) to the mitral annulus (MA) to deliver an annuloplasty device into the CS to shrink the annulus, thus reducing MR with no need for open cardiac surgery.

In humans, the distance between the CS and MA, however, can be more than negligible, and the CS can lie on the left atrial wall for almost its entire course. Moreover, because coronary arteries can run between the CS and MA, they could theoretically be compressed by PMA devices.

The aim of the present study was to evaluate in normal human hearts the spatial relation between the CS and MA and coronary arteries to test anatomic bases for the efficacy and safety of PMA methods.

Methods

To define surgical anatomy of the AV junction, excised cadaveric human hearts, obtained from patients who died of noncardiac causes and were subjected to clinically motivated routine autopsy examination, were obtained for dissection. Hearts with congenital anomalies or with previous cardiac surgery were excluded from the study. Sixty-one hearts were entered into the analysis. The study was approved by the institutional ethics committee.
was defined as a single artery running in the posteroseptal space by an epicardial approach. A risky AVNA was difficult to achieve by an epicardial approach. An endocardial approach, based on the annulus plane, not the diagonal line connecting them (see the Figure).

Great care was taken to measure the length of the vertical line measured. Because the mitral valve annulus lies deeper than the CS, and the distance from the CS to the mitral valve annulus was

level of the middle of both the P2 and P3 scallops of the mitral valve, wall, mitral valve leaflets, and left ventricular wall were made at the left ventricle at the level of the P3 segment of the posterior mitral valve leaflet. Distance between CS inferior border plane (CSP) and MA superior border plane (MAP) was measured on the fresh heart. LA indicates left atrium; LVFW, left ventricular free wall.

Dissection was performed by a surgeon experienced in both mitral valve surgery and the epicardial approach to the AV junction with conventional vascular instrumentation. To define a standard topographic reference, the relative position of an investigated vessel with respect to another one crossing it was defined as deeper if closer to the epicardial surface of the left atrium or left ventricle.

The heart was inspected, and coronary artery dominance (left, right, or balanced) was defined. Length and mode of termination (bifurcation or trifurcation) of the left main (LM) trunk were noted. The anterior interventricular vein (AIV) was identified and followed along its course up to its confluence into the great cardiac vein/CS. In case of overlapping of the AIV and left anterior descending coronary artery (LAD), first diagonal artery (DA), or ramus branch (RB), the relative positions of the vessels were noted. The great cardiac vein was followed all along the posterior mitral valve annulus and the posteroseptal space up to its confluence into the right atrium. The position of the circumflex artery (CX) relative to the annulus (above, below, or at the same level), CS (deeper or superior), and left atrial wall (epicardial or intramural) was noted, as it was for total number of major (>1 mm) marginal branches of the CX. Mode of termination of the CX was characterized as diminutive, radial posterolateral, marginal, posterior, or posterior descending according to McAlpine. Two longitudinal sections including the left atrial wall, mitral valve leaflets, and left ventricular wall were made at the level of the middle of both the P2 and P3 scallops of the mitral valve, and the distance from the CS to the mitral valve annulus was measured. Because the mitral valve annulus lies deeper than the CS, great care was taken to measure the length of the vertical line included between the CS inferior border plane and the mitral valve annulus plane, not the diagonal line connecting them (see the Figure).

The AV node artery (AVNA) was identified in the posteroseptal space by an epicardial approach. An endocardial approach, based on surgical access through the atrial wall located between the inferior border of the CS ostium and the attachment of septal leaflet of the tricuspid valve, was added in cases in which AVNA identification was difficult to achieve by an epicardial approach. A risky AVNA was defined as a single artery running in the posteroseptal space close to the mitral valve annulus.

**Statistical Analysis**

Categorical data are presented as absolute values and percentages; continuous data are summarized as mean±SD. The $\chi^2$ or Fisher exact test, as appropriate, was used to evaluate the relationship between the CX artery course with respect to CS (deep or superior) and (1) coronary artery circulation dominance, (2) mode of termination of the CX, (3) mode of termination of the LM (bifurcation or trifurcation), and (4) position of the CX with respect to mitral valve annulus (above, below, or same level).

The Student $t$ test, the Mann-Whitney $U$ test, or the Wilcoxon rank-sum test was used as appropriate to evaluate the relationship between the CX artery course with respect to the CS (deep or superior) and CS-MA distance, LM length, and number of CX branches with a >1-mm diameter.

