Supplemental Online Content

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*. Published online July 28, 2021. doi:10.1001/jamacardio.2021.2621

This supplemental material has been provided by the authors to give readers additional information about their work.

eResults Supplement to Sensitivity Analysis Results

Results of the sensitivity analyses are shown in Table S5. For the 6-month complication endpoint and the reintervention endpoint, the results were robust to the type of model used (Fine-Gray or Cox model). All endpoints were robust to the type of weighting scheme used (overlap weights or IPTW weights). For all endpoints the results were consistent when the entire cohort of all implanted patients were used. Notably, while the risk for reintervention was lower for leadless-VVI compared to transvenous-VVI when the pre-defined cohort of patients implanted prior to 30 June 2018 was used (adjusted HR: 0.63, 95% CI: 0.36 – 1.12, P=0.112) this reduction became significantly lower when the entire cohort of implanted patients were used (adjusted HR: 0.59, 95% CI: 0.37 – 0.94, P=0.028).

Online-Only Tables:

eTable 1. Current Definitions of Procedural Terminology for Implants

Device Procedure	CPT Codes	ICD-10-PCS Codes
MICRA		
Insertion	0387T	02HK3NZ
Replacement	0387T	02HK3NZ *plus* 02PA3NZ
Revision (e.g., repositioning)	33999	02WA3NZ
Removal	0388T	02PA3NZ
PACEMAKER (CONVENTIONAL), SINGLE CHAMBER with SINGLE TRANSVENOUS RIGHT VENTRICULAR LEAD		
Insertion of whole system	33207	0JH604Z *or* 0JH605Z *plus* 02HK3JZ
Replacement of whole system	33207 *plus* 33233 *and* 33234	0JH604Z *or* 0JH605Z *plus* 02HK3JZ *plus* 0JPT0PZ *plus* 02PA3MZ
Insertion of generator only	33212	0JH604Z *or* 0JH605Z
Replacement of generator only	33227	0JH604Z *or* 0JH605Z *plus* 0JPT0PZ
Insertion of RV lead only	33216	02HK3JZ
Replacement of RV lead only	33216 *plus* 33234	02HK3JZ *plus* 02PA3MZ
Revision (e.g., repositioning generator or lead)	33215	02WA3MZ
	33218	02WA3MZ
	33222	0JWT0PZ
Removal of whole system	33233 *and* 33234	0JPT0PZ *plus* 02PA3MZ
Removal of generator only	33233	0JPT0PZ
Removal of lead only	33234	02PA3MZ
PACEMAKER (CONVENTIONAL), DUAL CHAMBER with TRANSVENOUS RIGHT ATRIAL AND RIGHT VENTRICULAR LEAD (e.g., for pacemaker syndrome)		
Insertion of whole system	33208	0JH606Z *plus* 02H63JZ *plus* 02HK3JZ
Upgrade from single chamber to dual chamber pacemaker system	33214	0JH606Z *plus* 02H63JZ *plus* 0JPT0PZ
CRT-P with TRANSVENOUS RIGHT VENTRICULAR LEAD and CORONARY SINUS LEAD with or without RIGHT ATRIAL LEAD		
Insertion of whole CRT-P system	33207 *or* 33208 *plus* 33225	0JH607Z *plus* 02HK3JZ, *plus* 02H43JZ *with or without* 02H63JZ
Upgrade from single chamber pacemaker system to CRT-P, by adding a CS lead while using existing generator and existing RV lead	33224	02H43JZ

