Non-Invasive Visualization of the Cardiac Venous System in Coronary Artery Disease Patients Using 64-Slice Computed Tomography

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OBJECTIVES	This study was designed to evaluate the value of 64-slice computed tomography (CT) to visualize the cardiac veins and evaluate the relation between variations in venous anatomy and history of infarction.
BACKGROUND	Cardiac resynchronization therapy (CRT) is an attractive treatment for selected heart failure patients. Knowledge of venous anatomy may help in identifying candidates for successful left ventricular lead implantation.
METHODS	The 64-slice CT of 100 individuals (age 61 ± 11 years, 68% men) was studied. Subjects were divided into 3 groups: 28 control patients, 38 patients with significant coronary artery disease (CAD), and 34 patients with a history of infarction. Presence of the following coronary sinus (CS) tributaries was evaluated: posterior interventricular vein (PIV), posterior vein of the left ventricle, and left marginal vein (LMV). Vessel diameters were also measured.
RESULTS	Coronary sinus and PIV were identified in all individuals. Posterior vein of the left ventricle was observed in 96% of control patients, 84% of CAD patients, and 82% of infarction patients. In patients with a history of infarction, a LMV was significantly less observed as compared with control patients and CAD patients (27% vs. 71% and 61%, respectively, $p <$ 0.001). None of the patients with lateral infarction and only 22% of patients with anterior infarction had a LMV. Regarding quantitative data, no significant differences were observed between the groups.
CONCLUSIONS	Non-invasive evaluation of cardiac veins with 64-slice CT is feasible. There is considerable variation in venous anatomy. Patients with a history of infarction were less likely to have a LMV, which may hamper optimal left ventricular lead positioning in CRT implantation. (J Am Coll Cardiol 2006;48:1832–8) © 2006 by the American College of Cardiology Foundation

Cardiac resynchronization therapy (CRT) has become an attractive treatment option for highly symptomatic heart failure patients with a broad QRS complex on the surface electrocardiogram and poor left ventricular (LV) systolic function (1–3). In selected patients, CRT reduces symptoms and improves exercise capacity. The CARE-HF (Cardiac Resynchronization–Heart Failure) trial also reported a significant reduction of morbidity and mortality compared to optimized medical treatment (4). However, in large randomized trials, up to 30% of the patients undergoing CRT do not respond favorably to this invasive treatment (5). To improve the success rate, several issues, including echocardiographic evaluation of mechanical dyssynchrony and the evaluation of viability in the target region for the LV pacing lead, should be addressed during the selection of potential candidates (6). Another important pre-implantation issue is knowledge of the cardiac venous anatomy of the candidate. Even if viable tissue is identified in the

region with the latest mechanical activation, endocardial CRT implantation will be successful only if the LV lead can be positioned in a vein draining this region. Ideally, venous anatomy should be assessed before implantation non-invasively in the outpatient clinic to determine whether a transvenous approach is feasible. The feasibility of multislice computed tomography (MSCT) to visualize the venous anatomy was recently demonstrated in a study with 16-detector row computed tomography (CT) (7). The authors described a marked variability in venous anatomy, confirming previous invasive studies (8). The absence of coronary sinus tributaries may be related to scar formation secondary to previous myocardial infarction (MI) in the region drained by these specific veins. In the present study, the cardiac venous anatomy of 100 subjects undergoing non-invasive coronary angiography with 64-slice MSCT was retrospectively evaluated. The study aims were 1) to evaluate the feasibility of 64-slice MSCT to depict the cardiac venous system and 2) to evaluate the relationship between variations in cardiac venous anatomy and previous MI.

METHODS

Study population. The anatomy of the cardiac venous system was retrospectively studied in 100 consecutive sub-

Abbreviations and Acronyms

CAD	=	coronary artery disease
CRT	=	cardiac resynchronization therapy
CS	=	coronary sinus
GCV	=	great cardiac vein
LMV	=	left marginal vein
LV	=	left ventricular
MI	=	myocardial infarction
MSCT	=	multi-slice computed tomography
PIV	=	posterior interventricular vein
PVLV	=	posterior vein of the left ventricle
3-D	=	3-dimensional

jects (68 men, age 61 ± 11 years) in whom MSCT was performed for non-invasive evaluation of the coronary arteries. The population was divided in 3 groups. Twenty-eight subjects had normal coronary arteries (control patients). Thirty-eight patients had significant coronary artery disease (CAD) without a history of previous infarction. Thirty-four patients had CAD and a history of MI; mean time between occurrence of the MI and CT acquisition was 49 ± 7 months.

