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# Can the Placement of the Left Ventricular Lead Regarding its Distance From the Ostium of the Middle Cardiac Vein Increase the Rate of Responder Patients to Cardiac Resynchronization Therapy?

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## ABSTRACT

**Objective:** Despite appropriate patient selection criteria and procedural information and technological advances, a high number of patients with cardiac resynchronization therapy (CRT) still remains non-responsive to treatment. In this study, it was aimed to investigate the relation between the distance between the middle cardiac vein (MCV) and the placement of the left ventricular (LV) lead and the response to CRT implantation.

**Material and Methods:** Angiographic and clinical data of a total of 53 patients were analyzed retrospectively. Patients were divided into two separate groups as responders and non-responders according to the benefit of CRT after at least six months of clinical follow-up. The distance between the coronary sinus (CS) branch where the LV lead was placed and the MCV ostium was measured, and the relation between this distance and response to CRT was examined.

**Results:** Mean age of the patients was 63.53 ± 11.11 years, and 19 (35.8%) patients were females. Ischemic etiology was significantly higher in the non-responders group than in the responder group [14 patients (41.2%) vs 13 patients (72.2%), p= 0.031]. The distance from MCV to the tributary where LV lead was placed was not statistically different between the groups (44.8 ± 18.3 mm vs. 37.8 ± 17.3 mm; p= 0.531); however, this distance was significantly correlated with the reduction of hospitalization after implantation of the CRT.

**Conclusion:** In general, the recommended target for the location of the LV lead in CRT implantation is the lateral and posterior tributaries of the CS, nevertheless this issue has not been clearly clarified. In this study, we found that the distance between the LV lead tributary and MCV may be associated with a decrease in the frequency of hospitalization due to heart failure.

**Keywords:** Cardiac resynchronization therapy, middle cardiac vein, responders

## ÖZ

**Sol Ventrikül İleti Kablosunun Orta Kardiyak Ven Ağzından Uzaklığa Göre Yerleştirilmesi, Kardiyak Resenkronizasyon Tedavisine Yanıt Veren Hasta Oranını Arttırabilir mi?**

**Giriş:** Uygun hasta seçim kriterlerine ve işlemsel bilgi ve teknolojik gelişmelere rağmen kardiyak resenkronizasyon tedavisi (KRT) uygulanan yüksek oranda hasta, tedaviye yanıt vermemeye devam etmektedir. Bu çalışmada, biz orta kardiyak ven (OKV) ağzı ile sol ventrikül (LV) iletim kablosu yerleşimi arasındaki mesafe ile KRT uygulanmasına yanıt arasındaki ilişkiyi araştırdık.

**Gereç ve Yöntemler:** Toplam 53 hastanın anjiyografik ve klinik verileri geriye dönük olarak analiz edildi. Hastaların yaş ortalaması 63.53 ± 11.11 yıl olup 19'u (%35.8) kadındı. Hastalar en az altı aylık klinik takipten sonra KRT'nin yararına göre yanıt verenler ve yanıt vermeyenler olarak iki ayrı gruba ayrıldı. LV iletim kablosunun yerleştirildiği koroner sinus (KS) dalı ile OKV ağzı arasındaki mesafe ölçüldü ve bu mesafeyle KRT'ye yanıt arasındaki ilişki incelendi.

**Bulgular:** İki grup arasında demografik ve klinik özellikler açısından karşılaştırıldığında, yanıt vermeyen grupta iskemik etiyoloji yanıt veren gruba göre anlamlı derecede yüksekti [14 hastaya (%41.2) karşı 13 hasta (%72.2), p= 0.031]. OKV ağzı ile LV iletim kablosunun yerleştirildiği yan dala olan mesafe, gruplar arasında istatistiksel olarak farklı değildi (44.8 ± 18.3'e karşı 37.8 ± 17.3; p= 0.531) ancak bu mesafe KRT uygulanmasından sonra hastaneye yatıştaki azalma ile anlamlı olarak ilişkiliydi.

**Sonuç:** Genel pratikte, KRT implantasyonunda LV iletim kablosu yeri için önerilen hedef, KS'nin yan ve arka dallarıdır ancak bu konu yeterince açıklığa kavuşturulmamıştır. Bu çalışmada, LV iletim kablosunun yerleştiği yan dal ile OKV ağzı arasındaki mesafenin kalp yetmezliğine bağlı hastaneye yatış sıklığında azalma ile ilişkili olabileceğini bulduk.