Upgrade from single chamber pacemaker system to CRT-P, by removing old generator and replacing it with CRT-P generator, adding CS lead, and using existing RV lead - without an RA lead	33228 *or* 33229 *plus* 33225	0JH607Z *plus* 0JPT0PZ *plus* 02H43JZ
Upgrade from single chamber pacemaker system to CRT-P, by removing old generator and replacing it with CRT-P generator, adding CS lead, adding RA lead, and using existing RV lead	33206 *plus* 33233 *plus* 33225	0JH607Z *plus* 0JPT0PZ *plus* 02H43JZ *plus* 02H63JZ
CRT-D with TRANSVENOUS RIGHT VENTRICULAR LEAD and CORONARY SINUS LEAD with or without RIGHT ATRIAL LEAD		
Insertion of whole CRT-D system	33249 *plus* 33225	0JH609Z *plus* 02HK3KZ *plus* 02H43KZ *with or without* 02H63KZ
Upgrade from single chamber pacemaker system to CRT-D, by removing old generator and replacing it with CRT-D generator, adding CS lead, and using existing RV lead - without an RA lead	33240 *plus* 33233 *plus* 33225	0JH607Z *plus* 0JPT0PZ *plus* 02H43JZ
Upgrade from single chamber pacemaker system to CRT-D, by removing old generator and replacing it with CRT-D generator, adding CS lead, adding RA lead, and using existing RV lead	33249 *plus* 33233 *plus* 33225	0JH607Z *plus* 0JPT0PZ *plus* 02H43JZ
Complication Measure	**Definitions**	
EMBOLISM AND THROMBOSIS		
DEEP VEIN THROMBOSIS	I82.401 or I82.402 or I82.403 or I82.409 or I82.411 or I82.412 or I82.413 or I82.419 or I82.421 or I82.422 or I82.423 or I82.429 or I82.4Y1 or I82.4Y2 or I82.4Y3 or I82.4Y9 or I82.4Z1 or I82.4Z2 or I82.4Z3 or I82.4Z9 I82.621 or I82.622 or I82.623 or I82.629 I82.A11 or I82.A12 or I82.A13 or I82.A19	
PULMONARY EMBOLISM	I26.01 or I26.02 or I26.09 or I26.90 or I26.92 or I26.99	
THROMBOSIS DUE TO CARDIAC PROSTHETIC DEVICES, IMPLANTS AND GRAFTS	T82.867+	
EMBOLISM DUE TO CARDIAC PROSTHETIC DEVICES, IMPLANTS AND GRAFTS[3]	T82.817+	
EVENTS AT PUNCTURE SITE		
ARTERIOVENOUS FISTULA	I77.0	
VASCULAR PSEUDOANEURYSM	I72.4	

CARDIAC EFFUSION/PERFORATION	
CARDIAC PERFORATION	I97.51
PERICARDIAL EFFUSION	I97.51 + (I30.9 or I31.3)
CARDIAC TAMPONADE	I31.4
DEVICE-RELATED COMPLICATION	
MECHANICAL BREAKDOWN OF CARDIAC ELECTRONIC DEVICE	T82.11++
DEVICE DISLODGEMENT OR DISPLACEMENT OF CARDIAC ELECTRONIC DEVICE	T82.12++
OTHER MECHANICAL COMPLICATION OF CARDIAC ELECTRONIC DEVICE	T82.19++
INFECTION AND INFLAMMATORY REACTION DUE TO OTHER CARDIAC AND VASCULAR DEVICES, IMPLANTS AND GRAFTS	T82.7+++
HEMORRHAGE DUE TO CARDIAC PROSTHETIC DEVICE, IMPLANT AND GRAFTS	T82.837+
PAIN DUE TO CARDIAC PROSTHETIC DEVICE, IMPLANT AND GRAFTS	T82.847+
STENOSIS DUE TO CARDIAC PROSTHETIC DEVICE, IMPLANT AND GRAFTS	T82.857+
POCKET COMPLICATION	T82.897+
OTHER	
ACUTE MYOCARDIAL INFARCTION DURING CARDIAC SURGERY	I97.190 or I97.790
HEMATOMA – POST PROCEDURAL	I97.638
HEMORRHAGE – POST PROCEDURAL	I97.618
INTRAOPERATIVE CARDIAC ARREST	I97.710 or I97.120
PERICARDITIS	I30.9 or I31.9
VASCULAR COMPLICATION – BLEEDING OR FAILURE OF VASCULAR CLOSURE DEVICE REQUIRING INTERVENTION	I97.418 or I97.618
HEMOTHORAX	(J95.62 or J95.831) plus J94.2
	J95.72 plus J94.2

