【別添】

Micra 経カテーテルペーシングシステム（Micra AV）に関する費用対効果評価 [第 1.0 版]

9. 補足資料

補足資料として、以下をまとめた。

- 同定した臨床研究(論文)の一覧表
- システマティックレビューに組み込んだ臨床研究(論文)の詳細表

[redacted]

- 植込み後 30 日間に合併症が発生することによる追加的な死亡率
- SF-36 で計測された HRQoL 値の変換

同定した臨床研究(論文)の一覧表

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
Arai et al, 2022	Leadless pacemaker implantation with postprocedural computed tomography (CT)	Grouped by placement of leadless pacemaker – septal or non-septal	N=67; N=28 Septal group N=39 Non-Septal group	Mean±SD, Unpaired t-test, Mann-Whitney U test, Fisher exact test, Pearson's product-moment correlation, EZR version 1.36, R software	Arai H, Mizukami A, Hanyu Y, Kawakami T, Shimizu Y, Hiroki J, Yoshioka K, Ohtani H, Ono M, Yamashita S, Iwatsuka R, Ueshima D, Matsumura A, Goya M, Sasano T. Leadless pacemaker implantation sites confirmed by computed tomography and their parameters and complication rates. *Pacing Clin Electrophysiol* 2022; 45: 196-203.
Arps et al, 2021	Micra TPS in subjects without persistent AF	N/A (retrospective analysis)	N=50	Mean +/- SD, t-test, Wilcoxon rank sum test, McNemar test	Arps K, Piccini JP, Yapejian R, et al. Optimizing mechanically sensed atrial tracking in patients with atrioventricular-synchronous leadless pacemakers: A single-center experience. Heart Rhythm O2. 2021;2(5):455-462.
Barletta et al, 2020	Micra TPS in subjects <79 years	Micra TPS in subjects >=80 years	N = 109 (46 above 80 years)	Mean ±SD, t-tests, Mann-Whitney U test, Fisher's exact test	Barletta V, Zucchelli G, Parollo M, et al. Leadless pacing in the elderly: never too old for something new. Monaldi Arch Chest Dis. 2020;90(4). doi:10.4081/monaldi.2020.1255

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
Bhatia et al, 2021	Micra TPS implantation with extraction or abandoned Micra device	Micra TPS implantation with no extraction	All Micra N=302 Abandoned N=12 Extraction N=11	Mean ±SD, Median and categorical variables as %, Fisher's exact test, SAS version 9.4	Bhatia NK, Kiani S, Merchant FM, Delurgio DB, Patel AM, Leon AR, Lloyd MS, Westerman SB, Shah AD, El-Chami MF. Life cycle management of Micra transcatheter pacing system: Data from a high-volume center. J Cardiovasc Electrophysiol 2021; 32: 484-490.
Bicong et al, 2022	leadless pacemaker implantation with previous CIED infection and lead extraction	N/A (retrospective analysis)	N=39	numbers and percentages for categorical variables, means ± SDs for normally distributed continuous variables, and medians with 25th–75th percentile for	Bicong, L., Allen, J. C., Arps, K., Al-Khatib, S. M., Bahnson, T. D., Daubert, J. P., Frazier-Mills, C., Hegland, D. D., Jackson, K. P., Jackson Il, L. R., Lewis, R. K., Pokorney, S. D., Sun, A. Y., Thomas, K. L. & Piccini, J. P. Leadless pacemaker implantation after lead extraction for cardiac implanted electronic device infection. Journal of cardiovascular electrophysiology 2022, 33(3), 464-470.

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
				nonnormally distributed continuous variables	
Clementy et al, 2021	Micra TPS in critically ill patients	Conventional transvenous pacing in critically ill patients	N=99 consecutive patients implanted with Micra TPS LPM	JMP 9.0 software, Mean ±SD, χ^2 or Fisher's exact test, Student's t-test, Mann-Whitney-Wilcoxon test, Kaplan-Meier method	Clementy N, Coelho R, Veltmann C, Marijon E, Tolosana J, Galand V, Ploux S, Eschalier R, Simeon E, Blessberger H, Mueller-Leisse J, Pujol-Lopez M, Martins R, Ritter P, Steinwender C, Babuty D. Leadless pacemakers in critically ill patients requiring prolonged cardiac pacing: A multicenter international study. J Cardiovasc Electrophysiol 2021; 32: 2522-2527.
El-Chami et al, 2022	Leadless pacemaker implantation in Medicare beneficiaries	Transvenous VVI, contemporaneous control group	N=6,219 de novo Leadless VVI; N=10,212 de novo Transvenous VVI	T-tests, Chi-squared tests, Propensity score overlap weights, logistic regression model, Fine-Gray competing risk models, Cox	El-Chami MF, Bockstedt L, Longacre C, Higuera L, Stromberg K, Crossley G, Kowal RC, Piccini JP. Leadless vs. transvenous single-chamber ventricular pacing in the Micra CED study: 2-year follow-up. Eur Heart J 2022; 43: 1207-1215.

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
				proportional hazards model, SAS version 9.4	
El-Chami et al, 2022a	Micra system patients with anticoagulation therapy (AC)	Interrupted anticoagulation or no anticoagulation	N=5,585 Group 1 (no AC), N=5,795 Group 2 (interrupted AC), N=5,415 Group 3 (continuous AC)	Student t tests, Wilcoxon rank sum test, Fisher exact test, Firth penalized likelihood, Logistic regression models SAS Version 9.4 or R Version 4.0.2, PSweight package in R Version 1.1.4	El-Chami MF, Garweg C, Iacopino S, Al-Samadi F, Martinez-Sande JL, Tondo C, Johansen JB, Prat XV, Piccini JP, Cha YM, Grubman E, Bordachar P, Roberts PR, Soejima K, Stromberg K, Fagan DH, Clementy N. Leadless pacemaker implant, anticoagulation status, and outcomes: Results from the Micra Transcatheter Pacing System Post-Approval Registry. Heart Rhythm 2022; 19: 228-234.
El-Chami et al, 2021	Micra implant with concomitant AVNA.	Micra implant with no concomitant atrioventricular node	N=192 Patients undergoing AVNA, N=2,616 Patients not	Wilcoxon Rank sum test, Fisher's exact test, logistic regression model, Cox proportional hazards, Standardized	El-Chami MF, Shinn T, Bansal S, Martinez-Sande JL, Clementy N, Augostini R, Ravindran B, Sagi V, Ramanna H, Garweg C, Roberts PR, Soejima K, Stromberg K, Fagan DH, Zuniga N, Piccini JP. Leadless pacemaker implant with concomitant atrioventricular node ablation: Experience with the Micra transcatheter

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
		ablation (AVNAs	undergoing AVNA	mean differences, SAS v9.4 or R v4.0.2	pacemaker. J Cardiovasc Electrophysiol 2021; 32: 832-841.
Garweg et al, 2020	Class I or II indication for Micra, with previous valve intervention	Class I or II indication for Micra, without previous valve intervention	N=170 (54 with previous valvular intervention, 116 without)	Mean ±SD, Mann-Whitney U test, Mann-Whitney U test, Kolmogorov-Smirnov test, Chi-squared test, Wilcoxon signed-rank test, Pearson's correlation coefficient, ANOVA with Bonferroni correction	Garweg C, Vandenberk B, Foulon S, et al. Leadless pacemaker for patients following cardiac valve intervention. Arch Cardiovasc Dis. 2020;113(12):772-779.
Garweg et al, 2021	Micra implantation using MARVEL 2 algorithm to provide AV synchronous pacing	No use of MARVEL 2 algorithm	N=75 patients implanted with Micra LPM and received MARVEL 2 algorithm AV Block N=42, 1:1	Mean ± SD or Median and interquartile range, Paired t-tests, Wilcoxon signed rank test, SAS v9.4	Garweg C, Khelae SK, Chan JYS, Chinitz L, Ritter P, Johansen JB, Sagi V, Epstein LM, Piccini JP, Pascual M, Mont L, Willems R, Splett V, Stromberg K, Sheldon T, Kristiansen N, Steinwender C. Behavior of AV synchrony pacing mode in a leadless pacemaker during variable AV conduction and arrhythmias. J Cardiovasc Electrophysiol 2021; 32: 1947-1957.

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
			AVC N=18, Other rhythms N=13		
Haddadin et al, 2022	leadless pacemaker implantation	N/A Retrospective database study	N = 7,821	Means, median, SD, percentages, multiple hierarchical logistic regression,	Haddadin, F., Majmundar, M., Jabri, A., Pecha, L., Scott, C., Daher, M., Kumar, A., Kalra, A., Fram, R., Haddadin, F., Almahameed, S., DeSimone C. V., Cha, Y.-M., Mulpuru, S. K., Ellenbogen, K. A., Saeed, M., Chelu, M. G. & Deshmukh, A. J. Clinical outcomes and predictors of complications in patients undergoing leadless pacemaker implantation. Heart Rhythm 2022. Article in Press.
Hauser et al, 2021	MACE associated with Micra LICP (leadless intracardiac pacemaker) implantation	CapSureFix lead usage during first 30 days after implant	Micra LICP N=363, CapSureFix N=960	Pearson χ^2 or Fisher's exact test, R version 3.6.0 in R Studio Version 1.1.463	Hauser RG, Gornick CC, Abdelhadi RH, Tang CY, Casey SA, Sengupta JD. Major adverse clinical events associated with implantation of a leadless intracardiac pacemaker. Heart Rhythm 2021; 18: 1132-1139.
Hauser et al, 2022	Database search for consequences of Micra	NA	N=563, Perforations that manifeste	Pearson's chi-square or Fisher's exact tests, R version 4.0.1	Hauser RG, Gornick CC, Abdelhadi RH, Tang CY, Kapphahn-Bergs M, Casey SA, Okeson BK, Steele EA, Sengupta JD. Leadless pacemaker perforations: Clinical consequences and related

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
	LPM perforations and related device and operator use problems.		d clinically during Micra implantation within 30 days of implant		device and user problems. J Cardiovasc Electrophysiol 2022; 33: 154-159.
Higuchi et al, 2020	Micra TPS implanted subjects, stable pacing threshold	Micra TPS implanted subjects, increased pacing threshold	N=60 (9 in stable threshold group, 51 in increased pacing threshold)	Shapiro-Wilk test, Mann-Whitney U test, Student's t-test, Welch t-test, Fisher's exact probability test, ROC curve	Higuchi M, Shinoda Y, Hasegawa T, et al. Predictors of increase in pacing threshold after transcatheter pacing system implantation due to micro-dislodgement. Pacing Clin Electrophysiol. 2020;43(11):1351-1357.
Houmsse et al, 2020	Micra TPS implanted subjects with an IVC filter	NA	N=23	Mean (SD), Median (IQR)	Houmsse M, Karki R, Gabriels J, et al. Implantation of leadless pacemakers via inferior vena cava filters is feasible and safe: Insights from a multicenter experience. J Cardiovasc Electrophysiol. 2020;31(12):3277-3285.
Jelisejevas et al, 2021	Micra TPS Implantation access from left femoral artery	Micra TPS Implantation access from right femoral artery	N=143; N=18 left femoral access; N=125 Right	Jamovi project version 1.2, Shapiro-Wilk test, Mean ± SD, Student t-test, Mann-Whitney U-	Jelisejevas J, Breitenstein A, Hofer D, Winnik S, Steffel J, Saguner AM. Left femoral venous access for leadless pacemaker implantation: patient characteristics and outcomes. *Europace* 2021; 23: 1456-1461.

