Leadless versus Transvenous Single-Chamber Ventricular Pacemakers: Three Year Follow-Up of the Micra CED Study

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Abstract

Background: The Micra Coverage with Evidence Development (CED) Study is a novel comparative analysis of Micra (leadless VVI) and transvenous single-chamber ventricular pacemakers (transvenous VVI) using administrative claims data. **Objective:** To compare chronic complications, device reinterventions, heart failure hospitalizations, and all-cause mortality after 3 years of follow-up. **Methods:** U.S. Medicare claims data linked to manufacturer device registration information were used to identify Medicare beneficiaries with a *de novo* implant of either a Micra VR leadless VVI or transvenous VVI pacemaker from March 9, 2017-December 31, 2018. Unadjusted and propensity score overlap-weight adjusted Fine-Gray competing risk models were used to compare outcomes at 3 years. **Results:** Leadless VVI patients (N=6,219) had a 32% lower rate of chronic complications and a 41% lower rate of reintervention compared with transvenous VVI patients (N=10,212) (chronic complication hazard ratio [HR] 0.68; 95% CI, 0.59-0.78; reintervention HR 0.59; 95% CI 0.44-0.78). Infections rates were significantly lower among patients with a leadless VVI (<0.2% versus 0.7%, P<0.0001). Patients with a leadless VVI also had slightly lower rates of heart failure hospitalization (HR 0.90; 95% CI 0.84-0.97). There was no difference in the adjusted 3-year all-cause mortality rate (HR 0.97; 95% CI, 0.92-1.03). **Conclusion:** This nationwide comparative evaluation of leadless VVI versus transvenous VVI *de novo* pacemaker implants demonstrated that the leadless group had significantly fewer complications, reinterventions, heart failure hospitalizations, and infections than the transvenous group at 3 years, confirming that the previously reported shorter-term advantages associated with leadless pacing persist and continue to accrue in the medium-to-long-term.

Introduction

The Micra Coverage with Evidence Development (CED) Study is a novel comparative analysis of Micra (leadless VVI) and transvenous single-chamber ventricular pacemakers (transvenous VVI) using Medicare administrative claims data. This unique study allows the Centers for Medicare and Medicaid Services (CMS) to provide coverage for leadless pacemakers while continuing to assess the performance of the technology as it becomes more widely implemented in real-world practice.[1] The acute (30-day), 6-month, and 2-year outcomes have been previously reported,[2,3] with leadless VVI associated with higher rates of acute pericardial effusion (0.8% vs. 0.4%), but lower rates of chronic complications and reinterventions at both 6 months and 2 years of follow-up (31% lower rate of chronic complications (3.6% vs. 6.5%) and 38% lower rate of device reintervention (3.1% vs. 4.9%) at 2 years). The Micra CED Study results have been consistent with the findings of the Micra transcatheter pacing system (TPS) investigational device exemption (IDE) study[4] and Micra leadless pacemaker post-approval registry (Micra PAR),[5] demonstrating the utility of real-world data in complementing traditional clinical and registry studies as a source of evidence for insight into utilization, safety, and outcomes in general practice. The Micra CED Study will continue to follow leadless pacing

patients in the Medicare population until CMS determines there is enough evidence to support or negate national coverage, making it a valuable source of evidence for comparative performance of leadless and transvenous pacemakers into the medium- and long-term. The study design also allows for the comparison of relevant health care utilization endpoints. In the present analysis, we compare for the first time rates of heart failure hospitalization between patients implanted with a leadless VVI vs. transvenous VVI pacemaker. The objective of this analysis is to compare and report on chronic complications, device reinterventions, heart failure-related hospitalizations, and all-cause mortality between leadless VVI and transvenous VVI pacemakers after 3-years of study follow-up.

Methods

The overall Micra CED Study design has been described previously.[2,3,6] The purpose of the study is to evaluate complications, utilization, and outcomes of the leadless VVI pacing system in the US Medicare population. The primary objectives of the Micra CED study were to estimate the acute (30-day) complication rate and the 2-year survival rate associated with the leadless pacing system. The study uses manufacturer device registry information to identify Medicare beneficiaries implanted with a Micra leadless pacemaker (Model MC1VR01, Medtronic, Inc) using a previously-described- linking algorithm.[6] The study also identifies a contemporaneous cohort of patients implanted with a transvenous VVI pacemaker from any manufacturer during the study period directly from their Medicare claims. The study was approved by the Western Institutional Review Board with a waiver of informed consent and is registered on ClinicalTrials.gov (NCT03039712).

