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ORIGINAL SCIENTIFIC PAPER
Arrhythmias

Hypertensive vs. normotensive blood pressure response to advanced conduction disorders: comparison of baseline non-invasive haemodynamic evaluation

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Aims Patients with advanced conduction disorders exhibit diverse haemodynamic profiles, from cardiogenic shock to severe hypertension. Peripheral vascular resistance (PVR) significantly contributes to compensatory mechanisms during bradycardia. This study aimed to assess the haemodynamic responses of patients presenting with high-degree atrioventricular (AV) block.

Methods and results We retrospectively analyzed 261 consecutive patients with advanced conduction disorders who underwent pacemaker implantation from October 2020 to December 2022. Patients were classified into three groups: normotensive (<160 mmHg), hypertensive (≥160 mmHg), and unstable (requiring emergent temporary pacing). Additionally, 73 stable patients underwent non-invasive haemodynamic assessment. Of 261 patients, 99 (37.9%) were normotensive, 118 (45.2%) hypertensive, and 44 (16.9%) unstable. Hypertensive patients frequently had hypertension history (77.1%), presented with higher escape rhythms (39.1 ± 6.7 vs. 31.5 ± 10.4 and 38.1 ± 9.9 in unstable and normotensive patients, respectively), and exhibited higher ejection fractions (58.2 ± 8 vs. 53.2 ± 12 and 53.9 ± 11, respectively). They demonstrated fewer low cardiac output signs, including acute kidney injury and elevated lactate levels. PVR was significantly elevated in the hypertensive group. The unstable group experienced the highest 30-day mortality and higher 1-year mortality, though the latter did not reach statistical significance. Factors independently associated with a hypertensive response included higher heart rate, higher ejection fraction, and calcium channel blocker pre-treatment.

Conclusion Haemodynamic presentations in high-degree AV block are heterogeneous. A hypertensive response represents a distinct clinical phenotype characterized by preserved cardiac function, higher escape rhythms, increased PVR, and fewer end-organ hypoperfusion signs.

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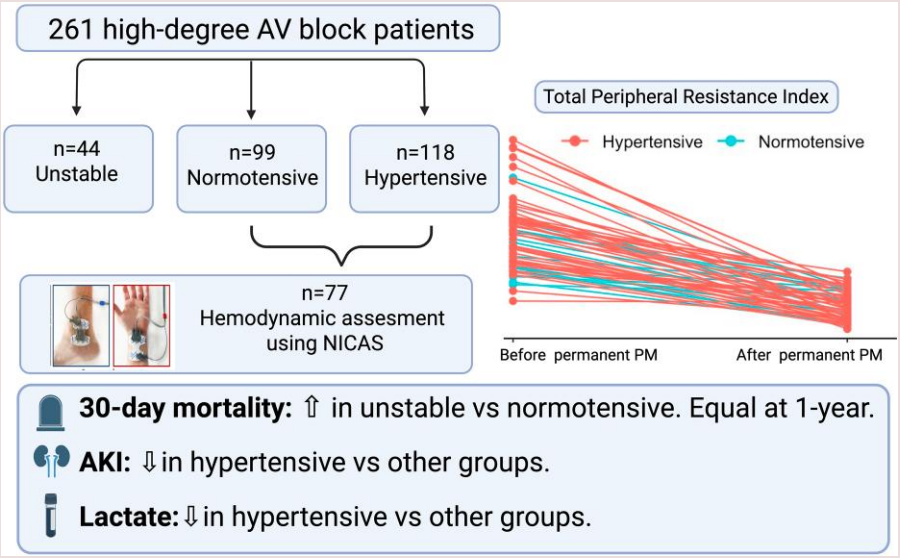
Graphical Abstract



Keywords Complete atrioventricular block • High-degree atrioventricular block • Hypertensive response • Bradycardia • Haemodynamics • Pacemaker implantation

Introduction

Patients with high-degree atrioventricular (AV) block can present with a wide range of clinical manifestations, depending on their haemodynamic response. These manifestations may vary from profound haemodynamic instability to paradoxical hypertension. The haemodynamic consequences of acquired complete AV block are influenced by several factors, including the ventricular escape rate, the duration of the abnormal rate, and the temporal relationship between atrial and ventricular activity, ventricular function, Peripheral vascular resistance (PVR), and coexisting medical conditions.[1]

During the low cardiac output (CO) state which results from the low heart rate (HR), several compensatory haemodynamic changes occur, including increased stroke volume (SV), increased systolic pressure, increased pulse pressure, and increased pulmonary pressure.[2] A pronounced hypertension response is an underreported (but common) reversible phenomenon with high-degree AV block and is likely secondary to an increased SV and decreased CO.[3] The diverse haemodynamic changes in response to high-degree AV block have not been studied profoundly by dedicated haemodynamic studies.

NICaS is a non-invasive whole-body bioimpedance monitoring system applied to assess haemodynamics and fluid balance. Upon measuring bioimpedance, haemodynamic changes throughout the cardiac cycle and total body water (TBW) measures can be made.

Our aim was to investigate the haemodynamic response of all consecutive patients who presented to our cardiac intensive care unit with high-degree AV block.

Methods

Study population

We performed a single-center prospective cohort study in the cardiac intensive care unit of a tertiary hospital in Israel. The study included 261 consecutive patients who presented with advanced conduction disorder and required pacemaker implantation between October 2020 and December 2022. Advanced conduction disorder included 2:1 AV block, high-degree AV block with advanced AV conduction ratio ≥3:1, and third-degree (complete) AV block with independent atrial and ventricular rhythm.

Haemodynamic response was divided into three groups: hypertensive, normotensive, and unstable.

(1) Hypertensive response was defined as systolic blood pressure equal to or above 160 mmHg.
(2) Normotensive response was defined as blood pressure below 160 mmHg and no temporary pacemaker implantation.
(3) Unstable response was defined as patients who required emergent temporary pacemaker implantation.

