Safety and Feasibility of His-Purkinje System Pacing for Over 85-year-old Patients with Symptomatic Bradycardia: A Comparative Study with A Younger Cohort.

Zhongyuan Ren[1], Songyun Wang[2], Peng Jia[1], Jun Zhang[1], Jing Xiong[3], Jingying Zhang[1], Haotian Yang[1], Xiang Li[1], Yawei Xu[1], and Dongdong Zhao[1]

[1]Shanghai Tenth People's Hospital
[2]Renmin hospital of Wuhan University
[3]Shanghai Tenth People's Hospital, Tongji University, School of Medcine

April 27, 2020

Abstract

Introduction: His-Purkinje system (HPS) pacing emerges as an ideal strategy to restore cardiac synchrony. However, there is insufficient evidence to confirm the safety of HPS pacing in advanced age patients who are vulnerable to invasive procedures. Methods: We aimed to evaluate the short-term feasibility and safety of HPS pacing in symptomatic bradycardia patients over 85 years of age by comparing the pacing parameters and clinical outcomes with a younger cohort. 189 out of 198 consecutive patients underwent HPS pacing with symptomatic bradycardia were included. Among them 37 and 152 were aged over 85 years and below 85 years respectively. Peri- and post-procedure pacing parameters, cardiac function and clinical events were thoroughly evaluated during follow-up. Results: Compared with the younger cohort, the elderly had worse renal function and cardiac function. All 189 patients underwent successful HPS pacing, among whom 28 were paced at His-bundle. Paced QRS duration was shortened non-significantly compared with intrinsic, which showed no difference between cohorts. Pacing threshold and impedance decreased significantly without difference between cohorts. Lead dislodgement and pocket hematoma/infection only occurred in 2 (1.3%) and 4 (0.7%) younger patients, respectively. Through a 10.5±3.0 months follow-up, A non-significant improvement in cardiac function was indicated by echocardiographic indices. Clinical events incidences were comparable, except a higher incidence of myocardial infarction (8.1% vs 0.7%) observed in the advanced age cohort. Conclusion: Compared with the younger, HPS pacing could safely restore physiological conduction and reserve cardiac function in advanced age patients with symptomatic bradycardia.

Title: Safety and Feasibility of His-Purkinje System Pacing for Over 85-year-old Patients with Symptomatic Bradycardia: A Comparative Study with A Younger Cohort.

Authors : Zhongyuan Ren M.D.[1, 2*], Songyun Wang, M.D., PhD[3*], Peng Jia M.D.[1], Jun Zhang M.D.[1], Jing Xiong, M.D., PhD[1], Jingying Zhang M.D.[1], Haotian Yang M.D.[1], Xiang Li. M.D. [1], Yawei Xu M.D., PhD[1#], Dongdong Zhao M.D., PhD[1#]

* Zhongyuan Ren and Songyun Wang contributed equally to the work.

Institutions :

[1] Department of Cardiology, Shanghai Tenth People's Hospital, Tongji University School of Medicine, Shanghai, 200072, China.

[2] Soochow University Medical College, No. 199 Ren-ai Road, SIP, Suzhou, 215123, China.

[3] Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan University School of Medicine, Wuhan, Hubei Province, 430060, China.

Corresponding author : Dongdong Zhao, MD, PhD, Department of Cardiology, Shanghai Tenth People's Hospital, Tongji University School of Medicine. 301 Yanchang Rd., Shanghai, 200072, China, e-mail:*zhaodd@tongji.edu.cn.*

Co-Corresponding author: Yawei Xu M.D., PhD, Department of Cardiology, Shanghai Tenth People's Hospital, Tongji University School of Medicine. 301 Yanchang Rd., Shanghai, 200072, China. e-mail:*xuyawei@tongji.edu.cn*

Funding: This work was supported by the National Nature Science Foundation of China [grant numbers 81900292, 81900456], Fundamental Research Funds for the Central Universities [grant number 2042018kf0102], and Renmin Hospital of Wuhan University [grant number RMYD2018M37].

Disclosure : None.

Abstract

Introduction: His-Purkinje system (HPS) pacing emerges as an ideal strategy to restore cardiac synchrony. However, there is insufficient evidence to confirm the safety of HPS pacing in advanced age patients who are vulnerable to invasive procedures.

Methods : We aimed to evaluate the short-term feasibility and safety of HPS pacing in symptomatic bradycardia patients over 85 years of age by comparing the pacing parameters and clinical outcomes with a younger cohort. 189 out of 198 consecutive patients underwent HPS pacing with symptomatic bradycardia were included. Among them 37 and 152 were aged over 85 years and below 85 years respectively. Peri- and post-procedure pacing parameters, cardiac function and clinical events were thoroughly evaluated during follow-up.