Data and Cohort Identification

For this analysis, Medicare claims (inpatient, outpatient, and carrier) and enrollment data were used to identify Medicare fee-for-service (FFS) beneficiaries implanted with a leadless VVI or transvenous VVI pacemaker from March 9, 2017 (the first date of Medicare coverage for leadless VVI pacemakers) through December 31, 2018. Pacemaker implants were identified using the International Classification of Diseases, 10$^{\text{th}}$ Revision, Procedure Coding System (ICD-10) and the Current Procedural Terminology (CPT) codes for inpatient and outpatient implants respectively (**Appendix Table 1**). The index date for outcomes ascertainment was defined as the date of each patient's first observed pacemaker implant procedure during the study period. Patients with evidence of a prior cardiovascular implantable electronic device (CIED) were excluded to facilitate comparison of*de novo* pacemaker implants and to reduce the risk of misattribution of outcomes related to a prior device. Patients with less than 12 months of continuous enrollment in FFS Medicare were excluded to ensure that patient baseline clinical and demographic characteristics could be adequately captured. Among the patients implanted with a transvenous VVI pacemaker, the cohort was limited to patients implanted in facilities with evidence of leadless implants over the same time period, to increase the likelihood that patients in the study cohort would have had access to and a chance to receive either system. See**Appendix Figure 1** for the study cohort diagram.

Baseline and Implant Encounter Characteristics

Patient demographic characteristics (age, sex, US region) were ascertained using data from the CMS enrollment file. Patient baseline comorbidities were defined as the presence of diagnosis and procedure codes on any encounter claim during the 12 months prior to implant (see full ICD-10 and CPT code list in **Appendix 2** .) Comorbidities included end-stage renal disease (ESRD), renal dysfunction, coronary artery disease, peripheral vascular disease, tricuspid valve disease, atrial fibrillation, left bundle branch block, supraventricular tachycardia, ventricular arrythmia, steroid use, diabetes, heart failure, chronic obstructive pulmonary disease, hyperlipidemia, and hypertension. History of any cardiovascular events and procedures (acute myocardial infarction, coronary artery bypass graft, transcatheter aortic valve, and percutaneous coronary intervention) were also included. A Charlson Comorbidity Index (CCI) score was also calculated for each patient.[7] Characteristics of the implant encounter hospitalization were also identified, including whether the implant occurred in the inpatient or outpatient hospital setting, whether the patient was admitted for the implant procedure hospitalization through the emergency department, whether the patient was implanted

during the weekend, the time from admission to the implant procedure, and whether the patient had a concomitant cardiac procedure (transcatheter aortic valve replacement or atrial fibrillation ablation) during the pacemaker implant procedure.

Outcomes

This analysis focuses on chronic complications, device reinterventions, heart failure-related hospitalizations and all-cause mortality at 3 years as acute complications have been reported previously.[2] Chronic complications have been reported previously and include those prospectively defined using the relevant ICD-10 and CPT codes as complications most likely attributable to the implant procedure or device itself that may continue to occur or persist outside the time period of the implant procedure. These included embolism, thrombosis, device-related complications, including device breakdown, dislodgment, infection, and pocket complications, pericarditis, and hemothorax (**Appendix Table 2**). Device reinterventions were identified using the relevant procedure codes and were defined as system revision, lead revision or replacement, system replacement (e.g. replacing a leadless VVI with another leadless VVI), system removal, switch to the alternative type of system (i.e. switch from leadless VVI to transvenous VVI or transvenous VVI to leadless VVI), upgrade to a dual chamber system, or upgrade to a cardiac resynchronization therapy (CRT) device. A post-hoc composite endpoint of any reinterventions requiring a wholly new device (composite of replacement, system switch, removal, upgrade to dual chamber system, upgrade to CRT) was also defined. The rationale for defining this post-hoc endpoint was that these types of reinterventions are particularly burdensome and costly to patients, providers, and payers. Date of death was determined from the Medicare Beneficiary Summary File.