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
			femoral access	test Pearson χ^2 or Fisher's exact test	
Kumar et al, 2021	Micra TPS in subjects with chronic/permanent AF associated with CHB, SSS	Transvenous pacemaker	N=443 (198 for Micra, 245 for transvenous)	Mean +/- SD	Kumar V, Agarwal R, Singh Yadav M, Dhir S, Kumar V. Implantation of the Micra transcatheter pacing system: A single center North India experience. Indian Pacing Electrophysiol J. 2021;21(1):19-24.
Martinez-Sande et al, 2021	Micra TPS implantation from left femoral artery	Transvenous pacemakers	N=443 (198 for Micra, 245 for transvenous)	Mean +/- SD, Propensity score matching, Cox regression analysis, multiple hypothesis testing with Benjamini-Hochberg procedure, Bayesian cohort analysis (posterior calculated using Metropolis-Hastings algorithm)	Martinez-Sande JL, Garcia-Seara J, Gonzalez-Melchor L, et al. Conventional single-chamber pacemakers versus transcatheter pacing systems in a "real world" cohort of patients: A comparative prospective single-center study. Indian Pacing and Electrophysiology Journal. 2021;21(2):89-94. doi:10.1016/j.ipej.2020.12.004
Nicosia et al, 2022	leadless single-	N/A	N = 577	means and SD;	Nicosia, A., Iacopino, S., Nigro, G., Zucchelli, G., Tomasi, L., D'Agostino, C., Ziacchi, M.,

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
	chamber pacemaker Micra TPS implants			minimum, maximum, and median with IQR, counts and percentages, Kruskal–Wallis test, chi-square test, Fisher`s exact test	Piacenti, M., De Filippo, P., Sgarito, G., Campisi, G., Nicolis, D., Foti, R. & Palmisano, P. Performance of transcatheter pacing system use in relation to patients' age. *Journal of Interventional Cardiac Electrophysiology*, 2022, 1-8.
Ngo et al, 2021	Systematic review of reported outcomes from Micra implantation.	Systematic review of reported outcomes from Nanostim implantation.	36 Studies, N=4335	Freedman-Tukey double arcsine transformation, Stata version 16.0, Stata user-written command Metaprop, I2 statistic	Ngo L, Nour D, Denman RA, Walters TE, Haqqani HM, Woodman RJ, Ranasinghe I. Safety and Efficacy of Leadless Pacemakers: A Systematic Review and Meta-Analysis. *J Am Heart Assoc* 2021; 10: e019212.
Oliviera et al, 2021	Micra leadless pacemaker	N/A (Systematic Review)	58 papers covering 4,739 subjects	Mean +/- SD	Oliveira SF, Carvalho MM, Adão L, Nunes JP. Clinical outcomes of leadless pacemaker: a systematic review. Minerva Cardiol Angiol. 2021;69(3):346-357.
Palmisano et al, 2021	Micra leadless pacemaker with femoral vein access	Transvenous pacemaker	N = 243 (leadless 91, transvenous 152)	Mean +/- SD, Student's t-test, Mann-Whitney U test, analysis of variance, Fisher's exact test, binary	Palmisano P, Guido A, Panico V, et al. Leadless pacemaker versus transvenous single-chamber pacemaker therapy: peri-procedural aspects, utilization of medical resources and patient acceptance. Expert Rev Med Devices. 2021;18(5):483-491

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
				logistic regression for propensity scores	
Piccini et al, 2021	Micra leadless pacemaker in Medicare beneficiaries	Transvenous pacemaker	N=5746 (leadless), N=9662 (transvenous)	Mean +/- SD, t-tests, Chi-squared test, univariate logistic regression, Fine-Gray competing risk modules, Cox proportional hazards models	Piccini JP, El-Chami M, Wherry K, et al. Contemporaneous Comparison of Outcomes Among Patients Implanted With a Leadless vs Transvenous Single-Chamber Ventricular Pacemaker. JAMA Cardiol. 2021;6(10):1187-1195.
Piccini et al, 2022	Micra leadless pacemaker in previous trials	N/A (pooled analysis)	N=32 (effusion), N=2785 (no effusion)	Mean +/- SD, binomial confidence intervals, multivariable risk production model, Lasso regression	Piccini JP, Cunnane R, Steffel J, et al. Development and validation of a risk score for predicting pericardial effusion in patients undergoing leadless pacemaker implantation: experience with the Micra transcatheter pacemaker. Europace. Published online January 13, 2022. doi:10.1093/europace/euab315
Russo et al, 2022	Micra leadless pacemaker in subjects with AF	Micra leadless pacemaker in subjects without AF	N=140	Mean +/- SD, median +/- IQR, Kolmogorov-Smirnov test, Shapiro-Wilk test, chi-squared tests with Yates correction where	Russo V, D'Andrea A, De Vivo S, et al. Single-Chamber Leadless Cardiac Pacemaker in Patients Without Atrial Fibrillation: Findings From Campania Leadless Registry. Front Cardiovasc Med. 2022;8:781335.

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
				appropriate, Student's t-test, Mann-Whitney U test, Wilcoxon signed-rank test, Kaplan-Meier analysis	
Sanchez et al, 2021	Micra leadless pacemaker in subjects with normal LVEF (>=50%)	Transvenous pacemaker	N=198 (131 for transvenous, 67 for leadless)	Mean +/- SD, Student's t-test, Chi-squared test, multivariate analysis	Sanchez R, Nadkarni A, Buck B, et al. Incidence of pacing-induced cardiomyopathy in pacemaker-dependent patients is lower with leadless pacemakers compared to transvenous pacemakers. J Cardiovasc Electrophysiol. 2021;32(2):477-483.
Sasaki et al, 2022	Micra leadless pacemaker for subjects with bradyarrhythmia (Class I and II)	Transvenous pacemaker	N=193 (leadless 110, transvenous 83), N=116 with propensity score matching (leadless 58,	Mean +/- SD, median, IQR, Student's t-test, Wilcoxon rank-sum test, Fisher's exact test, Kaplan-Meier method and log-rank test, logistic regression model	Sasaki K, Togashi D, Nakajima I, et al. Clinical Outcomes of Non-Atrial Fibrillation Bradyarrhythmias Treated With a Ventricular Demand Leadless Pacemaker Compared With an Atrioventricular Synchronous Transvenous Pacemaker — A Propensity Score-Matched Analysis —. Circulation Journal. Published online 2022. doi:10.1253/circj.cj-21-088

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
			transvenous 58)		
Takato et al, 2020	Class I and IIa recommendations for Micra leadless implant with bradyarrhythmia	NA	N=51	Friedman's test, Wilcoxon signed rank	毛利 崇人, 佐藤 俊明, 冨樫 郁子, 上田 明子, 三輪 陽介, 星田 京子, 野々口 紀子, 田代 身佳, 百瀬 裕一, 勝目 有美, 副島 京子, リードレスペースメーカ植込み後の急性期および長期成績, 杏林医学会雑誌, 2020, 51 巻, 4 号, p. 257-263, 公開日 2020/12/25
Vincent et al, 2022	Micra leadless pacemaker	Transvenous pacemaker	Micra: n = 16,825 Transvenous: n = 565,845	Pearson X^2 test, t-test, 1-way analysis of variance, numbers and percentages	Vincent, L., Grant, J., Peñalver, J., Ebner, B., Maning, J., Olorunfemi, O., Goldberger, J. J. & Mitrani, R. D. Early trends in leadless pacemaker implantation: Evaluating nationwide in-hospital outcomes. Heart rhythm, 2022. Article in press
Zucchelli et al, 2021	Micra leadless pacemaker (Class I indication)	Transvenous pacemaker	N = 200 (100 in leadless, 100 in transvenous)	Mean +/- SD, median, percentages, unpaired and paired t-tests, Mann-Whitney U	Zucchelli G, Tolve S, Barletta V, et al. Comparison between leadless and transvenous single-chamber pacemaker therapy in a referral centre for lead extraction. Journal of Interventional Cardiac Electrophysiology.

Name of clinical study	Intervention	Comparator	Sample size	Statistics	Reference
				test, Fisher's exact test	2021;61(2):395-404. doi:10.1007/s10840-020-00832-9

システマティックレビューに組み込んだ臨床研究(論文)の詳細表

Arai et al, 2022	
Study site	Kameda Medical Center, Japan
Participant recruitment period	September 2017 to November 2020
Target population	All patients who underwent CT after recommended ventricular demand pacing (VVI) pacemakers due to atrial fibrillation, age, comorbidities, or low pacemaker dependency.
Key exclusion criteria	Patient did not have CT scan after leadless pacemaker implantation
Details of intervention method	Micra transcatheter pacing system guided by vascular ultrasound through right femoral vein. Using contrast injection, the position of the delivery catheter was confirmed.
Details of comparator	Non-septal placement of the pacemaker
Study design	Retrospective single-center study
Blinding method	NA
Primary endpoint	Cardiac injury related to implantation site
Key secondary endpoints	Pacing failure
Statistical analysis methods	Mean±SD Unpaired t-test Mann-Whitney *U* test Fisher exact test Pearson's product-moment correlation EZR version 1.36 R software
Sample size	N=67; N=28 Septal implantation group N=39 Non-septal implantation group
Follow-up period	Immediately, 1 week and 2 months after procedure
Main background factors of subjects	All must have had CT scan after leadless pacemaker implantation
Results of primary endpoints	Cardiac injury 4 out of 39 all in non-septal group
Results of key secondary endpoints	Pacing failure 4 out of 28 all in septal group
Limitations of the study	Retrospective single-center study Limited patient number Only patients who underwent CT for medical reasons after leadless pacemaker implantation were enrolled Procedural characteristics decided by operators Differences in timing of CT scan

Arai et al, 2022	
Conclusions	Even though there are inferior results from Septal implantation, this is still recommended because of the reduced risk of postprocedural complications.