Results : Compared with the younger cohort, the elderly had worse renal function and cardiac function. All 189 patients underwent successful HPS pacing, among whom 28 were paced at His-bundle. Paced QRS duration was shortened non-significantly compared with intrinsic, which showed no difference between cohorts. Pacing threshold and impedance decreased significantly without difference between cohorts. Lead dislodgement and pocket hematoma/infection only occurred in 2 (1.3%) and 4 (0.7%) younger patients, respectively. Through a 10.5±3.0 months follow-up, A non-significant improvement in cardiac function was indicated by echocardiographic indices. Clinical events incidences were comparable, except a higher incidence of myocardial infarction (8.1% vs 0.7%) observed in the advanced age cohort.

Conclusion : Compared with the younger, HPS pacing could safely restore physiological conduction and reserve cardiac function in advanced age patients with symptomatic bradycardia.

Keywords : physiological pacing, left bundle branch pacing, His-bundle pacing, bradycardia, super-aged, elderly, safety.

Introduction

Physiological pacing—the concept of imitating the normal cardiac conduction pathway—has long been put forward as a means of restoring atrioventricular synchrony(1). This concept has been historically redefined since the first His-bundle pacing attempt to achieve ventricular synchrony in 2000(2). Thereafter, a growing body of evidence shows the efficacy of His-bundle pacing. However, most studies utilize advanced pacemakers for a limited population(3-5), which cannot be generalized to patients requiring a more cost-effective therapy.

In addition, early battery depletion often occurred as a result of the elevated pacing threshold, impeding the application of His-bundle pacing[6]. Huang et al. optimized the technique by pacing at the distal His-bundle[7] or even closer to the left bundle branch (LBB), presenting a narrow QRS with steady pacing parameters[8]. Based on this observation, in 2017 they reported the first case of LBB pacing to correct an LBB block in a heart failure patient with steady pacing parameters[9]. Presently, the evidence indicates that His-Purkinje system (HPS) pacing poses a promising alternative for correcting bradycardia[6,10].

Although the criteria of successful His-bundle[11] and LBB pacing[12] have been well-defined, we still lack practical experience under specific conditions, such as cardiomyopathy and myocardial infarction, which are common in super-aged patients.

As the conductive pathway degenerates, bradycardia occurs more frequently in super-aged patients, which can only be corrected by the implantation of a pacemaker [13]. Nevertheless, elderly patients have distinctive features compared with the general population: more tortuous veins[14], lower BMI, and lower cardiac mass[15]. These differences increase the potential risks of the implantation procedure. Additionally, comorbidities like hypertension, ischemic heart disease and chronic renal disease[13] are pervasive in the elderly population, further worsening the prognosis for pacemaker implantation. Therefore, super-aged patients should be evaluated with extreme care, especially when performing HPS pacing, which requires more invasive manipulation including transseptal lead placement. However, currently no study has discussed the feasibility and safety of HPS pacing in the advanced age population.

Our study was designed to validate the safety and prognose of HPS pacing in patients over 85 with symptomatic bradycardia through comparison with a younger cohort, in order to provide the preliminary evidence in advanced age patients.

Methods

Study Sample

From October 2018 to June 2019, 198 consecutive patients were admitted indicating a need for pacemaker implantation in accordance with the 2013 ESC guidelines[16] , lead failure requiring revision, or pacemaker replacement due to battery depletion. Among them, 189 patients had symptomatic bradycardia were included, encompassing 37 patients aged over 85 and 152 younger patients. These patients underwent either permanent His-bundle or LBB pacing. Patients were excluded if they indicated and underwent cardiac resynchronization therapy (CRT) or an implantable cardioverter-defibrillator (ICD). Written forms of consent were acquired from every patient before the procedure. Our study complied with the Declaration of Helsinki and it was approved by the local ethical committee.

HPS pacing

His-bundle pacing

The His-bundle pacing procedure was similar to that used in previous studies[6,8]. Briefly, through the left subclavian vein or axillary vein (**Figure 1 A**), an 8.5F sheath was placed after a fixed curved sheath (C315His, Medtronic) distally advanced beyond the tricuspid annulus. A Select Secure lead (model 3830, 69CM, Medtronic, Minneapolis, MN, USA) was then cannulated to locate the His-bundle by capturing the His-bundle potential displayed on electrocardiogram (ECG, Bard recorder, Bard Electrophysiology Laboratory System, MA). Subsequently, pacing parameters were monitored and an eligible site was chosen with criteria described by Su et al.[8]. During implantation, intrinsic QRS duration, paced QRS duration, and pacing stimulus to LV activation time (p-LVAT) were all measured.

LBB pacing

For LBB pacing, a similar maneuver to the one described above was applied to locate His-bundle. Afterwards, under a right anterior oblique (RAO) 30deg view, activation mapping was conducted 1cm anterior to His-bundle to locate the ideal site—the proximal LBB, where left and right activations fuse incompletely and show a negative "W" waveform on lead V1. Then, the electrode was manipulated perpendicularly to the interventricular septum (IVS) and screwed clockwise until it reached the LV subendocardium.