A heart failure-related hospitalization was defined as an inpatient hospitalization with an ICD-10 diagnosis code for heart failure in the primary position on an inpatient claim following discharge from the implant procedure hospitalization or encounter. A composite endpoint of heart failure hospitalization or death was also defined, as this is a common measure in the heart failure literature.[8] These heart failure hospitalization endpoints were newly-defined for the present analysis and were not previously reported on in the Micra CED Study.[2,3] Similar to reporting on upgrades to CRT, heart failure hospitalizations can provide evidence of and serve as a proxy measure for pacing-induced cardiomyopathy or potentially worsening heart failure among pacemaker patients and may be useful for evaluating long-term device performance. This novel endpoint is designed to be hypothesis generating and is the first health care utilization-related endpoint reported from the Micra CED Study. Medicare claims were available through December 31, 2020; patients alive and without an event were censored on that date.

Statistical Analysis

The statistical adjustments used in the analysis were prespecified and have been used for all comparative analyses of the Micra CED Study cohort. Propensity score overlap weights[9,10] were used to account for differences in baseline and encounter characteristics between the leadless-VVI and transvenous-VVI cohorts. Unadjusted and overlap-weight adjusted 3-year complication, reintervention, and heart failure hospitalization rates were estimated using the cumulative incidence function. Fine-Gray competing risk models were used to compare the unadjusted and adjusted risk for 3-year chronic complications, device reinterventions, and heart failure hospitalizations between study groups, and Cox proportional hazards models were used to compare all-cause mortality and the composite of heart failure hospitalization and all-cause mortality through 3 years. A sub-analysis of the heart failure hospitalization endpoints was also conducted among patients in the study cohort without a history of heart failure at baseline. Because heart failure hospitalizations are not a primary or pre-specified secondary endpoint of the Micra CED Study, the inclusion of this endpoint is designed to be hypothesis-generating. Thus, no statistical correction for the additional endpoint was made and all endpoints were evaluated at a significance level of $P<.05$ and all P values were 2-tailed. Events occurring in between one and 10 patients were suppressed to protect beneficiary privacy as required by CMS.[11] All statistical analyses were conducted in SAS version 9.4 (SAS Institute).

Results

There were 6,219 leadless and 10,212 transvenous *de novo* implant procedures identified during the study period contributing to the analysis cohort (**Table 1**). Patient baseline characteristics of this cohort have been previously reported.[3] Compared with transvenous, patients implanted with a leadless VVI pacemaker were more likely to have ESRD (12.0% vs. 2.3%, P<0.001), renal dysfunction (48.8% vs. 42.1%, P<0.001), and a higher mean Charlson Comorbidity Index score (5.1±3.4 vs. 4.6±3.0, P<0.001). Mean follow-up time for patients implanted with a leadless VVI pacemaker was 675 days, compared to 727 days for transvenous (P<0.001). After applying the propensity score overlap weights, all measured baseline and encounter characteristics were well balanced with all standardized mean differences near zero. There were 2,937 patients implanted with a leadless VVI pacemaker and 4,821 patients implanted with a transvenous VVI pacemaker in the sub-analysis of heart failure hospitalization endpoint analysis cohort without a prior history of heart failure.

Chronic Complications

Table 2 shows the adjusted rates for chronic complications and reinterventions. Chronic complication rates were significantly lower in patients implanted with a leadless VVI pacemaker compared with the transvenous (adjusted, 4.9%, vs. 7.1%, P<0.0001), driven by lower device-related complication rates (adjusted 2.6% vs. 5.2%, P<0.0001). In the time-to-event model, patients implanted with a leadless pacemaker had significantly fewer overall chronic complications at 3 years compared with patients implanted with a transvenous pacemaker (**Figure 1A** ; unadjusted hazard ratio (HR) 0.73; 95% CI 0.64–0.84, P= <0.0001; adjusted HR 0.68; 95% confidence interval (CI) 0.59–0.78, P< 0.0001). Unadjusted chronic complication rates are shown in **Appendix Table 3.**

Reinterventions

Reintervention rates were also significantly lower in the patients implanted with a leadless VVI pacemaker compared with the transvenous (adjusted, 3.6%, vs. 6.0%, P=0.0002). System revisions, removals, and upgrades to both dual chamber and CRT devices were significantly lower in the patients implanted with a leadless VVI pacemaker compared with the transvenous, while system replacements were significantly higher. For the composite endpoint of reinterventions requiring a new device (inclusive of system removal, system replacement, system switch or upgrade to dual chamber or CRT), patients implanted with a leadless VVI pacemaker had significantly fewer reinterventions requiring a new device (adjusted, 3.6% vs. 5.0%, P=0.02). In the time-to-event model, patients implanted with a leadless pacemaker had a lower rate of reintervention compared with patients implanted with a transvenous pacemaker (**Figure 1B** ; unadjusted HR 0.60; 95% CI 0.45–0.80, P=0.0006; adjusted HR 0.59; 95% CI 0.44–0.78, P=0.0002). Unadjusted reintervention rates are shown in **Appendix Table 3.**

