# Characterization of the suitability of coronary venous anatomy for targeting left ventricular lead placement in patients undergoing cardiac resynchronization therapy

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| **Aims** | Recent studies suggest differences in coronary venous anatomy between patients with ischaemic (I) and non-ischaemic (N) cardiomyopathy. We hypothesize that these differences may affect the potential for left ventricular (LV) lead targeting in patients undergoing cardiac resynchronization therapy. |
| **Methods and results** | The retrograde contrast venograms were retrospectively reviewed in 133 patients (age $68 \pm 9$ years, 101 males). The quantity and distribution of veins were recorded as well as the final lead position. There were no major differences in the distribution of LV lead positions between I and N [posterior vein, 14.0% (I) vs. 15.8% (N); posterolateral vein, 21.1 vs. 18.4%; lateral vein, 59.7 vs. 50.0%; anterolateral vein, 3.5 vs. 13.2%; $P = \text{NS}$]. Excluding the middle and great cardiac veins, in total only 59 of 133 patients had more than one suitable vein as potential targets for LV lead placement (I, 36.8% vs. N, 50.0%; $P = 0.16$). |
| **Conclusion** | Underlying aetiology does not affect the quantity and distribution of coronary veins available for LV lead placement. The limitations of venous anatomy restrict LV lead placement to a single vein with little scope for site selection in almost half of all the patients. Given these limitations, in many patients, prospective targeting of LV lead placement may require a direct surgical approach. |
| **Keywords** | Cardiac resynchronization therapy • Coronary veins • Left ventricular lead placement |

## Introduction

Cardiac resynchronization therapy (CRT), in a relatively short space of time, has evolved into a well-established treatment for selected patients with advanced heart failure. Responders are offered the potential of enhanced systolic function, reversal of left ventricular (LV) remodelling, reduction in hospital admissions, and improved survival and clinical symptoms.[1–5] Non-responders still continue to represent a consistently high proportion (25–30%) of all recipients of biventricular stimulation. This may in part relate to inappropriate patient selection but also to deficiencies in therapy implementation. Along with lack of LV dyssynchrony, extensive myocardial scarring, posterolateral

transmural infarction, and inappropriate device programming, suboptimal LV lead position is implicated in non-response.[6,7] Left ventricular performance shows a greater improvement in patients in whom the LV is paced at the most delayed site compared with patients in whom it is paced at any other site.[8,9] Concordance between the position of the LV pacing lead and the latest area of activation is associated with the greatest improvements in reverse chamber remodelling in a graduated manner according to the degree of separation between lead tip and maximal dyssynchronous segment.[10] Recent work has demonstrated that correlation between pacing site and site of maximal dyssynchrony translates into better clinical outcomes of improved mortality and heart failure hospitalizations.[11] Left ventricular lead placement

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is restricted by the variability of coronary venous anatomy. In addition, there may be issues related to lead instability, inadequate pacing and sensing thresholds, and diaphragmatic pacing. Non-invasive visualization of coronary venous anatomy is a novel and feasible application of multidetector computed tomography (MDCT).[12–14] In keeping with previous invasive studies, variation of coronary anatomy between individual patients is consistently reported in published series.[15–17] Differences between groups of patients are also suggested by authors who report a paucity of lateral veins in subgroups of patients with either a history of myocardial infarction or previous coronary artery bypass grafting (CABG).[13,14] The absence of coronary sinus tributaries may be related to scar formation causing regression of venous drainage to non-viable segments. The impact of these acquired anatomical differences on the potential for LV lead targeting has not been investigated. We hypothesize that the suggested differences in the quantity and distribution of coronary veins between patients with ischemic and non-ischemic cardiomyopathy may affect the potential for LV lead targeting in patients undergoing CRT with and without ischaemic heart disease. In this observational study, we reviewed the implant retrograde coronary sinus venograms at the time of CRT implantation to assess the potential for targeted LV lead placement.

# Methods

## Study population

In this single-centre study, data were retrospectively reviewed from 139 patients who underwent CRT between October 2006 and July 2008. Selection for device implantation was based on New York Heart Association (NYHA) class III or IV symptoms, despite optimal drug treatment, impaired LV systolic function (ejection fraction <35%), and QRS durations >120 ms. In all patients, the devices were implanted in the electrophysiology laboratory under local anaesthetic. Intravenous sedation was given where required.

