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RESEARCH LETTER

Inappropriate Shock Rates and Long-Term Complications due to Subcutaneous Implantable Cardioverter Defibrillators in Patients With and Without Heart Failure: Results From a Multicenter, International Registry

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Data on patients with heart failure (HF) with reduced ejection fraction and mildly-reduced (HFmrEF) ejection fraction implanted with a subcutaneous implantable cardioverter defibrillator (S-ICD) are limited to a single analysis from the UNTOUCHED trial (Understanding Outcomes with the S-ICD in Primary Prevention Patients with Low Ejection Fraction).[1] Using real-world data from the largest multi-center physician-initiated S-ICD registry (iSUSI, former Experience From the Italian S-ICD Registry-project,[2] ClinicalTrials.gov-Identifier: NCT05390047), we assessed long-term clinical outcomes of S-ICDs in HF patients. This registry has been approved by local institutional review boards. Data supporting the findings of this study are available from the corresponding author, upon reasonable request. The HF cohort included patients with HF with reduced ejection fraction and HF with mildly-reduced ejection fraction, defined according to the latest European Guidelines[3]; this cohort was compared with non-HF patients. The primary outcome of the study was the 1-year inappropriate shocks (IS) incidence rate across the 2 cohorts. As secondary outcome, appropriate shocks and device-related complications were assessed. Cox regression analysis was used to test association between baseline and intraprocedural variables and study outcomes, after testing for proportionality of hazards either graphically or through Schoenfeld residuals. Univariable analyses were performed; all variables with a *P* value of <0.10 were fit into a multivariable model to adjust for confounders.

In total, 1409 patients were enrolled: HF with reduced ejection fraction+HF with mildly-reduced ejection fraction patients represented 57.3% (n=807) of the entire cohort. HF patients were older (55.4±13.7 versus 44.0±15.7 years, *P*<0.001), more frequently male (81.2% versus 71.3%, *P*<0.001) and they were more likely to present cardiovascular risk factors and comorbidities than non-HF patients. Moreover, HF patients were implanted in primary prevention more frequently (74.4% versus 45.2%, *P*<0.001). Ischemic (48.9% versus 8.5%, *P*<0.001) and nonischemic (34.2% versus 5.3%, *P*<0.001) dilated cardiomyopathy were more likely to represent the underlying cardiac disease in the HF group, while hypertrophic cardiomyopathy (18.6% versus 1.5%, *P*<0.001), arrhythmogenic right ventricular cardiomyopathy (2.2% versus 8.1%, *P*<0.001) and primitive electrical diseases were more frequent in the non-HF group. Over a median follow-up of 21.3 [10.0–34.6] months in the HF group versus 23.0 [13.8–38.7]

Key Words: defibrillators ■ heart failure ■ incidence ■ registries ■ stroke volume ■ subcutaneous tissue ■ ventricular dysfunction

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For Sources of Funding and Disclosures, see page 59.

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Nonstandard Abbreviations and Acronyms

HF	heart failure
IS	inappropriate shocks
S-ICD	subcutaneous implantable cardioverter defibrillator
TV	transvenous

months in the non-HF group, 133 patients (9.4%) experienced IS, and 133 ventricular arrythmias were adequately treated, with the 2 groups showing similar rates of appropriate shocks (9.2% versus 9.8%, *P*=0.689). No significant differences in the 1- and 2-year IS rate (1-year: 5.1% versus 5.4%, *P*=0.803; 2-year 8.0% versus 7.9%, *P*=0.945) were observed between groups. Kaplan-Meier estimates showing no differences between HF versus non-HF patients (also stratified by left ventricular ejection fraction) for IS and appropriate shock rate have been reported in Figure A–D. At multivariate analysis for the primary outcome, older age (aHR=0.974 [0.955–0.992], *P*=0.005), lower left ventricular ejection fraction (aHR=0.954 [0.926–0.984], *P*=0.003), and an activated SMART Pass algorithm (aHR=0.321 [0.184–0.560], *P*<0.001) decreased the risk of IS (Figure E and F), while arrhythmogenic right ventricular cardiomyopathy (aHR=3.364 [1.206–9.384], *P*=0.020) increased the risk of IS. Seventy-six patients experienced device-related complications more frequently in the HF cohort (1-year: 4.8% versus 2.7%, *P*=0.041; 2-year: 6.2% versus 3.8%, *P*=0.031), with no significant differences regarding any specific outcome of interest at the 2-year follow-up mark: lead infection (1.1% versus 0.7%, *P*=0.381), pocket infection (1.9% versus 0.8%, *P*=0.107), pocket hematoma (3.2% versus 2.8%, *P*=0.668). All lead infections were treated with system revision/lead extraction, while n=3 pocket infections were managed conservatively.