An eligible site must meet following criteria:

1. LBB potential recorded at the pacing tip
2. Unipolar pacing shows RBB block feature on ECG
3. Selective or non-selective capture of LBB recorded under different outputs To ensure safe and stable pacing, pacing threshold, sensing and impedance were all measured. A decremental conduction test was then applied to ensure the correction of conductive lesions. The intrinsic and paced QRS durations, and p-LVAT were measured, and the pacing site was optimized with the shortest p-LVAT in order to improve cardiac function and prognosis (**Figure 2**).

In order to prevent perforation and optimize fixation, we used digital subtraction angiography (DSA) to approximate the lead depth in the IVS by injecting contrast media via the puncture sheath and C315 sheath (**Figure 1 D-F**). For patients with IIdeg to IIIdeg AV block or complete LBB block, we placed a temporary pacemaker in case of a complete AV block resulting from injury of the His-bundle or proximal LBB.

Device programming

Generally, the pacing lead was connected in accordance with the cardiac rhythm. For sinus rhythm or chronic AF patients, the lead was connected to atrial port or ventricular port respectively. Pacing output and AV delay was adjusted individually to achieve optimal QRS morphology before discharge. During follow-up, pacing parameters, AV delay and pacing proportion were routinely monitored.

Follow-up management

In the 1st, 3rd and 12th months following the procedure, patients were required to have outpatient follow-ups, or inpatient follow-ups if they were immobilized. Comprehensive medical histories were taken and physical examinations conducted by experienced cardiologists. Device programming, 24-hour Holter, and transthoracic echocardiography (TTE) were evaluated.

Statistical analysis

Continuous parameters were described as a mean +- standard deviation (SD) if they conformed to normal distribution, while those without a normal distribution were presented as the median and interquartile ranges (IQR). The p-value was generated from 2 sample t-tests or a Mann-Whitney test according to the equality of variance, or singed-rank test if a normal distribution was not presented. Repeated measures analysis of variance was applied to analyze the repeated measurements of pacemaker and echocardiographic parameters. Categorical variables were described as percentages (%) and p-values were analyzed with χ^2tests or Fisher exact tests (when theoretical frequency was lower than 5). A 2-sided P-value of <0.05 was considered statistically significant. SAS 9.4 software (SAS Institute Inc., Cary, NC, USA) was used to conduct the analysis.

Results

Sample characteristics

Generally, the elder cohort was 10 years older than the younger. The indications of pacemaker replacement were similar between cohorts, while 4 (2.6%) younger patients had lead failure necessitated lead revision. Of note, compared with the younger cohort, the elderly had significantly deteriorated renal function indicated by estimated glomerular filtration fraction (eGFR, 54.8±24.3 ml/min/1.73m^2 VS 87.1±31.8 ml/min/1.73m^2), and worse cardiac function indicated by higher NYHA (New York Heart Association) grading and proBNP level despite similar left ventricular ejection fraction (LVEF). The other comorbidities and medications were similar. Detailed information is listed in **Table 1** .

Periprocedural details

HPS pacing was achieved in all 189 patients with short fluoroscopic time. Satisfactory electrical synchrony was indicated by narrow paced QRS wave (107.4±8.8 ms vs 106.6±10.7 ms) and short p-LVAT (75.6±10.2 ms vs 74.4±8.6 ms), which showed no difference between the young and elder cohorts. Pacing parameters were similar between cohorts. And no complications including ventricular perforation were observed. Further periprocedural details are presented in **Table 2** . Fluoroscope procedures are shown in **Figure 1** and ECGs in **Figure 2** .

Follow-up

All patients underwent a mean follow-up of 10.5±3.0 months. Comparing pacing parameters monitored in the 3rd month, threshold and impedance showed a similar decreasing pattern. Sensing rose significantly in the younger patients, while it stayed stable in the elderly (**Figure 3**). Though without a significant difference, pacemaker-related events only occurred in the younger, including 2 (1.3%) lead dislodgement underwent lead revision, 1 (0.7%) pocket hematoma underwent drainage and 3 (2.0%) pocket infections requiring debridement.

The overall prognosis was similar between cohorts, with comparable mortality (1 (2.7%) elder patient resulted from intestinal obstruction and 1 (0.7%) younger patient due to ventricular fibrillation). In the 3rd month, However, cardiac events occurred more frequently in the elderly, including a higher incidence of myocardial infarction (8.1% vs 0.7%, p=0.03) and a non-significant higher rehospitalization rate (27.0% vs 13.8%, p=0.05). Follow-up details are shown in **Table 3** .

TTE in the 3rd month completed in 31 young and 12 elder patients revealed similar non-significant improvements of cardiac function **(Figure 4)** . Notably, only 1 younger patient had heart failure with acutely dropped LVEF (from 60% to 24%) which resulted from pneumonia with massive pleural effusion recovered from thoracocentesis.