Data regarding baseline characteristics, clinical presentation, echocardiography parameters, laboratory parameters, and hospital outcome were collected retrospectively. The study was approved by the institutional review board ethics committee in compliance with the Declaration of Helsinki.

NICaS study

A dedicated haemodynamic study was performed on 73 patients using the non-invasive NICaS system. For the haemodynamic study, we excluded patients who were haemodynamically unstable, required inotropes/vasopressors, or required emergent temporary pacemaker implantation. Other excluded patients were patients with severe peripheral vascular disease or severe peripheral oedema.

NICaS (NI Medical Ltd, Ra'anana, Israel), a non-invasive cardiac system, is a bedside monitoring system designed for a comprehensive assessment of the body haemodynamics.[4] It is based on bioimpedance changes measured throughout the peripheral tissues' vasculature during systole and diastole, using two surface limb leads.[4,5] Making available near-instantaneous results, NICaS is capable of estimating TBW, CO and cardiac index (CI), SV, and total systemic peripheral resistance (TPR). Also, a one-lead ECG monitor is recorded. CO and other haemodynamic and respiratory parameters

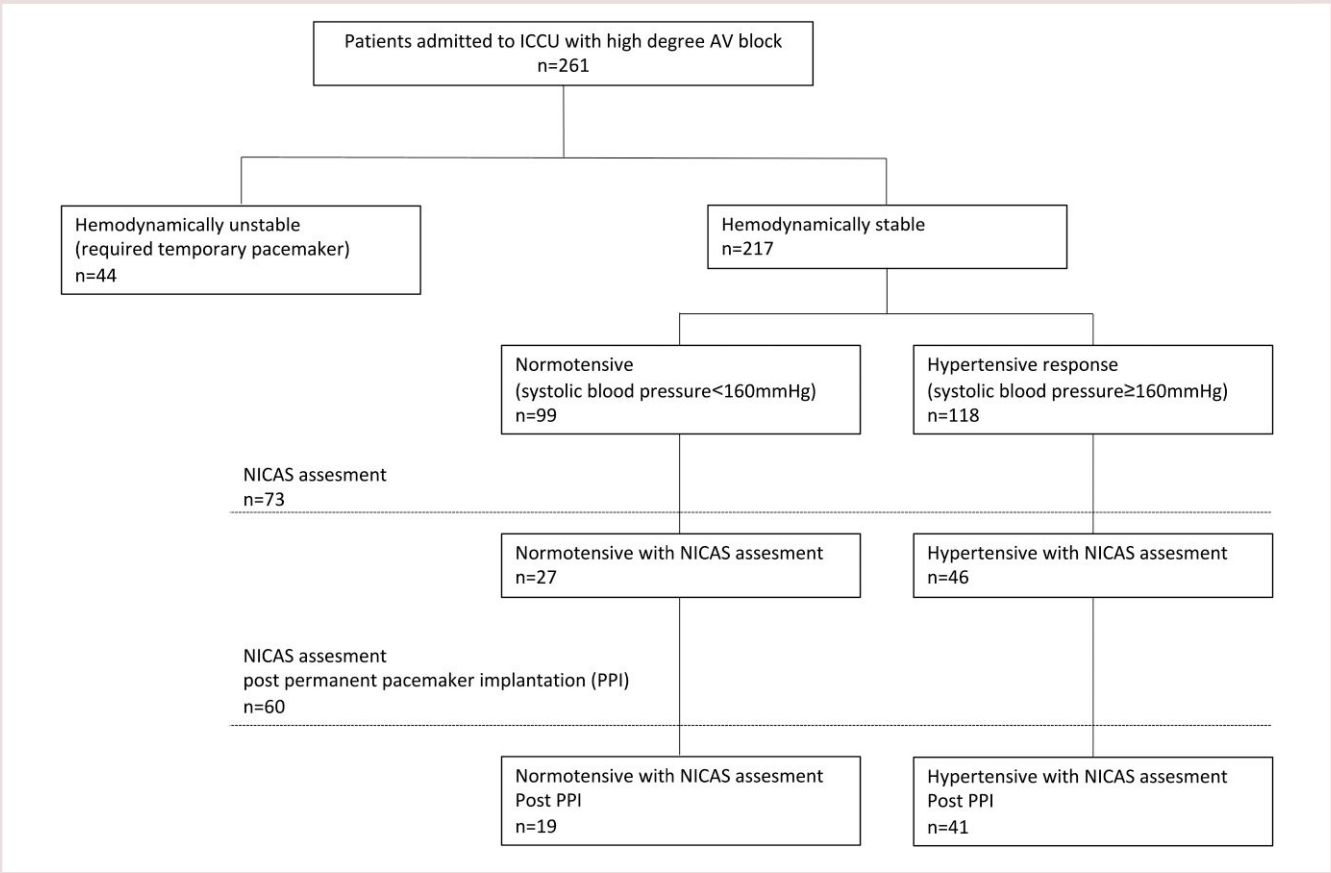


Figure 1 Patient flowchart.

are calculated by a proprietary algorithm (see Supplementary material online, *Figure S1* and Supplementary material online, *Table S1*). Upon measuring bioimpedance changes throughout the cardiac cycle, and dependent on additional data (as blood haematocrit and sodium), SV calculations and other haemodynamic measures can be made. Accordingly, patients' weight, systolic and diastolic BP, blood haematocrit, sodium, and peripheral oxygen saturation data were taken separately and given as input for NICaS at each analysis. All measurements were performed in a supine position after 5 min at rest. At least three measurements were performed at each analysis, and the recorded measurement was an average of all three readings to ensure analysis validity. This method has been validated against invasive haemodynamic assessment techniques, including thermodilution, and has demonstrated accuracy in estimating CO, SV, and other parameters across various cardiac and clinical settings.[6–10] Additionally, this method has proven accurate in estimating CO, SV, and other measurements for a range of cardiac and other clinical settings.[7,10–12] NICaS measurements are performed almost routinely in our cardiac intensive care unit for patients presenting with a low CO state from any cause.