Arps, 2021	
Study site	Duke University, USA
Participant recruitment period	Feb 2020 – Jan 2021
Target population	Patients who received an AV synchronous leadless pacemaker (Micra) without persistent AF
Key exclusion criteria	Persistent AF at implantation
Details of intervention method	Using the standard technique as detailed by El Chami et al. 2016. Devices were interrogated prior to discharge, with manual atrial mechanical (MAM) test used to optimize atrial sensing features and maximize atrial tracking in sinus rhythm.
Details of comparator	None
Study design	Retrospective single-center cohort study
Blinding method	NA
Primary endpoint	Pacing burden
Key secondary endpoints	Tracking index, total AVS, >70% AVS
Statistical analysis methods	Mean +/- SD, t-test, Wilcoxon rank sum test, McNemar test
Sample size	N = 50
Follow-up period	1-2 follow-ups
Main background factors of subjects	Mean age was 69 +/- 16.8 years, 48% female
Results of primary endpoints	The median pacing burden was 10% [0%, 92%], and 33 patients (67%) had <50% total RV pacing (median 1.2% [0%, 9%]).
Results of key secondary endpoints	The mean tracking index (AM-VP divided by total VP) was 37% ± 33% in those with <50% pacing and 47% ± 35% in patients with ≥50% pacing. In 13 patients with history of paroxysmal AF, the mean tracking index was 26% ± 27%. The median total AV synchrony was 83% [49%, 98%] overall and 59% [0%, 74%] in those requiring ≥50% pacing. In patients with complete heart block, the mean tracking index was 41% ± 31%, and median total AV synchrony was 69% [16%, 96%]. A majority of patients (35/50, 70%) had device programming changes at their first postimplant follow-up visit.

Arps, 2021	
Limitations of the study	Single center study with limited sample size. Quantification of AV synchrony was extrapolated from device interrogated data and could not be validated with continuous ambulatory telemetry. No structured mechanism to report symptom burden or quality of life. Patient selection for leadless TPS was based on clinician judgement. Mode changes and adjustment in pacing parameters were performed at each clinician's discretion using MAM testing for guidance.
Conclusions	In patients with AV-synchronous leadless pacemakers, programming changes are frequent and are associated with increased atrial tracking and increased AV synchrony in patients with complete heart block.

Barletta et al, 2020	
Study site	Azienda Ospedaliero-Universitaria Pisania, Italy
Participant recruitment period	May 2014 – July 2019
Target population	All subjects eligible for Micra leadless pacemaker, <79 years
Key exclusion criteria	<18 years, hemodynamic instability, mechanical tricuspid valve prosthesis, IVC filter, morbid obesity, femoral venous occlusion
Details of intervention method	Standard technique, femoral vein access, non-apical site where possible
Details of comparator	All subjects eligible for leadless pacemaker, >=80 years
Study design	Prospective observational cohort study
Blinding method	None
Primary endpoint	Electrical parameters during follow-up
Key secondary endpoints	Clinical follow-up
Statistical analysis methods	Mean ±SD, t-tests, Mann-Whitney U test, Fisher's exact test
Sample size	N=109 (46 elderly)
Follow-up period	18.05 months
Main background factors of subjects	77.7 years overall (85.85 for elderly cohort, 71.57 for young cohort), 76.15% male
Results of primary endpoints	No differences were observed between groups at 12 month F-U in pacing threshold, impedance or R wave amplitude.

Barletta et al, 2020	
Results of key secondary endpoints	No acute complications were observed, including venous access issues, fever or acute signs of infection. No device related events were registered.
Limitations of the study	Small, single-center study
Conclusions	The implant is an effective and safe procedure in elderly patients, with similar electrical performance and outcome compared with younger patients at mid-term follow-up.

Bhatia et al, 2021	
Study site	Emory Healthcare, Atlanta GA, USA
Participant recruitment period	April 1, 2014 – October 31, 2019
Target population	Patients implanted with Micra TPS during long-term follow-up
Key exclusion criteria	No Micra TPS implanted
Details of intervention method	Retrospectively identified patients who underwent Micra TPS implantation using medical history, indications, imaging, procedural characteristics, follow-up electrical measurements, and outcomes.
Details of comparator	All successful Micra implantations via femoral access.
Study design	Observational retrospective cohort study
Blinding method	None
Primary endpoint	Rate and reasons for Micra extraction/abandonment
Key secondary endpoints	Low revision rate, safety and efficiency
Statistical analysis methods	Mean ±SD, Median and categorical variables as %, Fisher's exact test, SAS version 9.4
Sample size	All Micra N=302, Abandoned N=12, Extraction N=11
Follow-up period	1105.5 ± 529.3 days
Main background factors of subjects	72.7 ± 15.4 median age, Male 54.6%, HTN 83.4%, Diabetes 35.8%, Coronary Heart disease 40.1%
Results of primary endpoints	Median time for extraction was 78 days Reasons: • upgrade for pacing induced cardiomyopathy (n = 3), • increased thresholds or failure to capture on previous Micra TPS (n = 3), • bridging from extraction to implantation of another device (n = 3),

Bhatia et al, 2021	
	• tricuspid valve endocarditis secondary to intravenous drug use (n = 1), • aortic valve endocarditis (n = 1). Median time of abandonment was 398.5 days Reasons: • upgrade for pacing-induced cardiomyopathy (n = 6) • an increase in thresholds/failure to capture (n = 3), • battery depletion due to elevated thresholds (n = 2) • pacemaker syndrome (n=1) Devices implanted after abandonment included CRT (n = 5, 41.7%), Micra TPS (n = 2, 16.7%), transvenous pacing system (n = 4, 33.3%),
Results of key secondary endpoints	Mean fluoroscopy time was 5.14 ± 3.6 min. Revisions required for Micra TPS 6% (primarily pacing cardiomyopathy) Determined that RV can accommodate several Micra TPS
Limitations of the study	Retrospective study Study only at one center with inherent patient selection and procedural outcomes Small number of patients Not able to rule out device problems in patient not in follow-up Adverse events may occur after follow-up period
Conclusions	In this large single-center study, 6% of patients implanted with a Micra required a system modification during long-term follow-up, most commonly due to the requirement for CRT pacing. These patients were managed successfully with extraction or abandonment.

Bicong et al, 2022	
Study site	Duke University Medical Center
Participant recruitment period	November 11, 2014 to November 18, 2019.
Target population	Patients (1) who had a previous CIED infection (2) followed by lead extraction, and (3) underwent device reimplantation with a Micra VR leadless pacemaker
Key exclusion criteria	Patients without follow-up information after hospital discharge
Details of intervention method	Modified Seldinger technique was used to access the femoral vein with direct ultrasound guidance. The delivery

Bicong et al, 2022	
	tool with the Micra Transcatheter Pacing System (Medtronic) was used.
Details of comparator	N/A
Study design	Single arm retrospective review of electronic medical records
Blinding method	N/A
Primary endpoint	Not specified. Endpoints include: Patient demographics, indication for Micra implantation, past medical history, previous CIED infection, implant characteristics, device electrical performance, adverse events in follow-up, including implant procedural complications, pacemaker syndrome, new-onset heart failure, recurrent infection, and death.
Key secondary endpoints	See above
Statistical analysis methods	Patient characteristics are summarized as numbers and percentages for categorical variables, means ± SDs for normally distributed continuous variables, and medians with 25th–75th percentile for non-normally distributed continuous variables. Adverse outcomes were assessed through post-implantation follow-up, and summarized with numbers and percentages.
Sample size	N=39
Follow-up period	Mean (± SD) = 24.8 (± 14.7) Median = 24.6 Minimum—Maximum = 0.5 - 47.5 25th percentile—75th percentile = 12.2 - 38.3
Main background factors of subjects	Patients with CIED infection with subsequent lead extraction and who underwent leadless pacemaker implantation
Results of primary endpoints	three major complications in three patients related to device implantation.
Results of key secondary endpoints	Not specified
Limitations of the study	retrospective cohort study in a single quaternary care center, small cohort
Conclusions	Leadless pacemaker implantation is associated with a low reinfection rate in patients with previous CIED infection and lead extraction. Leadless pacing may be a safer alternative to transvenous devices in patients with bradycardia indications who undergo CIED removal for infection.

Clementy et al, 2021	
Study site	9 major tertiary European LPM implanting centers
Participant recruitment period	September 2015 – August 2019
Target population	Consecutive patients implanted with a Micra LPM during the hospitalization in an intensive care unit
Key exclusion criteria	Previous implantation of a pacemaker
Details of intervention method	Implantation of Micra TPS in critically ill patients.
Details of comparator	Conventional transvenous pacing
Study design	Retrospective observational study
Blinding method	None
Primary endpoint	Safety and efficacy of LPM implantation in the high-risk population of patients
Key secondary endpoints	Follow-up
Statistical analysis methods	JMP 9.0 software, Mean ±SD, χ^2 or Fisher's exact test, Student's t-test, Mann-Whitney-Wilcoxon test, Kaplan-Meier method
Sample size	N=99 consecutive patients implanted with Micra TPS LPM
Follow-up period	Median follow-up 19 months
Main background factors of subjects	Mean age 75 years, Male 52%, AFib 53%, Charlson Comorbidity index 7±3, Diabetes 28%
Results of primary endpoints	Successful implantation 98%, Implantation failure 2%, Death 1%, Tamponade 3%, Pericardial effusion w/o drainage 1%, elevated threshold 1%
Results of key secondary endpoints	In-hospital and 30-day mortality rates were 6% and 7%, 91 patients discharged after median of 5 days
Limitations of the study	Study may not reflect the general population requiring permanent pacing in ICU Overall procedure costs with LPM not removed Decrease in ICU stay may decrease some costs LPMs implanted were one chamber devices
Conclusions	LPM appears as an acceptable alternative to conventional temporary transvenous pacing in selected critically ill patients requiring prolonged cardiac pacing, especially regarding the risk of infection.

El-Chami et al, 2022	
Study site	United States
Participant recruitment period	March 9, 2017 to December 31, 2018
Target population	Leadless VVI pacemakers in the US Medicare fee-for-service population.
Key exclusion criteria	Medicare beneficiaries
Details of intervention method	The study used administrative claims data to enroll patients, ascertain patient characteristics, identify comorbidities, and measure outcomes.
Details of comparator	Transvenous VVI, contemporaneous control group
Study design	Continuously enrolling, observational, cohort study
Blinding method	NA
Primary endpoint	Device reinterventions, chronic complications, and mortality at 2 years between leadless VVI and transvenous VVI patients
Key secondary endpoints	NA
Statistical analysis methods	*T*-tests, Chi-squared tests, Propensity score overlap weights, logistic regression model, Fine-Gray competing risk models, Cox proportional hazards model, SAS version 9.4
Sample size	N=6,219 *de novo* Leadless VVI; N=10,212 *de novo* Transvenous VVI
Follow-up period	2 years
Main background factors of subjects	Medicare claims and enrollment data was used to identify beneficiaries implanted with Micra leadless pacemaker. Identified patients implanted with a transvenous VVI pacemaker using the International Classification of Diseases, limited transvenous VVI patients to hospitals that implanted leadless VVI pacemakers during the study period.
Results of primary endpoints	Reintervention rates were significantly lower in leadless VVI patients. System revisions, removals, and upgrades to CRT were significantly lower in the leadless VVI patients. Overall chronic complication rate was significantly lower in the leadless VVI patients. 30-day all-cause mortality rate was not significantly different between leadless VVI and transvenous VVI patients
Results of key secondary endpoints	NA

El-Chami et al, 2022	
Limitations of the study	Medicare administrative claims data are a secondary database used primarily for billing purposes. Not able to obtain device interrogation data to access programmed lower rates, pacing thresholds and battery longevity. Possibility of residual confounding or selection bias cannot be completely eliminated. Analysis does not include patients implanted beyond December 2018 and outcomes beyond December 2019
Conclusions	In a real-world study of US Medicare patients, the Micra leadless VVI pacemaker was associated with a 38% lower adjusted rate of reinterventions and a 31% lower adjusted rate of chronic complications compared with transvenous VVI pacing. There was no difference in adjusted all-cause mortality at 2 years.