Discussion

Our study compared the clinical profiles of 37 patients aged over 85 with 152 younger patients admitted with symptomatic bradycardia and underwent HPS pacing, suggesting that in the advanced age population with symptomatic bradycardia: 1. HPS pacing can also be safely performed with extensive care, 2. HPS pacing can achieve similar cardiac synchrony and stability in the short term, 3. The short-term prognosis of HPS pacing was comparable with younger patients.

Chinese aging population stands out as a major issue, with report estimating over 150 million Chinese citizens will be over 80 by 2050[17]. As in our study, the median age of younger cohort was 77 years. Besides, bradycardia—resulting from either aging or potential disease progression—is more pervasive in geriatrics. Therefore, pacemaker implantation investigating super-aged patients has long been a focus [13]. However, as a community, elderly patients have more comorbidities, worse general conditions and limited life expectancy. Pacing strategy necessitates a more comprehensive consideration compared with younger patients. Although studies have indicated that conventional physiological pacing (dual chamber pacing) cannot improve the likelihood of survival[18] and cost more, less complications and a better quality of life by physiological pacing should be considered as well[13].

On one hand, HPS comprises the normal conduction pathway, which is an ideal site to achieve physiological pacing. Pacing from HPS mimics routine cardiac conduction to the greatest extent with a narrow QRS wave. Research has proven that His-bundle pacing improves cardiac function comparably with RV pacing[19] or CRT[20]. Besides, LBB pacing can also narrow QRS and reserve cardiac function comparably with RV pacing[21]or CRT[22]. In addition, both His-bundle[8] and LBB[10] pacing can be performed with stable pacing parameters. Similarly, in our study, we observed comparable electrical synchrony with narrowed QRS and reserved cardiac function indicated by LVEF albeit the change was non-significant. And pacing parameters were kept stable during a short-term. Moreover, those indices showed no difference between younger and elder cohorts. Hence, HPS pacing could achieve stable and physiologic cardiac synchrony in advanced age patients as well.

On the other hand, safety is a major concern for super-aged patients. Studies on the elderly have shown that elderly patients had more tortuous veins (as shown in **Figure 2 A**), lower BMI and lower cardiac mass[15], accounting for the higher risk of complications such as pneumothorax, lead dislodgement and loss of capture[14]. Therefore, pacemaker implantations should be performed with excessive care.

First, the fluoroscopic time was comparable to that previously reported[10]. Before the procedure, we thoroughly evaluated patients' medical histories and conducted examinations like chest X-rays to reveal any underlying risks. Moreover, as we performed implantation via the left subclavian or axillary vein, taking extreme caution, no pneumothorax occurred during follow-up. According to recent study, alternative puncture sites such as the cephalic and auxiliary vein should be considered, as well as ultrasonic guidance if the risk of pneumothorax is high[23]. Thus, in order to ensure safety, we recommend a thorough evaluation of patient profiles before procedure and careful manipulation when performing pacemaker implantation in either young or elder patients.

Secondly, lead dislodgement is rare for His-bundle pacing and LBB pacing, as Vijayaraman et al. reported 3 acute cases[10] and Wang et al. reported 2 late ones[21]. The manipulation of His-bundle pacing has been well-described and performed[8]. In addition, ever since 2017 when Huang et al. published the first case of LBB pacing[9], the maneuver of LBB pacing has been standardized with less complications. In our study, lead dislodgement occurred in 2 younger patients underwent His-bundle pacing early in our center, while no case occurred in the elder cohort. Both had successful lead repositioned at LBB. Presumably, extensive fibrosis of myocardium caused by either myocardial infarction or cardiomyopathy render the fixation of the electrode difficult, as Zhang et al. reported 1 failed implantation due to fibrosis after an anterior myocardial infarction[24]. However, we currently still lack a convenient and effective way to evaluate fibrosis and avoid such complications. Based on our experience, we recommend the criteria to assess lead depth and minimize the risk of lead dislodgement: 1. Unipolar pacing impedance at the distal tip should be $> 500\ \Omega$ (sharp decrement indicates perforation into LV); 2. Once LBB potential has been recorded and pacing parameters were acceptable, screwing was halted instantly; 3. Under DSA, we judged the lead depth by continuously injecting contrast (**Figure 2 D-F**). In addition, when retracting the delivery sheath, we observed a rebound of the distal portion of the lead, which indicated a steady fixation[12].

