ORIGINAL ARTICLE

A Modular Communicative Leadless Pacing–Defibrillator System

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ABSTRACT

BACKGROUND

The subcutaneous implantable cardioverter–defibrillator (ICD) is associated with fewer lead-related complications than a transvenous ICD; however, the subcutaneous ICD cannot provide bradycardia and antitachycardia pacing. Whether a modular pacing–defibrillator system comprising a leadless pacemaker in wireless communication with a subcutaneous ICD to provide antitachycardia and bradycardia pacing is safe remains unknown.

METHODS

We conducted a multinational, single-group study that enrolled patients at risk for sudden death from ventricular arrhythmias and followed them for 6 months after implantation of a modular pacemaker–defibrillator system. The safety end point was freedom from leadless pacemaker–related major complications, evaluated against a performance goal of 86%. The two primary performance end points were successful communication between the pacemaker and the ICD (performance goal, 88%) and a pacing threshold of up to 2.0 V at a 0.4-msec pulse width (performance goal, 80%).

RESULTS

We enrolled 293 patients, 162 of whom were in the 6-month end-point cohort and 151 of whom completed the 6-month follow-up period. The mean age of the patients was 60 years, 16.7% were women, and the mean (±SD) left ventricular ejection fraction was 33.1±12.6%. The percentage of patients who were free from leadless pacemaker–related major complications was 97.5%, which exceeded the prespecified performance goal. Wireless-device communication was successful in 98.8% of communication tests, which exceeded the prespecified goal. Of 151 patients, 147 (97.4%) had pacing thresholds of 2.0 V or less, which exceeded the prespecified goal. The percentage of episodes of arrhythmia that were successfully terminated by antitachycardia pacing was 61.3%, and there were no episodes for which antitachycardia pacing was not delivered owing to communication failure. Of 162 patients, 8 died (4.9%); none of the deaths were deemed to be related to arrhythmias or the implantation procedure.

CONCLUSIONS

The leadless pacemaker in wireless communication with a subcutaneous ICD exceeded performance goals for freedom from major complications related to the leadless pacemaker, for communication between the leadless pacemaker and subcutaneous ICD, and for the percentage of patients with a pacing threshold up to 2.0 V at a 0.4-msec pulse width at 6 months. (Funded by Boston Scientific; MODULAR ATP ClinicalTrials.gov NCT04798768.)

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The transvenous implantable cardioverter–defibrillator (ICD) is the established method for treating life-threatening ventricular arrhythmias in patients at risk for sudden death from cardiac causes.[1] However, patients are at risk for lead-related complications caused by conductor failure, breakdown of insulation, and infection, and this risk increases over time.[2] The subcutaneous ICD was developed to circumvent transvenous lead-related complications. The safety and performance of subcutaneous ICDs are well established.[3,4] Lead-related complications happen less frequently and overall device-related complications, including infections, are less serious among patients with subcutaneous ICDs than among patients with transvenous ICDs.[5,6] However, the subcutaneous ICD can provide neither prolonged bradycardia nor antitachycardia pacing therapy. Antitachycardia pacing can terminate ventricular arrhythmias, particularly ventricular tachycardia, thereby possibly allowing avoidance[7] of painful shock delivery.[8] Because it does not have the capability to provide antitachycardia pacing, the subcutaneous ICD is contraindicated in patients who require antitachycardia pacing for arrhythmia termination.[16] The MODULAR ATP (Effectiveness of the EMPOWER Modular Pacing System and EMBLEM Subcutaneous ICD to Communicate Antitachycardia Pacing) study[9] investigated the safety and performance of a modular pacing–defibrillator system — the subcutaneous ICD in wireless communication with a leadless pacemaker — in patients with an indication for ICD implantation who were at risk for sudden death caused by ventricular arrhythmias that could be terminated by antitachycardia pacing (see video).[9-15]

Methods

Study Design and Oversight

The MODULAR ATP study is an ongoing, prospective, multinational, single-group study; the study design has been described previously.[9] The study was designed to assess the safety and performance of an investigational modular pacing–defibrillator system comprising a subcutaneous ICD coupled with a leadless pacemaker (EMPOWER, Boston Scientific). The study was sponsored by Boston Scientific and approved by the institutional review board at each center. Written informed consent was obtained from patients and documented in accordance with the principles of the Declaration of Helsinki, the International Council for Harmonisation guidelines for Good Clinical Practice, and all pertinent governance in the individual countries. An independent data monitoring committee oversaw safety data and study conduct. An independent clinical events committee reviewed adverse events and episodes of arrhythmia that were treated. The sponsor collected and monitored study data and performed outcome analyses according to the statistical analysis plan and the protocol, available with the full text of this article at NEJM.org. All drafts of the manuscript were written by the first two authors (who had final authority over the content) and an author who is an employee of the sponsor and were reviewed and edited by the other authors. The authors vouch for the accuracy and completeness of the data and for the fidelity of the study to the protocol.

