Original Article

Efficacy and safety of leadless ventricular pacemaker: a single-center retrospective observational study

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Background: The Micra leadless pacemaker (MLP) has been demonstrated to be safe and effective as a substitute for conventional transvenous ventricular pacemakers (TVP). However, its application in the general population is still restricted. The aim of this retrospective study was to assess the safety and efficacy of MLP.

Methods: Clinical data and device parameters were gathered on every patient receiving MLP implantation between 1 January 2019 and 31 December 2023, in the First Affiliated Hospital of Soochow University. The efficacy of MLP on the primary composite endpoint, atrioventricular (AV) synchrony, hospitalization, and post-implantation quality of life was assessed. Safety outcomes included implantation procedural characteristics, acute and chronic complications, and stability of pacing parameters. Meanwhile, we compared pacing parameters, AV synchrony, and improvement of life quality between patients who had been implanted with the MicraTM VR (Medtronic Micra™ MC1VR01) and Micra™ AV (Medtronic Micra™ MC1AVR1). Multivariate linear regression models were used to unearth potential predictors of echocardiography or electrocardiogram (ECG) parameters on pacing parameters.

Results: A total of 94 patients were included, and implantation was successful in all of the cases. A single patient experienced effusion hours after the implantation, indicating a low rate of both acute and chronic complications. In patients with complete AV block (AVB), Micra AV increased AV synchrony from 23.2%±6.3% to 80.8%±5.7%. After 28 days of implantation, the patients' Minnesota Living with Heart Failure Questionnaire (MLHFQ) score decreased from 27.1±18.6 to 20.0±17.6, and none of them required hospital readmission. Left ventricular end-diastolic diameter (LVEDD, 50.0±6.7 cm), left ventricular end-systolic diameter (LVESD, 32.6±3.9 cm), and ECG R wave in lead V5 (RV5, 1.3±0.6 mV) can be employed for the prediction of pacemaker threshold [0.50 (0.38–0.67) mV], sensing voltage (10.1±4.7 mV), and impedance (785.9±226.4 Ohm) correspondingly.

Conclusions: Despite being a small, single-center, retrospective study, our study provided data for assessing the safety and efficacy of MLP. Clinicians and patients can make well-informed therapy decisions by being aware of its benefits and forecasting pacing parameters.

Keywords: Leadless pacemaker; Micra; cardiac pacing; myocarditis

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Introduction

In clinical settings, patients with bradyarrhythmias have benefited from permanent cardiac pacing (1). Complications of transvenous ventricular pacemakers (TVP), including lead dislodgement, malfunction, infection, vascular thrombosis, endocarditis, tricuspid regurgitation, hematoma, and pneumothorax, are more prevalent than previously recognized (2,3). Leadless pacing, as an alternative form of transvenous pacing, primarily reduced the lead- and pocket-related complications (4). Micra leadless pacemakers (MLPs) offer a new option for patients with no superior vena cava pathway or recurrent infections associated with pacing systems (5-7). At the same time, MLPs do not affect the patients' limb movement and aesthetics, which significantly improves their self-confidence and overall experience of their medical care. The first generation of MLP (Micra™ VR; Medtronic, Dublin, Ireland) could only provide single-chamber ventricular rate response pacing, which limited its application for some patients. Then, the second-generation MLP (Micra™ AV; Medtronic) appeared, which is based on a 3-axis accelerometer that provides contactless atrial sensing and allows for atrioventricular (AV) synchronous pacing (8), further advancing the application of MLP.

Some studies have shown a greater incidence of pericardial effusion and perforation in patients undergoing MLP compared to TVP, at a rate of 0.8%, which is nevertheless regarded as safe (3,9-11). In general, MLP has clear advantages and is anticipated to gain increased traction in the coming years. However, additional clinical studies are required to confirm the efficacy and safety of MLP, especially among Asian patients. We performed this retrospective study to assess the safety and efficacy of MLP in a real-world setting. We present this article in accordance with the STROBE reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-181/rc).

Highlight box

Key findings

- Our study investigates safety and efficacy of Micra leadless pacemaker (MLP) in different populations. Post-implantation pacing parameters can be predicted preoperatively by echocardiography and electrocardiogram (ECG).

What is known and what is new?

- As an alternative form of transvenous ventricular pacemaker, the MLP has been demonstrated to be safe and efficacious.
- Additional clinical data is presented to substantiate this conclusion. Additionally, the pacing parameters following implantation were identified as having a considerable influence on the longevity of pacemakers. Echocardiography and ECG were employed to predict the requisite pacing parameters.

What is the implication, and what should change now?

