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ORIGINAL INVESTIGATIONS

Clinical Inferences of Cardiovascular Implantable Electronic Device Analysis at Autopsy

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ABSTRACT

BACKGROUND Cardiovascular implantable electronic device (CIED) removal and interrogation are recommended at autopsy in suspected cases of sudden cardiac death, but data on the role of nonselective post-mortem CIED (pacemaker or defibrillator) analysis in this setting are lacking.

OBJECTIVES This study undertook an institutional registry analysis to determine the utility of systematic routine CIED removal, interrogation, and analysis at autopsy.

METHODS From May 19, 2009, to May 18, 2015, autopsy subjects with a CIED at a Johns Hopkins University medical institution (Baltimore, Maryland) underwent CIED removal and interrogation by an electrophysiologist for clinical alerts. The CIED was then submitted for technical analysis by the manufacturer. The CIED interrogation, the manufacturer's technical analysis, and the final autopsy report were all cataloged in the Johns Hopkins Post-mortem CIED Registry.

RESULTS A total of 2,025 autopsies were performed; 84 subjects had CIEDs removed and analyzed. These devices included 37 pacemakers and 47 defibrillators. Overall, 43 subjects had died suddenly, and 41 had not died suddenly. Significant clinical alerts (sustained tachyarrhythmias or an elevated fluid index value) were seen in 62.8% cases of sudden deaths. In the nonsudden death cohort, 19.5% displayed a significant clinical alert. Significant association of CIED alerts were noted when comparing sudden deaths versus nonsudden deaths ($p < 0.001$), defibrillators versus pacemakers ($p < 0.005$), and cardiac versus noncardiac causes of death ($p < 0.001$). Manufacturer analyses revealed a case of premature pacemaker battery depletion, as well as a hard reset in a defibrillator as a result of cold exposure.

CONCLUSIONS Post-mortem CIED analysis was clinically useful in assisting with determination of the timing, mechanism, and cause of death in the majority of sudden deaths and in almost 20% of nonsudden deaths. The authors advocate CIED removal with analysis as an important diagnostic tool in all autopsies and to assist manufacturers in identifying potentially fatal device failures. (J Am Coll Cardiol 2016;68:1255-64) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CIED = cardiovascular implantable electronic device

FDA = Food and Drug Administration

Cardiovascular implantable electronic devices (CIEDs) encompass permanent pacemakers, implantable cardioverter-defibrillators, and insertable loop recorders. CIED analysis is recommended at autopsy (1,2), but it is rarely performed (3–5). Selective autopsy case reports, case series, and a large study registry have shown the utility of post-mortem CIED interrogation but have been limited to suspected cases of sudden cardiac death (3,6–10). Consequently, the utility of nonselective CIED analysis at autopsy regardless of suspected cause of death remains unknown. We undertook an institutional registry analysis to determine the clinical role of systematic routine CIED removal, software interrogation, and hardware analysis at autopsy.

METHODS

AUTOPSY SUBJECTS. Over a period of 6 years, from May 19, 2009, to May 18, 2015, all autopsies undertaken at 2 Johns Hopkins University medical institutions in Baltimore, Maryland, (Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center) used a protocol for routine CIED identification and removal. All autopsy subjects identified as having a CIED were included in the Johns Hopkins Post-mortem CIED Registry ("the registry"). The subjects underwent either complete autopsy or limited autopsy with, at minimum, inclusion of the heart and CIED generator. Consent for autopsy was obtained post-mortem from next of kin or legal guardians.

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CIED ANALYSIS. CIED generators were routinely removed by an autopsy technician using recommended precautions (11–13). In particular, a manufacturer-specific bidirectional hex wrench was used for disconnection of the CIED generator header from the attached indwelling leads to avoid cutting leads, which may trigger inappropriate device therapies and false device alerts. The CIED generator was stored at room temperature until it was interrogated with a manufacturer-specific computer programmer by a board-certified clinical cardiac electrophysiologist (S.K.S.). Appropriate battery and lead parameters, alerts, and electrograms were reviewed and cataloged in the registry. Significant clinical and technical alerts were also reviewed and confirmed by a second board-certified clinical cardiac electrophysiologist (J.E.M.).

SIGNIFICANT CIED ALERTS. Significant clinical alerts included those triggered by sustained atrial or ventricular tachyarrhythmias within 24 h of death or an elevated OptiVol (Medtronic, Minneapolis, Minnesota) fluid index >60 Ohm-days in the weeks before death. An elevated OptiVol fluid index indicates significant thoracic fluid accumulation as determined by elevated intrathoracic impedance measurements, and this software algorithm is nominally activated in most defibrillators manufactured by Medtronic. By contrast, the intrathoracic impedance alert algorithm (CorVue, St. Jude Medical, St. Paul, Minnesota) found in most defibrillators manufactured by St. Jude Medical is not nominally activated. Significant technical alerts included premature battery depletion, evidence of lead malfunction (fracture or insulation breach), or random component failure.

INACCURATE CIED ALERTS. Inaccurate technical alerts triggered post-mortem as a result of automated algorithms (capture threshold, sensing, impedance testing) and inaccurate clinical alerts caused by false atrial or ventricular tachyarrhythmias derived from artifact detection were not considered significant and were not catalogued.

MANUFACTURER ANALYSIS. The CIED device was then submitted to the applicable manufacturer (Medtronic; Boston Scientific, Natick, Massachusetts; St. Jude Medical; or Biotronik, Lake Oswego, Oregon) for detailed technical analysis (guidelines for processing returned products are available from all manufacturers on request). Standardized manufacturer analysis entailed visual and mechanical inspection, software interrogation, and stabilization of the device at 37°C (to mimic in vivo conditions) before electrical bench testing to assess battery status, pacing and shocking capability accurately. If device failure was suspected, then destructive analysis was undertaken to assess for specific component failure.

AUTOPSY ANALYSIS. The attending pathologist undertook visual inspection, anatomic dissection and measurements, microscopic analysis, and, when appropriate, immunohistochemical staining, toxicology, and genetic studies. The attending pathologist was informed of the CIED interrogation results before their adjudication of the cause, mechanism, and time of death on finalization of the autopsy report. For example, if a subject with methicillin-resistant *Staphylococcus aureus* sepsis syndrome died suddenly and was noted to have bacterial endocarditis at autopsy and ventricular fibrillation on post-mortem implantable cardioverter-defibrillator interrogation corresponding to the time of death, then the cause of death would be "sepsis," the mechanism would be "bacterial endocarditis," and the time of death would be ascertained from their