MSCT. Imaging was performed with a 64-detector row Toshiba Multislice Aquilion 64 system (Toshiba Medical Systems, Otawara, Japan). Between 80 and 110 ml of contrast material (Iomeron 400, Bracco Altana Pharma GmbH, Konstanz, Germany) at an injection rate of 5 ml/min was used. Scanning was performed using simultaneous acquisition of 64 sections with a collimated slice thickness of 0.5 mm. Rotation time ranged from 400 to 500 ms depending on heart rate, and tube voltage was 120 kV at 300 mA. A segmental reconstruction algorithm allowed inclusion of patients with a range of heart rates without the need for pre-oxygenation or beta-blocking agents. Retrospective electrocardiogram gating was performed to eliminate cardiac motion artifacts. Data reconstruction was performed on a Vitrea post-processing workstation (Vital Images, Plymouth, Minnesota). During analysis, the observers were blinded to the group assignments of the participants.

Anatomic observations. The tributaries of the cardiac venous system (Fig. 1) were identified on volume-rendered reconstructions. Thereafter, the course of the veins was evaluated in 3 orthogonal planes using multiplanar reformatting. The presence of the following cardiac veins was evaluated: CS, anterior interventricular vein, posterior interventricular vein (PIV), posterior vein of the left ventricle (PVLV), and left marginal vein (LMV). The number of side branches of these tributaries was also evaluated.

Quantitative data. The ostium of the CS was defined as the site where the CS makes an angle with the right atrium in the crux cordis area. Multiplanar reformatting was used to determine the size of the ostium in 2 directions (Fig. 2). The diameters of the proximal parts of the PIV, PVLV, and LMV were measured. The proximal diameter of the great cardiac vein (GCV) and the distal diameter of the GCV
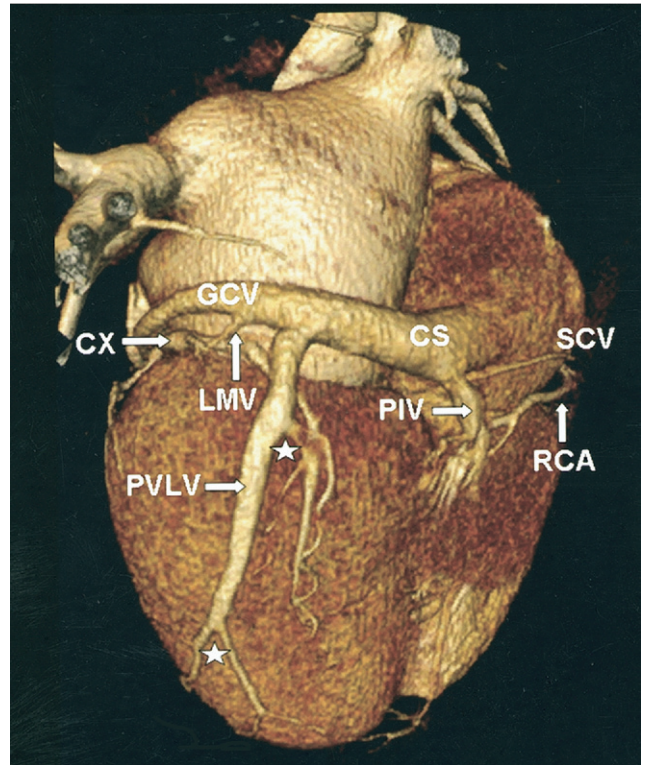

Figure 1. Volume-rendered reconstruction of the heart, posterolateral view. The first tributary of the coronary sinus (CS) is the posterior interventricular vein (PIV), running in the posterior interventricular groove. The second tributary of the CS is the posterior vein of the left ventricle (PVLV) with several side branches **(asterisks)**. The next tributary is the left marginal vein (LMV). The great cardiac vein (GCV) will then continue as anterior cardiac vein in the anterior interventricular groove. Also note the circumflex coronary artery (CX) and right coronary artery (RCA).

before continuing its course in the anterior interventricular groove as anterior cardiac vein were also evaluated. Finally, the distance between the origins of the various venous tributaries was measured on volume-rendered reconstructions (Fig. 3).

