


# Predictors of stroke volume improvement with AV-optimized conduction system pacing in patients with AV dromotopathy

Anja Zupan Mežnar<sup>1,2,\*</sup>, Tadej Žlahtič<sup>2</sup>, Miha Mrak<sup>1,2</sup>, Maja Ivanovski<sup>2</sup>, and David Žižek <sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Ljubljana, Vrazov trg 2, 1000 Ljubljana, Slovenia; and <sup>2</sup>Department of Cardiology, University Medical Centre Ljubljana, Zaloška 2, 1000 Ljubljana, Slovenia

Received 4 December 2025; revised 18 January 2026; accepted 16 February 2026; online publish-ahead-of-print 19 February 2026

## Abstract

### Aims

Patients with first-degree atrioventricular (AV) block and mechanical AV dyssynchrony can present with heart failure (HF)-like symptoms. AV-optimized conduction system pacing (CSP) can improve haemodynamics and symptoms, but selection criteria remain uncertain. We aimed to identify electrocardiographic and echocardiographic predictors of an acute haemodynamic response to AV-optimized CSP in symptomatic first-degree AV block.

### Methods and Results

Nineteen patients (mean age  $60.5 \pm 21.1$  years; 37% female) with symptomatic first-degree AV block underwent baseline electrocardiography and echocardiography followed by AV-optimized conduction system pacing and repeat echocardiographic assessment. Electrocardiographic parameters (PR interval, P wave duration/PR interval ratio) and echocardiographic indices (E/A wave confluence, A-Q interval, and DFT/RR ratio) were tested for association with change in left ventricular stroke volume (LVSV).

The mean PR interval was  $395 \pm 61$  ms, the mean A-Q interval  $155 \pm 65$  ms, and the mean DFT/RR ratio  $0.34 \pm 0.1$ . E/A wave confluence was present in 15 patients (79%). AV-optimized pacing increased LVSV by  $7.8 \pm 3.9$  ml, corresponding to an  $11.8 \pm 5.7\%$  relative increase ( $P < .01$ ). Echocardiographic parameters were associated with LVSV response, including A-Q interval ( $r = 0.63$ ,  $P = .004$ ), DFT/RR ratio ( $r = -0.59$ ,  $P = .008$ ), and E/A wave confluence ( $r = 0.57$ ,  $P = .01$ ). Electrocardiographic parameters were not associated with LVSV change.

### Conclusions

Echocardiographically assessed mechanical AV dyssynchrony, rather than electrocardiographic parameters, is associated with an acute haemodynamic response to pacing. Echocardiographic evaluation may help identify patients with prolonged PR interval who could benefit from AV-optimized CSP.

### Keywords

Atrioventricular dyssynchrony • Atrioventricular conduction block • Conduction system pacing • Atrioventricular optimization