## Invasive coronary venography

Retrograde radio-opaque contrast injection was performed to delineate coronary venous anatomy following coronary sinus intubation. An occlusive balloon catheter was inserted in the coronary sinus to maximize coronary venous opacification in cases where coronary venography was deemed to be incomplete. The images were recorded in the left anterior oblique (20–30°) and right anterior oblique (RAO) (20–30°) projections. The LV lead was positioned preferentially in the middle to distal aspect of a posterior or lateral ventricular branch of the coronary sinus. Following an overnight stay, patients underwent chest radiography (postero-anterior and lateral) to exclude lead displacement. The retrograde contrast venograms were retrospectively reviewed, and for each patient, the quantity and distribution of coronary veins were recorded as well as the final lead position on the pre-discharge chest radiograph. Coronary veins were documented for their presence as well as their deemed suitability to receive an LV pacing lead by two experienced implanters based upon vessel calibre, course, and tortuosity.
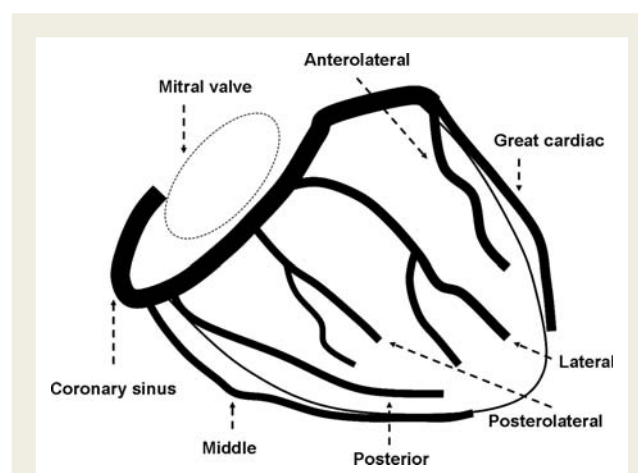
## Identification of coronary anatomy

The middle and great cardiac veins are the two most consistently present branches of the coronary venous system and so identification of the coronary veins on the venograms was performed by initially attempting to visualize these two veins.[18–21] Depending on their

position along the lateral border of the heart, the various branches draining into the coronary sinus were identified as posterior, postero-lateral, lateral, or anterolateral veins (*Figure 1*). For each patient, the final vein position of the LV lead was recorded.

## Left ventricular lead position

Lead positions were verified on post-implant chest radiographs in the postero-anterior and lateral views in all patients. In the lateral view, the cardiac silhouette was divided into three equal segments and lead tip classified as either anterior, lateral, or posterior (*Figure 2*).



**Figure 1** Schematic illustration of the coronary sinus and tributaries in an RAO view to show nomenclature used to identify coronary venous anatomy.
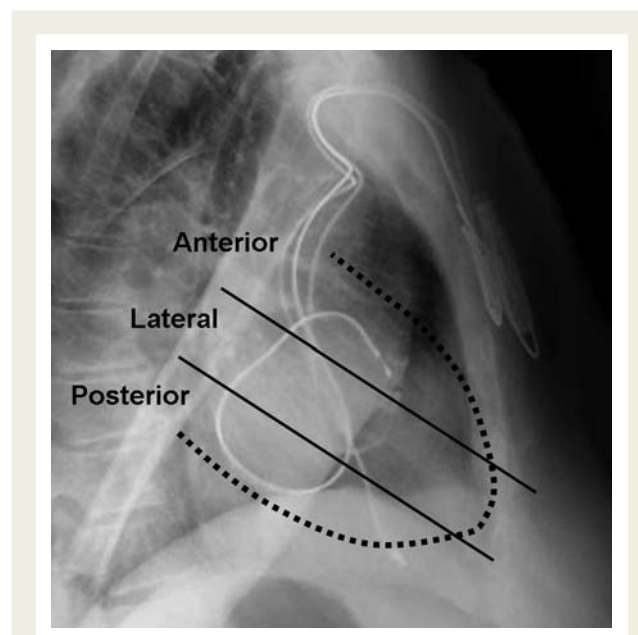


**Figure 2** In order to determine the LV lead position, the cardiac silhouette in the lateral chest radiograph is divided into three equal segments. In this example, the LV lead is seen in the anterior position.