Thirdly, ventricular perforation is another major complication. No extant study has focused on perforations in HPS pacing. Nevertheless, one study has shown several factors to correlate with ventricular perforation during conventional pacing, including the use of temporary pacemakers, use of steroids, use of helical screw leads, BMI of <20, and old age[15]. Their study indicates that a thinning of the cardiac wall for reasons unknown, and excessive leads in the RV increase risk of perforation. Inevitably, during HPS pacing, an active fixation 3830 lead was used and temporary pacemakers were routinely placed for AVB patients. Furthermore, patients aged over 85 had a more vulnerable cardiac wall, with a higher risk of myocardial infarction (18.9%) and higher usage of statins (43.2%). We presume that the risk of perforations during HPS pacing exceeds that of conventional pacing in advanced age population. Though we observed no perforation in our sample of 189 patients, which is in parallel with the incidence rate indicated by current HPS pacing studies (ranging from 0 to 3%[10,21,24,25]), we still need to stress that manipulation should be managed with extensive care. Most importantly, we should carefully screw the lead and evaluated the lead depth as described above. Meanwhile, in the occasion of temporary pacing, the lead is better fixed at the relatively thick area of the IVS. Although such maneuvers could empirically prevent perforation, larger studies focusing on safety are warranted to validate these conclusions. In conclusion, we believe HPS pacing in elderly patients poses a higher risk of perforation and extensive caution should be taken during procedure.

Last but not least, although our study showed HPS pacing can be achieved safely with satisfactory cardiac synchrony, we should reflect the necessity of HPS pacing for symptomatic bradycardia population with advanced age comprehensively. In our study, advanced age patients had more cardiac events, including higher myocardial infarction incidence and non-significant higher rehospitalization rate due to cardiovascular events. We believe the deteriorated cardiac function and higher proportion coronary heart disease might contribute to the recurrent cardiovascular symptom. Currently, only a 20-year evidence of pacing in patients over 90 years old provided similar outcomes of single or dual chamber pacing[(13)]. Although the evidence is not adequate to illustrate the necessity of HPS pacing in advanced age population, it can be a desirable choice in an experienced center with the premise of safety. More importantly, we should realize that it is general conditions, rather than age, that directly affect the safety of the procedure. Therefore, evaluation of general conditions should be prioritized ahead of age before HPS pacing.

Limitations

First, the conclusion cannot be extrapolated as we only included patients with symptomatic bradycardia patients. Secondly, although both His-bundle and LBB pacing can be physiological, the difference between them was not stressed, which was beyond the scope of this paper. A well-designed, larger-scaled, comparative study is required. Thirdly, During the procedure, His-bundle and LBB potentials cannot be recorded exhaustively, which might result from a complete LBB block or a distal complete AVB. Moderate to severe tricuspid regurgitation could impede the recording of His-bundle or LBB potential as well. In addition, the duration of follow-up examinations was too short to observe long-term clinical events. Study with a longer follow-up period is necessary to validate the long-term necessity and benefits of these procedures. Last but not least, due to immobility and impaired cognitive function, compliance rates among elderly patients is low (including relatively younger patients as well), which makes follow-up difficult and often incomplete. A more considerate follow-up strategy is required for the aged population.

Conclusion

Compared with a younger cohort, physiological pacing could be achieved at HPS with a considerable success rate and level of safety in the elderly population with symptomatic bradycardia. Long-term follow-up is warranted to validate the benefits of HPS pacing.

Acknowledgment

Great thankfulness to all the work done by electrophysiology team.

References

1. Prech M, Grygier M, Mitkowski P et al. Effect of restoration of AV synchrony on stroke volume, exercise capacity, and quality-of-life: can we predict the beneficial effect of a pacemaker upgrade? Pacing Clin Electrophysiol 2001;24:302-7.

2. Deshmukh P, Casavant DA, Romanyshyn M, Anderson K. Permanent, direct His-bundle pacing: a novel approach to cardiac pacing in patients with normal His-Purkinje activation. Circulation 2000;101:869-77.

3. Su L, Xu L, Wu SJ, Huang WJ. Pacing and sensing optimization of permanent His-bundle pacing in cardiac resynchronization therapy/implantable cardioverter defibrillators patients: value of integrated bipolar configuration. Europace 2016;18:1399-405.

4. Huang W, Su L, Wu S et al. Benefits of Permanent His Bundle Pacing Combined With Atrioventricular Node Ablation in Atrial Fibrillation Patients With Heart Failure With Both Preserved and Reduced Left Ventricular Ejection Fraction. J Am Heart Assoc 2017;6.

5. Sharma PS, Naperkowski A, Bauch TD et al. Permanent His Bundle Pacing for Cardiac Resynchronization Therapy in Patients With Heart Failure and Right Bundle Branch Block. Circ Arrhythm Electrophysiol 2018;11:e006613.

6. Sharma PS, Dandamudi G, Naperkowski A et al. Permanent His-bundle pacing is feasible, safe, and superior to right ventricular pacing in routine clinical practice. Heart Rhythm 2015;12:305-12.

7. Vijayaraman P, Huang W. Atrioventricular block at the distal His bundle: Electrophysiological insights from left bundle branch pacing. HeartRhythm Case Rep 2019;5:233-236.

8. Su L, Wu S, Wang S et al. Pacing parameters and success rates of permanent His-bundle pacing in patients with narrow QRS: a single-centre experience. Europace 2019;21:763-770.