Patients

Patients 18 years of age or older with an indication for ICD implantation[16,17] who had a preexisting subcutaneous or transvenous ICD that was to be extracted and who were considered to be at high risk for monomorphic ventricular tachycardia[16] were eligible for enrollment if they did not require pacing at baseline, had chronotropic incompetence, or required pacing for ventricular dyssynchrony. The risk of monomorphic ventricular tachycardia was defined as a history of nonsustained monomorphic ventricular tachycardia with a left ventricular ejection fraction of up to 50% or a substantial cardiac scar, a history of sustained ventricular tachycardia or ventricular fibrillation with a left ventricular ejection fraction of up to 50%, a history of syncope that was arrhythmic in origin, a history of ischemic cardiomyopathy with a left ventricular ejection fraction of up to 35%, or a history of nonischemic cardiomyopathy with a left ventricular ejection fraction of up to 35% and a substantial cardiac scar. A full description of the inclusion and exclusion criteria is provided in the Supplementary Appendix, available at NEJM.org.

A video showing the modular pacing–defibrillator system is available at NEJM.org

Study Procedures

The investigational leadless pacemaker, when implanted with a subcutaneous ICD, delivers antitachycardia and bradycardia pacing (Fig. S1 in the Supplementary Appendix).[10-15] The leadless

pacemaker is implanted in the right ventricle through a dedicated delivery catheter and introducer sheath and can be retrieved by a dedicated retrieval catheter. The pacemaker is able to verify the rate of a ventricular arrhythmia after the subcutaneous ICD detects an arrhythmia and to deliver antitachycardia pacing if the sensed rate is 158 to 261 beats per minute.[18,19] The leadless pacemaker can also function as an independent, single-chamber, rate-responsive bradycardia pacemaker.

Study investigators underwent a prespecified training program and competence assessment before study participation began.[20] The leadless pacemaker was delivered and deployed under fluoroscopy. Fixation and electrical testing were performed. Device recapture and redeployment were allowed as needed to achieve acceptable electrical settings and position as determined by the implanter. If the pacemaker location and performance were acceptable, the pacemaker was released from the tether. Patients who received a new subcutaneous ICD underwent implantation of the subcutaneous ICD and the pacemaker simultaneously or implantation of the subcutaneous ICD within 30 days after pacemaker implantation, according to the standard-of-care methods at the study site and the subcutaneous ICD user-manual instructions.[21] Patients with a previously implanted subcutaneous ICD underwent pacemaker implantation alone. Procedure medications, venous closure, and hemostasis methods were chosen at the implanter's discretion. Antitachycardia pacing requests were programmed as "on" for all therapy zones.

After the system implantation (Fig. S2), patients underwent system testing before discharge and during follow-up visits at months 1, 6, and 12 and every 6 months thereafter. System testing was performed during periods of induced arrhythmias and resting heart rates. This testing included defibrillation testing during induced ventricular fibrillation and termination with a shock delivered by the subcutaneous ICD during asynchronous pacing at the maximum pacing output setting to test the interaction between pacing stimuli and subcutaneous-ICD arrhythmia detection, as well as subcutaneous-ICD sensing during overdrive pacing to detect oversensing. Additional visits were mandated, in accordance with the protocol, for reportable adverse events, arrhythmia episodes, or device deficiencies (see the Supplementary Appendix for additional information on system testing and safety reporting).

END POINTS

The safety end point was freedom from major complications related to the leadless pacemaker at 6 months after implantation, evaluated against a performance goal of 86% (see the Supplementary Appendix for additional information). A major leadless pacemaker–related complication was defined as any complication related to the pacemaker, its implantation procedure, or its therapy delivery that resulted in system revision, permanent loss of pacemaker function, hospitalization, or death. All adverse events were adjudicated by the clinical events committee.

The primary performance end points were successful communication between the pacemaker and the ICD, evaluated against an 88% performance goal, and a pacing threshold up to 2.0 V at a 0.4-msec pulse width, evaluated against a performance goal of 80% (both measured at the 6-month visit). Successful wireless communication was determined by testing during which the subcutaneous ICD requested the pacemaker to deliver pacing at a rate faster than the patient's intrinsic rhythm. Since device communication can be affected by the relative orientation of the devices, the end point was assessed with the patient in four different body postures. All end points and objectives are summarized in Table S1.