In our cohort, the 1-year rate of IS in HF patients was 4.66%, similar to the non-HF group. Compared with other S-ICD trials, our overall IS rate was slightly lower than the EFFORTLESS trial and the IDE study (S-ICD System Investigational Device Exemption Clinical Investigation; 1-year IS rates of 8.1% and 13.1%, respectively), but higher than the more recent UNTOUCHED trial (3.1%).[1,4] A potential explanation for this finding is the overall younger age of our population, as well as the higher number of arrhythmogenic right ventricular cardiomyopathy patients (n=66, 4.7%), that presented a higher risk of IS. Comparing transvenous implantable cardioverter defibrillators with S-ICDs, a pivotal meta-analysis[5] has shown a similar IS rate between patients with similar underlying characteristics. However, T-wave oversensing was more prevalent in S-ICD patients. One significant finding from this study was the association between a lower left ventricular ejection fraction and a higher IS rate, corroborating the only report available on this topic (UNTOUCHED trial[1]). If the UNTOUCHED investigators did not postulate a potential underlying mechanism, we believe that this might be explained by significant differences in device programming, at in least in part. Indeed, the shock zone programming was significantly lower in HF patients, due to the significant higher number of patients receiving the S-ICD in primary prevention in this group. Moreover, T-wave oversensing was the underlying most frequent cause of IS in both works (55% versus 50%); thus, a less aggressive shock zone might lead to double counting and IS. Our study has some limitations: this is an observational nonrandomized study, with differences in the baseline variables that were inherently linked to the mismatched clinical phenotype of HF and non-HF patients. Moreover, no comparisons were made with transvenous-ICDs that represent the cornerstone of SCD prevention in HF patients. Therefore, our findings should be confirmed with future studies. In conclusion, HF patients have higher device-related complications but similar inappropriate and appropriate shock rates.

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APPENDIX

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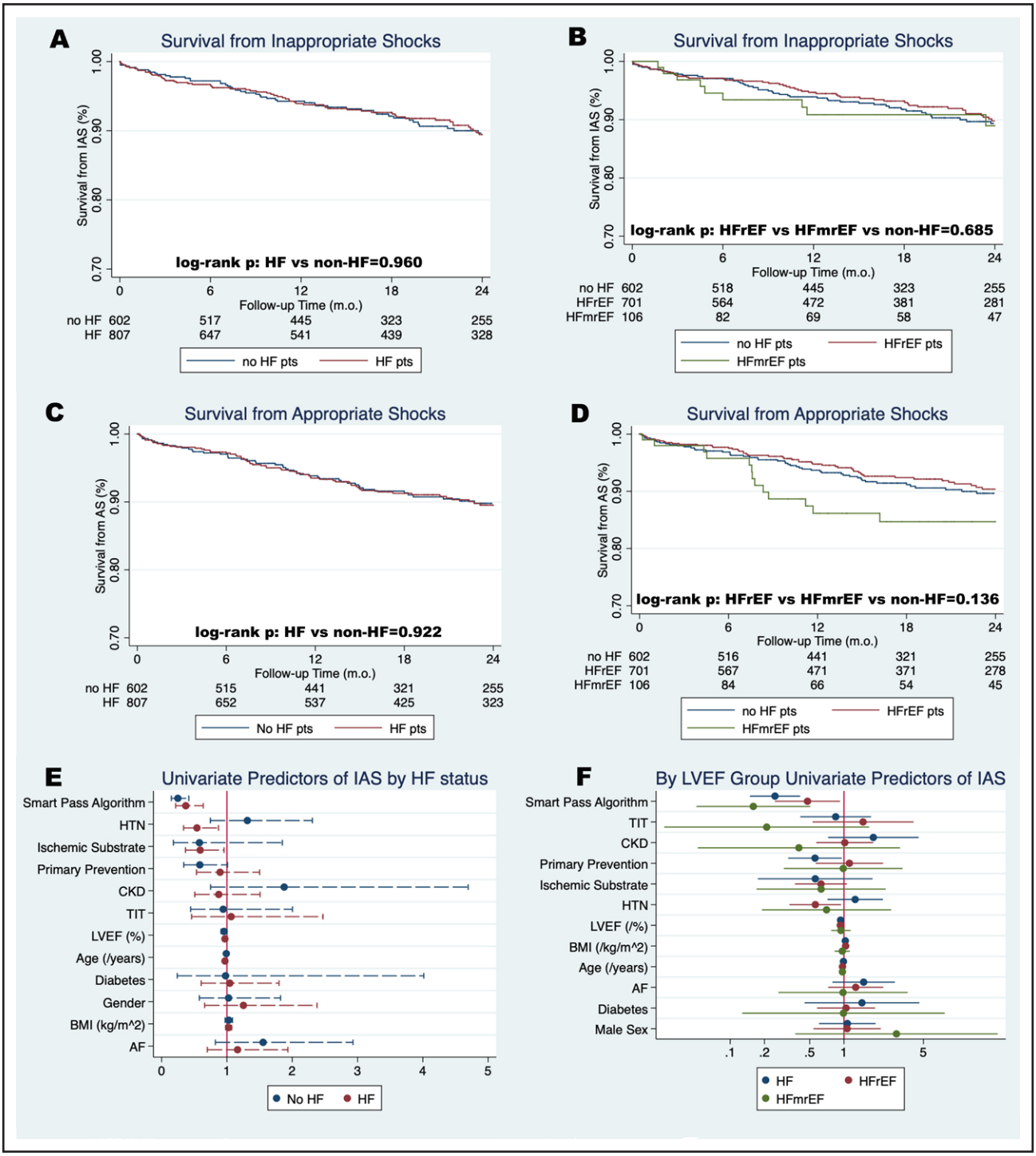

Figure. Survival from inappropriate shocks in the 2 study cohorts (A) and by LVEF stratification (B).
Survival from appropriate shocks in the 2 study cohorts (**C**) and by LVEF stratification (**D**). **E–F**, Univariate predictors of inappropriate shocks in the 2 study cohorts (**C**) and by LVEF stratification (**D**). AF indicates atrial fibrillation; BMI, body mass index; CKD, chronic kidney disease; HF, heart failure; HTN, hypertension; IAS, inappropriate shocks; LVEF, left ventricular ejection fraction; mrEF, mildly reduced ejection; rEF, reduced ejection fraction; and TIT, 2-incision technique.