Statistical analysis. A statistical software program, SPSS 12.0 (SPSS Inc., Chicago, Illinois), was used for statistical analysis. Continuous variables are presented as mean ± SD. Categorical variables are presented as absolute number (percentage). Analysis of variance was used to study differences between the groups regarding continuous variables; chi-square testing was used to study differences regarding categorical data. A p value <0.05 was considered statistically significant.

RESULTS

Baseline characteristics. In Table 1, baseline characteristics of the individuals are summarized. Compared with control patients, patients with significant CAD or a history of infarction were older and were more frequently men. They also had a higher frequency of cardiac risk factors including hypercholesterolemia and smoking.
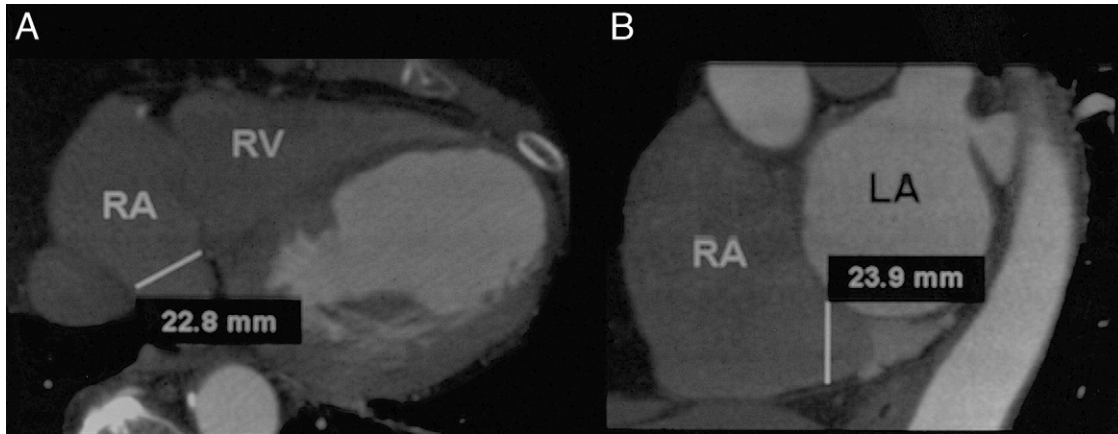
Figure 2. Measurement of the diameter of the coronary sinus (CS). The ostium of the CS was defined as the site where the CS makes an angle with the right atrium in the crux cordis area. This is best seen on the transverse plane. The diameter is first measured in the anteroposterior position **(A)**. Multiplanar reformatting was then used to determine the size of the ostium in the supero-inferior direction on the coronal plane **(B)**. LA = left atrium; RA = right atrium; RV = right ventricle.

Left ventricular ejection fraction was significantly lower in patients with a history of infarction. Regarding the coronary artery lesions, none of the control patients had significant coronary stenosis (by definition). In the CAD group, 10 patients had lesions occluding ± 50% of the coronary lumen and 25 patients had lesions occluding ≥75% of the lumen. A significant stenosis was present in the left anterior descending coronary artery in 78% of patients, in the left circumflex coronary artery in 38%, and in the right coronary artery in 30%. For patients with a

Figure 3. Example of measurement of the distance between the origins of the tributaries of the coronary sinus. LMV = left marginal vein; PIV = posterior interventricular vein; PVLV = posterior vein of the left ventricle.

history of infarction, these percentages were 88%, 46%, and 42%, respectively. Regarding the location of the infarction, 23 patients (68%) had a previous anterior infarction, 4 (12%) a lateral infarction, and 7 (21%) an inferior infarction. Twelve of the 34 infarction (35%) patients had a non–Q-wave infarction and 22 (65%) had a Q-wave infarction.