- MLPs are suitable for application in the general population, including those with a history of myocarditis. It is recommended that echocardiography and ECG be conducted with greater precision prior to implantation. The type of pacemaker should be chosen with greater care if the predicted parameters are unfavorable.

Methods

Study design and population

This observational study was designed to evaluate the safety and efficacy of MLP by consecutively enrolling 94 patients who were implanted with Micra TPS (35 implanted with Micra VR, 59 implanted with Micra AV) at the Department of Cardiology, First Affiliated Hospital of Soochow University between 1 January 2019 and 31 December 2023 (*Figure 1*). All patients had compatible guideline-supported pacing indications. We recommend MLP implantation in patients with abnormal TVP implantation pathways, recurrent pacemaker infections or high risk of infection, end-stage renal disease and hemodialysis, and other comorbidities that make TVP implantation particularly difficult or at high risk of complications. We believe that MLP should be considered in patients with arrhythmias including atrial fibrillation, intermittent second-degree, high-grade AV block, and sinus arrest or sinus block, and a low percentage of expected ventricular pacing. Patients with a high proportion of expected ventricular pacing (>40%) coupled with a reduced or mildly reduced left ventricular ejection fraction (LVEF), moderate-to-severe tricuspid regurgitation, and an abnormal inferior vena cava pathway were deemed unsuitable for implantation of an MLP (12,13). The decision to implant a leadless system rather than a conventional device was individualized, taking into account the patients' preferences. The study was approved by the Ethics Committee of the First Affiliated Hospital of Soochow University (No. [2024]203), and informed consent was signed prior to the procedure. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Implantation procedure and data collection

Experienced operators performed implantation of the MLP

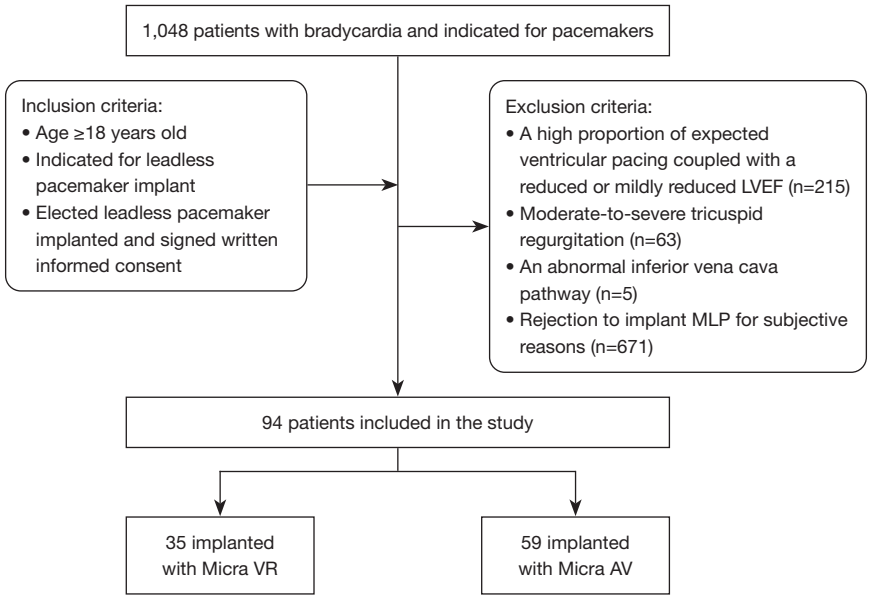

Figure 1 Patient selection and exclusion criteria and the numbers of patients included. LVEF, left ventricular ejection fraction; MLP, Micra leadless pacemaker; Micra AV, Medtronic Micra™ MC1AVR1; Micra VR, Medtronic Micra™ MC1VR01.

according to standard operating procedures (14). History, clinical examination, laboratory tests, electrocardiogram (ECG), and echocardiograph were routinely performed in all patients before implantation according to local practice and guidelines. Procedural characteristics and pacing parameters were recorded intraoperatively and at follow-up. We also used the Minnesota Living with Heart Failure Questionnaire (MLHFQ) score to assess clinical improvement and evaluated complications after pacemaker implantation by follow-up telephone calls. The MLHFQ is a multidimensional assessment tool that evaluates three primary domains: physical, emotional, and social. The physical domain consists of 8 items, the emotional domain consists of 5 items, and the social domain consists of 6 items. Each item was scored from 0 to 5; the total score ranged from 0 to 105, with higher scores indicating more severe impairment of health-related quality of life (15). Follow-up visits were scheduled at 28 days and 1 year after discharge.