El-Chami et al, 2022a	
Study site	United States
Participant recruitment period	NA
Target population	Micra system patients with anticoagulation therapy (AC)
Key exclusion criteria	No Micra system implanted
Details of intervention method	Patients undergoing Micra VR implant attempt who were enrolled in the Micra Post-Approval Registry (PAR). Implanting Micra requires large-bore venous access and navigation of the delivery system in the right ventricle to implant the device.
Details of comparator	Interrupted anticoagulation or no anticoagulation
Study design	Prospective, nonrandomized, registry study
Blinding method	NA
Primary endpoint	Safety and performance
Key secondary endpoints	NA
Statistical analysis methods	Student t tests, Wilcoxon rank sum test, Fisher exact test, Firth penalized likelihood, Logistic regression models SAS Version 9.4 or R Version 4.0.2, PSweight package in RVersion 1.1.4
Sample size	N=5,585 Group 1 (no AC), N=5,795 Group 2 (interrupted AC), N=5,415 Group 3 (continuous AC)
Follow-up period	NA

El-Chami et al, 2022a	
Main background factors of subjects	Patients undergoing Micra VR implant attempt who were enrolled in the Micra Post-Approval Registry (PAR) were included in this analysis.
Results of primary endpoints	Rate of acute complications by AC strategy was 3.1%, 2.6%, and 1.5% for group 1, 2, and 3, respectively Most major complication in all groups was pacing issues Combined rate of vascular and pericardial effusion events regardless of severity was 6.5%, 4.8%, and 3.6% for groups 1, 2, and 3, respectively, Rate of pericardial effusion regardless of severity was 1.2%, 0.8%, and 0.5% in groups 1,2 3 respectively.
Results of key secondary endpoints	NA
Limitations of the study	Study not randomized Data on type of AC (DOAC vs warfarin) was not collected Patients on AC are older
Conclusions	The overall incidence of vascular and pericardial effusion complications after Micra implant is low. Implantation of Micra using a strategy of uninterrupted AC seems to be safe, with no increased risk of vascular or pericardial effusion events compared to a strategy that relies on interruption of AC.

El_Chami et al, 2021	
Study site	United States
Participant recruitment period	NA
Target population	Patients enrolled in the Micra Transcatheter Pacing (IDE) Study, Continued Access (CA) study, and Post-Approval Registry (PAR)
Key exclusion criteria	Not included in the above studies
Details of intervention method	Enrolled patients with Class I or II pacing indications with no co-morbidity restrictions.
Details of comparator	Patients not undergoing concomitant atrioventricular node ablation (AVNA)
Study design	Observational cohort study
Blinding method	NA

El_Chami et al, 2021	
Primary endpoint	Safety and performance of Micra when AVNA is performed at time of device implantation
Key secondary endpoints	NA
Statistical analysis methods	Wilcoxon Rank sum test, Fisher's exact test, logistic regression model, Cox proportional hazards, Standardized mean differences, SAS v9.4 or R v4.0.2
Sample size	N=192 Patients undergoing AVNA, N=2,616 Patients not undergoing AVNA
Follow-up period	20.4 ± 15.6 months
Main background factors of subjects	Mean age 77.4 ± 8.9 years, 72% female
Results of primary endpoints	Pacing capture threshold (PCT) at implant was 0.58 ± 0.35 V at a pulse duration of 0.24 ms among patients with AVNA compared to 0.65 ± 0.49 in patients without AVNA (p = .12).
Results of key secondary endpoints	NA
Limitations of the study	Residual confounding due to unmeasured factors cannot be ruled out in an observational study Sample size small leading to wider confidence intervals The study does not have a comparison group of patients undergoing AVNA weeks to months post LP implant. No comparator group of patients undergoing concomitant AVNA with TV-PPM implant.
Conclusions	Concomitant AVN ablation and leadless pacemaker implant is feasible. Pacing thresholds are stable over time. However, patient comorbidities and the risk of major complications are higher in patients undergoing AVNA.

Garweg et al, 2020	
Study site	University Hospital of Leuven, Belgium
Participant recruitment period	July 2015 – Nov 2019
Target population	Class I or II indication for Micra, with previous valve intervention
Key exclusion criteria	Standard exclusion criteria for Micra
Details of intervention method	Standard technique
Details of comparator	Class I or II indication for Micra, without previous valve intervention
Study design	Prospective observational cohort study
Blinding method	None

Garweg et al, 2020	
Primary endpoint	Successful implantation, electrical performance
Key secondary endpoints	Complications
Statistical analysis methods	Mean ±SD, Mann-Whitney U test, Mann-Whitney U test, Kolmogorov-Smirnov test, Chi-squared test, Wilcoxon signed-rank test, Pearson's correlation coefficient, ANOVA with Bonferroni correction
Sample size	N=170 (54 with previous valvular intervention, 116 without)
Follow-up period	12 months
Main background factors of subjects	82.0 years mean (82.5 years in valvular, 82.0 years in non-valvular), 61.8% male (43.7% in valvular, 65.6% in non-valvular)
Results of primary endpoints	Micra TPS was successfully implanted in all patients. Over time, electrical performances were similar in both groups.
Results of key secondary endpoints	Complete AV block in one subject in valvular group and had a loss of function at 6 month follow-up. Implantation of second device was successful. Flash pulmonary oedema occurred in a patient previously treated by TAVI> Loss of device function occurred in one subject in non-valvular group. No deaths related to Micra or procedure were observed.
Limitations of the study	Small number of subjects All procedures were performed by the same operator Absence of a direct comparison No reporting on right ventricular and tricuspid valve function
Conclusions	The Micra™ leadless pacemaker is a safe and efficient pacing option in patients after valve intervention. The absence of pacing lead through the tricuspid valve as well as a reduction in device infections during follow-up are significant advantages for this population.

Garweg et al, 2021	
Study site	USA, Europe, Malaysia, Hong Kong
Participant recruitment period	NA
Target population	Test MARVEL 2 in patients with AVC status who have Micra LPM implanted
Key exclusion criteria	Patients who have persistent 3^0 AV block with normal sinus rhythm and in the presence of sinus arrhythmia, sinus bradycardia (<40 bpm), or atrial/ventricular premature beats and atrial arrhythmias.
Details of intervention method	To confirm the ability of a downloaded algorithm (hereafter referred to as the MARVEL 2 algorithm) to provide AV synchronous pacing by mechanically sensing atrial contraction via the accelerometer signal
Details of comparator	No MARVEL 2 algorithm used
Study design	Prospective, non-randomized multicenter clinical trial
Blinding method	None
Primary endpoint	Demonstrate the superiority of the MARVEL 2 algorithm
Key secondary endpoints	Safety
Statistical analysis methods	Mean ± SD or Median and interquartile range, Paired t-tests, Wilcoxon signed rank test, SAS v9.4
Sample size	N=75; AV Block N=42, 1:1 AVC N=18, Other rhythms N=13
Follow-up period	The performance of the AV synchronous pacing mode and associated mode switches was characterized over the entire study duration which averaged 153 ± 29 min.
Main background factors of subjects	Mean age 77.5±11.8, Male 60%, HTN 69.3%, Diabetes 17.3%, AFib 18.7%, Coronary artery disease 30.7%
Results of primary endpoints	The mode switching algorithm reduced VP in patients with 1:1 AVC and appropriately switched to VDD during AV block. No pacing safety issues were observed during arrhythmias.
Results of key secondary endpoints	The safety of the AVC mode switch was confirmed in patients with persistent third-degree AV block as it did not induce ventricular pauses greater than 1500ms, arrhythmias, or symptoms.

Garweg et al, 2021	
Limitations of the study	Small patient number No ventricular using a leadless pacing system was evaluated at rest in a limited patient sample for a short duration Behavior of the MARVEL 2 algorithm during the different rhythms and varying AVC was assessed at rest and its performance during activities need to be studied.
Conclusions	The mode switching algorithm reduced VP in patients with 1:1 AVC and appropriately switched to VDD during AV block. No pacing safety issues were observed during arrhythmias.

Haddadin et al, 2022	
Study site	Data were extracted from the National Readmission Database (NRD), a nationally representative database comprising discharge records from 28 states, with approximately 35 million weighted discharges annually (excluding rehabilitation and long-term acute-care facilities). NRD represents approximately 58.2% of all hospitalizations in the United States.
Participant recruitment period	2016 – 2018
Target population	all adults (≥ 18 years) who underwent leadless pacemaker implantation
Key exclusion criteria	Patients discharged in December were excluded to ensure 30-day follow-up
Details of intervention method	Patients with a leadless pacemaker implantation according to ICD10 code 02HK3NZ
Details of comparator	N/A
Study design	Single arm retrospective database study
Blinding method	N/A
Primary endpoint	Clinical outcomes included in-hospital all-cause death, stroke, venous thromboembolism, any bleeding, and the need for blood transfusion.
Key secondary endpoints	Immediate procedure-related complications included vascular complications, pericardial effusion with and without the need for pericardiocentesis, and device dislodgment.
Statistical analysis methods	Continuous variables: mean ± SD or median (interquartile range).