Heart Failure Hospitalizations and All-Cause Mortality

Heart failure hospitalization rates were slightly lower among patients implanted with a leadless VVI pacemaker compared to transvenous in the overall patient cohort (adjusted, 19.9% vs. 22.0%, P=0.005) as well as among patients without prior history of heart failure (adjusted, 11.2% vs. 13.6%), P=0.003) (**Appendix Table 4**). In the time-to-event models, patients with a leadless pacemaker had a slightly, but significantly lower, rate of heart failure hospitalization compared with patients implanted with a transvenous pacemaker through 3 years (**Figure 1C** ; unadjusted HR 0.90; 95% CI 0.84–0.97, P=0.006; adjusted HR 0.90; 95% CI 0.83–0.97, P=0.005). Among patients without history of heart failure, the lower rates among patients implanted with a leadless VVI pacemaker were more pronounced (unadjusted HR 0.83; 95% CI 0.72–0.94, P=0.005; adjusted HR 0.81; 95% CI 0.71–0.93, P=0.003) (**Appendix Figure 2**).

The unadjusted 3-year all-cause mortality rate was significantly greater in the patients implanted with a leadless VVI pacemaker compared with the transvenous (HR, 1.09; 95% CI, 1.03-1.15, P=0.003); however, there was no difference in the adjusted 3-year all-cause mortality rate between leadless and transvenous (**Figure 1D** ; HR, 0.97; 95% CI, 0.92-1.03, P=0.32) after accounting for differences in baseline characteristics.

For the composite endpoint of time to heart failure hospitalization or death, there was no difference in the

unadjusted rates for either the full cohort or those patients without history of heart failure (full cohort: unadjusted HR 1.03; 95% CI 0.98-0.1.08, P=0.28; sub-cohort: unadjusted HR 1.00, 95% CI 0.93-1.08, P=0.98). After statistical adjustment, there were small differences, with patients implanted with a leadless VVI pacemaker having slightly lower rates than transvenous (full cohort: adjusted HR 0.94; 95% CI 0.89-0.99, P=0.01; sub-cohort: adjusted HR 0.92, 95% CI 0.85-0.99, P=0.03) (**Appendix Figures 3A and 3B**).

Discussion

In this nationwide comparative evaluation of 6,219 leadless VVI versus 10,212 transvenous VVI *de novo* pacemaker implants, leadless VVI pacemakers were associated with a 32% reduction in the rate of chronic complications and a 41% reduction in the rate of reintervention at 3 years. These results build off of the published 2-year results of the Micra CED Study, which showed a 31% reduction in complications and a 38% reduction in reinterventions at 2 years in this cohort.[3] Lower rates of complications among leadless pacing patients have now been observed in both clinical trials and real-world clinical practice.[4,5] This present analysis suggests the reductions in the risk of complications and reinterventions associated with leadless pacing, previously seen at 6 months and 2 years of follow-up, persist and continue to accrue in the medium-to-long-term. This analysis provides valuable new information on the expected rate of accrual of additional complications and need for system revision over time. At the 3-year endpoint, most complications that patients continue to experience are related to device (device breakdown, mechanical failure, etc.) or pocket in the transvenous VVI arm. Because the differential benefit of leadless pacing is largest with respect to these device-related complications, it would be reasonable to assume that the benefits observed at 2 and now 3 years would persist over longer time horizons.

The present analysis also provides new insight into the robustness of the 2-year results, particularly related to device reinterventions. This present analysis found a 29% lower rate of reinterventions requiring a new device (device removal and replacement, and upgrades to dual-chamber and CRT devices) among leadless VVI patients, demonstrating that the lower rate of reintervention is not solely driven by the need for lead revisions and lead-related reinterventions, which are less invasive and costly than reinterventions requiring a whole new system.