STATISTICAL ANALYSIS

The end points and statistical analyses are summarized in Table S2 and are based on one-sided hypotheses. A prespecified hierarchical testing procedure was developed in such a way that the performance end points would be evaluated after the safety end point was met, and ancillary objectives would be evaluated if the performance end points were met. The study included a group sequential design with a prespecified early analysis of the safety end point after at least 134 patients underwent system implantation and completed their 6-month visit, with 90% power and a one-sided 1.2% significance level. The safety end point would be assessed under the assumption that a proportion, approximating the survival analysis percentage of patients with freedom from major pacemaker-related complications, would be 93%, with a performance goal of 86%, which is similar to that used for other leadless pacemakers (see the Supplementary Appendix).[22,23] If the safety end point was met at this early analysis, the 6-month end points would not be evaluated in the full study cohort.

We calculated the first performance end point (successful device communication) using a repeated-measure logistic-regression model, across the four tested postures during the 6-month visit (Fig. S3). We assumed that communication would be successful in 95% of communication tests across all patients and postures, with a performance goal of 88%. To provide the study with 80% power at a one-sided 2.5% significance level, we estimated that 152 tests would need to be performed in 38 patients. Details on data usability criteria are provided in Table S3, and additional information regarding the derivation of the performance goal is provided in the Supplementary Appendix.

The second performance end point (the percentage of patients with an adequate pacing threshold [≤2.0 V at a 0.4-msec pulse width]) was measured at the 6-month visit. To provide 90% power at a one-sided 2.5% significance level, we estimated that data from 57 patients would be needed. We selected the performance goal of 80% for this end point, which is similar to that used for other leadless pacemakers.[22,23]

The overall type I error rate for the end points was controlled with the use of the intersection–union test method. Tipping-point analyses were conducted to assess the effect of missing data for each end point. Other study results, such as death, overall system-related complications, and therapy performance in response to arrhythmia episodes, were observational in nature. The widths of the reported confidence intervals have not been adjusted for multiplicity, and the intervals should not be used in place of hypothesis testing. Missing data were assumed to be missing at random, and death was treated as a competing risk. Additional statistical analysis methods and more details about the handling of missing data are available in the Supplementary Appendix. Statistical analyses were performed with the use of SAS, version 9.4 (SAS Institute). The data cutoff date was January 24, 2024.

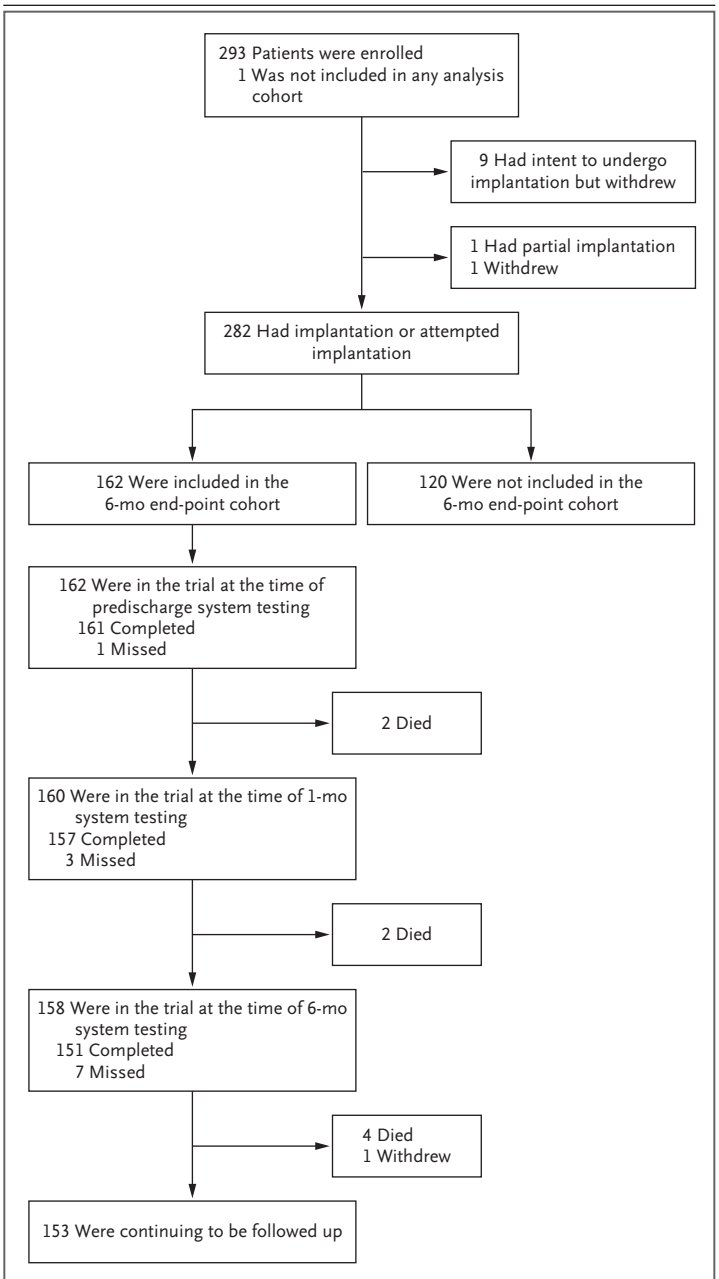

Figure 1. Enrollment and Follow-up.