End point

The composite efficacy end points were improvement of post-implantation life quality as measured by a reduction in the MLHFQ score from baseline at 28 days and freedom from readmission for arrhythmia within 6 months. High AV synchronization (>70%) was an additional valid endpoint in patients implanted Micra AV. The composite safety end points were the proportion of patients experiencing acute and chronic complications during the 28-day and 6-month follow-up and stable pacemaker parameters at 28 days. Low radiation dose was considered a secondary safety end point.

Acute complications were defined as those occurring within 28 days of implantation and included embolism and thrombosis, puncture site events, cardiac effusion and/or perforation, device-related complications, and other complications such as device-related acute myocardial infarction, postoperative hematoma or bleeding, intraoperative cardiac arrest, pericarditis, vascular complications, hemothorax, and pneumothorax. Chronic complications were defined as those that occurred after 28 days and were most likely due to complications of device implantation or the device itself, including thrombosis, device-related complications (including device malfunction, dislodgement and infection), and pericarditis (3,16).

Cardiac cycles were defined as synchronous if a ventricular marker followed the P-wave by ≤300 ms. The percentage of AV synchrony was calculated from the patients' Holter monitoring as the number of synchronized cycles divided by the total number of cardiac cycles.

According to consensus statement of Chinese experts, the intraoperative pacing parameters of MLP are generally required to meet the following criteria: threshold

≤1 V/0.24 ms, sensation ≥5 mV, and impedance of 400–1,500 Ohm (17).

Statistical analysis

Continuous variables were expressed as mean ± standard or median (interquartile range), and the Shapiro-Wilk test was used to determine whether the data followed a normal distribution; categorical variables were expressed as numbers (percentages). The Student's *t*-test or the Mann-Whitney *U* test was used to compare continuous variables between groups, as appropriate. Comparison of categorical variables was performed by χ^2 analysis or the Fisher exact test, as appropriate. Differences were considered statistically significant at P<0.05. Given that echocardiography and ECG can reflect cardiac structure, function, and electrical activity, we sought to investigate whether the variables associated with them were related to pacing parameters. Univariable and multivariable linear regression analyses were also performed to determine the effect of each variable on pacing parameters. Multivariable regression included all the significant variables in the univariable analysis. Results are presented as β [95% confidence interval (CI)]. Statistical analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA).

Results

Study population and baseline characteristics

More than 1,000 patients were implanted with pacemakers for bradyarrhythmias during the study period, with MLP implanted in less than 10% of those cases. Lack of awareness of MLP and high prices were the main reasons. The complete characteristics of the participants included in the study are displayed in *Table 1*. The most common indication for initial pacing was third-degree AV block (AVB) (35.1%). The remaining underlying conduction abnormalities leading to device implantation were symptomatic second-degree AVB (31.9%), bradycardia associated with persistent or permanent atrial tachyarrhythmias (13.8%), and sinus node disease (19.1%). Some 24.5% of patients experienced 1 or more episodes of syncope.

The proportions of patients grouped by symptom severity were comparable: 51.1% of patients had mild to moderate symptoms [New York Heart Association (NYHA) II], and 8.5% had severe symptoms (NYHA IV). We used the Barthel Index to assess the ability to perform activities of daily living, with a score of 97 [85–100], indicating that in principle the patient is able to carry out the activities of daily living on his/her own. The patient underwent preoperative echocardiography. The mean LVEF was 62.2%±5.1%, mean left ventricular end-systolic diameter (LVESD) was 32.6±3.9 cm, the mean left ventricular end-diastolic diameter (LVEDD) was 50.0±6.7 cm, and the mean left atrial anteroposterior diameter (LAD) was 42.3±6.5 cm. The mean R wave in lead V5 (RV5) before implantation was 1.3±0.6 mV. All patients were free of heart valve diseases, including moderate to severe tricuspid regurgitation and tricuspid stenosis.