As discussed in El-Chami et. al.,[3] rates of device reintervention can be influenced by both adverse events, like pacing-induced cardiomyopathy, as well as patient selection. The advantage that leadless pacemakers have in terms of absence of leads can also be a limitation in that leadless pacemaker systems can be less adaptable to modular upgrades, such as an addition of a CRT lead. The current study shows no significant difference in all-cause mortality after adjustment for differences in baseline patient characteristics and a 10% lower rate of heart failure hospitalizations at 3 years. These results are comforting and suggest the reduction in reinterventions observed among leadless-VVI patients are not coming at the expense of worse pacing outcomes (such as untreated pacing-induced cardiomyopathy). In fact, these results appear to bolster previous findings suggesting lower rates of pacing-induced cardiomyopathy among patients implanted with a leadless pacemaker, potentially due to greater frequency of mid-septal placement associated with leadless implants.[12] It would be valuable to explore this hypothesis further in a randomized clinical trial.

The Micra CED Study also continues to demonstrate the benefits of leadless pacing with regards to device infection. While the total rate of device infection requiring full device removal in the transvenous VVI comparator arm is low (0.7%), it is significantly higher than in the leadless VVI arm. CMS reporting rules prevent us from displaying cell values less than 10 in order to prevent patient identification. If we assume that the value is actually 10, the infection rate requiring device removal in the leadless group is only 0.16%. Prior literature has demonstrated the serious risk of patient mortality and other adverse clinical and economic outcomes posed by device infection.[13]

To our knowledge, this is the first analysis to report on heart failure hospitalizations among leadless pacing patients and is possible because the large sample size and long-term follow-up of the Micra CED study allows for the capture of an adequate number of events of interest. The ability to capture and report on this endpoint highlights some of the significant advantages of using real-world data to supplement traditional

clinical studies for post-market device evaluation.

Limitations

There are several limitations inherent to this observational study using administrative data. First, Medicare administrative claims data are a secondary database used primarily for billing purposes, not for clinical research purposes; therefore, traditional clinical adjudication is not conducted. It is possible that reinterventions, complications, or comorbidities could be missed, improperly coded, or inadequately documented in administrative claims. However, our prior analyses suggest that this probability is low,[6] and, if anything, claims-based studies tend to overestimate adverse events.[14] We would also not expect this to have a differential impact between the two study arms. Second, as with any observational study, the possibility of residual confounding following statistical adjustment for measured confounders cannot be completely eliminated. Third, because our study does not include device interrogation data, we are unable to assess variables such as programmed lower rates, pacing thresholds, and battery longevity which may be of particular interest when assessing the need for device reintervention. Finally, due to data availability, this analysis is limited to the Medicare FFS population and does not capture outcomes beyond December 31, 2020.

Conclusion

In a real-world study of US Medicare patients, the leadless VVI pacemaker was associated with a 32% lower rate of chronic complications (4.9% vs. 7.1%) and a 41% lower rate of device reinterventions (3.6% vs. 6.0%) at 3 years. Rates of heart failure hospitalization were slightly lower among leadless VVI patients, and all-cause mortality rates were similar among leadless VVI and transvenous VVI patients at 3 years, suggesting no trade-off between lower rates of device reintervention and chronic right ventricular-only pacing outcomes for patients. Infections rates were remarkably lower in the leadless group. The Micra CED Study continues to illustrate the feasibility of utilizing real-world data to generate evidence measuring the safety and effectiveness of new technology and continues to complement existing clinical evidence demonstrating the benefits of leadless pacing.

Author Contributions: All authors met the IJCME criteria for authorship. All authors had access to the data according to the terms of the data use agreement with CMS and all authors fully reviewed and vouch for the accuracy of reported results. Academic authors had independent final review and approval of publication.

Data Availability Statement: The authors are not owners of the dataset (dataset is owned by the Centers for Medicare and Medicaid Services) and do not have the right to share the data.

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Table 1: Baseline characteristics of patients undergoing*de novo* implantation with a leadless VVI pacemaker vs. a transvenous VVI pacemaker