Haddadin et al, 2022	
	Categorical variables: frequency (percentage). After adjusting for covariates, multiple hierarchical logistic regression analyses were used to measure the predictors of immediate procedural complications during the index admission. Covariates included age, gender, primary payer, median household income, hospital bed size, hospital procedure volume, elective vs urgent admission, Elixhauser comorbidity index, and baseline comorbid conditions.
Sample size	N = 7,821
Follow-up period	30 days
Main background factors of subjects	N/A
Results of primary endpoints	All-cause death, n (%) = 513 (6.6) Acute venous thromboembolism, n (%) = 443 (5.7) Acute stroke, n (%) = 285 (3.6) Any bleeding, n (%) = 1179 (15.1) Blood transfusion, n (%) = 693 (8.9)
Results of key secondary endpoints	Total procedure-related complication rates, n (%) = 588 (7.5) All vascular complications, n (%) = 181 (2.31) Vascular complications requiring repair, n (%) = 26 (0.33) Procedure-related bleeding, n (%) = 194 (2.48) Pericardial effusion without pericardiocentesis, n (%) = 146 (1.9) Pericardial effusion requiring pericardiocentesis, n (%) = 82 (1.0) Thoracotomy among patients with effusion, n (%) = 26 (11.5) Device dislodgment, n (%) = 40 (0.51) Removal or repositioning of leadless pacemaker, n (%) = 253 (3.25) Postprocedure length of stay (d) = 2 days (1–6) Cost (US$) = $34,483 (23,602–57,040)
Limitations of the study	Risk of errors and inaccuracies in coding for diseases and procedures. NRD does not capture readmissions to non-participating hospitals, out-of-hospital death, or postmortem diagnosis for the cause of death. No comparison group.

Haddadin et al, 2022	
	No information on post-discharge medications, medications adherence, and post-discharge outpatient follow-up. No information on device interrogation, capture threshold, device sensitivity, number of deployment attempts, deployment location in the right ventricle, and echocardiographic, laboratory, and imaging data.
Conclusions	Overall complications related to leadless pacemaker placement was slightly higher than in post-approval registry studies. Rate of serious complications remained relatively low and comparable to prior studies in a high-risk population with multiple comorbidities.

Hauser et al, 2021	
Study site	USA, FDA MAUDE database
Participant recruitment period	2016 – 2020
Target population	Micra LPM implanted patients who had major adverse events (MACE) as well as using CapSureFix leads
Key exclusion criteria	No MACE, did not use Micra LICP (leadless intra cardiac pacemaker) or use of CapSureFix leads
Details of intervention method	To describe Micra implantation MACE and compare them to implant procedure MACE for Medtronic CapSureFix active-fixation transvenous pacing leads.
Details of comparator	CapSureFix lead usage during first 30 days after implant
Study design	5-year Retrospective study
Blinding method	None
Primary endpoint	Describe MACE in Micra compared to CapSureFix transvenous active-fixation ventricular pacing leads
Key secondary endpoints	NA
Statistical analysis methods	Pearson χ^2 or Fisher's exact test, R version 3.6.0 in R Studio Version 1.1.463
Sample size	Micra LICP N=363, CapSureFix N=960
Follow-up period	NA
Main background factors of subjects	NA

Hauser et al, 2021	
Results of primary endpoints	MACE for Micra LICP is <1% Less MACE for implantation of CapSureFix leads There were 11.0 times more deaths and 3.4 times more cases of acute cardiac tamponade for Micra implants compared to CapSureFix ventricular lead placements MACE: Deaths Micra 26.4%, CapSureFix 2.4%; Tamponade Micra 79.1%, CapSureFix 23.4%; CPR Micra 21.8%, CapSureFix 1.1%
Results of key secondary endpoints	NA
Limitations of the study	True numbers of MACE are not known, due to nonreporting. Underreporting in CapSureFix is more likely because it is an older product Search terms may have missed MACE Possible that MAUDE reports contain erroneous narrative information
Conclusions	Because of possibility of catastrophic myocardial and vascular tears and perforation, Micra implants should be performed in hospital with emergency cardiothoracic surgery capabilities.

Hauser et al, 2022	
Study site	USA, FDA MAUDE database
Participant recruitment period	June 9, 2016 – July 31, 2021
Target population	Micra VR and Micra AV MAUDE reports submitted by Medtronic, Inc
Key exclusion criteria	Not available data in MAUDE database
Details of intervention method	Database search for consequences of Micra LPM perforations and related device and operator use problems.
Details of comparator	NA
Study design	Retrospective study
Blinding method	None
Primary endpoint	Deaths, major adverse clinical events (MACEs), and device and/or operator use problems
Key secondary endpoints	NA
Statistical analysis methods	Pearson's chi-square or Fisher's exact tests, R version 4.0.1

Hauser et al, 2022	
Sample size	N=563, Perforations that manifested clinically during Micra implantation within 30 days of implant
Follow-up period	NA
Main background factors of subjects	NA
Results of primary endpoints	27% Deaths, Cardiac tamponade 89%, Pericardial effusions 11%, Emergency surgery 26%. Perforations caused by: Device problems 25%, Operator use problems 14%, combined device and operator problems 11%
Results of key secondary endpoints	NA
Limitations of the study	Incidences of MACE in MAUDE are unknown. Because of long-term longitudinal surveillance study, Micra MAUDE reports could be higher Possible for some MACE were not reported to the manufacturer or to the FDA and are not in the MAUDE database. High percentage of MACE in USA could be due to underreporting in other countries Do not know the qualifications, experience, or caseload of the implanting physicians or hospitals.
Conclusions	Micra perforations reported in MAUDE are often associated with death and major complications requiring emergency intervention. Device and use problems account for at least half of perforations. Studies are needed to identify who is at risk for a perforation and how MACE can be avoided or mitigated.

Higuchi et al, 2020	
Study site	Mito Saiseikai General Hospital, Japan
Participant recruitment period	October 2017 – April 2020
Target population	Micra TPS implanted subjects, stable pacing threshold
Key exclusion criteria	Missing data from attrition
Details of intervention method	Pull and hold method
Details of comparator	Micra TPS implanted subjects, increased pacing threshold
Study design	Retrospective study
Blinding method	None
Primary endpoint	Procedural data, transition of pacing threshold
Key secondary endpoints	Complications
Statistical analysis methods	Shapiro-Wilk test, Mann-Whitney U test, Student's t-test, Welch t-test, Fisher's exact probability test, ROC curve
Sample size	N=60 (9 in stable threshold group, 51 in increased pacing threshold)
Follow-up period	7 months
Main background factors of subjects	89.1 years in stable pacing, 85.9 years in increased pacing, 56% female in stable pacing, 53% in increased pacing
Results of primary endpoints	No difference sin number of deployments, tines or indwelling site. Longer implantation time, lower impedance and higher pacing threshold in increased pacing group. 44% in increased pacing did not have improved pacing thresholds after 3 months. Improved pacing thresholds for most in stable group.
Results of key secondary endpoints	No cases of CV mortality or rehospitalization. Two cases of pacing failure in increased pacing group without reimplantation. One lymph leakage at puncture site in increased pacing group and one pericardial effusion not requiring intervention in stable pacing.
Limitations of the study	Limit in accurately determining number of tines stably anchored to the myocardium by pull and hold Follow-up was short – 7 months
Conclusions	An IPT was noted shortly after Micra-TPS implantation owing to micro-dislodgement because of insufficient anchoring of

Higuchi et al, 2020	
	the device to the myocardium. Impedance >660 Ω and threshold <1.0 V/0.24 ms may predict an increase in pacing threshold.

Houmsse et al, 2020	
Study site	Nine centers in the USA/Canada (Wexner Medical Center, Mayo Clinic, NY/Long Island Jewish Medical Center, Fairfield Medical Center, Trihealth, Penn State Health Milton S Hershey Center, Emory University, Texas Cardiac Arrhythmia, McGill University)
Participant recruitment period	February 2014 to May 2020
Target population	Micra TPS implanted subjects with an IVC filter
Key exclusion criteria	None
Details of intervention method	NA
Details of comparator	None
Study design	Multicenter, retrospective study
Blinding method	None
Primary endpoint	Procedural outcome
Key secondary endpoints	Long-term complications
Statistical analysis methods	Mean (SD), Median (IQR)
Sample size	N=23
Follow-up period	7 months
Main background factors of subjects	73.8 years mean age, 52.2% male gender
Results of primary endpoints	Successful in 21 out of 22 subjects (one subject had IVC filter removed before the procedure). No device related complications or MACE. 3 patients had in-hospital mortality – septic shock, complications of prosthetic valve endocarditis and refractory heart failure
Results of key secondary endpoints	No delayed complications observed
Limitations of the study	Retrospective study with experienced operators Small sample size Unclear whether the IVC filters were rendered ineffective

Houmsse et al, 2020	
Conclusions	Safety and feasibility of Micra implantation via an IVC filter

Jelisejevas et al, 2021	
Study site	Switzerland
Participant recruitment period	June 2015 – May 2020
Target population	Clinical indication for a single-chamber pacemaker and provided written informed consent to the procedure
Key exclusion criteria	Not needing implantation of Micra TPS
Details of intervention method	Implantation access from left femoral artery
Details of comparator	Implantation access from right femoral artery
Study design	Retrospective, non-randomized single center study
Blinding method	NA
Primary endpoint	Safety of left access
Key secondary endpoints	NA
Statistical analysis methods	Jamovi project version 1.2, Shapiro-Wilk test, Mean ± SD, Student t-test, Mann-Whitney U-test Pearson χ^2 or Fisher's exact test
Sample size	N=143 consecutive patients undergoing Micra TPS implantation; N=18 (13%) Left femoral access; N=125 (87%) Right femoral access
Follow-up period	30 days interventional period
Main background factors of subjects	Mean age 79.8±7.5 yrs, Male 65%, Coronary artery disease 32%, Diabetes 20%, Chronic renal failure 64%
Results of primary endpoints	Implantation rate 99.2% for Right femoral, 100% left femoral access 14 deaths (11%) in median 257 days, Fluoroscopy and procedure times were not significantly different Reason for left femoral access is previous transfemoral TAVI causing poorer right access.
Results of key secondary endpoints	NA

Limitations of the study	Small study RCT should be conducted with comparison of two femoral venous approaches
Conclusions	A left femoral venous access for Micra TPS implantation is safe and effective with an excellent implantation success rate similar to a conventional right femoral venous access without longer implantation and fluoroscopy times.

Kowlgi et al, 2022	
Study site	three Mayo Clinic (Rochester, MN; Jacksonville, FL; and Phoenix, AZ) sites
Participant recruitment period	March 1 to September 1, 2020
Target population	All patients undergoing MicraTM-AV implants
Key exclusion criteria	Patients with less than 3 months follow-up (n = 6) Patients with persistent atrial arrhythmia (n = 7)
Details of intervention method	indication for MicraTM AV implant was complete heart block in 23 (53%) patients, symptomatic bradycardia in 13 (30%) patients, and AF with rapid ventricular rates planned for AV node ablation in 7 (16%) patients
Details of comparator	Endpoints were compared between patients with and without atrial synchronous ventricular pacing (AsVP) ≥ 70%.
Study design	Retrospective database analysis
Blinding method	N/A
Primary endpoint	demographics, clinical presentation, medications, relevant comorbidities, and implant-related complications
Key secondary endpoints	N/A
Statistical analysis methods	median (interquartile range [IQR]), mean ± standard deviation, percentages, Fisher exact test, paired samples t-test, Wilcoxon rank-sum test
Sample size	N = 43
Follow-up period	3 months, median follow-up duration of the whole cohort was 138 (103−190.5) days.
Main background factors of subjects	Twenty-eight patients (65%) achieved AsVP ≥ 70%, and 15 (35%) had inadequate AsVP
Results of primary endpoints	65% of patients achieved AsVP ≥ 70%

	Patients with adequate AsVP had smaller body mass indices, a lower proportion of congestive heart failure, and prior cardiac surgery.
Results of key secondary endpoints	N/A
Limitations of the study	Retrospective review that has the inherent pitfalls with potential confounding factors in the analysis of AV synchrony. Modest sample size, follow-up durations are non-uniform.
Conclusions	In comparison to the original study, a significantly lower proportion of AV synchrony was noted, mostly attributable to physiological reasons combined with a learning curve that exists for any new technology.

