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Antibacterial Envelope Is Associated With Low Infection Rates After Implantable Cardioverter-Defibrillator and Cardiac Resynchronization Therapy Device Replacement

Results of the Citadel and Centurion Studies

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ABSTRACT

OBJECTIVE This study sought to determine whether the nonabsorbable TYRX Antibacterial Envelope (TYRX) reduces major cardiovascular implantable electronic device (CIED) infections 12 months after implant.

BACKGROUND TYRX is a monofilament polypropylene mesh impregnated with minocycline and rifampin specifically designed to hold a CIED in place and elute antimicrobials over time. There are limited data on its ability to reduce CIED infections.

METHODS We prospectively enrolled patients who underwent generator replacement with an implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy device (CRT), treated with TYRX. The primary endpoints were major CIED infection and CIED mechanical complications. Given the differences in infection rates among ICD and CRT patients, 3 different control populations were used: a published benchmark rate for ICD patients, and both site-matched and comorbidity-matched controls groups for CRT patients.

RESULTS Overall, a major CIED infection occurred in 5 of 1,129 patients treated with TYRX (0.4%; 95% confidence interval: 0.00 to 0.90), significantly lower than the 12-month benchmark rate of 2.2% ($p = 0.0023$). Among the TYRX-treated CRT cohort, the major CIED infection rate was 0.7% compared with an infection rate of 1.0% and 1.3% ($p = 0.38$ and 0.02) in site-matched and comorbidity-matched control groups, respectively. Among the ICD group, the 12-month infection rate was 0.2% compared with the published benchmark of 2.2% ($p = 0.0052$). The most common CIED mechanical complication in study patients was pocket hematoma, which occurred in 18 of the 1,129 patients (1.6%; 95% confidence interval: 0.8 to 2.5), which is comparable with a published rate of 1.6%.

CONCLUSIONS Use of TYRX was associated with a lower major CIED infection rate. (TYRX™ Envelope for Prevention of Infection Following Replacement With a CRT or ICD; [NCT01043861/NCT01043705])
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ABBREVIATIONS AND ACRONYMS

CIED = cardiovascular implantable electronic device

CRT = cardiac resynchronization therapy

CRT-D = cardiac resynchronization therapy with DEFIBRILLATOR

CRT-P = cardiac resynchronization therapy with pacing function only

ICD = implantable cardioverter-defibrillator

TYRX = TYRX antibacterial envelope

Infection is a major complication of cardiovascular implantable electronic device (CIED) therapy and is associated with substantial morbidity, mortality, and expense (1–3). Although systemic antibiotics help reduce CIED infections (4,5), the incidence of CIED infections is increasing (6–9). Hence, novel adjunctive measures to prevent infection could improve CIED therapy outcomes.

The TYRX antibacterial envelope (TYRX), impregnated with minocycline and rifampin, was cleared by the Food and Drug Administration in 2008 for stabilization of CIED implants. The first-generation TYRX is made of nonabsorbable polypropylene mesh and elutes over time. Although an absorbable version was recently cleared for use, all patients in this study were treated with the first-generation, nonabsorbable product. Several nonrandomized retrospective studies have demonstrated that TYRX use is associated with a 60% to 100% relative risk reduction for CIED infection (10–12). However, TYRX envelope performance in a large, prospective CIED population has not been previously reported.

We report on the findings of 2 prospective registry studies conducted to evaluate the effectiveness of TYRX in reducing CIED infections in high-risk patients undergoing implantable cardioverter-defibrillator (ICD) (Citadel Study) and cardiac resynchronization therapy (CRT) (Centurion Study) implantations.

METHODS

STUDY DESIGN. Citadel and Centurion were separate multicenter, prospective, cohort studies that enrolled patients undergoing CIED replacement or upgrade with an ICD (Citadel) or CRT (Centurion) with TYRX. After the interim analysis in 2012, the studies were combined and the analysis plan was updated to analyze patients with TYRX in a single analysis.

The CIED procedure was performed according to usual standards of care including administration of pre-procedural intravenous antibiotics.

Patient follow-up visits were scheduled for 1 to 8 weeks, 3 months, 6 months, and 12 months after implantation. At each visit, wound sites were inspected and patients were assessed for presence of CIED infection, mechanical complication, and other adverse events. The trial protocol was approved by the institutional review board at each participating center, or a central institutional review board registered with the Food and Drug Administration and the Office of Human Rights Protections (Goodwyn Institutional Review Board, Cincinnati, Ohio). All patients provided written, informed consent.

STUDY POPULATION. Eligible patients included those >18 years old undergoing CIED replacement with an ICD (Citadel) or CRT (Centurion), were >18 years with a TYRX (**Figure 1**), and could follow-up in person. Use of an antibiotic eluting flat sheet (TYRX ST Antibacterial Soft Tissue Device, TYRX, Inc., Monmouth Junction, New Jersey) was permitted in lieu of the TYRX Envelope. The antibiotic eluting flat sheet was used in <5% of patients.

Patients were excluded from enrollment if they had a contraindication to receiving TYRX, a current CIED infection, a planned lead extraction, a clinical diagnosis of an active infection at the time of the CIED procedure, were pregnant, could not provide appropriate signed informed consent, had a life expectancy of <6 months, or were expected to undergo heart transplantation within 6 months.

CONTROL GROUPS. Both studies were nonrandomized registries; hence, no formal control group was used. In an attempt to place the findings in proper context, previously published or site-matched and comorbidity-matched controls were used. Additionally, because complication rates differ between ICD

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