The patient who had partial implantation underwent implantation of the subcutaneous ICD but not the leadless pacemaker because the patient was found to not be eligible for enrollment between the procedures. The patients who were not included in the 6-month end-point cohort had undergone implantation after the implantation date of the 134th patient to complete the 6-month visit.

RESULTS

PATIENTS

From July 2021 through January 2024, a total of 293 patients were enrolled at 38 centers (Fig. 1). Owing to variable timing of follow-up visits, the 6-month end-point cohort included 162 patients who had undergone implantation on or before the implantation date of the 134th patient to complete the 6-month follow-up visit (Fig. S4). The mean age of the patients was 60 years, 16.7% were women, 61.1% had ischemic cardiomyopathy, and the mean (±SD) left ventricular ejection

Table 1. Patient Characteristics at Baseline.*

Characteristic	Patients (N=162)
Age — yr	60±12
Sex — no (%)	
Female	27 (16.7)
Male	135 (83.3)
Body-mass index†	29.8±5.9
Race — no. (%)‡	
White	110 (67.9)
Black or African heritage	12 (7.4)
Other	10 (6.2)
Not disclosed	31 (19.1)
Indication for ICD — no. (%)	
Primary prevention	87 (53.7)
Secondary prevention	75 (46.3)
New York Heart Association classification — no. (%)	
Class I	40 (24.7)
Class II	82 (50.6)
Class III	38 (23.5)
Class IV	2 (1.2)
Left ventricular ejection fraction — %	33.1±12.6
Diabetes — no. (%)	57 (35.2)
Hyperlipidemia — no. (%)	103 (63.6)
Renal dysfunction — no. (%)	32 (19.8)
History of cardiac disease — no. (%)§	
Ischemic cardiomyopathy	99 (61.1)
Nonischemic cardiomyopathy	59 (36.4)
Other cardiac diseases	52 (32.1)
No history of cardiac disease	9 (5.6)
Ventricular arrhythmias — no. (%)¶	
Ventricular tachycardia	86 (53.1)
Sustained and nonsustained	19 (11.7)
Monomorphic, nonsustained	35 (21.6)
Monomorphic, sustained	31 (19.1)
Stable	24 (14.8)
Ventricular fibrillation	28 (17.3)
Sustained and nonsustained	2 (1.2)
Nonsustained	3 (1.9)
Sustained	23 (14.2)
No ventricular arrhythmias	67 (41.4)
Previous cardiovascular implantable electronic device — no. (%)‖	
Transvenous pacemaker	0
Transvenous defibrillator	16 (9.9)
Subcutaneous defibrillator	69 (42.6)

* Plus–minus values are means ±SD. Percentages may not total 100 because of rounding. ICD denotes implantable cardioverter–defibrillator.
† Body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Race was voluntarily reported by the patients. Patients could select more than one category, so the sum of the numbers may exceed the total number of patients.
§ Patients could have more than one category of cardiac disease history.
¶ Patients could have multiple ventricular arrhythmia substrates.
‖ A total of eight patients reported having a previous transvenous ICD as well as a subcutaneous ICD.

fraction was 33.1±12.6%. A total of 87 patients (53.7%) received a subcutaneous ICD for primary prevention (Table 1 and Table S4). The representativeness of the study population is shown in Table S5. The median duration of follow-up was 12.4 months, and 151 patients completed the 6-month follow-up visit. A total of 162 patients had complete data for the safety end point, 147 for the first performance end point, and 151 for the second performance end point (Table S6).

DEVICE IMPLANTATION AND TESTING

All leadless pacemaker and ICD devices were successfully implanted, with 66 patients (40.7%) undergoing isolated pacemaker implantation and 96 (59.3%) undergoing both pacemaker and ICD implantation (Table S4). For isolated pacemaker implantation, the median duration of the procedure was 35.0 minutes, and the median duration of fluoroscopy was 6.7 minutes; for dual pacemaker and ICD implantation, the median duration of the procedure was 79.0 minutes, and the median duration of fluoroscopy was 7.2 minutes. In 5 patients, multiple attempts at implanting the pacemaker were required (see the Supplementary Appendix). Three of these patients underwent intraprocedural retrieval of the pacemaker; in these patients, the median procedure and fluoroscopy durations were 134.0 and 36.9 minutes, respectively. Intraprocedural pacemaker repositioning was required in 43 patients (26.5%), with 21 (13.0%) needing more than one repositioning during the implantation procedure. There were no full dislodgments from the myocardium (as indicated by worsening electrical variables or detected on imaging) requiring reintervention.