**Anahtar Kelimeler:** Kardiyak resenkronizasyon tedavisi, orta kardiyak ven, yanıt verenler

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## INTRODUCTION

Since the promising studies of Dr. Mower and Serge Cazeau in the early 1990s, cardiac resynchronization therapy (CRT) has been an important treatment strategy for heart failure patients with low ejection fraction and intraventricular conduction defects (1,2). Despite the advances in CRT devices technology and the improvement of knowledge of appropriate patient selection criteria over time, about 30% of the patients do not benefit from CRT implantation, and these cases are defined as non-responders.

The response to CRT implantation is related not only on the clinical characteristics of the patients, but also on procedural variables, in particular, on the anatomical features of the coronary sinus tributaries. Previous studies have reported that targeting the posterior and lateral walls for left ventricular (LV) lead placement is associated with better outcomes compared to other sites; however, more information is needed on which branch of the coronary sinus should be targeted to increase the amount of responder patients (3,4).

The middle cardiac vein (MCV) is located along the posterior interventricular groove of the heart and is adjacent to the interventricular septum. Therefore, we hypothesized that taking into account of the ostium location of MCV may be helpful as a cornerstone when determining the appropriate LV lead position. The aim of this study was to investigate the relation between the distance from the MCV ostium to the tributary of coronary sinus in which the LV lead is placed and the response to CRT.

## MATERIALS and METHODS

### Study Population

A total of 53 patients who underwent successful CRT implantation between January 2016 and November 2021 were included in this single-center retrospective and descriptive study. Despite the optimal medical treatment before the procedure, New York Heart Association (NYHA) functional class 2-4, in the surface electrocardiogram (ECG), left bundle branch block (LBBB), morphology, ejection fraction (EF) <40% and prolonged QRS duration (>130 msn) were determined as criteria for the implantation of CRT. Patients with non-LBBB interventricular conduction disease, severe valvular heart disease, serious liver and kidney failure were excluded from the study. Demographic, clinical features and angiographic images of all patients were retrospectively analyzed. Response to CRT was determined as regards the change in the following criteria after at least six months of follow-up;

1) NYHA functional capacity,

2) Hospitalization due to heart failure,

3) EF and

4) QRS duration.

Those who improved in terms of the criteria mentioned above after CRT implantation were defined as the responder group, and patients who did not have any changes or worsened were defined as the non-responder group.

### Angiographic Examination

Angiographic images of the patients were examined by two experienced cardiologists who were blind to the patients' clinical circumstances. After calibration, study parameters were measured at the moment when the coronary sinus and its tributaries were completely filled with a radiopaque agent at left anterior oblique (LAO) 30° views. In this view, the tributaries of the coronary sinus are divided into three zones, which are depicted from six o'clock to 12 o'clock (Figure 1). The distance between the MCV ostium and the tributary ostium where the LV lead was placed was measured.

This study was approved by Bakırköy Dr. Sadi Konuk Research and Training Hospital Clinical Research Ethics Committee (Decision Number: 2022-02-06, Date: 17.01.2022) and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

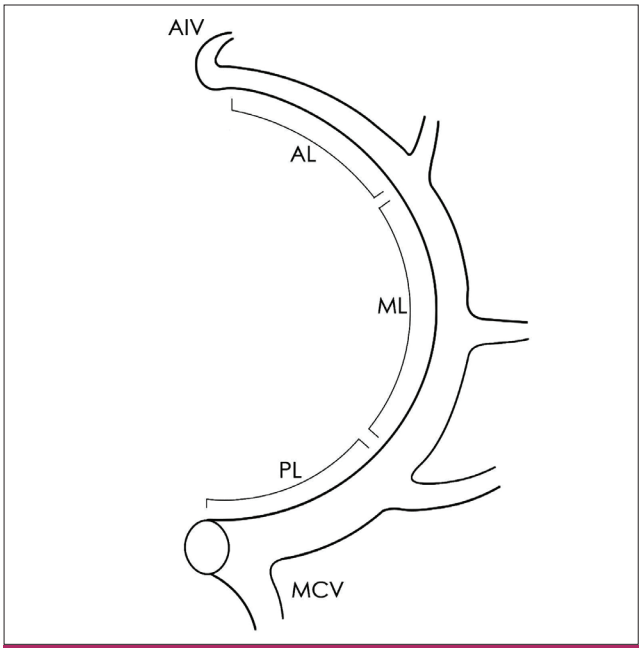


**Figure 1.** Depiction of the coronary sinus and its tributaries.
MCV: Middle cardiac vein, PL: Posterolateral branch, ML: Midlateral branch, AL: Anterolateral AIV: Anterior interventricular vein.