Patients were assessed by NICaS at the following time points—at presentation and following pacemaker implantation. The haemodynamic parameters measured were SV, SV index (SVi), CO, CI, TPR, and TBW. The NICaS software enabled collected data to be transferred directly to an XLS file, a feature that minimized possible errors.

Statistical analysis

Statistical analyses were performed using BlueSky Statistics version 10.3.1 (BlueSky Statistics, Chicago, IL, USA), IBM SPSS Statistics version 27 (IBM Corp., Armonk, NY, USA), and R version 4.5.0 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables are presented as mean ± standard deviation (SD) or median and interquartile range (IQR), while categorical variables are summarized as frequencies and percentages.

Comparisons among the three groups were conducted using one-way analysis of variance (ANOVA) for continuous variables with normal distribution, assessed based on skewness and kurtosis. For variables that were not normally distributed, the Kruskal–Wallis test was applied. *Post hoc* analyses and pairwise comparisons between groups were performed using Student's *t*-test or Wilcoxon rank-sum (Mann–Whitney *U* test) test as appropriate, with Bonferroni correction for multiple comparisons. Categorical variables were compared using the chi-square test.

A logistic regression models were constructed to identify predictors of both hypertensive and unstable responses, using the other two groups as the reference. The models included covariates such as baseline characteristics, medication use, and presenting symptoms.

Comparisons of 1-year all-cause mortality were performed using a Cox proportional hazards model adjusted for baseline characteristics, including age, gender, and other variables significantly differing at baseline. Kaplan–Meier survival curves were generated, and log-rank test *P*-values were reported.

Statistical significance was defined as a two-tailed *P*-value <0.05 for all analyses.

Results

During the study period, a total of 261 patients were admitted with high-degree AV block, predominantly men (60.2%) with a mean age of 79.4 ± 10.5. Of which, 99 patients (37.9%) presented with normotensive response, 118 patients (45.2%) presented with hypertensive response, and 44 patients (16.9%) were unstable and required temporary pacemaker implantation. The patient flowchart is presented in *Figure 1*, and blood pressure distribution is presented in *Figure 2*.

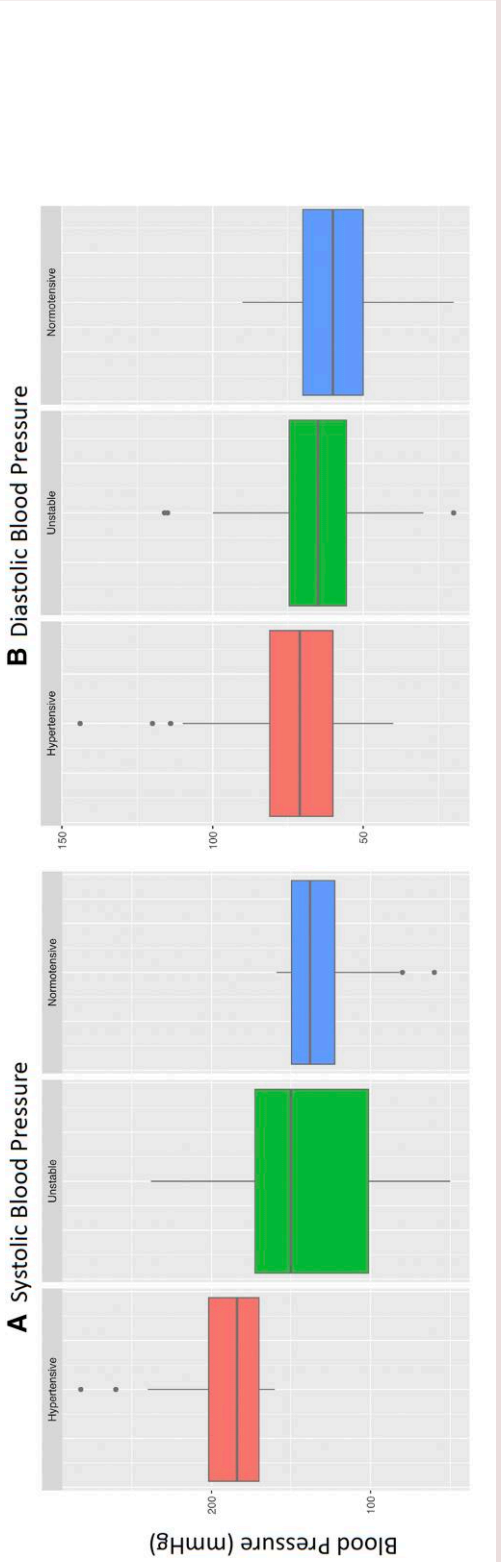


Figure 2 Blood pressure across the different haemodynamic groups.

Normotensive patients were significantly younger than hypertensive and unstable patients (76.2 ± 12.3, 80.1 ± 10.1, and 80.6 ± 10.5, respectively, $P = 0.019$). Patients presenting with high-degree AV block and a hypertensive response had a higher—but not statistically significant—prevalence of hypertension (77.1%), and a significantly lower prevalence of dyslipidaemia compared with the normotensive and unstable groups (63.3% vs. 76.5% and 79.5%, respectively; $P = 0.045$). Peripheral vascular disease, coronary disease, diabetes, and renal failure were equally prevalent (*Table 1*). Patients who presented with high-degree AV block and hypertensive response had a higher LV ejection fraction (58.2 ± 7.9%) compared with patients with normotensive or unstable response (53.9 ± 11.1% and 53.2 ± 11.6%, respectively, $P = 0.003$). Regarding chronic medications, patients presenting with a hypertensive response were more frequently treated with calcium channel blockers (37.3%) compared with normotensive (22.2%) and unstable (29.5%) patients, although this difference did not reach statistical significance ($P = 0.061$). Conversely, beta-blocker use was significantly lower in hypertensive patients (26.3%) compared with normotensive (37.8%) and unstable (47.7%) patients ($P = 0.024$). Furosemide, spironolactone, and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers were equally prevalent (*Table 1*).