Anatomic observations. No patients had to be excluded because of suboptimal study quality. The CS, anterior interventricular vein, and PIV were observed in nearly all patients (100%, 100%, and 99%, respectively). The PVLV was observed in 96% of the control patients, in 84% of the CAD patients, and in 82% of the patients with previous infarction (p = NS). The LMV was significantly less often identified in patients with a previous infarction as compared with CAD patients and control patients (27% vs. 61% vs. 71%, p < 0.001) (Fig. 4). An example of a patient with a previous infarction and absence of the LMV is presented in Figure 5. None of the patients with a history of a lateral infarction had a LMV; only 22% of the patients with a history of an anterior infarction had a LMV, whereas 43% of the patients with a previous inferior infarction had a LMV. In the 12 non–Q-wave infarction patients, the PVLV was present in 11 (92%) and the LMV was present in 5 (42%). In the 24 Q-wave infarction patients, the PVLV was present in only 17 (77%) and the LMV in 4 (18%).

In patients with a previous infarction, the presence of both a PVLV and LMV was observed significantly less often than in CAD patients and normal patients (26.5% vs. 60.5% vs. 71.4%, p < 0.01, Fig. 6). Patients with a PIV exhibited 1 side branch in 7%, 2 side branches in 28%, and 3 side branches in 2% of patients; 63% of these patients had no side branches. In the patients in whom a PVLV was identified, 1 side branch was observed in 2%, 2 side branches in 16%, and 3 side branches in 1% of patients; 81% had no side branches. In patients with a LMV, 1 side branch was present in 4% and 2 side branches in 23% of patients; 73% of these patients had no side branches. No significant
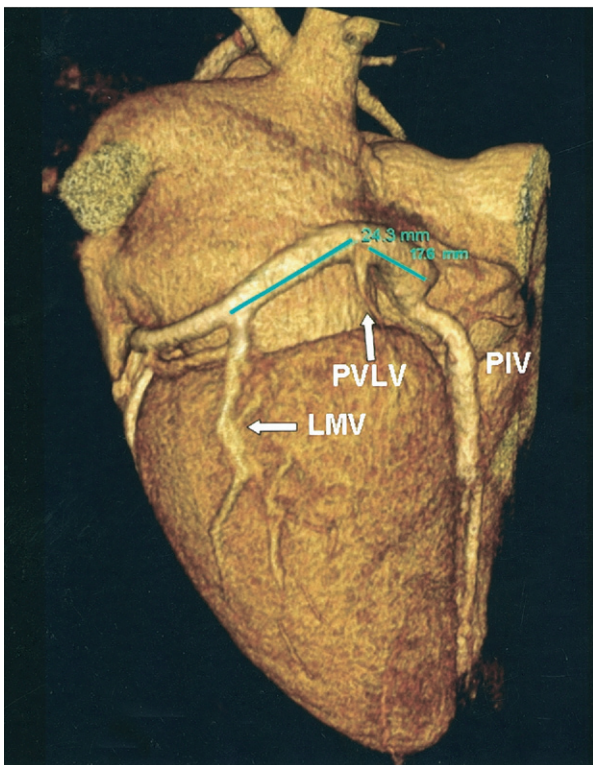
Table 1. Baseline Characteristics of the Study Population

	Control Patients (n = 28)	CAD (n = 38)	Infarction (n = 34)	p Value
Age (yrs)	56 ± 11	64 ± 10	62 ± 11	0.02
Male gender	14 (50%)	26 (68%)	28 (82%)	0.03
LV ejection fraction	64 ± 9%	58 ± 14%	50 ± 13%	0.0001
Cardiac risk factors				
Hypertension	10 (40%)	17 (50%)	11 (37%)	NS
Hypercholesterolemia	11 (44%)	24 (71%)	22 (73%)	0.047
Smoking	4 (16%)	10 (29%)	14 (47%)	0.048
Diabetes mellitus	9 (35%)	14 (40%)	3 (10%)	0.02
Family history of CAD	7 (28%)	7 (21%)	12 (39%)	NS

CAD = coronary artery disease; LV = left ventricular.

differences regarding the number of side branches were observed between control patients and patients with CAD with or without previous infarction.