## Statistical analysis

GraphPad Prism version 5 was used for the statistical analysis. For categorical data, Fisher's exact $T$-test was used. For continuous data, Student's $T$-test was used to compare means between two groups. A value of $P < 0.05$ was considered as statistically significant.

# Results

## Baseline characteristics

A total of 139 patients were assessed of which 6 subjects were excluded due to insufficient venography data. From the remaining 133 patients (age $68.2 \pm 8$ years, 101 males), transvenous CRT was abandoned in 2 patients due to the absence of any suitable

**Table I** Baseline characteristics of all patients

| Characteristic | Ischaemic (n = 57) | Non-ischaemic (n = 76) | P-value |
|---|---|---|---|
| Age (mean ± SD) | 66 ± 10 | 69 ± 11 yrs | NS |
| Male n (%) | 41 (72) | 60 (79) | NS |
| NYHA III/IV | 53/4 | 70/7 | NS |
| Diabetes mellitus, n (%) | 20 (35) | 30 (40) | NS |
| LV end-systolic volume, mL (mean ± SD) | 124 ± 19 | 120 ± 19 | NS |
| LV end-diastolic volume, mL (mean ± SD) | 70 ± 7 | 68 ± 12 | NS |
| EF, % (mean ± SD) | 23 ± 6 | 22 ± 6 | NS |
| QRS, ms (mean ± SD) | 158 ± 23 | 161 ± 25 | NS |
| Use of ACEI or ARB, n (%) | 54 (95) | 75 (97) | NS |
| Use of β-blockers, n (%) | 38 (67) | 54 (71) | NS |
| Use of spironolactone, n (%) | 32 (56) | 48 (63) | NS |
| Use of loop diuretics, n (%) | 57 (100) | 15 (100) | NS |

coronary vein in one and failure to cannulate the coronary sinus in the other. Both patients underwent surgical epicardial LV lead placement and data from both patients are included in the analysis. Fifty-seven patients had a history of ischaemic heart disease defined as coronary stenoses >50% in at least one epicardial artery, and of this group, 31 patients had previously undergone CABG. The baseline characteristics of all the patients according to underlying aetiology are shown in *Table 1*.

## Final left ventricular lead positions

Left ventricular lead positions were: posterior vein, ischaemic patients (I) 14.0% vs. non-ischaemic patients (N) 15.8% ($P = 1.00$); posterolateral vein 21.1 vs. 18.4% ($P = 0.36$); lateral vein 59.7 vs. 50.0% ($P = 0.29$); anterolateral vein 3.5 vs. 13.2% ($P = 0.11$); and the middle vein in one patient (I). There were no major differences in the distribution of final LV lead positions between I and N (*Figure 3*). Within the ischaemic group, there were no differences between patients according to the history of previous CABG. The LV lead had to be revised in eight patients (I, five patients and N, three patients) due to dislodgement within the first 6 weeks. Of this group prior to re-positioning, in one patient, the lead was placed anteriorly, in four patients laterally, and in three patients posteriorly.