Patients with high-degree AV block and hypertensive response presented with significantly higher escape rhythm (39.1 ± 6.7 BPM) while patients who presented with unstable response suffered more frequently from complete AV block (84.1%) and significantly lower escape rhythm (31.5 ± 10.4 BPM) and a lower rate of 2:1 AV block (*Table 1*).

Patients with high-degree AV block presented predominantly with symptoms of weakness and dyspnoea which were equally prevalent in all haemodynamic responses. Nevertheless, chest pain was more frequent in hypertensive response (16.1%), while syncope was significantly less frequent (23.7% compared with 31.6% in normotensive and 63.6% in hypertensive, $P < 0.001$).

Clinical outcomes

Thirty-day mortality was highest in the unstable group, occurring in three patients (6.8%), compared with three patients (2.5%) in the hypertensive group and none in the normotensive group. One-year mortality was also highest in the unstable group (18.2%) compared with the hypertensive (8.5%) and normotensive (10.1%) groups; however, this difference did not reach statistical significance. In the survival analysis, there was no significant difference in 1-year mortality among the three groups (log-rank $P = 0.17$; *Figure 3*). Similarly, in the Cox multivariate analysis, no significant differences were observed between the groups when using the hypertensive group as the reference across all three models (see Supplementary material online, *Table S2*).

The incidence of acute kidney injury was significantly higher in the unstable group (58.1%) compared with the hypertensive (20.5%) and normotensive (37.1%) groups ($P < 0.001$). In a multivariate analysis using the normotensive group as the reference, a hypertensive response was independently associated with reduced odds of AKI (OR 0.46, 95% CI: 0.23–0.92) while both age and baseline chronic kidney disease were independently associated with increased odds of AKI (see Supplementary material online, *Table S3*).

Lactate levels were lower in the hypertensive group (12 ± 6.5 mg/dL) compared with the normotensive (18.9 ± 14 mg/dL) and unstable (19.3 ± 13 mg/dL) groups ($P < 0.001$; *post hoc* analysis as significant for hypertensive vs. other groups). In a multivariate analysis using the normotensive group as the reference, a hypertensive response (coefficient of −5.93, 95% CI: −9.62 to −2.24) along with ejection fraction (EF) (coefficient of 0.32, 95% CI; −0.49 to −0.15) emerged as independent predictor of lower lactate levels (see Supplementary material online, *Table S4*).

The median duration of hospitalization was 1 day longer in the unstable group compared with the hypertensive group ($P = 0.003$). A summary of clinical outcome is presented in *Table 2*.

Table 1 Baseline characteristics and clinical presentation: comparison according to haemodynamic response

	Normotensive ($n = 99$)	Hypertensive ($n = 118$)	Unstable ($n = 44$)	*P*-value
Female gender	33 (33.3%)	52 (44.1%)	19 (43.2%)	0.242
Age (mean ± SD)	76.2 ± 12.3[a]	80.1 ± 10.1[a]	80.6 ± 10.5	0.019
Hypertension	68 (69.4%)	91 (77.1%)	33 (75%)	0.429
Dyslipidaemia	75 (76.5%)	75 (63.3%)	35 (79.5%)	0.045
Diabetes mellitus	45 (45.9%)	48 (40.7%)	24 (54.5%)	0.280
PAD	8 (8.2%)	5 (4.2%)	2 (4.5%)	0.435
Atrial fibrillation—persistent	12 (12.2%)	13 (11.0%)	5 (11.4%)	0.960
Atrial fibrillation—paroxysmal	9 (9.3%)	9 (7.6%)	1 (2.3%)	0.331
Coronary disease	42 (42.9%)	37 (31.4%)	15 (34.1%)	0.205
Chronic kidney disease	32 (32.7%)	31 (26.3%)	11 (25%)	0.501
GFR (mL/min/1.73 m^2)	67.6 ± 24.6	68.7 ± 22	74.9 ± 22.5	0.211
Anaemia	40 (41.2%)	40 (34.5%)	21 (47.7%)	0.274
Heart failure (HFrEF)	20 (20.4%)	13 (11%)	7 (15.9%)	0.162
Heart failure (HFpEF)	12 (12.2%)	14 (12%)	6 (13.6%)	0.959
EF (%)	53.9 ± 11.1	58.2 ± 7.9[b]	53.2 ± 11.6	0.003
Right heart failure	4 (4.1%)	3 (2.6%)	2 (4.7%)	0.748
Moderate to severe MR	18 (19.4%)	22 (19.1%)	5 (11.4%)	0.464
Moderate to severe TR	16 (17.4%)	20 (17.5%)	6 (13.6%)	0.826
Beta-blockers	37 (37.8%)	31 (26.3%)	21 (47.7%)	0.024
CCB (dihydropyridine)	22 (22.4%)	44 (37.3%)	13 (29.5%)	0.061
ACEI/ARB'S	38 (38.8%)	59 (50.0%)	18 (40.9%)	0.171
Furosemide	20 (20.4%)	24 (20.3%)	8 (18.2%)	0.947
Spironolactone	11 (11.2%)	13 (11.0%)	3 (6.8%)	0.695
Complete AV block	63 (64.3%)	69 (58.5%)	37 (84.1%)	0.010
2:1 AV block	52 (53.1%)	58 (49.2%)	12 (27.3%)	0.014
Sinus arrest	5 (5.1%)	2 (1.7%)	10 (22.7%)	<0.001
Heart rate (BPM)	38.1 ± 9.9	39.1 ± 6.7	31.5 ± 10.4[b]	<0.001
Systolic blood pressure (mmHg)	133.2 ± 18.9	189.8 ± 24.6[b]	139.1 ± 48.9	<0.001
Syncope/pre-syncope	31 (31.6%)	28 (23.7%)	28 (63.6%)	<0.001
Weakness	62 (63.3%)	60 (51.3%)	24 (54.5%)	0.203
Dizziness	35 (35.7%)	28 (23.7%)	9 (20.5%)	0.073
Dyspnoea	23 (23.5%)	32 (27.1%)	11 (25.0%)	0.827
Chest pain	13 (13.3%)	19 (16.1%)	0	0.020
Duration of symptoms—days [median (Q1,Q3)]	2 (1,7)	3 (1,7)	1 (1,7)	0.285