Quantitative measurements from MSCT. The quantitative measurements are presented in Table 2. Inter- and intra-observer agreement were assessed in 10 patients; percentage agreements were 94% and 97%, respectively. For all patients, the diameter of the CS in the supero-inferior direction was significantly larger as compared to the antero-posterior direction: 12.2 ± 3.3 mm versus 11.3 ± 3 mm (p = 0.002). The more distant tributaries of the CS had smaller diameters. Within the 3 groups (control patients, CAD patients, or patients with previous infarction), no significant differences were noted. The distances between the origins of the different vessels were also comparable among the 3 groups.

DISCUSSION

The main findings in the current study are 2-fold. First, non-invasive evaluation of the cardiac venous system in CAD patients is feasible using 64-slice MSCT. Second, variation of the cardiac venous anatomy in CAD patients appears related to a history of previous MI; patients with previous infarction have significantly less left marginal veins.

Figure 4. Presence of the CS and its main tributaries: PIV, PVLV, and LMV in the 3 subsets (control patients, patients with coronary artery disease [CAD], and patients with CAD and history of myocardial infarction). Abbreviations as in Figure 3. *p < 0.01; **p < 0.0001.

These observations may have important implications for selection of potential CRT candidates with a history of MI. **Non-invasive evaluation of the cardiac venous system.** Until recently, the cardiac venous system could only be evaluated invasively using retrograde venography, either by direct manual contrast injection or after occlusion of the coronary sinus (8,9). In 2000, few studies reported on the use of non-invasive imaging with electron beam CT to depict the cardiac venous system (10,11). Recently, Mao et al. (12) analyzed the electron beam CT of 231 patients and demonstrated that this technique provides 3-dimensional (3-D) visualization of most components of the coronary venous system. In 2003, Tada et al. (13) reported the feasibility of MSCT to obtain high quality 3-D images of the cardiac venous system in one patient. Recently, preliminary studies were published on the value of 16-slice MSCT to evaluate the cardiac veins (7,14,15). Since then, 16-slice MSCT has gradually been replaced by 64-slice MSCT, offering a higher spatial resolution with a decreased acquisition time. Abbara et al. (14) suggested that because of the shorter scanning time, venous opacification might be insufficient using scanning protocols tailored for imaging the coronary artery system. However, the feasibility of depicting the cardiac venous system with 64-slice MSCT was clearly demonstrated in the present study. Despite a shorter scanning time, the CS and its tributaries could be evaluated in all individuals. Prominent side branches, suitable for insertion of pacemaker leads, were adequately visualized, but the distal parts of side branches with a smaller diameter could not be detected in all patients.

Variations in cardiac venous anatomy. In the current report, the accepted terminology for the CS and its tributaries of the Nomina Anatomica (English version) as described by von Lüdinghausen (16) was used to permit comparison with previous studies. Of note, in various studies the PIV is often described as the middle cardiac vein. Both in anatomic series and imaging series, either invasive venography or non-invasive evaluation with CT, a substantial variation in anatomy was reported.