A total of 153 of the 162 patients had at least one evaluable ventricular defibrillation test; the tests could not be evaluated in 1 patient, induction testing was attempted but a sustained arrhythmia could not be induced in 3 patients, and testing was not attempted in 5 patients. A total of 14 patients received more than one defibrillation test (see the Supplementary Appendix). During ventricular fibrillation induced in 153 patients, no instances of delayed pacing or inhibited subcutaneous ICD therapy occurred. Among 145 of the 162 patients, during resting-heart-rate testing, there was no evidence of oversensing the paced QRS complexes in the selected subcutaneous ICD sense vector. For the remaining 17 patients, inter-

mittent oversensing occurred during testing, which was mitigated by a reprogramming of the pacemaker (see the Supplementary Appendix).

FOLLOW-UP

System-related complications are shown in Table 2. The cumulative incidence of complications related to the overall system was 8.6% (Fig. S5). None of the adverse events were attributed to the pacemaker or therapy delivery after the implantation procedure, and none of the patients requested inactivation of pacemaker therapy for any reason (Table S7). One patient withdrew from the study after undergoing heart transplantation. Eight deaths occurred, four within the first 6 months after implantation (Fig. 1 and Fig. S6). Three deaths were related to cardiac pump failure, two were not related to cardiac causes, and the cause of death was unknown for three patients. No deaths were adjudicated to be related to the device or the procedure (Table S8). During follow-up, two patients (1.2%) underwent successful pacemaker retrieval procedures without complications — one patient in whom the initial implantation was determined to be in the left ventricle and one patient in whom complete heart block developed, unrelated to the pacing–defibrillator system, who received a dual-chamber leadless pacemaker.

END POINTS

Among the 162 patients evaluated, 97.5% had freedom from major leadless pacemaker–related complications (the safety end point), with a lower boundary of the one-sided 98.8% confidence interval of 94.2%, which exceeded the performance goal of 86% (Fig. 2). When the analysis was performed without factoring in death as a competing risk, the lower boundary of the one-sided 98.8% confidence interval was 92.5%, which exceeded the performance goal of 86% (Fig. S7). Four major complications related to the leadless pacemaker occurred in 4 patients (Table 2). One patient had a sudden drop in heart rate and blood pressure during extubation immediately after implantation of the subcutaneous ICD and required cardiopulmonary resuscitation; the return of spontaneous circulation was achieved. Two patients had myocardial perforation with cardiac tamponade during the pacemaker implantation procedure; both recovered without sequelae after pericardiocentesis. The fourth patient was discovered, during routine echocardiography 126 days after implantation, to have had the pacemaker implanted in the left ventricle; this was believed to have occurred because of the inadvertent crossing of a patent foramen ovale. The pacemaker was extracted without complications, and a second pacemaker was successfully implanted in the right ventricle.

A total of 147 of the 162 patients had communication testing data at the 6-month visit. Successful communication between the subcutaneous ICD and the pacemaker (the first performance end point) was observed in 98.8% of the communication tests, with a lower boundary of the one-sided 97.5% confidence interval of 97.0%, which exceeded the 88% performance goal (Fig. 3A). Communication success is shown in Figure 3B for each posture and in Table S9.

A total of 151 of the 162 patients underwent threshold testing at the 6-month follow-up. Among these patients, 147 patients (97.4%) had pacing thresholds up to 2.0 V at 0.4-msec pulse width (the second performance end point), with a lower boundary of the one-sided 97.5% confidence interval of 93.4%, which exceeded the 80% performance goal (Fig. 3C). The mean pacing threshold was 0.70 V at implantation and 0.56 V at 6 months (Fig. 3D). The mean R-wave amplitude was 11.1 mV at implantation and 14.6 mV at the 6-month visit; the mean pacing impedance was 812 ohms at implantation and 713 ohms at the 6-month visit (Fig. S8). Tipping-point analyses are shown in Table S10. Baseline characteristics did not appear to differ between patients with and those without missing data for each end point (Tables S11, S12, and S13).