9. Huang W, Su L, Wu S et al. A Novel Pacing Strategy With Low and Stable Output: Pacing the Left Bundle Branch Immediately Beyond the Conduction Block. Can J Cardiol 2017;33:1736 e1-1736 e3.

10. Vijayaraman P, Subzposh FA, Naperkowski A et al. Prospective evaluation of feasibility and electrophysiologic and echocardiographic characteristics of left bundle branch area pacing. Heart Rhythm 2019;16:1774-1782.

11. Vijayaraman P, Chung MK, Dandamudi G et al. His Bundle Pacing. J Am Coll Cardiol 2018;72:927-947.

12. Huang W, Chen X, Su L et al. A beginner's guide to permanent left bundle branch pacing. Heart Rhythm 2019;16:1791-1796.

13. Antonelli D, Freedberg NA, Bushari LI, Feldman A, Turgeman Y. Permanent pacing in nonagenarians over 20-year period. Pacing Clin Electrophysiol 2015;38:48-53.

14. Armaganijan LV, Toff WD, Nielsen JC et al. Are elderly patients at increased risk of complications following pacemaker implantation? A meta-analysis of randomized trials. Pacing Clin Electrophysiol 2012;35:131-4.

15. Mahapatra S, Bybee KA, Bunch TJ et al. Incidence and predictors of cardiac perforation after permanent pacemaker placement. Heart Rhythm 2005;2:907-11.

16. Brignole M, Auricchio A, Baron-Esquivias G et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Eur Heart J 2013;34:2281-329.

17. Fang EF, Scheibye-Knudsen M, Jahn HJ et al. A research agenda for aging in China in the 21st century. Ageing Res Rev 2015;24:197-205.

18. Healey JS, Toff WD, Lamas GA et al. Cardiovascular outcomes with atrial-based pacing compared with ventricular pacing: meta-analysis of randomized trials, using individual patient data. Circulation 2006;114:11-7.

19. Abdelrahman M, Subzposh FA, Beer D et al. Clinical Outcomes of His Bundle Pacing Compared to Right Ventricular Pacing. J Am Coll Cardiol 2018;71:2319-2330.

20. Sharma PS, Dandamudi G, Herweg B et al. Permanent His-bundle pacing as an alternative to biventricular pacing for cardiac resynchronization therapy: A multicenter experience. Heart Rhythm 2018;15:413-420.

21. Wang J, Liang Y, Wang W et al. Left bundle branch area pacing is superior to right ventricular septum pacing concerning depolarization-repolarization reserve. J Cardiovasc Electrophysiol 2020;31:313-322.

22. Zhang W, Huang J, Qi Y et al. Cardiac resynchronization therapy by left bundle branch area pacing in patients with heart failure and left bundle branch block. Heart Rhythm 2019;16:1783-1790.

23. Nash A, Burrell CJ, Ring NJ, Marshall AJ. Evaluation of an ultrasonically guided venepuncture technique for the placement of permanent pacing electrodes. Pacing Clin Electrophysiol 1998;21:452-5.

24. Zhang J, Wang Z, Cheng L et al. Immediate clinical outcomes of left bundle branch area pacing vs conventional right ventricular pacing. Clin Cardiol 2019;42:768-773.

25. Li X, Li H, Ma W et al. Permanent left bundle branch area pacing for atrioventricular block: Feasibility, safety, and acute effect. Heart Rhythm 2019;16:1766-1773.

Table 1. Baseline characteristics of HPS pacing patients.

Variables	Young (<85) N=152	Elderly ([?]85) N=37	P value
Age, yrs	77 [68, 81]	87 [86, 89]	**<0.0001**
Gender (male), n (%)	86 (56.6)	18 (48.6)	0.38
BMI, kg/m^2	24.0±3.9	23.8±3.3	0.76
IVS thickness, mm	10 [10, 11]	10 [10, 11]	0.34
LVEF, %	60 [55, 62]	59 [52, 60]	0.20
NT-proBNP, pg/ml	461.0 [178.8, 1203.5]	1617.0 [619.0, 2941.0]	**<0.0001**
eGFR, ml/min/1.73m^2*	87.1±31.8	54.8±24.3	**<0.0001**
NYHA, n (%)			**0.006**
IV	10 (6.6)	8 (21.6)	
III	25 (19.0)	7 (18.9)	
II	40 (26.3)	10 (27.0)	
I	77 (50.7)	12 (32.4)	
Indications, n (%)			0.52
SSS	45 (29.8)	13 (35.1)	
AF with long R-R interval	36 (23.8)	6 (16.2)	
AVB +	61 (40.4)	16 (43.2)	
Battery depletion	5 (3.3)	2 (5.4)	
Lead failure	4 (2.6)	0	
Medical history, n (%)			
Renal insufficiency	10 (6.6)	13 (35.1)	**<0.0001**
AF	52 (34.2)	11 (29.7)	0.60
Previous stroke	23 (15.3)	7 (18.9)	0.50
DCM	2 (1.3)	1 (2.7)	1.00
HCM	5 (3.3)	2 (5.4)	0.90
Coronary heart disease	49 (32.2)	17 (46.0)	0.12
myocardial infarction	17 (11.2)	7 (18.9)	0.32
Hypertension	108 (71.1)	25 (67.6)	0.68
Diabetes mellitus	37 (24.3)	8 (21.6)	0.73
Medications, n (%)			
Antiplatelet agents	42 (27.6)	11 (29.7)	0.70
Oral anticoagulants	19 (12.5)	4 (10.8)	1.00
Statins	48 (31.6)	16 (43.2)	0.18