ACEI, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; EF, ejection fraction; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; GFR, glomerular filtration rate; PAD, peripheral artery disease; MR, mitral regurgitation; TR, tricuspid regurgitation;
[a]Indicates that the two marked values in the same row are significantly different from each other only ($P < 0.05$, Bonferroni-corrected *post hoc* analysis).
[b]Indicates that the marked value is significantly different from both other columns ($P < 0.05$, Bonferroni-corrected *post hoc* analysis).

NICaS analysis

We performed a comprehensive non-invasive haemodynamic evaluation upon admission in 73 consecutive stable patients who presented with high-degree AV block (*Table 3*).

Patients were categorized according to their blood pressure response at presentation into normotensive ($n = 27$) and hypertensive ($n = 46$) groups. Additionally, a comparative analysis was performed to evaluate the changes in haemodynamic parameters before and after pacemaker implantation among the 59 patients with complete data.

The average HR at presentation was 38.9 ± 5 bpm, with a CO of 2.5 ± 0.6 L/min and a CI of 1.4 ± 0.4 L/min/m^2. Average blood pressure was significantly higher in the hypertensive group compared with the normotensive group (171.4 ± 29.9 mmHg vs. 136.1 ± 19.3 mmHg, $P < 0.001$).

When comparing between groups, there was no statistically significant difference in HR (38 ± 5 vs. 40 ± 5 bpm, $P = 0.131$). However, patients with a hypertensive response had significantly higher TPR (3401 ± 1082 dynes·s/cm^5 vs. 2703 ± 841, $P = 0.009$) and TPR index (5954 ± 1889 vs. 4852 ± 1486 dynes·s/cm^5/m^2, $P = 0.011$) (*Table 3*). All other haemodynamic parameters, including CO and CI, were similar between hypertensive and normotensive patients (CO: 2.4 ± 0.6 vs. 2.5 ± 0.6 L/min, $P = 0.400$; CI: 1.4 ± 0.4 vs. 1.5 ± 0.4 L/min/m^2, $P = 0.33$) (*Table 4*).

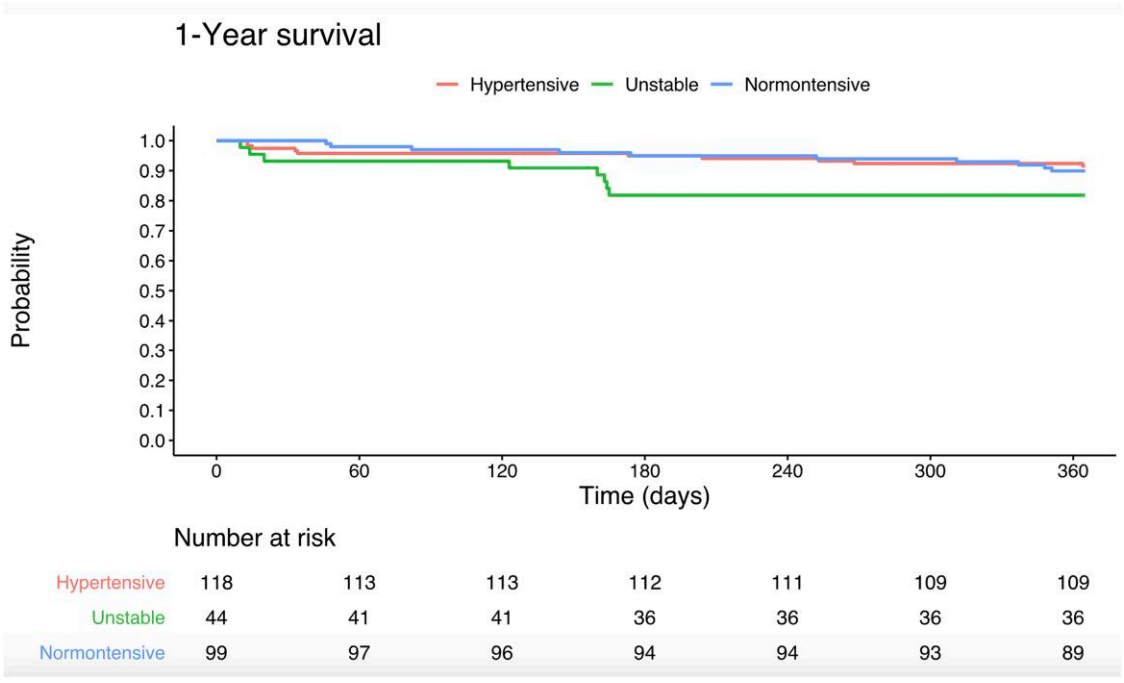


Figure 3 Kaplan–Meier plot for 1-year survival according to haemodynamic group.