### Statistical Analysis

Normality assessment of the data was performed using the Shapiro-Wilk test. Data with Gaussian and non-Gaussian distribution were expressed as mean ± standard deviation (SD) and median and interquartile range (IQR). Comparisons of the responder and non-responder groups were performed using independent Student's t- test or Mann-Whitney U test accordingly. Correlation of the distance from the MCV to the LV lead location with other clinical parameters was assessed using Spearman correlation analysis.

## RESULTS

Of the 53 patients included in the study, 34 were identified as responders according to the criteria mentioned above after six months of follow-up. The comparisons between responder and non-responder groups in terms of clinical, electrocardiographic and echocardiographic characteristics are shown in Table 1. The ischemic etiology of heart failure was determined statistically significantly higher in the non-responder group (13 patients in the group) than in the responder group (14 patients in group) (72.2% vs 41.2%, p= 0.031). There was no statistically significant difference between the two groups in terms of other clinical, ECG and echocardiographic features.

Features of the patients regarding the anatomy of the coronary sinus and location characteristics of the LV lead placement in responder and non-responder patients are shown in Table 2. In 38 of the patients, only one tributary was available to place the LV lead, while in 15 patients, two available tributaries were determined. Furthermore, in 37 patients, the LV lead was placed on non-anterior tributaries. The distance between MCV and the tributary in which LV lead was placed was measured as average 44.8 ± 18.3 mm in the responder group and as average 37.8 ± 17.3 mm in the non-responder group; however the difference was not statistically significant.

**Table 1.** Comparison of responder and non-responder patient groups in terms of baseline clinical electrocardiographic (ECG) and echocardiographic features

| | Responder (n= 34) | Non-responder (n= 19) | p |
|---|---|---|---|
| Age (years ± SD) | 61.9 ± 11.49 | 66.3 ± 10.33 | 0.179 |
| Sex (female) | 12 (35.3%) | 6 (33.3%) | 0.887 |
| Etiology of heart failure (ischemic) | 14 (41.2%) | 13 (72.2%) | **0.031** |
| HT | 22 (64.7%) | 14 (73.7%) | 0.498 |
| DM | 16 (47.1%) | 10 (52.6%) | 0.697 |
| CRF | 10 (29.4%) | 9 (47.4%) | 0.194 |
| COPD | 2 (5.9%) | 2 (10.5%) | 0.612 |
| NYHA functional class, n (%) | | | 0.193 |
| 2 | 2 (5.9) | 4 (23.5) | |
| 3 | 26 (76.5) | 11 (58.9) | |
| 4 | 6 (17.6) | 4 (17.6) | |
| Rhythm, n (%) | | | 0.712 |
| Sinus | 31 (91.2) | 15 (83.3) | |
| AF | 2 (5.9) | 2 (11.1) | |
| Other | 1 (2.9) | 2 (5.6) | |
| QRS duration (msn) | 176 ± 18 | 170 ± 19 | 0.163 |
| EF (%) | 25.4 ± 6.6 | 27.3 ± 5 | 0.763 |
| LV EDD (mm) | 63.7 ± 6.7 | 60.1 ± 5.6 | 0.822 |
| Type of CRT, n (%) | | | 0.407 |
| Defibrillator | 33 (97.1) | 18 (94.7) | |
| Pacemaker | 1 (2.9) | 1 (5.3) | |

HT: Hypertension, DM: Diabetes mellitus, CRF: Chronic renal failure, COPD: Chronic obstructive pulmonary disease, NYHA: New York Heart Association, AF: Atrial fibrillation, EF: Ejection fraction, LV EDD: Left ventricular end diastolic diameter, CRT: Cardiac resynchronization therapy, SD: Standard deviation.

**Table 2.** Comparison of coronary sinus anatomical features and LV lead placement characteristics in responder and non-responder patients

| | Responder (n= 34) | Non-Responder (n= 19) | p |
|---|---|---|---|
| CS ostium diameter (mm ± SD) | 9.6 ± 2.4 | 9.1 ± 2.1 | 0.346 |
| Number of suitable tributaries for LV lead placement | | | |
| 1 | 24 (72.7%) | 14 (73.7%) | 0.940 |
| 2 | 9 (27.3%) | 5 (26.3%) | |
| Tributary in which LV lead placed | | | |
| Anterolateral | 11 (32.4%) | 5 (27.8%) | 0.606 |
| Midlateral | 12 (35.2%) | 6 (33.3%) | |
| Posterolateral | 11 (32.4%) | 7 (37.9%) | |
| LV lead position | | | |
| Basal | 2 (6.1) | 2 (11.1) | 0.633 |
| Middle | 17 (51.5) | 7 (38.9) | |
| Apical | 14 (42.4) | 9 (50) | |
| The distance between the MCV and the tributary in which placed LV lead (mm ± SD) | 44.8 ± 18.3 | 37.8 ± 17.3 | 0.531 |

CS: Coronary sinus, LV: Left ventricular, MCV: Middle cardiac vein, SD: Standard deviation.