Pacemaker implantation and parameters

All devices were successfully implanted under fluoroscopy. The mean implantation time was 31.8±5.1 minutes (P=0.35), the fluoroscopy time was 11.6±3.0 minutes (P=0.89), and the radiation dose was 90.5±14.3 mGy (P=0.62) (*Table 2*). Intraoperative mean sensing voltage was 10.1±4.7 mV, with an impedance of 785.9±226.4 Ohm. Pacing thresholds were 0.50 (0.38–0.67) mV for all devices, 0.38 (0.38–0.50) mV in the Micra AV group, and higher in the Micra VR group at 0.50 (0.41–0.84) mV (*Table 2*). In the majority of patients, the device was placed in the mid or high right ventricular septum (92.6%). At 28-day follow-up, the mean sensation was 9.0±3.6 mV, impedance was 712.2±210.0 Ohm, and capture threshold was 0.45 (0.38–0.51) mV; both capture threshold and impedance were lower than they were during the intraoperative period. Overall, neither the Micra VR nor the Micra AV pacemaker characteristics were significantly altered. A total of 25 patients with normal sinus node function and predominantly complete AV block were included in the analysis. Normal sinus node function was established if patients with definite criteria for P waves were always positive in lead II and negative in lead aVR and their P-P intervals were from 0.6 to 1.0 seconds. Complete AV block was established when no P wave was conducted to the ventricles and ventricular contraction was maintained by a nodal or infranodal escape rhythm (8). Among these patients, 3 were implanted with Micra VR and 22 with Micra AV. The findings indicated an AV synchrony percentage of 80.8%±5.7% in a physiological atrial synchronous ventricular pacing mode (VDD) and 23.2%±6.3% in single-chamber ventricular pacing mode (VVI) (P<0.001) (*Figure 2*).

Table 1 Patient baseline characteristics

Parameters	All patients (n=94)	Micra AV (n=59)	Mira VR (n=35)
Demographics			
Male sex	59 (62.8)	35 (59.3)	24 (68.6)
Age (years)	78 [69–81]	74 [64–79]	78 [73–85]
Height (cm)	164.5±7.1	164.6±7.1	164.2±7.1
Weight (kg)	63.8±10.4	64.8±10.6	62.2±10.0
BMI (kg/m^2)	23.7±3.4	23.9±3.6	23.3±3.1
Previous syncope	23 (24.5)	14 (23.7)	9 (25.7)
Medical history			
Hypertension	62 (66.0)	38 (64.4)	24 (68.6)
Obesity as per BMI >30 kg/m^2	2 (2.1)	0 (0.0)	2 (5.7)
Atrial fibrillation	32 (34.0)	10 (16.9)	22 (62.9)
Congestive heart failure	38 (40.4)	26 (44.1)	12 (34.3)
Coronary artery disease	27 (28.7)	13 (22.0)	14 (40.0)
Diabetes	28 (29.8)	18 (30.5)	10 (28.6)
Prior stroke or TIA	16 (17.0)	9 (15.3)	7 (20.0)
CKD	8 (8.5)	6 (10.2)	2 (5.7)
COPD	4 (4.3)	2 (3.4)	2 (5.7)
Post-oncological disease	7 (7.4)	3 (5.1)	4 (11.4)
Charlson Comorbidity Index score	4 [3–6]	4 [3–5]	4 [4–6]
Medications at baseline			
ACEI/ARB	30 (31.9)	18 (30.5)	12 (34.3)
Beta-blockers	20 (21.3)	11 (18.6)	9 (25.7)
CCB	38 (40.4)	24 (40.7)	14 (40.0)
Antiplatelet agents	22 (23.4)	12 (20.3)	10 (28.6)
Anticoagulants	26 (27.7)	9 (15.3)	17 (48.6)
Echocardiographic data			
LVEF (%)	62.2±5.1	62.1±5.3	61.0±6.9
LVESD (cm)	32.6±3.9	32.1±4.0	33.1±4.6
LVEDD (cm)	50.0±6.7	48.5±5.1	50.5±7.1
LADs (cm)	42.3±6.5	40.0±4.9	44.7±7.7
Electrocardiogram			
RV5 (mV)	1.3±0.6	1.3±0.6	1.4±0.6

Table 1 (*continued*)

Table 1 (*continued*)

Parameters	All patients (n=94)	Micra AV (n=59)	Mira VR (n=35)
Clinical status			
Current NYHA functional class			
II	48 (51.1)	28 (47.5)	20 (57.1)
III	38 (40.4)	28 (47.5)	10 (28.6)
IV	8 (8.5)	3 (5.1)	5 (14.3)
Barthel index	97 [85–100]	100 [90–100]	95 [80–100]
Indication for pacing			
Sinus node diseases	18 (19.1)	10 (16.9)	8 (22.9)
Bradycardia associated with persistent or permanent atrial tachyarrhythmias	13 (13.8)	3 (5.1)	10 (28.6)
Symptomatic second-degree AVB	30 (31.9)	23 (39.0)	7 (20.0)
Third-degree AVB	33 (35.1)	23 (39.0)	10 (28.6)

Data are presented as n (%), median [IQR] or mean ± SD. Micra AV, Medtronic Micra™ MC1AVR1; Micra VR, Medtronic Micra™ MC1VR01; BMI, body mass index; TIA, transient ischemic attack; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II-receptor blocker; CCB, calcium antagonist; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVEDD, left ventricular end-diastolic diameter; LAD, left atrial anteroposterior diameter; RV5, R wave in lead V5; NYHA, New York Heart Association; AVB, atrioventricular block; IQR, interquartile range; SD, standard deviation.