Table 2 Clinical outcomes

	Normotensive ($n = 99$)	Hypertensive ($n = 118$)	Unstable ($n = 44$)	*P*-value
30-day mortality	0 (0%)	3 (2.5%)	3 (6.8%)	0.040[a]
1-year mortality	10 (10.1%)	10 (8.5%)	8 (18.2%)	0.200
Acute kidney injury	36 (37.1%)	24 (20.5%)	25 (58.1%)	<0.001[b]
Lactate level on admission (mg/dL)	18.9 ± 14.0	12 ± 6.5	19.3 ± 13	<0.001[b]
Hospitalization-days [median (Q1,Q3)]	3 (3,4)	3 (3,4)	4 (3,5)	0.003[c]

[a]Normotensive vs. unstable group was statistically significant in *post hoc* analysis.
[b]Hypertensive vs. other groups were statistically significant in *post hoc* analysis.
[c]Hypertensive vs. unstable group was statistically significant in *post hoc* analysis.

Non-invasive haemodynamic parameters, including the TPR index, were measured again after pacemaker implantation. Data were available for 59 patients (19 normotensive and 40 hypertensive). TPR index reserve was defined as the change between the two TPR index measurements divided by the baseline TPR index. Patients with a hypertensive response had a marginal significantly higher absolute TPR index reserve compared with normotensive patients ($P = 0.05$) (*Table 5*, *Figure 4*).

Separate analysis for heart failure patients is presented in Supplementary material online, *Figure S2*.

Multivariate analysis for predicting haemodynamic response

A multivariate analysis was conducted to identify factors independently associated with a hypertensive response, evaluating a range of covariates including baseline characteristics, medication use, and presenting symptoms. Using the other two groups as the reference, we found that older age (OR 1.03; 95% CI, 1.00–1.06), higher HR (OR 1.05; 95% CI, 1.01–1.10), higher EF (OR 1.04; 95% CI, 1.00–1.07), and pre-treatment with calcium channel blockers (OR 2.12; 95% CI, 1.11–4.07) were independently associated with increased odds of a hypertensive response. In contrast, the presence of syncope/pre-syncope and sinus arrest was associated with reduced odds. These results are detailed in Supplementary material online, *Table S5*.

Another multivariate analysis was performed to identify factors independently associated with haemodynamic instability using the combined normotensive and hypertensive response groups as the reference. The presence of syncope or pre-syncope (OR 3.75; 95% CI, 1.75–8.05) and sinus arrest (OR 8.36; 95% CI, 2.29–30.54) were associated with increased odds of haemodynamically unstable response. In contrast, higher HR was associated with reduced odds of instability (OR 0.92; 95% CI, 0.88–0.96). These findings are summarized in Supplementary material online, *Table S6*.

Discussion

This single-center study provides a comprehensive non-invasive assessment of the haemodynamic responses in patients presenting with high

Table 3 Non-invasive haemodynamic evaluation ($n = 73$)

	Normotensive response ($n = 27$)	Hypertensive response ($n = 46$)	*P*-value
Female gender	13 (48%)	16 (35%)	0.26
Age (mean ± SD)	71.5 ± 14.8	80 ± 10.3	0.005
Complete AV block	17 (65%)	31 (67%)	0.86
Syncope/pre-syncope	7 (27%)	11 (24%)	0.78
Hypertension	15 (58%)	32 (70%)	0.31
Dyslipidaemia	20 (77%)	28 (61%)	0.17
Diabetes mellitus	12 (46%)	20 (43%)	0.83
PAD	6 (23%)	5 (11%)	0.18
Atrial fibrillation—persistent	2 (8%)	4 (9%)	1
Atrial fibrillation—paroxysmal	5 (19%)	5 (11%)	0.48
Coronary disease	10 (38%)	19 (41%)	0.81
Chronic kidney disease	11 (42%)	20 (43%)	0.92
Anaemia	15 (58%)	22 (48%)	0.42
Heart failure (HFrEF)	6 (23%)	9 (20%)	0.72
Heart failure (HFpEF)	5 (19%)	6 (13%)	0.51
Moderate to severe MR	9 (35%)	10 (22%)	0.26
Moderate to severe TR	6 (23%)	8 (18%)	0.59
Beta-blockers	13 (50%)	13 (28%)	0.08
CCB (dihydropyridine)	4 (15%)	14 (30%)	0.16
ACEI/ARB'S	10 (38%)	21 (46%)	0.55
Furosemide	7 (27%)	11 (24%)	0.78
Spironolactone	3 (12%)	6 (13%)	1
AKI	14 (54%)	13 (28%)	0.031
Lactate	17.1 ± 7.9	11.9 ± 5.6	0.004

ACEI, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; EF, ejection fraction; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; PAD-peripheral artery disease; MR, mitral regurgitation; TR, tricuspid regurgitation;

Table 4 Non-invasive haemodynamic evaluation, haemodynamic parameters ($n = 73$)

	Normotensive response ($n = 27$)	Hypertensive response ($n = 46$)	*P*-value
BMI (kg/m^2)	26.4 ± 4.6	27.8 ± 6.8	0.38
BSA (m^2)	1.8 ± 0.3	1.8 ± 0.2	0.92
Blood pressure (mmHg)	136.1 ± 19.25	171.4 ± 29.9	<0.001
Heart rate (BPM)	40 ± 5	38 ± 5	0.13
SV (ml)	62 ± 15	62 ± 14	0.96
SI (mL/m2)	35 ± 8	34 ± 7	0.71
CO (L/min)	2.5 ± 0.6	2.4 ± 0.6	0.4
CI (L/min/m2)	1.5 ± 0.4	1.4 ± 0.4	0.33
TPR (dynes•s/cm^5)	2703 ± 841	3401 ± 1082	0.009
TPRI (dynes•s/cm^5/m^2)	4852 ± 1486	5954 ± 1889	0.011

BMI, body mass index; BSA, body surface area; CI, cardiac index; CO, cardiac output; SI, stroke volume index; SV, stroke volume; TPR, total peripheral resistance; TRRI, total peripheral resistance index.