First, the CS was analyzed. The CS is the most constant component of the cardiac venous system and was detected in all patients. The diameter of the CS was larger in the
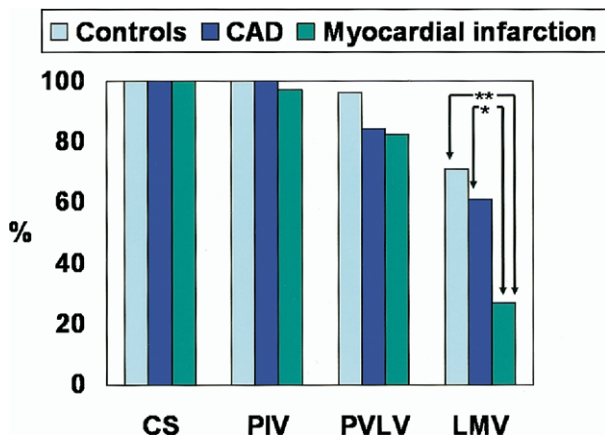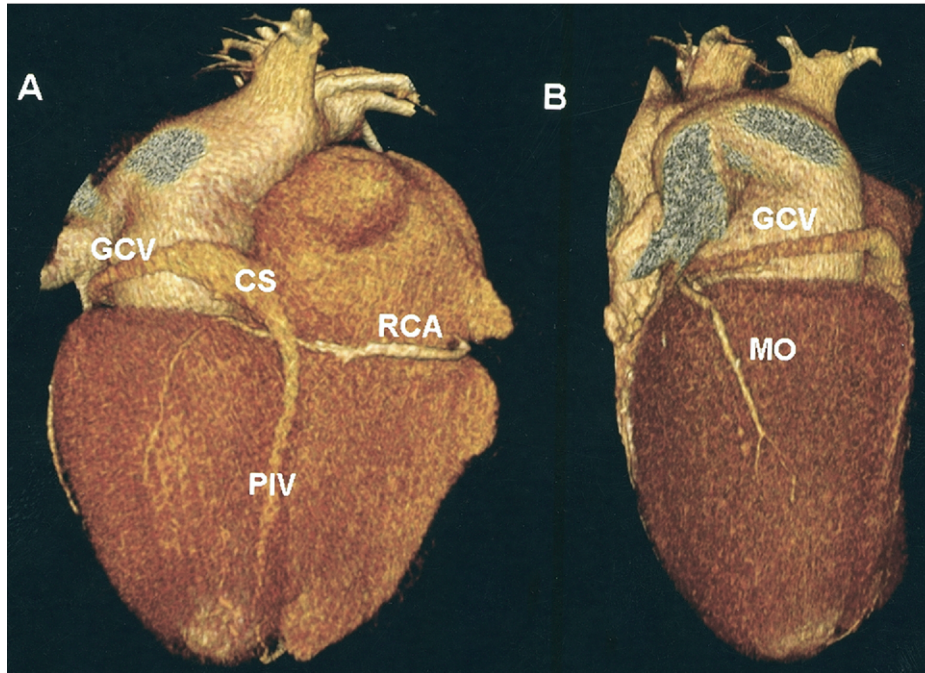
Figure 5. Example of absence of the posterior and left marginal vein in a patient with a history of an anterolateral infarction. **(A)** Posterior view; **(B)** left lateral view. The only tributary of the coronary sinus (CS) and great cardiac vein (GCV) is the posterior interventricular vein (PIV). Also note the obtuse marginal (MO) branch of the circumflex coronary artery and the right coronary artery (RCA).

supero-inferior direction as compared to the anteroposterior direction, indicating an oval shape of the ostium, confirming the 16-slice MSCT observations of Jongbloed et al. (7) and magnetic resonance imaging observations by Wittkampf et al. (17).

Second, the tributaries of the CS were evaluated. The PIV was observed in (nearly) all patients. The highest variability was observed in the number of tributaries between the PIV and the anterior interventricular vein. In anatomic series, the PVLV existed as a single large vessel in 63% of the cases (diameter ranging from 1.0 to 5.5 mm), and the prevalence of the LMV was between 73% and 88%