Table 2 Procedural characteristics

Characteristics	All patients (n=94)	Micra AV (n=59)	Micra VR (n=35)	P value
Procedure duration (min)	31.8±5.1	32.2±4.9	31.1±5.5	0.35
Radiation time (min)	11.6±3.0	11.5±3.0	11.6±3.0	0.89
Radiation dosage (mGy)	90.5±14.3	89.9±14.3	91.4±14.4	0.62
Final implantation site				0.75
RV apical septum/apex	7 (7.4)	4 (6.8)	3 (8.6)	
RV mid/high septum	87 (92.6)	55 (93.2)	32 (91.4)	
Threshold (mV)	0.50 (0.38–0.67)	0.38 (0.38–0.50)	0.50 (0.41–0.84)	0.004
Impedance (Ohms)	785.9±226.4	779.2±242.1	785.9±226.4	0.79
Sensing voltage (mV)	10.1±4.7	9.7±4.3	10.1±4.7	0.38
Pacing mode				<0.001
VVI	51 (54.3)	16 (27.1)	35 (100.0)	
VDD	43 (45.7)	43 (72.9)	0 (0)	

Data are presented as n (%), mean ± SD or median (IQR). Micra AV, Medtronic Micra™ MC1AVR1; Micra VR, Medtronic Micra™ MC1VR01; RV, right ventricular; VVI, single-chamber ventricular pacing mode; VDD, a physiological atrial synchronous ventricular pacing mode; SD, standard deviation; IQR, interquartile range.

Complications and post-implantation quality of life assessment

Complications arose in 1 patient during MLP implantation that required further intervention: the patient developed effusion hours after the implantation, which was performed under oral anticoagulation, and was safely discharged with improved outcomes following pericardiocentesis for drainage. As of 31 December 2023, all patients were free of chronic complications.

We used the MLHFQ to assess patients' quality of life. At 28 days after implantation of MLP, the patients' MLHFQ score decreased from 27.1±18.6 to 20.0±17.6 (P<0.001) (*Figure 3*). There was no difference in terms of changes in MLHFQ scores between patients receiving Micra AV and Micra VR at the 28-day follow-up visit (P=0.75).

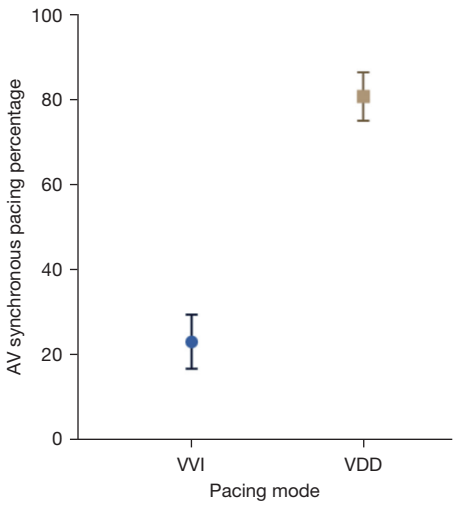

Figure 2 AV synchronous pacing percentage during VVI mode and VDD mode in patients with complete AV block and normal sinus rhythm. AV, atrioventricular; VVI, single-chamber ventricular pacing mode; VDD, a physiological atrial synchronous ventricular pacing mode.

Indicators related to and factors influencing the parameters of the pacemaker

Predictors of adverse pacing parameters are listed in *Tables 3-5*. In multivariate analysis, LVEDD (P=0.03) was independently associated with the pacing threshold. In some patients, interventricular septum e' may also be positively correlated with pacemaker threshold (*Table 3*). Of the echocardiography parameters, we found no predictors related to pacemaker impedance, but analysis of the preoperative ECG revealed a positive correlation between RV5 and impedance (P=0.02) (*Table 4*). Pacemaker perceived voltage was found to be related to LVESD (P=0.04) (*Table 5*).