Kumar, 2021	
Study site	Max Superspeciality Hospital, India
Participant recruitment period	Unspecified
Target population	Subjects with chronic/permanent AF associated with complete heart block, or SSS
Key exclusion criteria	Pacemaker syndrome, retrograde VA conduction, drop in arterial blood pressure with onset of ventricular pacing, pre-existing endocardial defibrillation, IVC filter, previous implanted leadless cardiac pacemaker
Details of intervention method	Steerable catheter through femoral vein, advanced into right ventricle and affixed to myocardium
Details of comparator	Transvenous pacemaker
Study design	Prospective, observational, single center study
Blinding method	NA
Primary endpoint	Adverse events or complications
Key secondary endpoints	Mean time from hospitalization to discharge
Statistical analysis methods	Mean +/- SD
Sample size	N = 443 (TPS 198, VVI-PM 245)
Follow-up period	3 years
Main background factors of subjects	Mean age of 71.71 +/- 8.44 years, male gender 71%
Results of primary endpoints	There was no adverse event or complications reported for any of the subjects.

Results of key secondary endpoints	Mean time from hospitalization to discharge was 1.5 days
Limitations of the study	Small sample size No control group
Conclusions	Leadless cardiac pacemaker was capable of providing effective and safe pacemaker function in a varied group of patients who had indications for long-term pacing therapy

Martinez-Sande, 2021	
Study site	University Clinical Hospital of Santiago de Compostela, Spain
Participant recruitment period	Jun 2015 – Dec 2019
Target population	Subjects with an indication for a single-chamber pacemaker implant
Key exclusion criteria	None
Details of intervention method	Femoral access for TPS, Cephalic dissection or subclavian puncture for VVI-PM (operator preference)
Details of comparator	Transvenous pacemakers (VVI-PM)
Study design	Prospective, observational, single center study
Blinding method	NA
Primary endpoint	Complication rate
Key secondary endpoints	Mortality rate
Statistical analysis methods	Mean +/- SD, Propensity score matching, Cox regression analysis, multiple hypothesis testing with Benjamini-Hochberg procedure, Bayesian cohort analysis (posterior calculated using Metropolis-Hastings algorithm)
Sample size	N = 443 (TPS 198, VVI-PM 245)
Follow-up period	22.3 +/- 15.9 months
Main background factors of subjects	Mean age was 81.5 years (TPS 79.2 +/- 6.6 years, VVI-PM 83.5 +/- 8.9 years), gender (TPS 62.1% male, VVI-PM 27.3% male)
Results of primary endpoints	The TPS group reported significantly lower total complications than the VVI-PM group (7, 3.5% vs. 21, 8.6% respectively, p = 0.0303). However, there were no differences in major complications between

	the groups (6, 3% vs. 14, 5.6% respectively, p = 0.1761). In a multivariable analysis of data matched by age, LVEF, chronic heart failure, anticoagulation status, and chronic kidney disease, the TPS group presented fewer complications than the VVI-PM group (Hazard ratio (HR) = 0.39, confidence interval (CI) 95%: 0.15–0.98; p = 0.013). The most frequent complications in patients with TPS were vascular (4, 2%), and associated with heart effusion (2, 1%). In patients with VVI-PM, the most frequent complications were pocket generator-related (12, 4.9%), pneumothorax (3, 1.2%), and electrode dislodgement (3, 1.2%)
Results of key secondary endpoints	During the follow-up, 62 patients died (14%), including 18 in the TPS group (9.1%) and 44 in the VVI-PM group (17.9%) with significant difference between the groups
Limitations of the study	Not a randomized trial Choice of each pacemaker was based on clinical conditions Number of patients included and follow-up likely underestimates infections in VVI-PM group Pocket-related complications in mid and long-term were not well represented
Conclusions	TPS patients had a lower overall complication rate than VVI-PM patients including matched-pair samples using a Bayesian analysis. These results confirm the good safety profile of TPS in daily clinical practice.

Nicosia et al, 2022	
Study site	15 Italian centers participating to the One Hospital ClinicalService project
Participant recruitment period	May 2016 to July 2019
Target population	Patients indicated for permanent cardiac pacing who underwent a TPS implant (TPS Micra Medtronic, Inc.)
Key exclusion criteria	N/A
Details of intervention method	Each center utilized their own standard-of-care practices and approaches during the implant.
Details of comparator	N/A
Study design	Single arm

Blinding method	N/A
Primary endpoint	All reported procedural, peri-procedural, and post-procedural complications were collected. Procedural Times of the total population of patients and statistical comparisons between the groups of patients according to age
Key secondary endpoints	N/A
Statistical analysis methods	means and SD; minimum, maximum, and median with IQR, counts and percentages, Kruskal–Wallis test, chi-square test, Fisher`s exact test
Sample size	N = 577
Follow-up period	median follow-up was 12.0 months (IQR: 5.9–23.8).
Main background factors of subjects	
Results of primary endpoints	Procedure-related complication occurrence was low (0.5%) Procedural duration and fluoroscopy time exposure were comparable among the four cohorts with no statistical difference between age groups.
Results of key secondary endpoints	N/A
Limitations of the study	Not reported
Conclusions	This multicenter real-world prospective data showed high safety levels for TPS implant at different ages. Procedural performance indicators were similar at the different ages, and complication rates were low and not related to the patient's age. Even procedural efficacy did not seem to be influenced by age.

Ngo et al, 2021	
Study site	NA, systematic review
Participant recruitment period	Studies published before June 6, 2020
Target population	Patients from observational studies of Nanostim and Micra leadless pacemaker implantation
Key exclusion criteria	No Micra or Nanostim LPM implanted
Details of intervention method	Systematic review of reported outcomes from Micra implantation.

Details of comparator	Systematic review of reported outcomes from Nanostim implantation.
Study design	Systematic review and meta-analysis (22 Prospective, 10 Retrospective, 4 not reported)
Blinding method	None
Primary endpoint	Safety, efficacy with acceptable pacing threshold
Key secondary endpoints	Implantation success, specific complications up to 90 days
Statistical analysis methods	Freedman-Tukey double arcsine transformation, Stata version 16.0, Stata user-written command Metaprop, I2 statistic
Sample size	36 Studies, N=4335
Follow-up period	90 days, 1 year
Main background factors of subjects	83.3 yrs old, Male 61%, HTN 69.7%, Diabetes 23.3%, Coronary artery disease 28.5%, AFib 66.7%
Results of primary endpoints	Micra pool incidence of complications at 90 days 0.46%, 1 year 1.77%. Nanostim 90 days 6.06% - 23.54% and 1 year 5.33% - 6.67%. Micra lower odds of complications as compared to conventional transvenous pacemaker implant (3.0% versus 7.43%) OR 0.49
Results of key secondary endpoints	At 1 year, 98.96% implanted with Micra had good pacing capture thresholds, Nanostim 90% - 100% good pacing capture thresholds
Limitations of the study	Data is entirely observational Small sample size and short follow-up time for most studies Meta analysis for Micra and Nanostim were performed separately Low number of studies using Nanostim Inconsistency in which complications were reported Efficacy and primary endpoints were different with each study
Conclusions	Most studies report outcomes for the Micra, which is associated with a low risk of complications and good electrical performance up to 1-year after implantation.

Oliviera, 2021	
Study site	NA
Study period	2015 to 2019
Inclusion Criteria	Studies which used leadless pacemakers in humans with heart disease

Exclusion criteria	Non-English/French/Spanish articles, animal studies, case reports, guidelines
Details of intervention method	NA
Details of comparator	NA
Study design	Systematic Review
Blinding method	None
Primary endpoint	Procedural success and failure
Key secondary endpoints	Complications during follow-up, Pacemaker indications
Statistical analysis methods	Mean +/- SD
Sample size	58 papers covering 4,739 subjects
Follow-up period	NA
Main background factors of subjects	NA
Results of primary endpoints	4,670 out of 4,739 implantations were successful
Results of key secondary endpoints	5.23% complication rate, most common were pacing issues (68), femoral access issues (64), procedure related cardiac injuries (47) 16 studies with complication rate below 10%, 21 studies with complication rate below 15%, 5 studies with complication rate between 15-20% 360 deaths were described during follow-up (117 from a cardiac cause, 11 from procedure/device) Main indication was chronic AF with slow ventricular rate, other indications included low level of physical activity or short expended lifespan, sinus-node dysfunction, second or third-degree AV block or bifascicular/trifascicular block
Limitations of the study	All studies were observational with a short follow-up period No RCTs which compared leadless pacemakers to conventional pacemakers Large heterogeneity between studies
Conclusions	Leadless pacemakers have a relatively low complication rate. They may be a good option in subjects with an indication for single-chamber pacing and in subjects with conditions precluding transvenous pacemaker implants.

Palmisano, 2021	
Study site	Giovanni Panico Hospital, Italy
Participant recruitment period	Feb 2016 – May 2020
Target population	Subjects undergoing single-chamber PM implantation for any cause
Key exclusion criteria	Leadless PM implantation after extraction of conventional PM or transvenous PM implantation after failed leadless PM attempt
Details of intervention method	Femoral vein catheter for implantation in septo-apical region of RV or other position if not accessible for leadless PM. Subclavian vein access positioned in right ventricular apical septum or right ventricular apex for transvenous PM.
Details of comparator	Transvenous pacemaker
Study design	Prospective, cohort-matched, single center study
Blinding method	None
Primary endpoint	Intra and post-procedural findings
Key secondary endpoints	Quality of life, patient acceptance, complications
Statistical analysis methods	Mean +/- SD, Student's t-test, Mann-Whitney U test, analysis of variance, Fisher's exact test, binary logistic regression for propensity scores
Sample size	N = 243 (leadless 91, transvenous 152)
Follow-up period	Baseline, 1 week, 3 months, 6 months
Main background factors of subjects	Mean age was 75.3 years for leadless and 80.6 years for transvenous. Gender was 72% male for leadless and 86% for transvenous.
Results of primary endpoints	Leadless implantation of Micra was significantly longer than transvenous, required more fluoroscopy and involved more team members. No significant differences in electrical parameters on implantation. Lower pain intensity for leadless compared to transvenous (persisted at 1 hour, no difference at 6 hours). Leadless had a lower rate of patients requiring analgesics in postoperative period. Mobilization was earlier for transvenous. Leadless had a shorter duration of hospitalization.
Results of key secondary endpoints	Leadless had a significantly higher quality of life as measured by SF-36 compared to transvenous at 1 week, 3 weeks and 6 months. FPAS was higher in leadless than transvenous (patient acceptance). Two transvenous developed pocket hematoma within 24 hours, with one requiring surgical

	drainage. No device related complications were observed for leadless. One leadless and one transvenous died in the follow-up.
Limitations of the study	Observational and non-random Total population was relatively small Duration was too short to assess long-term quality of life
Conclusions	L-PM implantation procedure is longer and requires more team members and longer postoperative immobilization than T-PM implantation. Patients who undergo L-PM implantation have less intra- and post-procedural pain and can be discharged earlier than those who undergo T-PM implantation. On medium-term follow-up, L-PM is associated with better QoL, on both physical and mental health scales, and greater patient acceptance than T-PM.