of cases (diameter varying from 1.0 to 3.0 mm) (15). Meisel et al. (8) studied 129 patients referred for cardioverter-defibrillator implantation with invasive venography and noted a PVLV in 55% and a LMV in 83%. In studies using non-invasive modality (electron-beam CT or 16-slice MSCT), the prevalence of the PVLV varied between 13% and 80% and the prevalence of the LMV between 38% and 93% (11–14). The number of patients with CAD was not specified in every study, and data on the prevalence and site of infarction were frequently lacking. Mao et al. (12) analyzed 231 patients and found the CS in 100%, the PIV in 100%, the posterior vein in 78%, and the marginal vein in
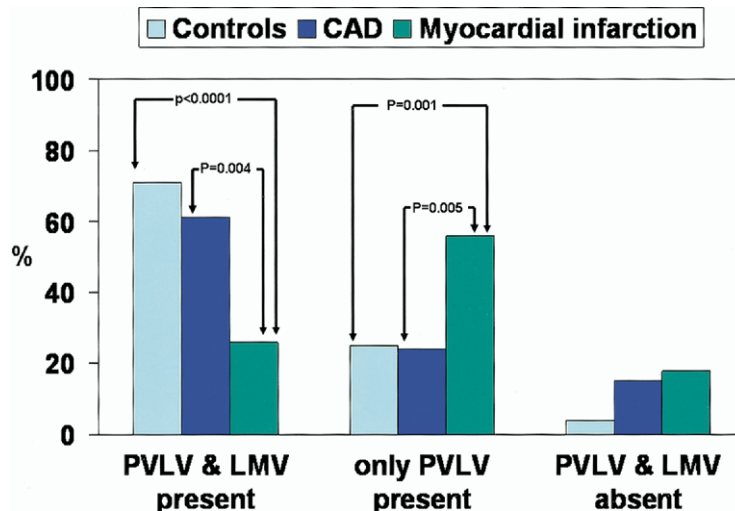

Figure 6. Prevalence of both the posterior vein of the left ventricle (PVLV) and the left marginal vein (LMV), only the PVLV, and neither PVLV and LMV according to subject category: control patients, coronary artery disease (CAD) patients, and myocardial infarction patients. Overall p = 0.003.

Table 2. Quantitative Measurements in Venous Anatomy From MSCT

	Control Patients (n = 28)	CAD (n = 38)	Infarction (n = 34)	p Value
Diameters				
CS anteroposterior (mm)	11.5 ± 2.4	11.2 ± 3.7	11.2 ± 2.9	NS
CS superoinferior (mm)	12.6 ± 3.2	11.7 ± 3.3	12.5 ± 3.3	NS
GCV proximal (mm)	7.2 ± 1.4	7.0 ± 1.8	7.4 ± 1.4	NS
GCV distal (mm)	4.9 ± 1.1	5.0 ± 1.0	5.1 ± 1.3	NS
PIV (mm)	5.0 ± 0.7	5.2 ± 1.3	5.2 ± 1.3	NS
PVLV (mm)	3.8 ± 0.7	3.9 ± 1.0	4.1 ± 1.1	NS
LMV (mm)	3.1 ± 0.8	3.6 ± 1.5	5.3 ± 5.8	NS
Distance between origin of				
PIV and PVLV (mm)	32 ± 17	27 ± 14	36 ± 22	NS
PVLV and LMV (mm)	41 ± 13	39 ± 15	38 ± 17	NS
PVLV and AIV (mm)	51 ± 16	55 ± 17	57 ± 10	NS
LMV and AIV (mm)	45 ± 9	44 ± 14	46 ± 13	NS

AIV = anterior interventricular vein; CS = coronary sinus; GCV = great cardiac vein; LMV = left marginal vein; PIV = posterior interventricular vein; PVLV = posterior vein.

81%. Abbara et al. (14) included 54 patients with suspected CAD referred for 16-slice MSCT. In 4 patients (7.4%), no LMV could be identified, and in 11 (20.4%) patients, no posterior vein could be found; however, none of the patients had a definite diagnosis of acute MI (14). Jongbloed et al. (7) studied 38 patients, including 18 CAD patients. The CS and PIV were observed in all patients; the PVLV was found in 95% of patients and the LMV in 60%.

A novelty of the current study is the demonstration of an association between these anatomic variations and the history of a MI. None of the patients with a previous lateral infarction had a LMV, and patients with anterolateral MIs and especially Q-wave infarctions were lacking the LMV. Post-mortem studies on cardiac veins in ischemic heart disease are scarce. Hansen (18) studied several series of patients who died from ischemic heart disease and detected thrombosis of the epicardial veins in large transmural infarctions. In all cases, the thrombosed veins were those draining the infarcted myocardium (19). Indirect evidence supporting the association between previous infarction and absent cardiac veins is provided by Komamura et al. (20), who used thermodilution measurements of GCV flow after reperfusion and demonstrated that salvaged myocardium after successful thrombolysis was not observed in patients demonstrating a progressive decrease in great cardiac vein flow.