**Table 3.** The correlation between the response parameters after CRT implantation and the distance from the MCV to the LV lead location

| | r | p |
|---|---|---|
| QRS differentiation | 0.246 | 0.088 |
| EF differentiation | -0.285 | 0.064 |
| NYHA functional status differentiation | 0.278 | 0.050 |
| Hospitalization due to heart failure | -0.325 | 0.023 |

CRT: Cardiac resynchronization therapy, MCV: Middle cardiac vein, LV: Left ventricular, EF: Ejection fraction, NYHA: New York Heart Association.

The relation between the distance from the MCV to the tributary of the coronary sinus where LV lead was placed and the parameters used to define the patients who were responders is shown in Table 3. The correlation found between the distance from the MCV to the LV lead position and the reduction in the frequency of hospitalization for heart failure after CRT implantation was in a negative direction and its effect was low despite being statistically significant (r= -0.325, p= 0.023). We did not find a statistically significant relation between the distance from the MCV to the LV lead position and other response parameters to CRT implantation.

## DISCUSSION

The most important finding of our study is the significant correlation between the distance from the MCV to the LV lead location and the decrease in the frequency of hospitalization due to heart failure after CRT implantation. However, we could not demonstrate similar correlation with other parameters (shortening of QRS duration, increasing of EF, NYHA functional status improvement) used to indicate the presence of a response to CRT implantation.

Similar to the result we found in our study, it is accepted that approximately 30% of the patients who undergo CRT do not receive an effective benefit from the implantation (5,6). In order to reduce this high non-responder rate, it is basically necessary to overcome the difficulties in two different stages;

1) Suitable patient selection and

2) accurate LV lead placement.

The implanter must handle other problems such as a stable lead position, an appropriate threshold, avoiding diaphragm stimulation and improving electrical conduction disorders in addition to a suitable and accessible tributary of CS to ensure effective LV stimulation. The MADIT-CRT study published in 2011 provided us with pioneering data showing that LV Lead placement is associated with clinical outcomes and showed that apical lead position is associated with an increase in deaths and hospital admissions (4). Another large-scale study recently published by Bohen et al. has demonstrated that lateral lead placement is associated with positive effects on long-term survival compared to anterior and posterior placements (7). Although there is no complete

consensus, in general, targeting areas outside of the anterior region (lateral and posterior) areas when placing the LV lead appears to be associated with higher responder rates and less negative clinical outcomes (5,8,9).

Identifying the latest electrical activation region and pacing from this area should be the main goal in order to reduce the prolonged QRS duration and achieve resynchronization of the cardiac conduction (10). As is well described, the stimulation of LV begins from the interventricular septum and proceeds to the lateral wall. In addition, MCV is one of the anatomical structures closest to this region where LV stimulation begins. Therefore, placement of the LV lead based on the origin of the conduction may provide additional benefit for increasing the response rate to CRT. In this study, we found that this distance is associated with reducing the frequency of hospitalization, which is one of the response parameters to CRT. While our study found a decrease in hospitalization time, there was no significant difference in QRS time reduction and ejection fraction improvement, which is consistent with the study published by Nakai et al., which has found that the improvement in clinical findings is higher than the improvements in ECG and echocardiographic findings (11).

The search for the optimal solution for resynchronization of ventricular conduction has initiated new pacing modalities. As of early results, his bundle pacing (HBP) and left bundle branch area pacing (LBP) modalities have appeared promising compared to conventional CRT to obtain a narrower QRS duration and better echocardiographic parameters (12,13). The result that all these new developments and searches show us is that more studies and developments are needed for the response to CRT.

### Limitations of the Study

Our study is a retrospective study with a relatively small number of cases. Supportive imaging methods such as tissue Doppler imaging, computed tomography and magnetic resonance imaging, which are used to see the detection of viable myocardial tissue in the target area of the LV lead before placement, were not used in this study. Other limitations are that the optimization process is not routinely performed for all cases after CRT implantation and also that the imaging methods necessary to demonstrate improvement in cardiac remodeling are not performed.