## Background

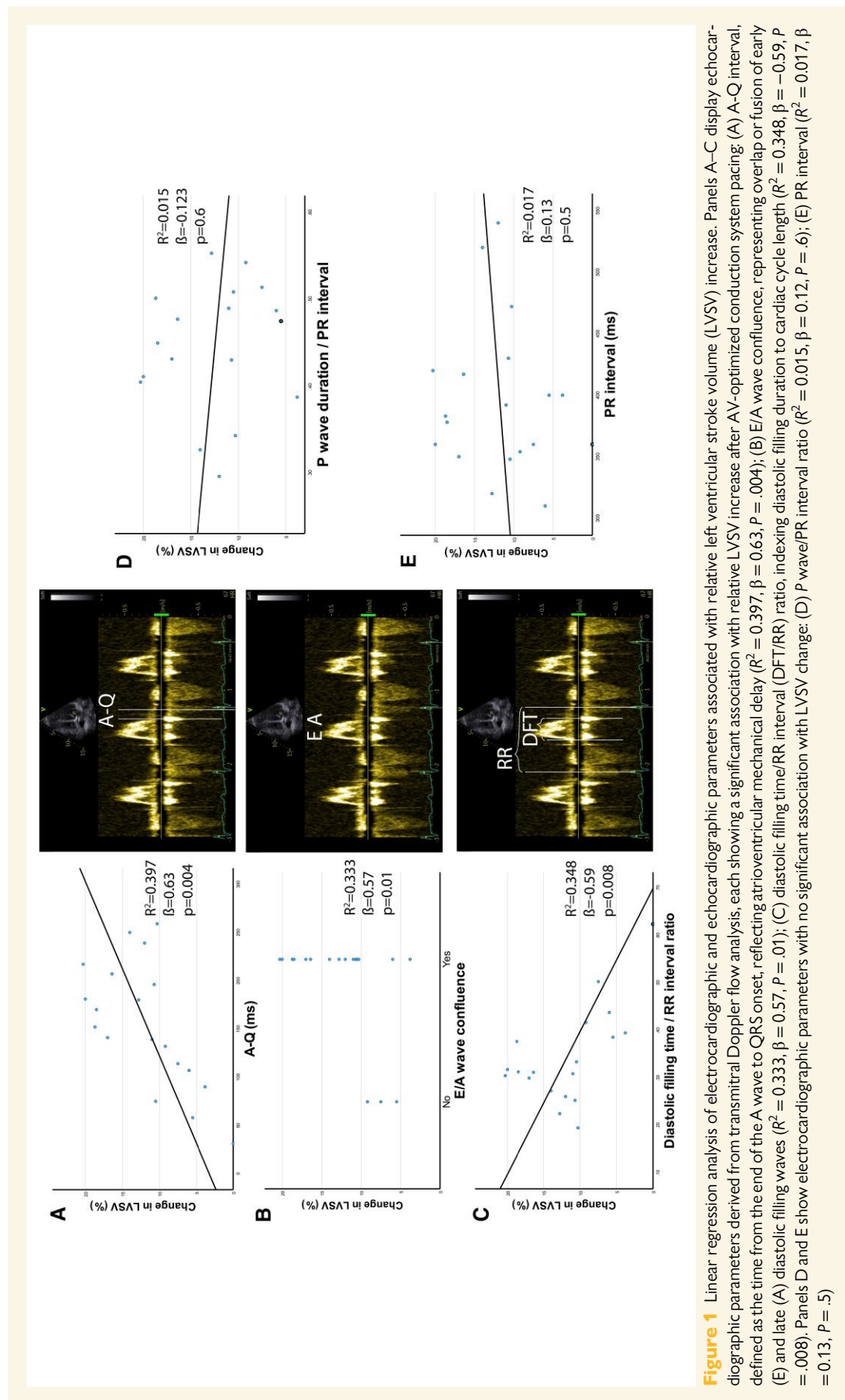
Patients with first-degree atrioventricular (AV) block and AV dyssynchrony may experience symptoms resembling heart failure (HF) owing to suboptimal ventricular filling and reduced left ventricular stroke volume (LVSV).<sup>1</sup> Although AV-optimized conduction system pacing (CSP)

has been shown to improve symptoms and LVSV in these patients, irrespective of baseline ejection fraction,<sup>2,3</sup> patient selection remains challenging. Notably, secondary analyses from the HOPE-HF trial suggested that the acute haemodynamic response to pacing is the most reliable predictor of clinical benefit, rather than baseline PR interval or echocardiographic E/A wave fusion.<sup>4</sup> However, this approach requires

\* Corresponding author. Tel: +386 1 522 85 68, Email: [anja.zupan.meznar@kclj.si](mailto:anja.zupan.meznar@kclj.si)

© The Author(s) 2026. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.



an invasive procedure before determining potential benefit, limiting its broader clinical adoption.

We hypothesized that echocardiographic assessment of AV dyssynchrony could help identify patients who are most likely to benefit from AV-optimized pacing.

## Aims

The aim of this study was to investigate electrocardiographic and echocardiographic parameters that predict a positive haemodynamic response to AV-optimized CSP in patients with symptomatic first-degree AV block.

## Methods

Between February 2020 and September 2022, patients screened for a single-centre, randomized, crossover AV dromotopathy study underwent prospectively planned baseline assessments, including PR interval measurement and echocardiography. The patient flow has been described previously.<sup>2</sup> This subanalysis includes individuals who received a CSP device (predominantly His bundle pacing) and had follow-up echocardiograms after AV-delay optimization. We included all 17 patients enrolled in the original randomized study and two additional patients who were excluded from that trial due to reduced left ventricular ejection fraction (total  $n = 19$ ). No other excluded patients underwent conduction system pacing. Exclusion criteria were: no symptoms, no echocardiographic AV dyssynchrony, PR interval shortening during exercise testing, pre-existing cardiac device, or a wide QRS complex. Electrocardiographic parameters (PR interval, P wave duration/PR interval ratio) and echocardiographic parameters (E/A wave confluence, A-Q interval [time interval between the end of A wave and the beginning of the QRS complex], and DFT/RR ratio [diastolic filling time/R wave to R wave interval ratio]), all measured from transmitral pulsed-wave Doppler with the sample volume placed at the mitral annulus level) were tested for association with change in LVSV after pacing.<sup>5</sup> Stroke volume was calculated from left ventricular outflow tract diameter and pulsed-wave Doppler velocity–time integral, obtained from apical five- and three-chamber views and averaged over at least five cardiac cycles. The values were cross-checked against the stroke volume obtained from the biplane Simpson's method. The echocardiographic acquisition and analysis protocol, including the AV-delay optimization procedure, has been described in detail previously.<sup>2</sup> Linear regression analysis was performed using SPSS v. 29.0.