One-way (single-factor) ANOVA or the Kruskal-Wallis 1-way ANOVA on ranks, with the Bonferroni or Kruskal-Wallis Z multiple-comparison test, was used to analyze differences in mean CS-MA distance, LM length, and number of CX branches with a >1-mm diameter between various modes of termination of the CX.

Multinomial logistic regression was used to evaluate the relation between CS-MA distance and LM length as the independent variable and number of CX branches with a >1-mm diameter (dichotomized as ≥2 or <2 branches) as the dependent variable. Statistical analysis was performed by the NCSS-PASS 2004 statistical package. The authors had full access to the data and take full responsibility for their integrity. All authors have read and agree to the manuscript as written.

**Results**

Dissection was successfully completed in all cases. Results are reported in the Table.

Right coronary artery dominance was observed in 93.4% of cases, left coronary artery dominance in 4.9%, and balanced circulation in 1.6%. The LM was bifurcated in 83.6% of cases and trifurcated in the remaining. The AIV crossed the LAD in 42.6% and the DA or RB in 100% of cases. The LAD was located between the AIV and the epicardium in 11.5% of cases. DA or RB was located between the AIV and the epicardium in 16.4% of cases. AVNA was lying close to the MA in 37.7% of the cases. A course of CX between CS and mitral valve annulus was noted in 63.9% of cases. Interestingly, a marginal CX was observed more commonly when the CX was superior to the CS than when it was deeper than the CS (91% versus 79.5%). A deeper CX was associated with a higher number of big (>1-mm diameter) marginal branches (1.6±0.7 versus 1.4±0.7 marginal branches; $P=0.06$). Statistical tests, however, failed to show significance for the observed trends.

**Detailed Results of Statistical Analysis**

No relationships could be demonstrated by $\chi^2$, Fisher exact, or Student $t$ tests between a deeper or superior course of the CX artery with respect to CS and coronary artery circulation dominance, mode of termination of the CX, mode of termination of the LM, position of the CX with respect to MA, distance of the CX to the MA, LM length, and number of CX branches with a >1-mm diameter.

ANOVA failed to show any relation between mode of termination of the CX and CS-MA distance (F ratio=0.79, $P=NS$), LM length (F ratio=1.10, $P=NS$), and number of CX branches with a >1-mm diameter (F ratio=1.34, $P=NS$).

Multinomial logistic regression analysis showed no significant relation between CS-MA distance (odds ratio [OR], 1.06; 95% CI, 0.93 to 1.21; $P=NS$) and LM length (OR, 0.96; 95% CI, 0.84 to 1.10; $P=NS$), and number of CX branches with a >1-mm diameter.
**Anatomic Findings**

<table>
<thead>
<tr>
<th>Anatomic Findings</th>
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<tbody>
<tr>
<td>LM length, mm</td>
<td>8.3±3.7</td>
</tr>
<tr>
<td>LAD deeper than crossing AIV, %</td>
<td>11.5</td>
</tr>
<tr>
<td>DA and RB deeper than crossing AIV, %</td>
<td>16.4</td>
</tr>
<tr>
<td>CS-to-MA distance at P3 level, mm</td>
<td>(range, 5–19; 9.7±3.2; median, 9)</td>
</tr>
<tr>
<td>CS-to-MA distance at P2 level, mm</td>
<td>(range, 1–15; 5.7±3.3; median, 5)</td>
</tr>
<tr>
<td>Risky AVNA, %</td>
<td>37.7</td>
</tr>
<tr>
<td>CX crossing CS, %</td>
<td></td>
</tr>
<tr>
<td>Diminutive type, %</td>
<td>2.5</td>
</tr>
<tr>
<td>Radial posterolateral type, %</td>
<td>2.5</td>
</tr>
<tr>
<td>Marginal type, %</td>
<td>79.5</td>
</tr>
<tr>
<td>Posterior type, %</td>
<td>7.7</td>
</tr>
<tr>
<td>Descending posterior type, %</td>
<td>7.7</td>
</tr>
<tr>
<td>CX branches &gt;1-mm diameter, n</td>
<td>(0–4, 1.6±0.7)</td>
</tr>
<tr>
<td></td>
<td>(1–2, 1.4±0.7)</td>
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</table>

**Discussion**

The main findings of this anatomic study are that the CS in the human heart lies behind the left atrial wall, not behind the mitral valve annulus, and that implanting a PMA device into the CS could theoretically result in compression of the DA and/or RB in 16.4% of cases, of the CX artery in 63.9% of cases, and of the AVNA in 37.7% of cases.