Continuous variables are described as mean ± SD or median with IQR, while categorical variables are presented as percentages (%). AF denotes atrial fibrillation, AVB atrial ventricular block, BMI body mass index, DCM dilated cardiomyopathy, eGFR estimated glomerular filtration fraction, HCM, hypertrophic cardiomyopathy, IVS interventricular septum, LVEF left ventricular ejection fraction, NT-proBNP N-terminal pro brain natriuretic peptide, NYHA New York Heart Association grading of cardiac function, SSS sick sinus syndrome.

* eGFR was calculated by MDRD formula.

+ AVB includes II° AVB Mobitz type 2 and III° AVB.

Table 2 Procedural details and pacing parameters.

Parameters	Young (<85) N=152	Elderly ([?]85) N=37	P value
LBB pacing, n (%)	128 (84.2)	33 (89.2)	0.44
Fluoroscopic time, min	11.4 [7.0, 16.2]	11.5 [7.2, 16.2]	0.93
Fluoroscopic dosage, mGy	130.1 [88.8, 273.7]	117.3 [89.8, 248.0]	0.74
Intrinsic QRS duration, ms	110.5±23.4	113.5±21.0	0.51
Paced QRS duration, ms	107.4±8.8	106.6±10.7	0.15
LBB block, n (%)	12 (8.0)	2 (5.4)	0.87
RBB block, n (%)	23 (15.2)	8 (21.6)	0.34
p-LVAT, ms	75.6±10.2	74.4±8.6	0.57
Lead depth, cm	12 [11, 12]	11 [11, 12]	0.07
Pacing parameters			
Threshold, V	0.9±0.6	0.8±0.3	0.12
Sense, mV	12.1±5.0	12.9±5.0	0.43
Impedance, Ω	708.0±168.1	699.8±170.0	0.79

p-LVAT denotes pacing to left ventricle activation time.

Table 3 Follow-up outcomes between younger and elder patients.

events	Young (<85) N=152	Elderly ([?]85) N=37	P value
Pacemaker related events			
Pneumothorax, n (%)	0	0	1.00
Lead dislodgement, n (%)	2 (1.3)	0	1.00
Pocket hematoma, n (%)	1 (0.7)	0	1.00
Pocket infection, n (%)	3 (2.0)	0	0.90
Clinical events			
Myocardial infarction, n (%)	1 (0.7)	3 (8.1)	**0.03**
Stroke, n (%)	1 (0.7)	2 (5.4)	0.18
Ventricular fibrillation, n (%)	1 (0.7)	0	1.00
Heart failure, n (%)	6 (4.0)	2 (5.4)	1.00
Pulmonary embolism, n (%)	1 (0.7)	0	1.00
Pleural effusion, n (%)	1 (0.7)	0	1.00

events	Young (<85) N=152	Elderly ([?]85) N=37	P value
Rehospitalization due to cardiovascular events, n (%)	21 (13.8)	10 (27.0)	0.05
Death due to cardiovascular events, n (%)	1 (0.7)	0	1.00
All-cause death, n (%)	1 (0.7)	1 (2.7)	0.84

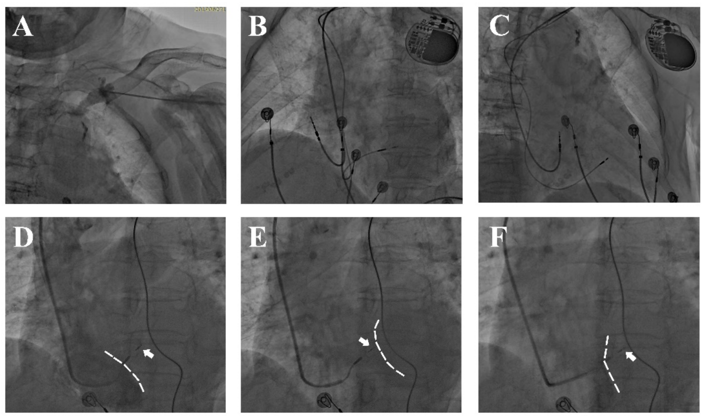

Figure 1. Fluoroscopy during LBB pacing. **A:** Venous angiography after puncture showed a tortuous left subclavian vein.**B, C:** Postprocedural fluoroscopy showed a fixed 3830 lead in the IVS and atrial lead in right atrial appendage. **D, E, F:**Lead depth measured by the relative position of 3830 electrode (*white arrow*) and IVS during screwing. **D, E** : Angiography via 8.5 F puncture sheath delineated RV silhouette (**D** ,*dashed white line*) while delayed contrast delineated LV silhouette (**E** , *dashed white line*). **F** : Angiography via C315 sheath showed RV side of IVS (*dashed white line*).