AV block. Several key findings emerged. Most patients (83%) were haemodynamically stable, with nearly half (45%) demonstrating a hypertensive response, defined as systolic blood pressure ≥160 mmHg.

This hypertensive profile was characterized by higher escape rhythms, higher EF, and reduced markers of end-organ hypoperfusion—namely, lower rates of AKI and lactate levels—compared with normotensive and unstable patients.

Table 5 Non-invasive haemodynamic changes before and after permanent pacemaker implantation based on blood pressure at presentation

	Normotensive response ($n = 19$)	Hypertensive response ($n = 40$)	*P*-value
Relative change in SV	0.02 ± 0.27	0.05 ± 0.33	0.689
Relative change in SI	−0.02 ± 0.21	0.06 ± 0.33	0.377
Relative change in CO	0.7 ± 0.41	0.98 ± 0.66	0.092
Relative change in CI	0.66 ± 0.43	0.99 ± 0.66	0.051
Relative change in TPRI	−0.52 ± 0.18	−0.61 ± 0.17	0.05

CI, cardiac index; CO, cardiac output; SI, stroke volume index; SV, stroke volume; TPRI, total peripheral resistance index.

Importantly, the hypertensive response was associated with significantly higher TPR and total peripheral resistance index (TPRI) which reflect elevated PVR, suggesting a compensatory mechanism of vasoconstriction aimed at preserving perfusion despite bradycardia. Multivariable analysis identified higher heart rates, better left ventricular function, calcium channel blocker (CCB) use, and interestingly higher age as independent predictors of this response. Overall, these findings highlight the hypertensive response as a distinct and underrecognized haemodynamic phenotype in patients with high-degree AV block, one that appears to confer a more favourable perfusion profile.

The association with CCBs is not fully understood. It is unlikely that CCBs themselves directly contributed to the hypertensive response observed. Rather, this association may reflect underlying clinical characteristics of the patients receiving these medications. One possible explanation is that they are frequently used in patients with more resistant forms of hypertension. Consequently, individuals treated with CCBs may represent a subgroup with inherently more severe hypertension and therefore a greater tendency to develop a hypertensive response. An alternative explanation is that patients with multiple comorbidities—such as chronic kidney disease, ischaemic heart disease, or heart failure—are more often prescribed other antihypertensive classes, such as ACE inhibitors or beta-blockers. Therefore, those treated with CCBs may constitute a comparatively healthier group, possessing greater cardiovascular reserve and a more intact compensatory mechanism, potentially facilitating a hypertensive response.

The association we found between syncope or pre-syncope and sinus arrest to haemodynamic instability highlights the need for heightened vigilance and close monitoring in this subgroup of patients. Patients presenting with both high-degree AV block and evidence of sinus node dysfunction may be at particularly high risk for further deterioration due to combined bradyarrhythmia and autonomic failure, necessitating prompt intervention and careful haemodynamic support.

Using NICaS, a non-invasive bioimpedance monitoring system, we performed detailed haemodynamic assessments on a subset of stable patients and particularly the patients with hypertensive response. These evaluations revealed that patients with hypertensive responses had significantly higher PVR indices compared with normotensive patients, while CO and CI were similar between the groups. This finding underscores the role of increased PVR rather than CO in driving the hypertensive response. Additionally, the greater TPR index reserve observed following pacemaker implantation among patients with hypertensive responses suggests a heightened vascular adaptability in this subgroup.

It should be noted that CO was reduced at presentation in both haemodynamically stable groups, with values around 2.5 L/min and a CI of ~1.5 L/min/m^2. As SV and stroke index (SI) were only borderline low, this reduction was primarily due to bradycardia rather than impaired contractility. The subsequent increase in CO after pacemaker implantation, without a marked change in SI, further supports this interpretation.

Our findings have important clinical implications. Recognizing the hypertensive response as a distinct haemodynamic profile may inform management strategies, particularly in terms of avoiding overly aggressive antihypertensive therapy on their admission that could compromise the compensatory response and end-organ perfusion. The use of non-invasive haemodynamic monitoring tools such as NICaS offers a practical approach to assess and guide therapy in this population, particularly in evaluating the response to pacemaker implantation.

When comparing clinical outcomes, it is not surprising that the unstable group had higher short-term mortality. However, 1-year mortality was similar across groups. Interestingly, a hypertensive response appeared to be protective against end-organ damage, as reflected by lower rates of AKI and lower lactate levels—not only compared with the hypotensive group but also with the normotensive group, highlighting that blood pressure should not be overtreated in this population.

We further examined this by conducting a multivariate analysis comparing the hypertensive response group to the normotensive group. The hypertensive response remained a strong independent predictor of both lower odds of AKI and lower lactate levels. This association persisted in a robust model that adjusted for baseline characteristics, including age, gender, metabolic comorbidities, left ventricular function (EF and HFpEF), and concomitant medications, highlighting the importance of haemodynamic profiling in predicting end-organ hypoperfusion and damage.

To our knowledge, this is the first study which comprehensively evaluated the haemodynamic response of high-degree AV block with an emphasis on hypertensive response. Physicians should be aware of this compensatory response at presentation which may be accompanied with extremely high blood pressure levels and approach them with restraint. In the modern era of machine learning, which has been successfully applied to predict adverse outcomes in various acute cardiovascular conditions integrating non-invasive haemodynamic data or classifying hypertensive responses to high-degree AV block may in the future enable more accurate risk stratification and prediction of adverse events in this population.[13]

This study has several limitations. It was conducted in a single center, which may limit the generalizability of the findings. The NICaS analysis was performed only in a subset of stable patients, excluding those with significant haemodynamic instability, which may introduce selection bias. However, it was impossible to perform a haemodynamic analysis in unstable circumstances. Additionally, the retrospective design for baseline data collection may have introduced information bias, and the study's observational nature precludes establishing causal relationships between the observed parameters and clinical outcomes. Additionally, we aimed to examine the haemodynamic profiles of different heart failure subgroups; however, the available data were limited.