Patient Characteristics	Leadless VVI (N=6,219)	Transvenous VVI (N=10,212)	P-Value
Demographic characteristics			
Age	79.5 ± 9.5	82.0 ± 8.1	<.0001
Female, N (%)	2741 (44.1%)	4412 (43.2%)	0.28
Midwest	1,351 (21.7%)	2191 (21.5%)	0.69
South	2506 (40.3%)	3904 (38.2%)	0.01
West	1,307 (21.0%)	1,842 (18.0%)	<.0001
Northeast	1,051 (16.9%)	2,266 (22.2%)	<.0001
Encounter characteristics			
Inpatient implant	3,309 (53.2%)	5,790 (56.7%)	<.0001
Days to implant	2.5±5.3	1.9±3.6	<.0001
Weekend implant	163 (2.6%)	353 (3.5%)	0.003
Admission through the ED	745 (12.0%)	1,105 (10.8%)	0.02
Clinical Characteristics			
ESRD	744 (12.0%)	238 (2.3%)	<.0001
Diabetes	2,805 (45.1%)	4,222 (41.3%)	<.0001
Atrial fibrillation	5,066 (81.5%)	9,088 (89.0%)	<.0001
Congestive heart failure	3,282 (52.8%)	5,391 (52.8%)	0.98
Chronic Obstructive Pulmonary Disease	1,931 (31.1%)	2,975 (29.1%)	0.01
Chronic steroid use	246 (4.0%)	327 (3.2%)	0.01
Coronary Artery Disease	3,489 (56.1%)	5,447 (53.3%)	0.001
Supraventricular tachycardia	476 (7.7%)	534 (5.2%)	<.0001
Ventricular arrythmia	979 (15.7%)	1,403 (13.7%)	0.0004
Hyperlipidemia	4,770 (76.7%)	7,578 (74.2%)	0.0003
Left bundle branch block	334 (5.4%)	543 (5.3%)	0.88

Patient Characteristics	Leadless VVI (N=6,219)	Transvenous VVI (N=10,212)	P-Value
Peripheral vascular disease	1,685 (27.1%)	2,736 (26.8%)	0.67
Prior coronary artery bypass graft	929 (14.9%)	1,460 (14.3%)	0.26
Prior acute myocardial infarction	1,242 (20.0%)	1,680 (16.5%)	<.0001
Prior percutaneous coronary intervention	979 (15.7%)	1,416 (13.9%)	0.001
Renal dysfunction	3,034 (48.8%)	4,294 (42.1%)	<.0001
Tricuspid valve disease	1,795 (28.9%)	2,945 (28.8%)	0.97
Transcatheter Aortic Valve Replacement	106 (1.7%)	154 (1.5%)	0.33
Concomitant atrial^{+} ablation	861 (13.8%)	1,125 (11.0%)	<.0001
Concomitant TAVR	170 (2.7%)	474 (4.6%)	<.0001
Charlson Comorbidity Index	5.1 ± 3.4	4.6 ± 3.0	<.0001
Follow-up time (days)	675 ± 364	727 ± 366	<.0001

$^{+}$ Concomitant procedures are defined as those occurring during the implant encounter. Atrial ablation includes CPT codes 93650, 93653, 93656, 93657, 02583ZZ with diagnosis of atrial fibrillation and may include atrial fibrillation as well as atrio-ventricular node ablation

Table 2. Adjusted reintervention and chronic complication rates at 3-years in leadless VVI versus transvenous VVI pacemaker patients

	Leadless VVI (N=6,219)	Leadless VVI (N=6,21
	Observed Events (%$^{+}$)	**3-Year Adjusted CIF I**
Chronic Complications		
Overall complications	310 (5.0%)	4.9% (4.6% - 5.2%)
Embolism and Thrombosis	<11 (<0.2%)*	*
Thrombosis due to cardiac device	<11 (<0.2%)*	*
Embolism due to cardiac device	<11 (<0.2%)*	*
Device-related complications++	172 (2.8%)	2.6% (2.5% - 2.7%)
Breakdown	91 (1.5%)	1.5% (1.4% - 1.8%)
Dislodgement	24 (0.4%)	0.4% (0.3% - 0.5%)
Other mechanical failure	64 (1.0%)	1.0% (0.9% - 1.2%)
Infection	<11 (<0.2%)*	*
Pain due to device	0 (0.0%)	*
Stenosis due to device	29 (0.5%)	0.5% (0.4% - 0.6%)
Pocket complications	N/A	N/A
Other complications	145 (2.3%)	2.1% (2.0% - 2.2%)
Pericarditis	104 (1.7%)	1.7% (1.4% - 1.9%)
Hemothorax	45 (0.7%)	0.7% (0.6% - 0.8%)
Reinterventions		
Any reintervention	199 (3.2%)	3.6% (3.2% - 3.9%)
System reinterventions		
Revisions	11 (0.2%)	0.2% (0.1% - 0.3%)
Lead-related reinterventions	N/A	N/A
Replacement	74 (1.2%)	1.2% (1.0% - 1.5%)
System switch (replacement with opposite type of device)	24 (0.4%)	0.5% (0.4% - 0.7%)
Removal	*	*
Upgrades		
Dual-chamber	26 (0.4%)	0.5% (0.3% - 0.6%)
CRT	76 (1.2%)	1.5% (1.3% - 1.7%)
Composite of reinterventions requiring new device+++	198 (3.2%)	3.6% (3.2% - 4.0%)

CIF, Cumulative Incidence Function; CRT, Cardiac Resynchronization Therapy, N/A: Not applicable; NE: Not estimable.