Piccini, 2021	
Study site	Medicare population, USA
Participant recruitment period	March 2017 – Dec 2018
Target population	Medicare beneficiaries implanted with Medtronic Micra
Key exclusion criteria	<12 months of continuous enrollment in Medicare prior to pacemaker implantation and with evidence of a prior cardiovascular implantable electronic device
Details of intervention method	Unspecified
Details of comparator	Transvenous pacemaker
Study design	Continuously enrolling observational cohort study
Blinding method	None
Primary endpoint	Acute complications
Key secondary endpoints	6-month complications, survival
Statistical analysis methods	Mean +/- SD, t-tests, Chi-squared test, univariate logistic regression, Fine-Gray competing risk modules, Cox proportional hazards models
Sample size	N=5746 (leadless), N=9662 (transvenous)
Follow-up period	Mean follow-up of 606.5 +/- 265.9 days
Main background factors of subjects	Mean age was 81.0 (8.7) years and 43.5% were female

Results of primary endpoints	Unadjusted overall acute complication rate was higher in patients with leadless (8.4% vs. 7.3%), no significant difference in adjusted overall complications (7.7% vs 7.4%), cardiac effusion/perforation within 30 days was significantly higher in leadless (0.8% vs. 0.4%), device related complications such as dislodgement, infection and pocket complications were lower with leadless (1.4% vs. 2.5%)
Results of key secondary endpoints	Leadless had a reduction in 6-month complications compared to transvenous (0.77 hazard ratio). Leadless had a lower rate of device revision compared to transvenous (0.63 hazard ratio). No difference in 6-month all-cause mortality (1.00 hazard ratio).
Limitations of the study	Non-randomized observational studies Complications may be missed or inadequately documented in administrative claims Residual confounding cannot be completed eliminated
Conclusions	Patients in whom a leadless pacemaker was implanted were observed to have higher rates of cardiac effusion or perforation within 30 days but lower device-related complication rates and requirements for device revision at 6 months

Piccini, 2022	
Study site	Micra IDE, Micra CA and Micra PAR studies (pooled cohort)
Participant recruitment period	December 2013 – March 2018
Target population	Subjects enrolled in previous Micra studies
Key exclusion criteria	Subjects missing >10 candidate variables, existing pacemaker or ICD
Details of intervention method	Unspecified
Details of comparator	None
Study design	Pooled analysis of prospective, non-randomized studies
Blinding method	None
Primary endpoint	Risk of pericardial effusion
Key secondary endpoints	Prediction of pericardial effusion risk
Statistical analysis methods	Mean +/- SD, binomial confidence intervals, multivariable risk production model, Lasso regression

Sample size	N=32 (effusion), N=2785 (no effusion)
Follow-up period	Study commencement to 2021
Main background factors of subjects	NA
Results of primary endpoints	32 subjects with symptomatic pericardial effusion (1.1%, 95% CI 0.8-1.6%)
Results of key secondary endpoints	C-index median was 0.73 for lasso logistic model, 0.73 for the scoring system
Limitations of the study	Modelling may be subject to confounding Unable to evaluate the location of attempted deployments and risk of perforation Echocardiograms were at the discretion of the physician and not protocol-driven or systematic Inability to divide into training or validation set
Conclusions	The overall rate of pericardial effusion following Micra implantation attempt is 1.1% and has decreased over time. The risk of pericardial effusion after Micra implant attempt can be predicted using pre-procedural clinical characteristics with reasonable discrimination.

Russo, 2022	
Study site	Campania Leadless Registry, Italy (Monaldi Hospital of Naples, University of Campania of Naples, Umberto I Hospital of Nocera Inferiore)
Participant recruitment period	July 2017 – Dec 2020
Target population	Inclusion in leadless pacemaker registry with Micra, subjects with AF
Key exclusion criteria	Subjects who did not consent to inclusion in the registry
Details of intervention method	Standard technique
Details of comparator	Inclusion in leadless pacemaker registry with Micra, subjects without AF
Study design	Retrospective review of multicenter registry
Blinding method	None
Primary endpoint	LLPM intraoperative data, perioperative complications
Key secondary endpoints	Syncope, cardiac hospitalization, pacemaker syndrome, all-cause death
Statistical analysis methods	Mean +/- SD, median +/- IQR, Kolmogorov-Smirnov test, Shapiro-Wilk test, chi-squared tests

	with Yates correction where appropriate, Student's t-test, Mann-Whitney U test, Wilcoxon signed-rank test, Kaplan-Meier analysis
Sample size	N=140
Follow-up period	Mean follow-up of 606.5 +/- 265.9 days
Main background factors of subjects	Mean age was 76.7 +/-11.24 years, men 64.3%
Results of primary endpoints	5% of subjects experienced perioperative complications (no difference between groups), no procedure-related death
Results of key secondary endpoints	Non-AF group showed higher percentage of ventricular pacing (52% vs 40%), LLPM electrical parameters remained stable and did not differ between two groups, no significant difference in outcome of interest between groups, no difference on Kaplan-Meier on combined endpoints, 10 subjects died, 7 subjects reported cardiac hospitalization and 5 reported syncope. None reported pacemaker syndrome.
Limitations of the study	Retrospective and non-randomised study design Small cohort size, differences in baseline characteristics, limited follow-up
Conclusions	LLPM may be considered a safe and reasonable treatment in patients without AF in need of pacing

Sanchez, 2021	
Study site	Ohio State University, USA
Participant recruitment period	Feb 2014 – June 2019
Target population	Normal LVEF (>=50% at baseline)
Key exclusion criteria	History of CRT and recovered LVEF who underwent extraction followed by single ventricle pacing, individuals who were not 100% pacemaker dependent
Details of intervention method	Standard technique in addition to AV node ablation (concurrently or during follow-up). TV group underwent ipsilateral venogram before axillary or subclavian access. RV lead implantation based on discretion of operator. Femoral venous approach used for leadless.
Details of comparator	Transvenous pacemaker

Study design	Retrospective review of prospectively maintained database
Blinding method	None
Primary endpoint	Incidence of pacing-induced cardiomyopathy (10% decrease in LVEF)
Key secondary endpoints	Acute and long-term procedure-related complications
Statistical analysis methods	Mean +/- SD, Student's t-test, Chi-squared test, multivariate analysis
Sample size	N=198 (131 for transvenous, 67 for leadless)
Follow-up period	Mean of 592 +/549 days for transvenous and 817 +/- 600 days for leadless
Main background factors of subjects	Mean age was 74 in transvenous and 73 for leadless. Female % was 95% in transvenous and 31% in leadless. LVEF was 59% for transvenous and 57 for leadless.
Results of primary endpoints	Overall, 18 (13.7%) patients in TVP and 2 (3%) in LP developed PICM after a median duration of 254 (interquartile range [IQR]: 470) days after implantation. The two patients in the LP group developed PICM after 180 and 350 days. The median duration before PICM in TVP group was 194 (IQR: 429). The incidence of PICM was significantly higher with TVP compared with LP ($p = .02$).
Results of key secondary endpoints	Incidence of acute periprocedural and follow-up complications (>30 days) was similar in both groups.
Limitations of the study	Retrospective single-center study Non-randomized study and device selection based on operator discretion
Conclusions	Pacemaker-induced cardiomyopathy is significantly lower in leadless compared to transvenous pacemakers.

Sasaki, 2022	
Study site	St Marianna University Hospital, Japan
Participant recruitment period	Sept 2017 – Sept 2020
Target population	Bradyarrhythmias based on Class I and II guideline recommendations
Key exclusion criteria	Reimplantation from lead failures, device upgrade or device infection, complete removal of prior device system

Details of intervention method	Manufacturer's protocol with target of RV mid-septal region (apical or high RV septum as backup)
Details of comparator	Transvenous pacemaker
Study design	Prospective, propensity score-matched, single center study
Blinding method	None
Primary endpoint	All-cause mortality
Key secondary endpoints	Cardiovascular mortality, late device-related adverse events, HF related hospitalization
Statistical analysis methods	Mean +/- SD, median, IQR, Student's t-test, Wilcoxon rank-sum test, Fisher's exact test, Kaplan-Meier method and log-rank test, logistic regression model
Sample size	N=193 (leadless 110, transvenous 83), N=116 with propensity score matching (leadless 58, transvenous 58)
Follow-up period	Median of 801 days (IQR 447-1,124 days) for leadless group and 649 days (IQR 375-808) in transvenous group
Main background factors of subjects	Mean age was 81 years in leadless and 82 years in transvenous. Female % was 62% in leadless and 35% in transvenous. LVEF was 63% in both leadless and transvenous cohorts.
Results of primary endpoints	Higher overall mortality in the leadless group over 4 year follow-up (28% vs. 4%, p = 0.059, non-significant)
Results of key secondary endpoints	Higher HF readmission rate in leadless group compared to transvenous (29% vs. 2%). No significant difference between leadless and transvenous for device-related AEs (0% vs 4%).
Limitations of the study	Retrospective observational investigation with loss to follow-up Based on a single-center experience Small sample size, reducing statistical power Risk of overlooking clinically important predictors from propensity score matching Operators were experienced for leadless, which may underestimate complications Data on medications unavailable
Conclusions	The implantation of a VVI-LPM for non-AF bradyarrhythmias increased the incidence of HF-related rehospitalization at the mid-term follow up compared to the use of a DDD-TPM