SPONTANEOUS ARRHYTHMIA EPISODES AND THERAPY

Antitachycardia pacing was delivered in response to 31 episodes of arrhythmia in 13 patients and successfully terminated 61.3% of the episodes (Fig. S9). Antitachycardia pacing accelerated the arrhythmia in 3 episodes. All episodes that were not terminated by antitachycardia pacing were terminated by ICD shock or terminated spontaneously or the arrhythmia stabilized to a rate below the conditional defibrillation zone. Appropriate therapy (antitachycardia pacing or shock) was delivered in 9.3% of patients, and shock was appropriately delivered in 6.2% of patients (Fig. S10). No instance of failure of therapy delivery caused by failure of device communication oc-

Table 2. Complications Related to the Pacing–Defibrillator System or Implantation Procedure.*

Complication	Events	Patients (N=162)
	no.	*no. (%)*
Any complication	18	16 (9.9)
Related to leadless pacemaker or procedure, during procedure	6	5 (3.1)
Myocardial perforation with tamponade†	2	2 (1.2)
Leadless pacemaker inadvertently implanted in left ventricle†	1	1 (0.4)
Adverse reaction, respiratory	1	1 (0.6)
Venous access site bleeding	1	1 (0.6)
Atrial fibrillation	1	1 (0.6)
Related to S-ICD system or procedure, during procedure	3	3 (1.9)
Adverse reaction, vasovagal syncope†‡	1	1 (0.6)
Adverse reaction, respiratory	1	1 (0.6)
Hypotension attributed to IV antibiotic	1	1 (0.6)
Hematoma, S-ICD pocket at ≤30 days after implantation	1	1 (0.6)
Related to S-ICD programmable generator	2	2 (1.2)
Premature cell-battery depletion	1	1 (0.6)
S-ICD migration or revision	1	1 (0.6)
Related to S-ICD electrode	2	2 (1.2)
Invasive intervention to address inappropriate tachycardia therapy, noise (noncardiac), electrode	1	1 (0.6)
Electrode migration or revision	1	1 (0.6)
Related to S-ICD system, therapy: invasive intervention to address ventricular tachycardia below rate cutoff with oversensing	1	1 (0.6)
Related to S-ICD system, diagnosis: random component failure, memory corruption	1	1 (0.6)
Related to S-ICD system, patient related: incisional or superficial infection >30 days after implantation, without explantation	1	1 (0.6)
Cardiovascular	0	0
Noncardiovascular	2	2 (1.2)
Unclassified	0	0

* Adverse event classifications as presented in this table were adjudicated by the clinical events committee. IV denotes intravenous, and S-ICD subcutaneous implantable cardioverter–defibrillator.
† These events were adjudicated as major complications and, thus, contributed to the safety end point.
‡ This adverse event was classified by the study-site investigator as an observation (see Table S7), but it was adjudicated as a complication.

curred. Inappropriate therapy was recorded in 36 episodes that occurred in 14 patients, with a majority caused by cardiac oversensing of slow ventricular arrhythmias (Table S14). Inappropriate therapy was delivered in 6.2% of the patients, and inappropriate shock was delivered in 4.9% (Fig. S11). No inappropriate episodes were caused by the oversensing of pacing (see the Supplementary Appendix).

DISCUSSION

In this prospective, multinational, single-group study, a modular pacing–defibrillator system comprising a leadless pacemaker receiving wireless communication from a subcutaneous ICD met the prespecified safety end point of freedom from major complications related to the leadless pacemaker and met the performance end points of

successful communication between the pacemaker and the ICD and a pacing threshold of up to 2.0 V at a 0.4-msec pulse width. System implantation was successful in all the patients; 97.5% of the patients were free from major leadless pacemaker–related complications at 6 months, and 91.4% were free from overall system-related complications (Fig. S5). Ventricular perforation occurred in 1.2% of the patients, a percentage similar to that reported with implantation of other single-chamber leadless pacemakers,[23,24] and was resolved with pericardiocentesis. There were no pacemaker dislodgments up to 6 months after implantation, a finding that contrasts with reports for other leadless pacemakers.[24,25] In two patients, device retrieval at a time remote from implantation was performed successfully.

Although the pacing–defibrillator system requires implantation of two separate devices, the percentage of patients with major pacemaker-related complications was 2.5%, which appears to be similar to the percentage of patients with such complications (4.0% and 6.7%) associated with single-chamber leadless pacemakers in two other studies.[23,24] The lower percentage in our study might be explained by our having selected investigators with ample experience implanting leadless pacemakers and subcutaneous ICDs. Despite the generally high number of coexisting conditions in patients requiring ICD implantation, none of the deaths in our study were deemed to be related to the device or the procedure.