+ Observed percentage defined as number of events divided by number of patients.

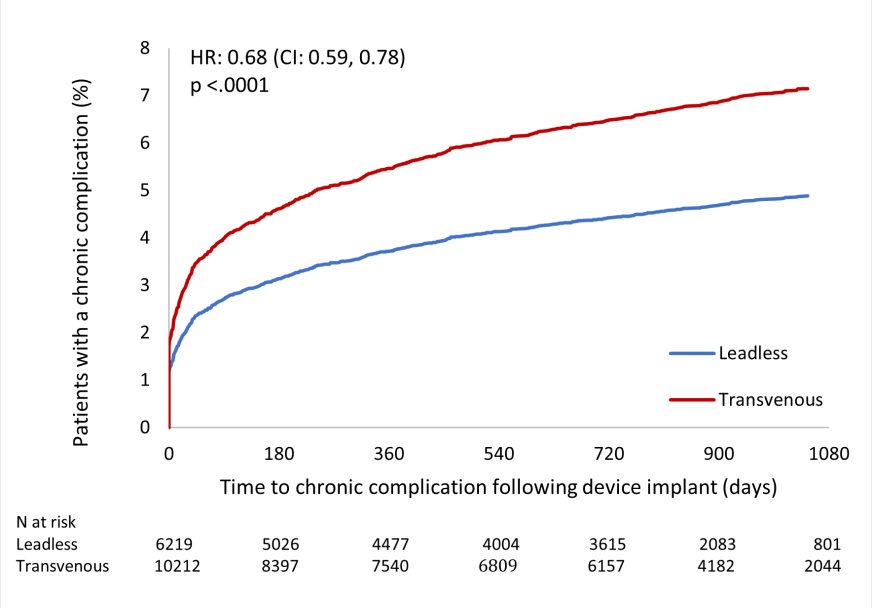
++ Includes complications related to the mechanical integrity of the device or codes explicitly stating device relatedness (e.g. device dislodgement, device infection, device pocket complication).

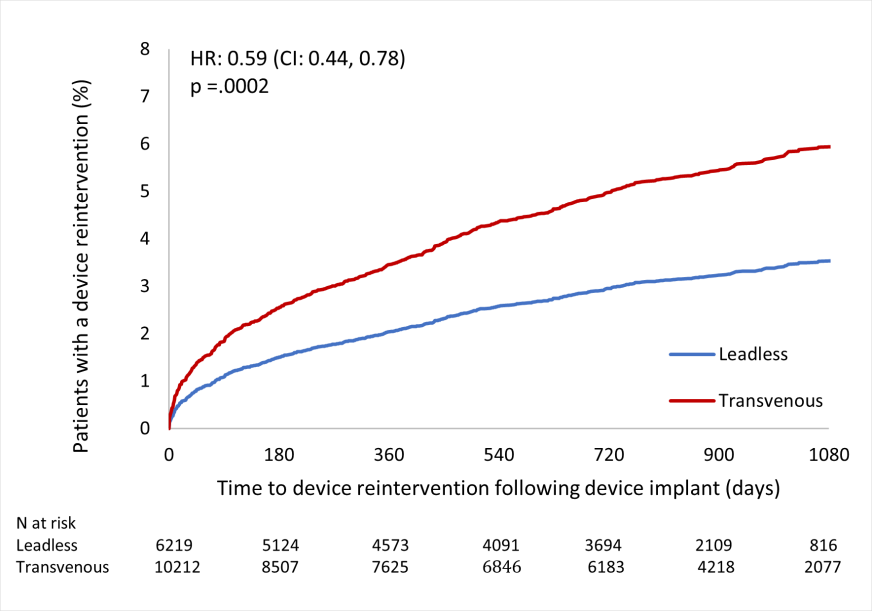
+++ Includes replacement, system switch, removal, upgrade to dual-chamber, and upgrade to CRT.

*CMS cell suppression requirement for cell values between 1 and 10.