PNEUMOTHORAX	J95.811 or J95.812
Patient Comorbidities	**Definition**
ATRIAL FIBRILLATION	Any codes in the following ranges: I48.0-I48.2 or I48.91
ATRIAL FLUTTER	Any codes in the following ranges: I48.3-I48.4 or I48.92
CONGESTIVE HEART FAILURE	Any code in the following ranges: I09.81 or I11.0 or I13.0 or I13.2 or I50.20-I50.9 or I97.130-I97.131
CHRONIC OBSTRUTIVE PULMONARY DISEASE	Any code in the following ranges: J43.0-J43.9 or J44.0-J44.9 or J47.0-J47.9 or J60-J63.6
CHRONIC STEROID USE	Z79.52
CORONARY ARTERY DISEASE	Any code in the following ranges: I25.10-I25.119 or I25.700-I25.739 or I25.790-I25.799 or I25.810 or I25.750-I75.769 or I25.811-I25.812 or I25.82-I25.84
DIABETES	Any code in the following ranges: E08.00-E08.9 or E09.00-E09.9 or E10.10-E10.9 or E11.00-E11.9 or E13.00-E13.9)
HISTORY OF SUPRAVENTRICULAR TACHYCARDIA	I47.1
HISTORY OF VENTRICULAR ARRYTHMIA	Any of the following codes: Z86.74 or I47.0 or I47.2 or I49.01 or I49.02 or I49.3
HYPERLIPIDEMIA	E78.1-E78.5
HYPERTENSION	Any code in the following ranges: I10 or I11.0-I11.9 or I12.0-I12.9 or I13.0-I13.2 or I15.0-I15.9 or I16.0-I16.9 or I97.3
LEFT BUNDLE BRANCH BLOCK	I44.7
PERIPHERAL VASCULAR DISEASE	Any code in the following ranges: I70.201-I70.299 or I70.301-I70.799 or I73.00-I73.9
PRIOR CORONARY ARTERY BYPASS GRAFT	Any code in the following ranges: Z95.1 or T82.211A-T82.218S or I25.700-I25.739 or I25.790-I25.799 or I25.810
PRIOR ACUTE MYOCARDIAL INFARCTION	Any code in the following ranges: I25.2 or I21.01-I21.4
PRIOR PERCUTANEOUS CORONARY INTERVENTION	Any code in the following ranges: Z95.5 or Z98.61 or T82.855A-T82.855S
RENAL DYSFUNCTION	Any code in the following ranges: K76.7 or N17.0-N17.9 or N18.1-N18.9 or N19 or N28.9 or N99.0 or R39.2
TRICUSPID VALVE DISEASE	Any code in the following ranges: I07.I-I07.9 or I08.1-I08.3 or I36.0-I36.9 or Q22.4 or Q22.8-Q22.9
CONCOMITANT ATRIAL ABLATION	93650 or 93653 or 93656 or 93657 or 02583ZZ + (I48.0-I48.2 or I48.91)
CONCOMITANT TRANSCATHETER AORTIC VALVE REPLACEMENT	33361or 33362 or 33363 or 33364 or 33365 or 33366 or 02RF38Z or 02RF38H
PRIOR TRANSCATHETER AORTIC VALVE REPLACEMENT	33361or 33362 or 33363 or 33364 or 33365 or 33366 or 02RF38Z or 02RF38H

eTable 2. Differences between acute and 6-month complications

Name	Acute Complication (Yes/No)	6-month Complication (Yes/No)
Embolism and Thrombosis		
Deep vein thrombosis	Yes	No
Pulmonary embolism	Yes	No
Thrombosis due to cardiac prosthetic devices, implants, and grafts	Yes	Yes
Embolism due to cardiac prosthetic devices, implants, and grafts	Yes	Yes
Events at Puncture Site		
Arteriovenous fistula	Yes	No
Vascular pseudoaneursym	Yes	No
Cardiac Effusion/Perforation		
Cardiac perforation	Yes	No
Pericardial effusion	Yes	No
Cardiac tamponade	Yes	No
Device Related Complication		
Mechanical breakdown of cardiac electronic device	Yes	Yes
Device dislodgement or displacement of cardiac electronic device	Yes	Yes
Other mechanical complication of cardiac electronic device	Yes	Yes
Infection and inflammatory reaction to other cardiac and vascular devices, implants and grafts	Yes	Yes
Hemorrhage due cardiac prosthetic device, implant and grafts	Yes	Yes
Pain due cardiac prosthetic device, implant and grafts	Yes	Yes
Stenosis due cardiac prosthetic device, implant and grafts	Yes	Yes
Pocket complication	Yes	Yes
Other		
Hematoma – post procedural	Yes	No
Hemorrhage – post procedural	Yes	No
Intraoperative cardiac arrest	Yes	No
Pericarditis	Yes	Yes
Vascular complication – bleeding or failure of vascular closure device requiring intervention	Yes	No
Hemothorax	Yes	Yes