## Results

Nineteen patients with complete datasets were analysed. The mean age was  $60.5 \pm 21.1$  years, 37% were female. All patients had marked first-degree AV block (mean PR interval  $395 \pm 61$  ms), measured at a mean heart rate of  $63 \pm 8$  bpm, and echocardiographic evidence of AV dyssynchrony. E/A wave confluence was observed in 15 patients (79%). The mean A-Q interval was  $155 \pm 65$  ms, and the mean DFT/RR ratio was  $0.34 \pm 0.1$ . AV optimized conduction system pacing increased LVSV by  $7.8 \pm 3.9$  ml, corresponding to an  $11.8 \pm 5.7\%$  relative increase. Left ventricular ejection fraction did not differ significantly before and after pacing ( $63.2 \pm 6.4\%$  vs.  $64.7 \pm 6.7\%$  with AV-optimized pacing).

Linear regression analysis showed that electrocardiographic parameters were not predictive of LVSV response to CSP. In contrast, echocardiographic parameters, particularly A-Q interval and DFT/RR, were significantly associated with the relative increase in LVSV. E/A wave confluence demonstrated a moderate positive correlation (Figure 1).

## Conclusions

Echocardiographically assessed mechanical AV dyssynchrony, rather than electrocardiographic parameters, appears to be the key

determinant of the haemodynamic response to pacing therapy. Consistent with HOPE-HF trial subanalysis, neither the PR interval nor the P wave/PR interval ratio reliably predicted benefit, reflecting that these measures capture electrical rather than mechanical aspects of AV dyssynchrony.<sup>4</sup>

In contrast, echocardiographic measures such as the A-Q interval, DFT/RR ratio, and E/A wave confluence demonstrated stronger associations with LVSV increase following AV-optimized CSP. The positive correlation between the A-Q interval and LVSV improvement suggests that a prolonged delay between atrial contraction and ventricular activation may identify patients most likely to benefit from AV-optimized CSP. Moreover, the inverse relationship between the DFT/RR ratio and LVSV increase highlights the importance of optimizing diastolic filling relative to the cardiac cycle. In this analysis, which included patients with markedly prolonged PR intervals, E/A wave confluence demonstrated only a moderate positive correlation. It is therefore unsurprising that in the HOPE-HF subanalysis, where the mean PR interval was  $249 \pm 59.2$  ms, there was no observed interaction between E/A wave confluence and the study endpoints.<sup>4</sup>

These findings suggest that echocardiographic assessment—particularly the A-Q interval and DFT/RR ratio—may assist in identifying patients with prolonged PR interval who could derive haemodynamic benefit from AV-optimized CSP. These results should be considered hypothesis-generating, and larger prospective studies are required to validate these parameters and determine whether their incorporation into patient selection and pacing algorithms improves clinical outcomes.

## Declarations

### Disclosure of Interest

The authors declare that they have no conflict of interest relevant to this manuscript.

### Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

### Funding

This work was supported by an institutional research grant from University Medical Centre Ljubljana (No. TP20190093).

## References

- Salden FCWM, Kutiyfa V, Stockburger M, Prinzen FW, Vernooij K. Atrioventricular dromotopathy: evidence for a distinctive entity in heart failure with prolonged PR interval. *Europace* 2018;**20**:1067–77. <https://doi.org/10.1093/europace/eux207>
- Zupan Mežnar A, Mrak M, Mullens W, Štublar J, Ivanovski M, Žižek D. AV-optimized conduction system pacing for treatment of AV dromotopathy: a randomized, cross-over study. *J Cardiovasc Electrophysiol* 2024;**35**:1340–50. <https://doi.org/10.1111/jce.16268>
- Whinnett ZI, Shun-Shin MJ, Tanner M, Foley P, Chandrasekaran B, Moore P, et al. Effects of haemodynamically atrio-ventricular optimized His bundle pacing on heart failure symptoms and exercise capacity: the His Optimized Pacing Evaluated for Heart Failure (HOPE-HF) randomized, double-blind, cross-over trial. *Eur J Heart Fail* 2023;**25**:274–83. <https://doi.org/10.1002/ehj.2736>
- Keene D, Kaza N, Srinivasan D, Ali N, Tanner M, Foley P, et al. Predictors of the efficacy of His bundle pacing in patients with a prolonged PR interval: a stratified analysis of the HOPE-HF randomized controlled trial. *Eur J Heart Fail* 2024;**26**:2261–8. <https://doi.org/10.1002/ehj.3367>
- Zupan Mežnar A, Mrak M, Žižek D. Letter regarding the article 'predictors of the efficacy of His bundle pacing in patients with a prolonged PR interval: a stratified analysis of the HOPE-HF randomized controlled trial'. *Eur J Heart Fail* 2024;**26**:2620–1. <https://doi.org/10.1002/ehj.3490>