Characterization of leadless pacemaker implantation for myocarditis

We found a history of viral myocarditis in 3 (20%) young patients (aged <60 years) who had had an MLP implanted

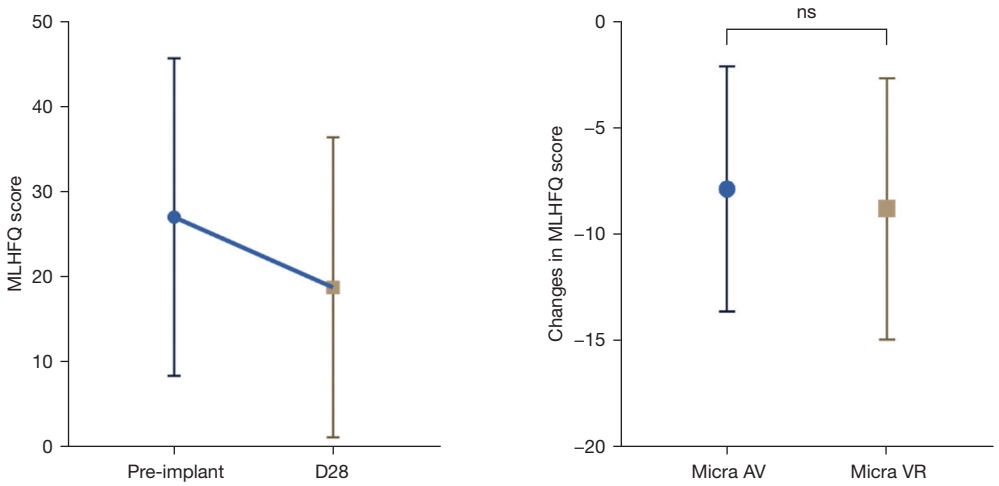

Figure 3 MLHFQ before and 28 days after implantation. MLHFQ, Minnesota Living with Heart Failure Questionnaire; D28, 28 days after implantation; Micra AV, Medtronic Micra™ MC1AVR1; Micra VR, Medtronic Micra™ MC1VR01; ns, not significant.

Table 3 Cardiac ultrasound-related predictors for high threshold

Variables	Univariate analysis		Multivariate analysis	
	β (95% CI)	P	β (95% CI)	P
Cardiac ultrasound-related impact on threshold				
LVEF	–0.007 (–0.019 to 0.006)	0.30	–	–
EDT	0.001 (–0.001 to 0.002)	0.56	–	–
Septal e' waves	0.071 (0.026 to 0.116)	0.002	0.070 (–0.005 to 0.145)	0.07
Lateral e' waves	0.042 (0.009 to 0.075)	0.02	–0.025 (–0.084 to 0.035)	0.41
E/e'	–0.020 (–0.050 to 0.010)	0.20	–0.015 (–0.047 to 0.016)	0.34
LAD	0.010 (–0.002 to 0.021)	0.09	–0.002 (–0.020 to 0.015)	0.80
LVEDD	0.023 (0.011 to 0.035)	<0.001	0.020 (0.002 to 0.039)	0.03
LVESD	0.006 (–0.011 to 0.024)	0.47	–	–
LVPW	–0.032 (–0.100 to 0.037)	0.36	–	–
IVS	0.002 (–0.045 to 0.049)	0.93	–	–

Univariate and multivariate linear regression models were fitted. CI, confidence interval; LVEF, left ventricular ejection fraction; EDT, deceleration time; E, early transmitral flow velocity; e', mitral annular velocity during diastole; LAD, left atrial anteroposterior diameter; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVPW, left ventricular posterior wall; IVS, interventricular septum.

Table 4 ECG-related predictors for high impedance

Variables	Univariate analysis		Multivariate analysis	
	β (95% CI)	P	β (95% CI)	P
ECG-related impact on impedance				
Heart rate	0.731 (–2.376 to 3.838)	0.64	–	–
Cardiac axis	0.443 (–0.523 to 1.409)	0.37	–	–
QRS duration	–0.611 (–2.231 to 1.010)	0.46	–	–
P-R interval	–0.462 (–1.318 to 0.395)	0.29	–0.04 (–1.447 to 0.239)	0.16
QTc	0.072 (–0.956 to 1.100)	0.89	–	–
RV5	77.987 (5.466 to 150.507)	0.04	90.532 (12.657 to 168.407)	0.02

Univariate and multivariate linear regression models were fitted. CI, confidence interval; ECG, electrocardiogram; QRS, QRS complex; QTc, corrected Q-T interval; RV5, R wave in lead V5.

for conduction block (*Table 6*). Viral myocarditis can lead to AVB, but reports of leadless pacemaker implantation in this population are rare.

Discussion

Real-world studies on MLP currently need to be enhanced, and our study helps to address this gap. The main findings of the study, which comprised 94 consecutive patients who underwent Micra TPS implantation, are listed below.