Takato, 2020	
Study site	Kyorin University, Japan
Participant recruitment period	March 2014 – Dec 2019
Target population	Class I and IIa recommendations for Micra leadless implant with bradyarrhythmia
Key exclusion criteria	Not specified
Details of intervention method	Femoral venous access
Details of comparator	None
Study design	Prospective cohort study
Blinding method	None
Primary endpoint	Electrical indicators
Key secondary endpoints	Complications
Statistical analysis methods	Friedman's test, Wilcoxon signed rank
Sample size	N=51
Follow-up period	22 months
Main background factors of subjects	Mean age was 79 years, 64% male
Results of primary endpoints	Resistance value decreased after 1 month compared to implantation, no significant change to right ventricular capture threshold
Results of key secondary endpoints	No reimplantation cases from pacing failure (increase in right ventricular capture threshold, inadequate sensing from decrease in right ventricular wave height or premature battery voltage consumption) No major acute complications, except for one case of intracardiac leakage of intraoperative contrast medium, 1 cardiovascular death up to 60 months, no major chronic complications, one case with pacemaker syndrome, one case with CRT for suspected herat failure from pacing induced cardiomyopathy
Limitations of the study	Retrospective single-center observational studies Small sample size with limited follow-up
Conclusions	No major acute complications, measured values were stable even up to 5 years

Vincent et al, 2022	
Study site	National Inpatient Sample (NIS) database
Participant recruitment period	2017 – 2019
Target population	Patients who underwent Micra® (Medtronic) LICP implantation (n = 16,825) or transvenous permanent pacemaker (n = 564,100) implantation, specified by ICD-10 procedure codes.
Key exclusion criteria	Age < 18, missing mortality data
Details of intervention method	Single-chamber leadless intracardiac pacemaker
Details of comparator	Transvenous pacemaker
Study design	Subsequent 1:1 case-control matching of patients undergoing LICP (n = 3,084) or transvenous pacemaker (n = 3,084) implantation by matching for patient age, gender, race, and significant comorbidities was performed.
Blinding method	
Primary endpoint	in-hospital all-cause mortality, pooled complication rate, and total duration of hospitalization
Key secondary endpoints	in-hospital complications (vascular, infectious, pericardial, requirement of pericardiocentesis, and device retrieval or replacement)
Statistical analysis methods	Pearson X2 test, t-test, 1-way analysis of variance, numbers and percentages
Sample size	Micra leadless pacemaker: n = 16,825 Transvenous pacemaker: n = 565,845 Single-chamber pacemaker: n = 1,255
Follow-up period	Index hospitalization only
Main background factors of subjects	Average patient age was 75.4 ± 12.8 years. majority of patients (55.2%) were male and self-identified as White/non-Hispanic (75.6%), compared to Black/African American (10.9%) or Hispanic (7.5%).
Results of primary endpoints	In-hospital all-cause mortality was 5.2% among leadless pacemaker implantations, with mortality rates decreasing between 2017 and 2019 (8.2% vs 4.2%). Average length of stay and total hospital charges increased. Pooled complication rates decreased
Results of key secondary endpoints	Postoperative infection and device retrieval rates decreased.

Limitations of the study	Patient data obtained is dependent on coded diagnoses that were not adjudicated and may be subject to error or omission. Outcomes are only reported during index hospitalization and do not capture readmission or out-of-hospital major adverse events or death over time.
Conclusions	LICP implantations were performed in patients of advancing age, increasing comorbidities, and heightened acuity of illness in comparison to the initial pivotal trials. Postprocedural complication rates and in-hospital all-cause mortality were higher in real world practice than previously reported. Between 2017 and 2019, pooled procedural complication rates decreased significantly, likely because of improving operator skill. Compared to transvenous pacemaker, leadless pacemaker implantation was associated with lower procedural complication rates but higher in-hospital mortality.

Zucchelli, 2021	
Study site	University Hospital of Pisa, Italy
Participant recruitment period	May 2014 – April 2019
Target population	Subjects who met Class I indication for pacing and were suitable for single-chamber ventricular stimulation
Key exclusion criteria	<18 years, hemodynamic instability, mechanical tricuspid valve prosthesis or inferior vena cava filter, morbid obesity that could impair remote Micra control, femoral venous occlusion, allergy to Micra TPS components, < 12 months life expectancy and risk of interference with any other electronic device
Details of intervention method	Femoral vein catheter for implant in right ventricle (non-apical position where feasible)
Details of comparator	Transvenous pacemaker
Study design	Prospective, comparison matched, single center study
Blinding method	None
Primary endpoint	Intra and post-procedural findings
Key secondary endpoints	Quality of life, patient acceptance, complications

Statistical analysis methods	Mean +/- SD, median, percentages, unpaired and paired t-tests, Mann-Whitney U test, Fisher's exact test
Sample size	N = 200 (100 in leadless, 100 in transvenous)
Follow-up period	12 months
Main background factors of subjects	77.5 years for leadless and 78.8 years for transvenous, 77% male for leadless and 67% for transvenous, LVEF 56% for leadless vs. 54.8% for transvenous
Results of primary endpoints	The implant procedure was successful in all patients. In group 1, the procedure duration was lower than in group 2 (43.86 ± 22.38 vs 58.38 ± 17.85 min, $p < 0.001$), while the fluoroscopy time was longer (12.25 ± 6.84 vs 5.32 ± 4.42 min, $p < 0.001$). There was no difference about the rate of septal implant at the right ventricle (76% vs 86%, $p = 0.10$). Patients were followed-up for a median of 12 months. No acute and chronic procedure-related complication was observed in group 1, while we reported acute complications in seven patients (7%, $p = 0.02$).
Results of key secondary endpoints	All electrical parameters remained stable during the entire follow-up in both groups. Mortality during follow-up was higher in TV-VVI PM vs Micra group (23 vs 7 deaths, $p = 0.003$). Ten patients experienced a complication in group 2 ($p = 0.004$), leading to system revision in six cases ($p = 0.038$).
Limitations of the study	Non-randomized observational study with small population Propensity score matched analysis was not used due to limited number of transvenous PMs, introducing a potential bias in the selection of control cases Single center experience Device longevity was only an estimate based on pacing threshold and impedance, without a measure of battery status
Conclusions	Micra implant is a safer procedure than TV-VVI PM implant even in real-life setting including patients at high risk of complications. It reduces acute complications and system revisions and minimize the risk of infective issue in patients needing ventricular pacing. Electrical measurements in such leadless pacemaker are stable and very low at long-

	term follow-up, with a longer estimated battery life than TV-VVI PM.

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植込み後 30 日間に合併症が発生することによる追加的な死亡率

An excess mortality of 9.5% observed during the first year in patients with early complication vs. no early complication was estimated from the POINTED registry . This percentage was multiplied by the absolute difference in complication events observed between the TC-PM and TV-PM cohorts at one month to obtain a nominal estimate for survival benefit associated with any reduced TC-PM early complication rate.

The estimation of 9.5% mortality during the first year is obtained from Palmisano et al. Figure 1.B: Excess mortality of approximately 9.5% is observed at 12 months (as evidenced by the difference in survival curves between patients with early complications as compared to patients without complications). Beyond 12 months, the survival curves do not show substantial difference in shape. We hence assumed no additional excess mortality beyond the 9.5% in the first year. The 9.5% survival difference was incorporated by multiplying it by the absolute difference in early complication rates between the TC-PM and TV-PM strategies. For example, if the early complication rate for TC-PM patients was 5%, then TC-PM patients were assumed to have a one-year mortality that was an absolute 9.5% x 5% = 0.475% lower than the TV-PM strategy’s mortality.

SF-36 で計測された HRQoL 値の変換

To obtain utility estimates for TC-PM and TV-PM, the identified SF-36 component data at baseline, one month, and six months were converted to a mean EQ-5D estimate using an established mapping algorithm (11,18). See Table S.4.1 for the SF-36 component score reported in the underlying study. See Table S.4.2 for the resulting mapped EQ-5D values.

Leadless Pacemaker (TC-PM)

SF-36 Component data per Cabanas-Grandio et al.	BL	1M	6M
Physical Functioning (PF)	44	61	63
Role Physical (RP)	23	59	64
Body Pain (BP)	51	66	69
Vitality (VT)	40	55	52
Role Emotional (RE)	61	74	75
Mental Health (MH)	61	73	75
Social Functioning (SF)	75	88	85
General Health (GH)	43	53	48

Transvenous Pacemaker (TV-PM)

SF-36 Component data per Cabanas-Grandio et al.	BL	1M	6M
Physical Functioning (PF)	41	45	42
Role Physical (RP)	22	18	36
Body Pain (BP)	52	64	60
Vitality (VT)	39	47	44
Role Emotional (RE)	62	61	68
Mental Health (MH)	61	70	65
Social Functioning (SF)	73	79	78
General Health (GH)	44	48	48

Table S.4.1: SF-36 component scores reported for Leadless pacemakers and Transvenous pacemakers at Baseline (BL), 1 month (1M), and 6 months (6M) post implant, as reported by Cabanas-Grandio et al.

Leadless Pacemaker (TC-PM)	Computed EQ5-D Score (based on Ara	***Absolute change to***	***Relative change to***

	et al., 2008 algorithm)	*baseline*	*baseline*
BL	0.586		
1M	0.727	0.141	24.1%
6M	0.743	0.157	26.8%
Transvenous Pacemaker (TV-PM)	Computed EQ5-D Score (based on Ara et al., 2008 algorithm)	***Absolute change to baseline***	***Relative change to baseline***
BL	0.577		
1M	0.654	0.077	13.1%
6M	0.617	0.039	6.7%

Table S.4.2: EQ-5D index scores derived by mapping SF-36 component scores shown in Figure S.4.1 using the algorithm by Ara et al, 2008.

At one year and for the remainder of the lifetime, we assumed the long-term EQ-5D estimate reported for TV-PM patients at five years (Lopez-Liria et al.) applied to both strategies, i.e., quality of life was assumed to be identical. For the periods 1 to 6 and 6 to 12 months, utility was modeled assuming a linear relationship between the values reported at respective follow-up points.

In the absence of other utility data that might help to estimate the temporary disutility associated with an endovascular intracardiac intervention, we looked at recent data of the UK TAVI trial as a proxy for TC-PM placement. As the data by Rombach et al. (Analysis of costs and quality of life at one year in the United Kingdom Transcatheter Aortic Valve Implantation (UK TAVI) Trial, presented at PCR Valves e-course, 2020) show, transcatheter aortic valve implantation (TAVI) patients reached their long-term utility as early as two weeks post procedure (the utility at two weeks was approximately the same as the utility observed at 12 months post index treatment). As such, it is safe to assume that the temporary disutility surrounding the procedure is at most 2 weeks. If we assume a decrement of 0.05 (patient remaining at baseline value) for one week, this

amounts to a QALY decrement of 0.05 * (1/52) =0.001. For TV-PM, we assumed temporary disutility to be twice as high (a decrement of 0.05 in utility for two weeks).

For any long-term complications in either TC-PM or TV-PM-treated patients, our analysis assumed a temporary reduction of 0.05 in utility for a period of one month.

The effect of all of these assumptions was tested in sensitivity analyses and, per results shown in the main paper, had minimal to negligible impact onto the cost-effectiveness findings.