## Characterization of venous anatomy

*Table 2* illustrates the quantity and distribution of coronary veins identified and the proportion of veins deemed as suitable targets for potential LV lead placement. For all patients, the breakdown according to aetiology is reported. In essence, the proportion of patients with one or more veins suitable for LV lead placement in each territory was 26.3% (posterior), 36.8% (posterolateral), 59.4% (lateral), and 24.8% (anterolateral) with no significant differences according to underlying aetiology. Excluding the middle and great cardiac veins, in total only 59 of 133 patients (44.4%) had
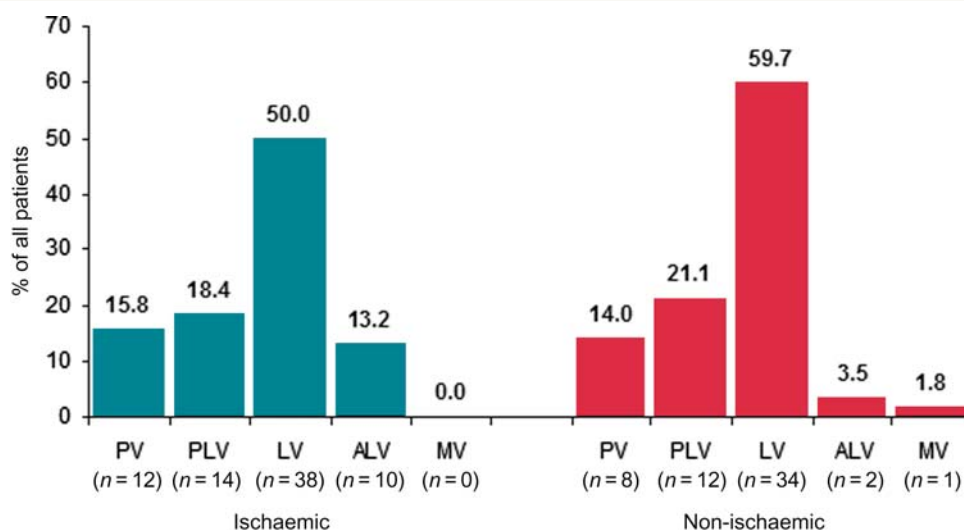
**Figure 3** Final left ventricular lead positions according to underlying aetiology of heart failure (n = 133). Posterior vein (PV, P = 1.00, ischaemic vs. non-ischaemic), posterolateral vein (PLV; P = 0.36), lateral vein (LV, P = 0.29), anterolateral vein (ALV, P = 0.11), and middle cardiac vein (MV).

**Table 2** Characterization of suitable veins in all patients and breakdown according to underlying aetiology

| Vein | No. suitable veins (total veins) | | | % patients with ≥1 suitable vein (*n*) | | | P-value |
|---|---|---|---|---|---|---|---|
| | All | NCM | ICM | All | NCM | ICM | |
| PV | 35 (50) | 20 (29) | 15 (21) | 26.3 (35) | 26.3 (20) | 26.3 (15) | 1.00* |
| PLV | 51 (68) | 31 (42) | 20 (26) | 36.8 (49) | 40.7 (31) | 31.5 (18) | 0.28* |
| LV | 94 (142) | 54 (90) | 40 (52) | 59.4 (79) | 55.2 (42) | 64.9 (37) | 0.27* |
| ALV | 36 (53) | 25 (37) | 11 (16) | 24.8 (33) | 30.2 (23) | 17.5 (10) | 0.09* |
| Total | 216 (313) | 130 (198) | 86 (115) | 44.3 (59) | 50.0 (38) | 36.8 (21) | 0.13* |

NCM, non-ischaemic cardiomyopathy; ICM, ischaemic cardiomyopathy; PV, posterior vein; PLV, posterolateral vein; LV, lateral vein; ALV, anterolateral vein. All (*n* = 133), NCM (*n* = 76), and ICM (*n* = 57).
*P-values refer to comparison of NCM vs. ICM.

**Table 3** Breakdown of characterization of suitable veins in ischaemic patients according to the previous history of CABG

| Vein | No. suitable veins (total) | | % patients with ≥1 suitable vein (*n*) | | P-value |
|---|---|---|---|---|---|
| | CABG | Non-CABG | CABG | Non-CABG | |
| PV | 10 (11) | 5 (10) | 32.2 (10) | 19.2 (5) | 0.27 |
| PLV | 12 (14) | 8 (12) | 32.2 (10) | 30.7 (8) | 0.91 |
| LV | 21 (27) | 19 (21) | 61.3 (19) | 69.2 (18) | 0.36 |
| LV | 7 (9) | 4 (7) | 22.6 (7) | 15.4 (4) | 0.35 |
| Total | 50 (61) | 36 (54) | 45.2 (14) | 26.9 (7) | 0.16 |

PV, posterior vein; PLV, posterolateral vein; LV, lateral vein; ALV, anterolateral vein. CABG (*n* = 31) and non-CABG (*n* = 26).

more than one suitable vein as potential targets for LV lead placement (I, 36.8% vs. N, 50.0%; *P* = 0.16). Within the ischaemic group, there were no differences according to a prior history of CABG (*Table 3*). There was a mean of 1.64 ± 0.94 suitable veins per patient (I, 1.51 ± 0.87 veins per patient vs. N, 1.73 ± 0.98 veins per patient; *P* = 0.18). Within the ischemic population, there were no differences according to a history of previous CABG (CABG, 1.61 ± 0.80 veins per patient vs. non-CABG, 1.38 ± 0.94 veins per patient; *P* = 0.322).