Clinical implications. The observation that patients with previous infarction are frequently lacking the LMV has important implications for the selection of potential candidates for CRT. Positioning the LV lead is the most challenging part of CRT implantation. Before a patient with previous infarction is referred for CRT implantation, a triad of questions (Fig. 7) has to be answered. First: where is the area of latest activation located? As shown by Ansalone et al. (21), the best clinical response occurs in patients who had their LV lead placed in or near the site of latest activation. Echocardiography with tissue Doppler imaging is an adequate non-invasive imaging modality to answer this question (22,23). Second: does the area of latest

mechanical activation not contain transmural scar tissue? Recently, Bleeker et al. (24) observed that patients with transmural posterolateral scar tissue on contrast-enhanced magnetic resonance imaging failed to respond to CRT. This observation underscored that assessment of LV dyssynchrony in patients with ischemic cardiomyopathy should be combined with assessment of scar tissue to verify whether the region that will be targeted for LV pacing does not contain transmural scar tissue. After having identified the region of latest activation without scar tissue, a final question has to be answered: are their cardiac veins, draining this target region, suitable for LV lead placement? Multi-slice CT can provide an answer to this question, which appears important in patients with a history of MI. If suitable cardiac veins are absent, a surgical approach is preferred over transvenous LV lead positioning.

Multi-slice CT is a reliable technique to depict the cardiac venous system, and the 3-D reconstruction will also allow segmental classification to map the cardiac veins and
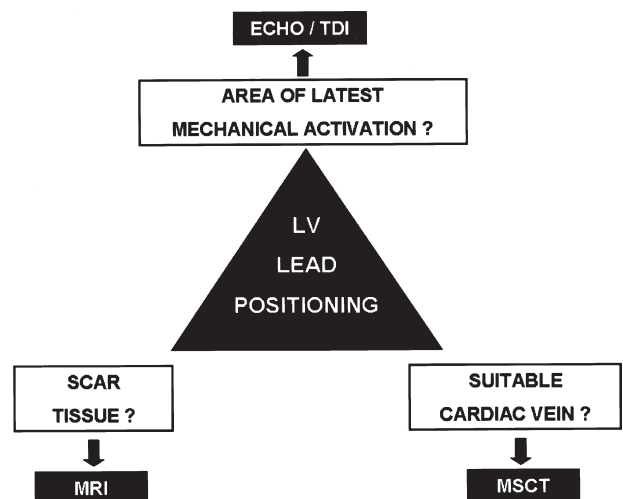

Figure 7. Non-invasive approach for left ventricular (LV) lead positioning. MRI = magnetic resonance imaging; MSCT = multi-slice computed tomography; TDI = tissue Doppler imaging.

tributaries in relation to the LV wall in a manner comparable to that of echocardiography (25). Multi-slice CT is able to detect anatomic and quantitative differences that may occur in CS and venous anatomy of heart failure patients who are candidates for CRT. Multi-slice CT will not only confirm the presence of a specific CS tributary but will also provide information on the course of the vessel, the side branches, the diameter, the distance from the CS, and the relation with adjacent structures. Depending on the experience of the implanting cardiologist, no invasive venography at all or only selected venography of the target cardiac vein may be sufficient to implant the lead successfully, on the basis of the MSCT data. In addition, information on cardiac venous anatomy acquired with MSCT could also be used during CRT implantation for 3-D navigation into the heart cavities and veins (26).

Study limitations. The 64-slice MSCT scans were tailored for optimal visualization of the coronary arteries. This could have caused suboptimal enhancement of the coronary veins, particularly of second- and third-degree side branches with a small diameter. Because atrial fibrillation is considered a contraindication for MSCT of the coronary arteries, only patients in sinus rhythm were included. Prospective confirmation of the current findings is needed in patients referred for CRT.

Conclusions. Non-invasive evaluation of the cardiac venous anatomy with 64-slice MSCT is feasible. There is considerable variation in cardiac venous anatomy. Patients with a history of MI were less likely to have a LMV, possibly limiting optimal LV lead positioning for CRT.

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