Pacing thresholds appeared to be consistently low through follow-up, with 97.4% of patients having 6-month pacing thresholds of up to 2.0 V, which exceeded the 80% performance goal. There were no pacemaker revisions required for inadequate pacing thresholds. R-wave amplitude and pacing impedance were within the acceptable boundaries and seemed to be similar to those of other leadless pacemakers.[23,24]

This pacing–defibrillation system relies on unidirectional communication from the subcutaneous ICD to the leadless pacemaker for antitachycardia pacing delivery. In our study, successful communication was observed in 98.8% of the communication tests performed at the 6-month visit, which exceeded the performance goal of 88%. Modular communication was shown across four different patient postures and appeared to be stable during follow-up. Pacing never resulted in undersensing of arrhythmia by the subcutaneous ICD during defibrillation testing or during clinical follow-up. Modular communicating pacemaker–defibrillators enable individual component upgrades or revisions without complete replacement of the hardware, eliminate single points of failure, and allow multichamber and multidevice interaction by means of intrabody communication without transvenous leads, which are a source of long-term complications of transvenous devices.[2]

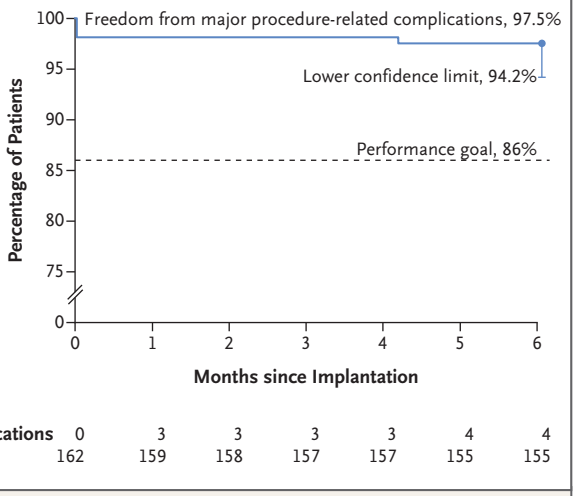

Figure 2. Freedom from Major Complications Related to the Leadless Pacemaker or Implantation Procedure.

Shown is the percentage of patients free from pacemaker- or procedure-related complications at 6 months, along with the lower boundary of the one-sided 98.8% confidence interval and the prespecified performance goal of 86%.

Antitachycardia pacing–mediated termination of ventricular arrhythmias occurred in 61.3% of episodes, which appears similar to the 46 to 72% of pacing attempts that were shown to be successful in large trials of ICDs[26,27] and the 70% reported in a study of an extravascular ICD.[28] However, patients with an extravascular ICD have reported pain or discomfort with antitachycardia pacing or pause-prevention pacing, which has resulted in requests for providers to disable the pacing feature[28] and in device extraction.[29] Inappropriate shocks were delivered in 4.9% of patients, which is higher than the 2.1% at 6 months that was reported in a recent trial of a subcutaneous ICD.[30] Because most of the inappropriate shocks