The majority of patients who underwent pacemaker implantation were elderly, with 84.0% of them being over 60 years old. These individuals typically had multiple health conditions, with hypertension being the most prevalent at 66.0%. According to a study of 6,146 community residents, high blood pressure and glucose levels could be associated with over 50% of AVB (18), indicating the need for early monitoring of cardiac conduction system in individuals

Table 5 Cardiac ultrasound-related predictors for high sensing

Variables	Univariate analysis		Multivariate analysis	
	β (95% CI)	P	β (95% CI)	P
Cardiac ultrasound-related impact on sensing				
LVEF	–0.096 (–0.068 to 0.259)	0.25	–	–
EDT	0.017 (–0.006 to 0.039)	0.15	0.017 (–0.005 to 0.039)	0.12
Septal e' waves	0.386 (–0.202 to 0.975)	0.19	0.343 (–0.242 to 0.928)	0.25
Lateral e' waves	0.162 (–0.265 to 0.588)	0.45	–	–
E/e'	–0.159 (–0.535 to 0.218)	0.40	–	–
LAD	–0.002 (–0.154 to 0.149)	0.98	–	–
LVEDD	–0.087 (–0.251 to 0.077)	0.29	–	–
LVESD	–0.242 (–0.468 to –0.016)	0.04	0.372 (–0.726 to –0.018)	0.04
LVPW	–0.474 (–1.357 to 0.409)	0.29	–	–
IVS	–0.277 (–0.881 to 0.328)	0.37	–	–

Univariate and multivariate linear regression models were fitted. CI, confidence interval; LVEF, left ventricular ejection fraction; EDT, deceleration time; E, early transmitral flow velocity; e', mitral annular velocity during diastole; LAD, left atrial anteroposterior diameter; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVPW, left ventricular posterior wall; IVS, interventricular septum.

Table 6 Characteristics of leadless pacemaker implantation for myocarditis

Characteristics	Patient 1	Patient 2	Patient 3
History of myocarditis (years)	16	7	30
NT-proBNP (pg/mol)	68.30	83.8	70.79
LVEF (%)	62	32	67
LVESD (mm)	29	51	29
LVEDD (mm)	77	60	46
Type of pacemaker	Micra VR	Micra AV	Micra AV
Indication for pacing	Symptomatic second-degree AVB	Symptomatic second-degree AVB	Third-degree AVB
Threshold (mV)	2.38	0.5	0.5
Impedance (Ohms)	600	780	610
Sensing (mV)	15.2	5.5	18.9
Pacing mode	VVI	VDD	VDD
Pacing percentage (%)	28.1	9.2	49.8

NT-proBNP, N-terminal pro-B-type natriuretic peptide; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVEDD, left ventricular end-diastolic diameter; Micra AV, Medtronic Micra™ MC1AVR1; Micra VR, Medtronic Micra™ MC1VR01; AVB, atrioventricular block; VVI, single-chamber ventricular pacing mode; VDD, a physiological atrial synchronous ventricular pacing mode.

with hypertension. With regard to blood pressure control strategies, recent studies suggest that intensive blood pressure control may not reduce the incidence of new conduction system disorders compared with standard blood pressure control (19), but there is a lack of research on the effects of antihypertensive medication choice or

renal denervation (RDN) on the incidence of emerging conduction system disorders in hypertensive patients.

MLP implantation is safe and effective in all age groups (16). With the exception of one patient who had a poor pacemaker threshold at the time of initial implantation, had the device removed and re-released multiple times, yet still had a poor threshold (final threshold of 2.13 mV), the majority of patients (98.9%) experienced a smooth implantation procedure. This patient steadfastly insisted on the implantation of an MLP despite being aware that this could have an impact on pacemaker longevity. The shorter operation duration and reduced radiation exposure for both the patient and the operator are in line with the idea of "green electrophysiology". Only one patient experienced a pericardial effusion within the first 24 hours following surgery, indicating a low rate of complications. The safety of implantation in special populations has also been considered. Among four patients who initially underwent implantation with a TVP followed by replacement with a Micra TPS due to peri-pocket tissue infection, there was one death due to severe comorbidities, and the other three did not experience any postoperative complications during the follow-up period. This suggests that leadless pacemakers may also be worth considering in this patient population (20). Our significant rate of acute complications was lower than the rate of 7.7% reported by Piccini *et al.* (3). Restricted to the follow-up time, additional data on long-term complication rates are required.

The Micra AV bridges the gap left by the Micra VR and expands the application of leadless pacemakers. The Micra AV resulted in an increase in AV synchrony, which correlates with long-term prognosis from 23.2%±6.3% to 80.8%±5.7%. This aligns with the findings of the MARVEL 2 study (8). In addition to objective complication rates and modifications in pacing parameters, subjective assessments from patients are crucial indicators. Patients' MLHFQ scores decreased at 28-day follow up, suggesting that implantation of an MLP is crucial for improving quality of life.