In conclusion, this study highlights the heterogeneous haemodynamic presentations of high-degree AV block, with hypertensive response emerging as a distinct and clinically relevant profile. The use of non-invasive haemodynamic monitoring provided valuable insights into the

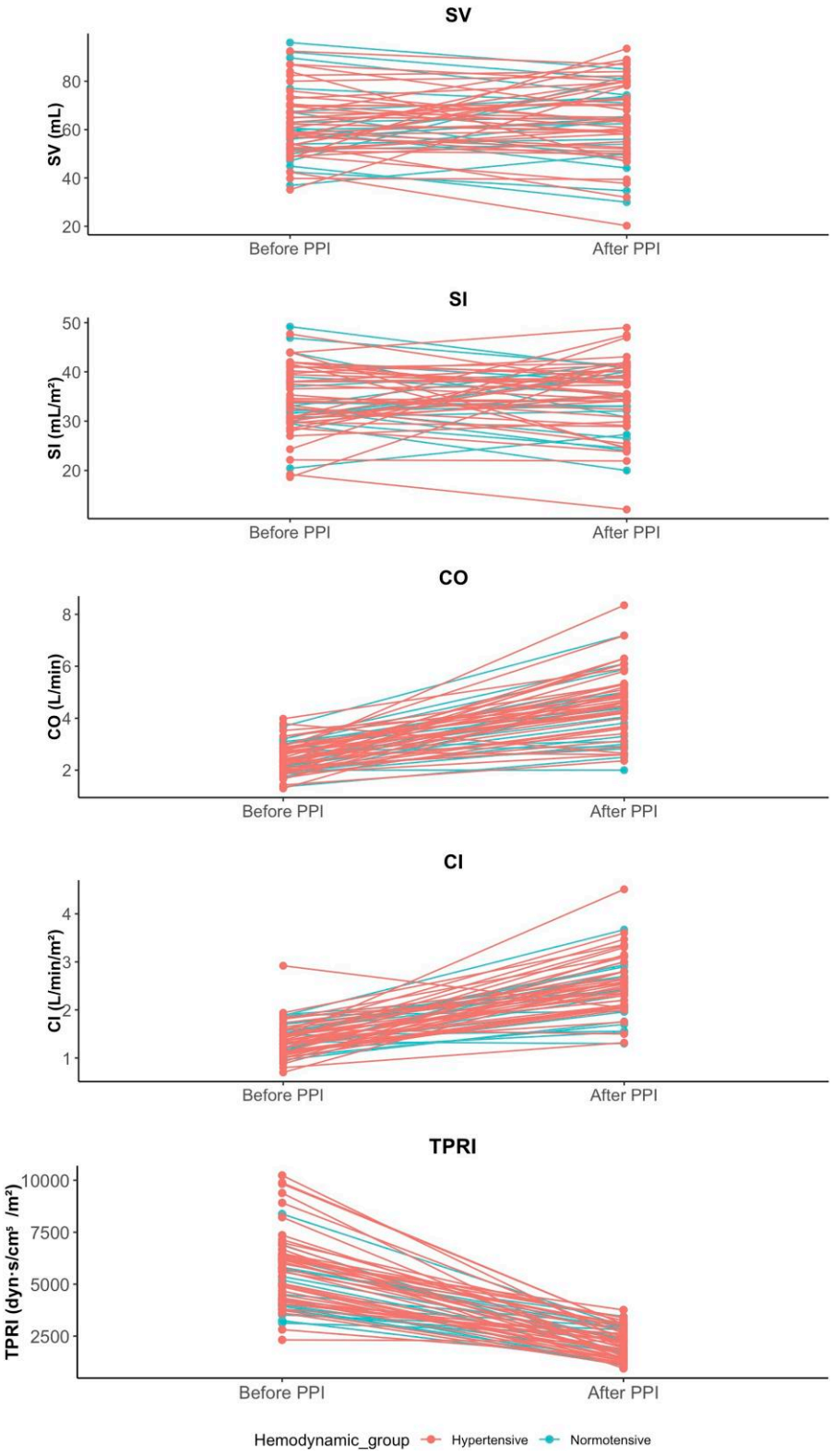


Figure 4 Change in haemodynamics in NICaS measurements before and after permanent pacemaker implantation. CI, cardiac index; CO, cardiac output; PPI, permanent pacemaker implantation; SI, stroke index; SV, stroke volume; TPRI, total peripheral resistance index.

mechanisms underlying this phenomenon. Further research is warranted to explore the pathophysiology of hypertensive responses and to evaluate the potential role of haemodynamic monitoring in optimizing management strategies for these patients.

Supplementary material

Supplementary material is available at *European Heart Journal: Acute Cardiovascular Care* online.

Author contributions

Katia Orvin (Conceptualization, Formal analysis, Investigation, Supervision, Writing – original draft), Shelly Vons (Data curation, Writing – review & editing) , Alon Barsheshet (Writing – review & editing), Ciel Zehavi (Data curation, Writing – review & editing), Gregory Golovchiner (Writing – review & editing), Georgy Rusadze (Data curation, Writing – review & editing), Ori Rahat (Writing – review & editing), Ran Kornowski (Writing – review & editing), Tsahi T. Lerman (Visualization, Writing – review & editing), Aharon Erez (Conceptualization, Formal analysis, Writing – review & editing)

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Data availability

The data underlaying this article will be shared on reasonable request to the corresponding authors.

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