Pneumothorax	Yes	No

eTable 3. Baseline characteristics of the subset of leadless-VVI and transvenous-VVI pacemaker patients included in the 6-month complication and device re-intervention measures

Patient Characteristics	Leadless-VVI (N=3,726)	Transvenous-VVI (N=7,246)	SMD	P-Value
Demographic characteristics				
Age	79.5 ± 9.5	82.0 ± 8.1	0.292	<0.0001
Female, N (%)	1,603 (43.0%)	3,188 (44.0%)	0.020	0.3296
Midwest	854 (22.9%)	1,594 (22.0%)	0.022	0.2721
South	1,467 (39.4%)	2,741 (37.8%)	0.032	0.1152
Northeast	659 (17.7%)	1,065 (22.2%)	0.112	<0.0001
Encounter characteristics				
Inpatient implant	1,994 (53.5%)	4,168 (57.5%)	0.081	<0.0001
Days to implant	2.6 ± 5.6	2.0 ± 3.7	0.121	<0.0001
Weekend implant	89 (2.4%)	260 (3.6%)	0.0705	0.0007
Admission through the ED	220 (5.9%)	489 (6.8%)	0.035	0.0885
Clinical Characteristics				
ESRD	464 (12.5%)	166 (2.3%)	0.396	<0.0001
Diabetes	1,675 (45.0%)	2,971 (41.0%)	0.080	<0.0001
Atrial fibrillation	3,029 (81.3%)	6,469 (89.3%)	0.227	<0.0001
Congestive heart failure	1,987 (53.3%)	3,814 (52.6%)	0.014	0.4916
Chronic Obstructive Pulmonary Disease	1,135 (30.5%)	2,071 (28.6%)	0.041	0.0403
Chronic steroid use	133 (3.6%)	234 (3.2%)	0.019	0.348
Coronary Artery Disease	2,100 (56.4%)	3,899 (53.8%)	0.051	0.011
Supraventricular tachycardia	297 (8.0%)	395 (5.5%)	0.101	<0.0001
Ventricular arrythmia	579 (15.5%)	981 (13.5%)	0.057	0.0045
Hyperlipidemia	2,858 (76.7%)	5,365 (74.0%)	0.062	0.0023
Left bundle branch block	204 (5.5%)	369 (5.1%)	0.017	0.3937
Peripheral vascular disease	1,038 (27.9%)	1,945 (26.8%)	0.023	0.2574
Prior coronary artery bypass graft	576 (15.5%)	1,052 (16.6%)	0.026	0.1893
Prior acute myocardial infarction	750 (20.1%)	1,201 (16.6%)	0.092	<0.0001
Prior percutaneous coronary intervention	591 (15.9%)	1,001 (13.8%)	0.058	0.0039
Renal dysfunction	1,816 (48.7%)	3,007 (41.5%)	0.146	<0.0001
Tricuspid valve disease	1,094 (29.4%)	2,081 (28.7%)	0.014	0.4825
Transcatheter Aortic Valve Replacement	70 (1.9%)	106 (1.5%)	0.032	0.1006
Concomitant atrial ablation[1]	512 (13.7%)	800 (11.0%)	0.082	<0.0001
Concomitant TAVR	96 (2.6%)	347 (4.8%)	0.118	<0.0001
Charlson Comorbidity Index	5.1 ± 3.4	4.5 ± 3.0	0.173	<0.0001