# Discussion

To our knowledge, this study reports the largest series of the quantity and distribution of coronary venous anatomy and the implications for the potential for LV lead targeting in patients undergoing CRT. We demonstrate that in almost half of all the patients undergoing CRT, the limitations of coronary venous anatomy restrict LV lead placement to a single vein with little scope for site selection. Furthermore, we show that the underlying aetiology of heart failure does not appear to make significant differences in the potential for LV lead targeting. In the light of studies using MDCT showing variations in coronary venous anatomy according to a prior history of previous myocardial infarction or CABG, our finding is a little unexpected.[13,14] Compared with MDCT, retrograde invasive venography at the time of CRT implant may be disadvantaged by the potential for poor visualization of early tributaries in the territory of the middle, posterior, and possibly the posterolateral territory while trying to achieve a

stable catheter position deeper in the coronary sinus. Additionally, the mid- to apical portions of coronary veins may not be well opacified. These factors may lead to an underestimate of the quantity and distribution of coronary venous anatomy and may be a limitation of our study. We do not believe that our findings are significantly impacted by this potential difference in the two techniques. If there are significant differences in coronary venous anatomy between patients with ischaemic and non-ischaemic cardiomyopathy, it does not appear to affect the potential for LV lead targeting. Furthermore, any differences between the two groups according to underlying aetiology are not reflected in the final lead position of LV leads. Only one study to date has compared head-to-head MDCT venography and invasive venography in CRT and not demonstrated any significant differences.[22] The cohort was however fairly small (*n* = 21) and the results require corroboration in a larger prospective study.

Variations in coronary venous anatomy determine LV lead position and affect CRT response. From the early work by Ansalone *et al.*[23] and more recently the use of techniques of tissue synchronization imaging,[9,10,22] real-time three-dimensional (3D)[8] and speckle tracking echocardiography[11,24] concordance between LV lead positions with respect to underlying dyssynchrony has a direct effect on clinical response, mortality, and hospitalizations. Early invasive studies show that even small changes in LV lead position are associated with exquisite changes in acute myocardial performance. Concurrent invasive measurements of pressure–volume loops during epicardial lead placement at multiple different sites in the LV show substantial variation in acute improvements in stroke

volume and d$P$/d$t_{max}$. In this acute haemodynamic study, a change of position of even 2 cm can significantly impact on response.[25] A great deal of variability exists in the distribution of LV mechanical dyssynchrony. The site of latest activation in 43% of patients in Ansalone *et al.*'s study[23] was not a lateral or posterolateral region, and in the study by Burgess *et al.* using real-time 3D echocardiography, the site of maximal mechanical delay in 52% was either the septal or the anteroseptal regions.[26] The optimal method for determining the site of maximal delay has not been established and the differences between echocardiographic techniques will be an important factor in assessing areas of intraventricular delay. When coronary lead position is reviewed in the context of area of latest activation as in the studies by Murphy *et al.*[10] and Becker *et al.*,[8] LV lead tip concordance to the area (or in the vicinity) of maximal delay was seen in only 64.8% (35 of 54) and 55.2% (32 of 58) patients, respectively. These observations as well as our current study suggest that the limitations of coronary venous anatomy across all groups of heart failure patients can be very restrictive for LV lead targeting for CRT via the transvenous route. On this basis, attempts to prospectively target LV lead placement should probably give greater consideration to the possibility of a surgical approach as first line rather than just rescue therapy for failed transvenous implants. Direct surgical epicardial LV lead placement may overcome these limitations and this approach provides the potential for a nearly unrestricted opportunity of lead implantation to the optimal target site.

## Limitations of our study

This study retrospectively analysed the coronary venous anatomy of 133 patients who received CRT devices. The patients were all treated by experienced operators in a well-established implant centre. Thus, the expected value of our results should be considered comparable to other similar centres. The purpose of the present study was not to establish whether patients had responded to CRT, merely to assess the potential targets for LV epicardial lead placement during implantation. Clearly, our analysis would be of greater value if response to CRT was correlated to the number of suitable epicardial veins per patient. Nevertheless, we feel the conclusions of the limitations of coronary venous anatomy illustrated in this work and the characterization of coronary veins in a large number of CRT patients still holds valid.

**Conflict of interest:** none declared.

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