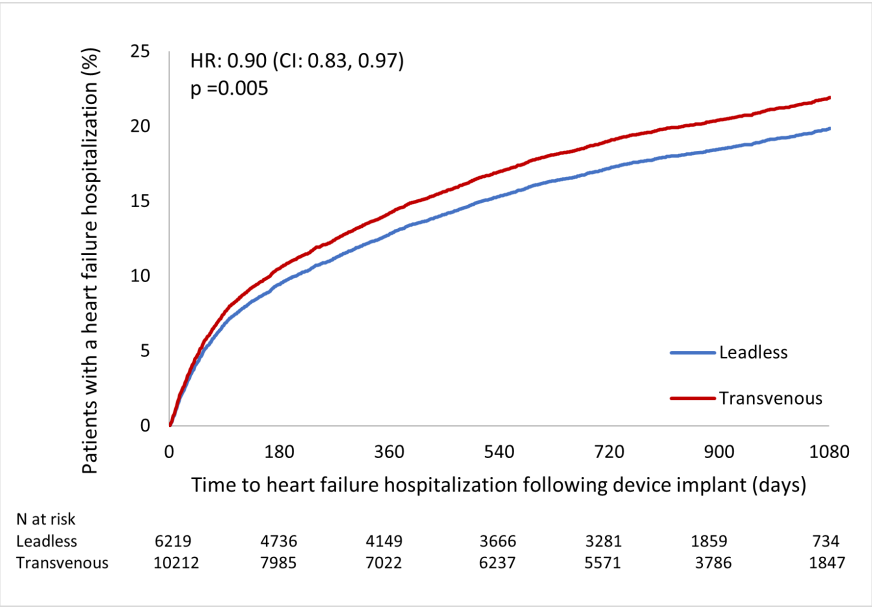
Figure Legends:

Figure 1. Adjusted time to event plots for chronic complications, device reinterventions, heart failure hospitalizations, and all-cause mortality out to 3 years of follow-up in patients treated with leadless VVI versus transvenous VVI pacing. A) Hazard ratio (HR) and cumulative incidence function for 3-year chronic complications based on the Fine-Gray competing risk model. B) HR and cumulative incidence function for 3-year device reinterventions based on the Fine-Gray competing risk model. B) HR and cumulative incidence function for 3-year heart failure hospitalizations based on the Fine-Gray competing risk model. D) HR and patient mortality rates based on the Cox proportional hazards model. CI = 95% confidence interval.

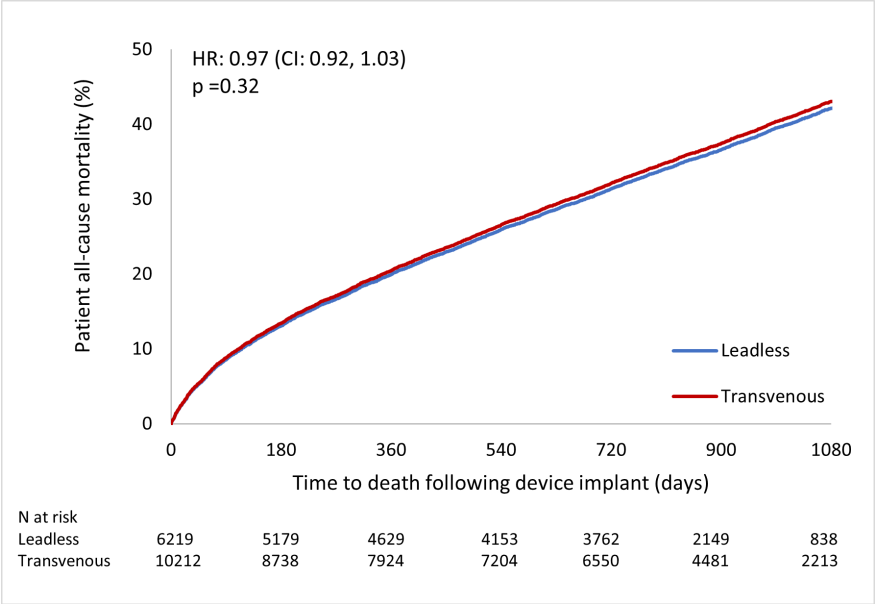




N at risk							
Leadless	6219	5124	4573	4091	3694	2109	816
Transvenous	10212	8507	7625	6846	6183	4218	2077



N at risk							
Leadless	6219	4736	4149	3666	3281	1859	734
Transvenous	10212	7985	7022	6237	5571	3786	1847



N at risk							
Leadless	6219	5179	4629	4153	3762	2149	838
Transvenous	10212	8738	7924	7204	6550	4481	2213