TVPM, transvenous pacemaker; SMD, standardized mean difference

[1]Concomitant procedures are defined as those occurring during the implant encounter. Atrial ablation includes CPT codes 93650, 93653, 93656, 93657, 02583ZZ with diagnosis of AF and may include AF as well as AV node ablation (see eTable 1).

eTable 4. Unadjusted 6-month complication rates

Complication Type	Leadless-VVI (N=3,726)		Transvenous-VVI (N=7,246)	
	Events (%)	6-Month CIF Estimates (95% CI)	Events (%)	6-Month CIF Estimates (95% CI)
Overall complications	129 (129, 3.5%)	3.5% (3.0%-4.0%)	299 (4.1%)	4.1% (3.7%-4.6%)
Embolism and Thrombosis	*	*	*	*
Thrombosis due to cardiac device	*	*	*	*
Embolism due to cardiac device	*	*	*	*
Device-related complication	66 (1.8%)	1.8% (1.4%-2.4%)	241 (3.3%)	3.3% (3.0%-3.7%)
Other complications	64 (1.7%)	1.7% (1.4%-2.1%)	57 (0.8%)	0.8% (0.6%-1.0%)
Pericarditis	50 (1.3%)	1.3% (1.1%-1.7%)	32 (0.4%)	0.4% (0.3%-0.6%)
Hemothorax	16 (0.4%)	0.4% (0.3%-0.7%)	29 (0.4%)	0.4% (0.3%-0.5%)

eTable 5: Summary of Sensitivity Analyses

Endpoint	Method	Patient Cohort	HR (95% CI)	P-value
6-month complications	Fine-Gray with overlap weights	All implanted patients (n=5,766 leadless-VVI and 9,662 transvenous-VVI)	0.77 (0.64 – 0.93)	0.007
	Fine-Gray with overlap weights *(pre-specified method)*	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.77 (0.62 – 0.96)	0.020
	Fine-Gray with IPTW weights	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.79 (0.64-0.98)	0.035
	Cox model with overlap weights	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.78 (0.63-0.97)	0.025
	Cox model with IPTW weights	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.80 (0.64-0.99)	0.043
	Unadjusted Fine-Gray	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.84 (0.68-1.03)	0.099
	Unadjusted Cox model	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.85 (0.69-1.05)	0.122
Reintervention	Fine-Gray with overlap weights	All implanted patients (n=5,766 leadless-VVI and 9,662 transvenous-VVI)	0.59 (0.37-0.94)	0.028
	Fine-Gray with overlap weights *(pre-specified method)*	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.63 (0.36 – 1.12)	0.112
	Fine-Gray with IPTW weights	Patients implanted before 30 June 2018 (n=3,726 leadless-	0.64 (0.37 – 1.12)	0.120

Endpoint	Method	Patient Cohort	HR (95% CI)	P-value
		VVI and 7,256 transvenous-VVI)		
	Cox model with overlap weights	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.63 (0.35 – 1.12)	0.117
	Cox model with IPTW weights	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.64 (0.37 – 1.12)	0.117
	Unadjusted Fine-Gray	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.67 (0.38 – 1.20)	0.177
	Unadjusted Cox model	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.67 (0.38 – 1.21)	0.184
6-month all-cause mortality	Cox model overlap weights	All implanted patients (n=5,766 leadless-VVI and 9,662 transvenous-VVI)	0.96 (0.87 – 1.06)	0.690
	Cox model with overlap weights *(pre-specified method)*	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	1.00 (0.89 – 1.12)	0.934
	Cox model with IPTW weights	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	0.98 (0.87 – 1.10)	0.720
	Unadjusted Cox model	Patients implanted before 30 June 2018 (n=3,726 leadless-VVI and 7,256 transvenous-VVI)	1.13 (1.01 – 1.27)	0.031

eTable 6. Results from a falsification test of hip fracture through 6-Months

	Leadless-VVI (N=3,726)	Transvenous-VVI (N=7,246)	P-Value
Hip fracture*	1.4%	1.1%	0.275
*Hip fracture identified with ICD-10 diagnosis codes S72.0XXX, S72.1XXX, S72.2XXX			

eFigure Standardized mean difference values of baseline characteristics before and after balancing with the overlap weight in the total (A) and 6-month (B) cohorts