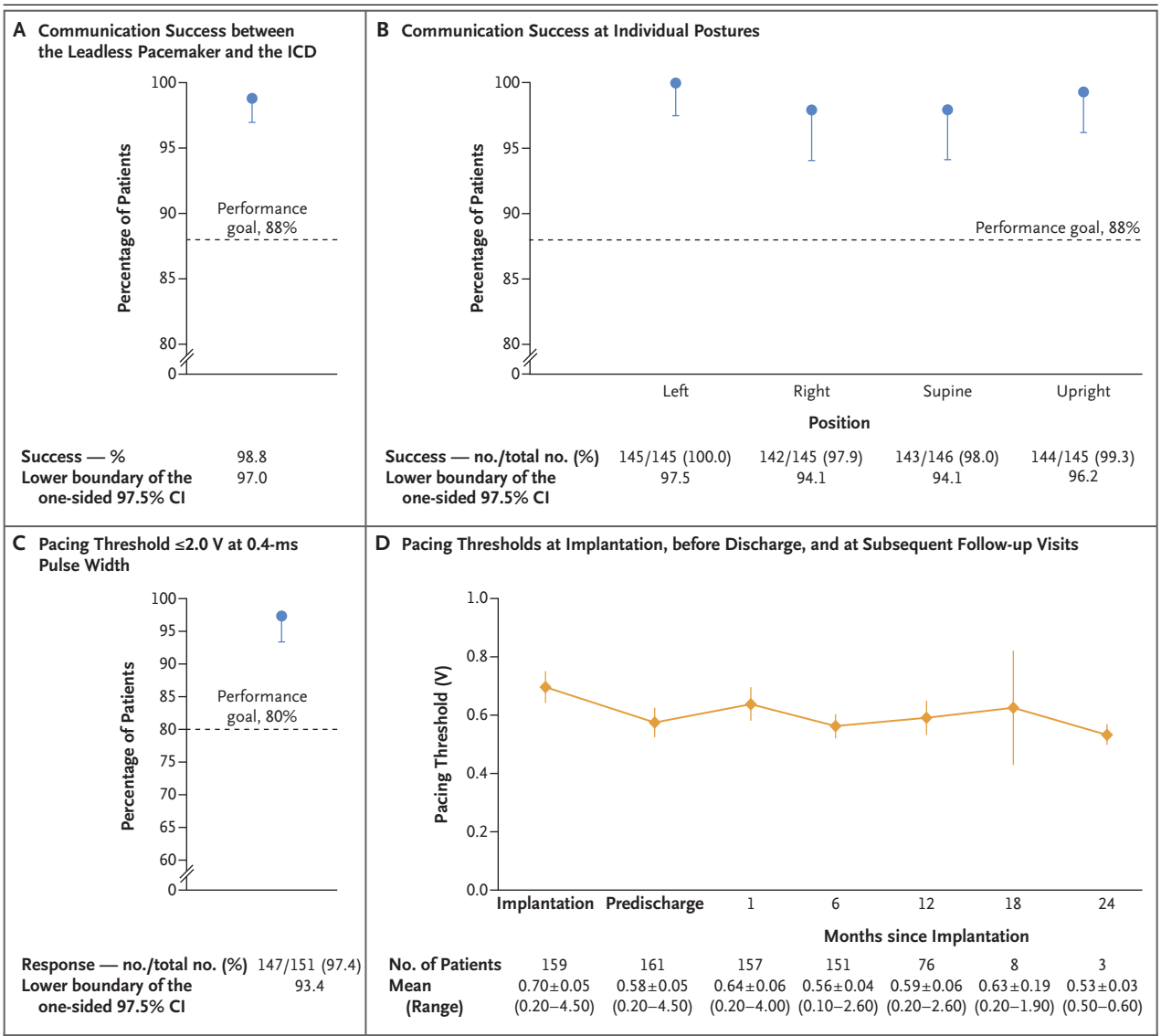

Figure 3. Wireless Communication between the Subcutaneous ICD and the Leadless Pacemaker and Electrical Performance of the Leadless Pacemaker.

Panel A shows the percentage of communication tests, evaluated in patients at four postures at the 6-month follow-up visit, in which communication between the leadless pacemaker and the subcutaneous ICD was successful, along with the lower boundary of the one-sided 97.5% confidence interval and the prespecified performance goal. Panel B shows the percentage of patients in whom communication was successful at each of four postures (lying on the left side, lying on the right side, supine, and upright), along with the lower boundary of the one-sided 97.5% confidence interval. The widths of the confidence limits have not been adjusted for multiplicity and should not be used in place of a hypothesis test. Panel C shows the percentage of patients with pacing thresholds up to 2.0 V at a 0.4-msec pulse width, along with the lower boundary of the one-sided 97.5% confidence interval and the prespecified performance goal. Panel D shows the patients' pacing thresholds at implantation, before discharge, and at subsequent follow-up visits. The mean (±SE) pacing thresholds and the range of the thresholds are shown below the graph. I bars represent standard errors; the widths of the standard errors have not been adjusted for multiplicity and should not be used in place of a hypothesis test.

were delivered in response to slower ventricular arrhythmias, this finding may be attributable to patient selection and device programming.

At present, the subcutaneous ICD has received a class IIa indication for patients who require an ICD and do not require pacing and a class III

indication (contraindicated) for patients who require an ICD with antitachycardia pacing for arrhythmia termination.[16] The inability of the subcutaneous ICD to deliver antitachycardia pacing has been a barrier to adoption of subcutaneous ICD therapy among patients who might otherwise benefit from avoiding transvenous lead implantation. The reported percentage of successful communication between the pacemaker and the ICD and antitachycardia pacing termination of arrhythmias with the pacing–defibrillator system might expand patient eligibility for a subcutaneous ICD.

Our study has limitations. The study is limited by the inherent disadvantages of a prospective, longitudinal, nonrandomized design with no comparator group. We evaluated the end points against prespecified goals for safety and performance on the basis of benchmarks from previously published literature. Therefore, we can report only on performance and not on efficacy. Our study enrolled patients with a high risk of ventricular tachycardia who were intentionally selected, and our findings may not be generalizable to other patients who require ICDs or who have ICDs already implanted.

The MODULAR ATP clinical study prospectively showed that the leadless pacemaker in wireless communication with a subcutaneous ICD exceeded performance goals for freedom from major leadless pacemaker–related complications, for communication between the leadless pacemaker and subcutaneous ICD, and for the percentage of patients with a pacing threshold of up to 2.0 V at a 0.4-msec pulse width at 6 months.

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APPENDIX

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