Recently, percutaneous, less invasive, and safer methods to perform mitral annuloplasty have been proposed to achieve the same clinical benefit of SMA with less morbidity and mortality. Feasibility and short-term efficacy of PMA have been successfully tested in animal models. Feasibility of PMA was demonstrated in an acute ovine model of acute ischemic MR by Liddicoat and colleagues. They emphasized limits of their model and warned against direct extrapolation of their results in a human setting. They clearly stated that long-term safety and efficacy of the PMA could not be derived by their model. Kaye and colleagues analyzed the effects of PMA in an acute ovine model of HF-related MR and observed a significant reduction in MA diameter and MR extent, accompanied by an acute increase in cardiac output and a reduction in pulmonary capillary wedge pressure. Daimon and colleagues tested the feasibility and efficacy of PMA in an ovine model of chronic ischemic MR. They observed a significant reduction in MR jet area resulting from a reduction in MA anteroposterior diameter and a reduction in tenting height and tenting area with no change in the intercommissural distance. At a maximum of 50 days after implant, no instances of device migration were documented; however, no data on MR extent evolution were provided. All these models were short-term models and did not report on the long-term effects of PMA.

A persistent, significant reduction in HF-induced MR with PMA was demonstrated at 4 weeks in dogs by Maniu and colleagues.

Catheter-based methods exploit the proximity of the CS to MA to deliver into the CS a device that causes a gradual change in septolateral distance of the MA, thus increasing leaflet coaptation and reducing MR.

The “close proximity” of the CS to the MA in humans has been based on an assumption derived from a study from Shinbane et al. intended to define anatomic relation between the CS and MA in view of ablation of left-sided accessory pathways. Distances of 14.1±3.1, 10.2±4.9, and 10.7±3.5 mm were documented between the MA and CS at distances of 20, 40, and 60 mm, respectively, from the CS ostium in 10 human hearts.

In 1992, Holman and colleagues published a detailed quantitative analysis of surgical anatomy of the AV junction relevant to surgical treatment of Wolff-Parkinson-White syndrome. In that study, the mean distance between the CS and MA was 8±3 mm, and the authors emphasized the inaccuracy of preoperative mapping studies that can result from the erroneous assumption that the CS lies immediately adjacent to the AV junction.

Using electron-beam CT angiography, Mao and colleagues recently studied 231 patients to define relationship between coronary veins and arteries. They found a DA or RB deeper than the AIV in 15% of cases and a CX deeper than the CS in 80.8% of cases. Unfortunately, no data were reported for the distance of the CS from the MA and the position of the AVNA relative to the MA.

In a recent report by Webb and colleagues of the initial human experience with PMA, early recurrence of MR, related to device failure, was reported in 3 of 4 patients. Because the study was discontinued, long-term performance of such methods, even with properly implanted and working devices, remains an unanswered question.

Our data reflect those reported in the literature and suggest that the CS in humans lies in a much higher position than the MA. Trigones, which is where surgeons begin and complete their annuloplasty, are at a distance away from the CS. Moreover, we found an interesting correlation between the depth of the CX and its distribution. When the CX was deeper than the CS, it gave a higher number of marginal branches of a significant diameter, thus distributing to a bigger portion of the LV, which implies that compressing such an artery could be even more dangerous.
Study Limitations
The number of anatomic samples used in the present study was insufficient to reach statistical power in the analysis of relative relationships between arterial and venous components of the coronary tree. From the point of view of the descriptive anatomist, however, the observation that the CS lies behind left atrial wall and not behind the mitral valve annulus should not be affected by this statistical limitation.

The distance between the CS and MA was measured on fresh isolated normal hearts. Left atrial dilatation could in theory alter this distance. A clinical study is needed to verify whether these data conform to in vivo findings.

Conclusions
Our results confirm that close proximity of the CS to the MA is not a paradigm. Surgical anatomy suggests that in humans PMA devices are likely to work by constricting that portion of the left atrium that lies in proximity of the MA, not by directly shrinking it. A theoretical anatomic base exists for a gradual “recoil” of the mitral valve annulus and of the base of the left ventricle with time. Long-term studies probably are needed to address this problem and to determine long-term efficacy of PMA. A quantitative analysis of the distance between the CS and MA should probably be part of the selection process of patients to undergo PMA.

Because a theoretical risk of compressing mainly the CX but also the DA or RB and AVNA exists, a study of the selection process of patients to undergo PMA.

Disclosures
None.

References
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