MLPs offer a significant reduction in complication rates compared to TVPs, which has facilitated the adoption of Micra TPS. However, compared to TVP, the pacing position of MLP is more difficult to modify, necessitating rigorous preimplantation examination. At the same time, post-implantation pacing parameters have a major effect on subsequent pacemaker longevity. Based on these considerations, we attempted to predict pacing parameters by routine preoperative testing to guide implantation. Multifactorial linear regression analysis showed that LVEDD was an independent predictor of pacemaker threshold. Nevertheless, in some patients, ventricular septum e' may positively correlate with threshold. LVESD was highlighted as an independent predictor of sensing voltage. The mechanism is not precise, but we speculate that some pathological changes in the myocardium may affect cardiac systolic function as well as threshold and sensing voltage. Echocardiography characteristics did not reveal any specific predictor of pacemaker impedance, but an examination of the preoperative ECG revealed a positive correlation between RV5 and impedance (P=0.02). RV5 generally reflects the depolarizing activity of the left ventricle, which may indicate pathological conditions such as left ventricular wall hypertrophy. It is not possible to tell if this is a direct reaction of LV electrical activity or an indirect result of septal electrical activity. It is noteworthy that the 95% CI of RV5 is wide, indicating that the model is not particularly stable and the regression equation is not highly significant. To further investigate the predictive value of RV5 for impedance, it would be beneficial to expand the sample size in future studies.

It was observed that certain patients without risk factors for conduction system diseases or a family history of genetic predisposition developed severe AVB early in life, which required pacemaker implantation. It is essential to be cautious when selecting pacemaker implantation due to the extended life expectancy of these patients. According to a closer review of their medical records, 3 patients who underwent MLP and were under 60 years of age (20%) had a documented history of myocarditis. Patient 2 experienced a relapse of viral myocarditis caused by cytomegalovirus (CMV) infection. Following intensive care treatment, the N-terminal pro-B-type natriuretic peptide (NT-proBNP) returned to normal. However, the LVEF remained low. At 4 months after receiving a MLP implantation, the LVEF improved to 56%, and Holter monitoring suggested that the pacing percentage had reached 9.2% by 1 year after implantation. Viral myocarditis can lead to conduction defects, even when there are no obvious changes to cardiac function. There is scarce information on the etiology; however, autoantibodies that target the conduction system may be produced. It is worth noting that patient 1 was strongly positive for anti-SSA and positive for anti-Ro-52 antibodies in the rheumatological immunological indices. A recent retrospective observational study that included

766 patients with heart failure (HF) found that anti-SSA was independently associated with AVB and bundle branch block (BBB) in patients with HF (21). Implanting MLP during the acute phase of myocarditis was not shown to lead to problems such as perforation, and there was some recovery of heart function and conduction after implantation; however, the limited number of instances prevents broad generalizations. Although the remaining patients did not show significant recovery of conduction function, we speculate that the degree of conduction dysfunction after myocarditis may be related to the duration of the disease, and whether early pacemaker implantation may help mitigate conduction and cardiac dysfunction remains to be investigated.

Limitations

First, this study had an observational retrospective design, which means that many important data were missing. For example, tricuspid regurgitation associated with cardiac implantable electronic devices and worsening tricuspid regurgitation after pacemaker implantation have received increasing attention in recent years and are thought to be associated with an increased risk of HF and death (22). However, our follow-up did not include relevant indicators. Second, the small sample size may not accurately represent the occurrence of long-term problems and the possibility of errors in the findings. Hence, the findings must be validated in a broader, multi-center cohort of patients with an extended follow-up period. However, this is a hypothesis-generating study that will allow further research to develop clinical trials. The absence of distinct long-term prognostic variations between Micra AV and Micra VR is attributed to the focus solely on the description of the AV synchronization rate without examining the influencing factors or doing additional follow-up. Third, few cardiovascular events occurred in our study population, so we were not able to perform prognostic statistical analyses of cardiovascular outcomes.

Conclusions

This study reports the safety and efficacy of MLP in a single center, and provides evidence that echocardiography and ECG characteristics may be related to pacing parameters. Although this was a small, single-center, retrospective study, we hope that it will enable further research into this topic, with the subsequent development of clinical trials.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Ethics Committee of the First Affiliated Hospital of Soochow University (No. [2024]203), and informed consent was signed prior to the procedure. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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