## CONCLUSION

Our study is the first study to use the distance between the MCV and the branch where the LV lead is placed. Moreover, we found that this distance may be associated with reducing the frequency of hospitalization in patients with CRT. Nevertheless, our findings need to be supported by large-scale prospective studies.

**Ethics Committee Approval:** This study was approved by Bakırköy Dr. Sadi Konuk Research and Training Hospital Clinical Research Ethics Committee (Decision Number: 2022-02-06, Date: 17.01.2022).

**Author Contributions:** Concept/Design: OP; Analysis/Interpretation: OP, ASE; Data Acquisition: ASE, MB; Writting: OP, ASE; Critical Revision: OP; Final Approval: OP.

**Conflict of Interest:** There is no conflict of interest.

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## REFERENCES

1. *Mower M. Method and apparatus for treating hemodynamic dysfunction by simultaneous pacing of both ventricles. US Patent (Patent Number: 4.928.688) 1990.*
2. *Cazeau S, Leclercq C, Lavergne T, Walker S, Varma C, Linde, C, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. N Engl J Med 2001;344(12):873-80. https://doi.org/10.1056/NEJM200103223441202*
3. *Saxon LA, Olshansky B, Volosin K, Steinberg JS, Lee BK, Tomassoni G, et al. Influence of left ventricular lead location on outcomes in the COMPANION study. J Cardiovasc Electrophysiol 2009;20:764-8. https://doi.org/10.1111/j.1540-8167.2009.01444.x*
4. *Singh JP, Klein HU, Huang DT, Reek S, Kuniss M, Quesada A, et al. Left ventricular lead position and clinical outcome in the multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy (MADIT-CRT) trial. Circulation 2011;123:1159-66. https://doi.org/10.1161/CIRCULATIONAHA.110.000646*
5. *Butter C, Georgi C, Stockburger M. Optimal CRT implantation-where and how to place the left-ventricularş lead? Curr Heart Fail Rep 2021;18(5):329-44. https://doi.org/10.1007/s11897-021-00528-9*
6. *Zhang X, Qian Z, Tang H, Hua W, Su Y, Xu G, et al. A new method to recommend left ventricular lead positions for improved CRT volumetric response and long-term prognosis. J Nuclear Cardiol 2021;28(2):672-84. https://doi.org/10.1007/s12350-019-01735-7*
7. *Behon A, Schwertner WR, Merkel ED, Kovács A, Lakatos BK, Zima E, et al. Lateral left ventricular lead position is superior to posterior position in long-term outcome of patients who underwent cardiac resynchronization therapy. ESC Heart Fail 2020;7(6):3374-82. https://doi.org/10.1002/ehf2.13066*
8. *Leyva F, Foley PW, Chalil S, Ratib K, Smith RE, Prinzen F, et al. Cardiac resynchronization therapy guided by late gadolinium-enhancement cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2011;13:29. https://doi.org/10.1186/1532-429X-13-29*
9. *Butter C, Auricchio A, Stellbrink C, Fleck E, Ding J, Yu Y, et al. Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. Circulation 2001;104(25):3026-9. https://doi.org/10.1161/hc5001.102229*
10. *Gold MR, Birgersdotter-Green U, Singh JP, Ellenbogen KA, Yu Y, Meyer TE, et al. The relationship between ventricular electrical delay and left ventricular remodelling with cardiac resynchronization therapy. Eur Heart J 2011;32(20):2516-24. https://doi.org/10.1093/eurheartj/ehr329*

11. *Nakai T, Ikeya Y, Kogawa R, Otsuka N, Wakamatsu Y, Kurokawa S, et al. What are the expectations for cardiac resynchronization therapy? A validation of two response definitions. J Clin Med 2021;10(3):514. https://doi.org/10.3390/jcm10030514*

12. *Vijayaraman P, Herweg B, Ellenbogen KA, Gajek J. His-optimized cardiac. resynchronization therapy to maximize electrical resynchronization: A feasibility study. Circ Arrhythm Electrophysiol 2019;12:e006934. https://doi.org/10.1161/CIRCEP.118.006934*

13. *Huang W, Chen X, Su L, Wu S, Xia X, Vijayaraman P. A beginner's guide to permanent left bundle branch pacing. Heart Rhythm 2019;16:1791-6. https://doi.org/10.1016/j.hrthm.2019.06.016*