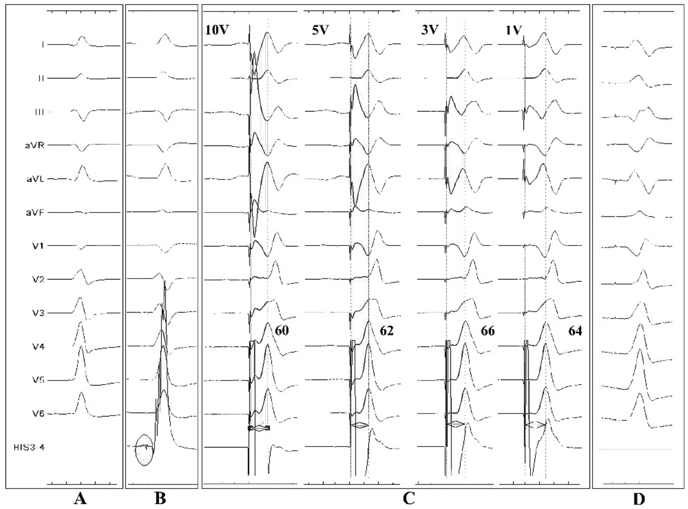

Figure 2. 12-lead and intracardiac electrocardiograms (ECG) during LBB pacing in a 96-year-old III° AVB patient. **A:**Intrinsic rhythm showed a QS morphology in V1 lead. **B:** LBB potential recorded by pacing tip (*black circle*) when the lead reached LV subendocardium. **C:** p-LVAT measured by unipolar pacing after fixation. Under different pacing output, QRS showed similar RBB block pattern and p-LVAT stayed short, indicating capture of LBB.**D:** Postprocedure ECG recording. A QR pattern was shown in V1 lead. Paced QRS duration was similar to intrinsic.

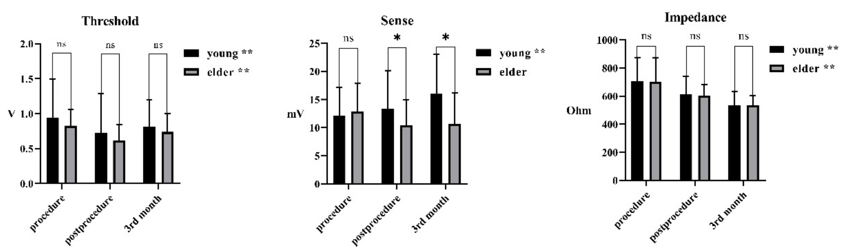

Figure 3. Pacing parameters before, after and in the 3rd month after implantation between young and elder cohorts. * and ** indicates statistical significance, $p<0.05$ and $p<0.01$ respectively, and ns denotes non-significance.

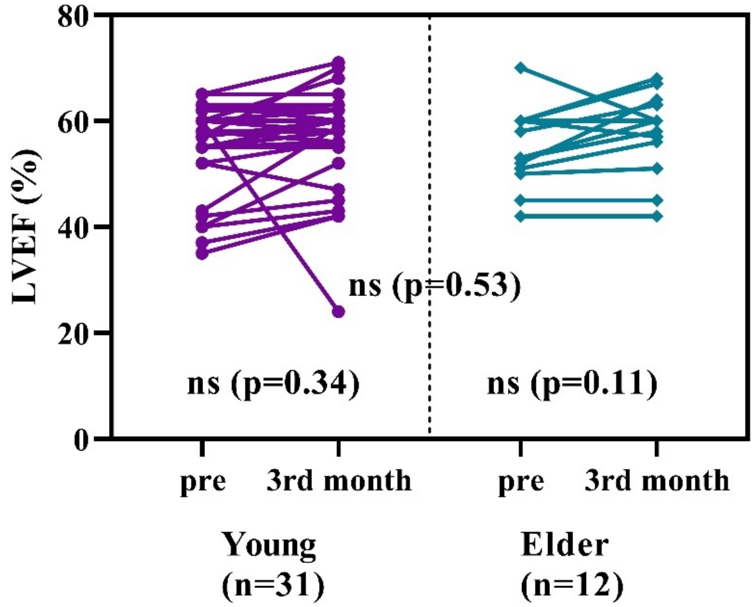

Figure 4. Comparison of cardiac function before and in the 3rd month of follow-up between cohorts. LVEF denotes left ventricle ejection fraction, ns for non-significance.