Overcoming reporting challenges: How to display, summarize, and model late reintervention outcomes, follow-up, and vital status information after surgery for atrial fibrillation

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BACKGROUND Postsurgical late reinterventions for atrial fibrillation (AF) include cardioversions (CV) or catheter ablations (CA). Commonly used methods for reporting and modeling the frequency and timing of CA or CV have well-known shortcomings.

OBJECTIVE The purpose of this study was to present intuitive and robust methods to visualize, summarize, and model late reinterventions type/timing and vital status simultaneously.

METHODS We present (1) the SMART plot (Summary of Mortality And Outcomes Reported Over Time); (2) the reintervention mean cumulative function (MCF); and (3) the proportional means model and the proportional rates model. We illustrate these methods in 3 groups: patients age $\leq$60 years, 60–75 years (reference), and $>$75 years who underwent surgical AF ablation.

RESULTS Patients age $>$75 years had a significantly lower MCF of CVs (hazard ratio [HR] 0.50, $P < .001$). MCF for CAs was not significantly lower for patients age $>$75 years (HR 0.57, $P = .13$). For combined reinterventions (CV or CA), the age group $>$75 years had a significantly lower MCF (HR 0.51, $P < .001$). There were no significant differences in late CV or CA reintervention patterns for patients age $\leq$60 years.

CONCLUSION The methods presented provide a comprehensive framework for displaying, summarizing, and modeling repeated late reinterventions after surgical AF ablation. Other areas of application are described, further emphasizing the potential for immediate use.

KEYWORDS Surgical ablation; Atrial fibrillation; Cardioversion; Catheter ablation; Late reintervention; Recurrent event

ABBREVIATIONS **AF** = atrial fibrillation; **AFL** = atrial flutter; **AT** = atrial tachycardia; **CA** = catheter ablation; **CARD** = Cardiovascular Research Database; **CV** = cardioversion; **FFAF** = freedom from atrial fibrillation; **PMM** = proportional means model; **PRM** = proportional rates model; **RF** = rate function; **SA** = surgical ablation; **SR** = sinus rhythm

(Heart Rhythm 2015;12:1456–1463)

Atrial fibrillation (AF) is the most common heart rhythm dysfunction in the United States, affecting more than 2.5 million individuals.[1,2] For symptomatic AF patients who are refractory to or intolerant of antiarrhythmic medication, AF treatment options include cardioversion (CV), catheter ablation (CA), or surgical ablation (SA). Appropriate risk/benefit ratio metrics are necessary when considering a sinus rhythm (SR) restoration intervention.[3–5]

Defining and reporting SR restoration "success" or "failure" after SA is somewhat equivocal and highly contextual.[6–9] The 2012 HRS/EHRA/ECAS Consensus Document

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on Catheter and Surgical AF Ablation defines "failure" as any symptomatic or asymptomatic episode of AF, atrial flutter (AFL), or atrial tachycardia (AT), of at least 30 seconds' duration, after the 3-month blanking period off antiarrhythmic drug therapy. Although this recommendation has been widely used and reported as an end-point of AF ablation trials, there is widespread recognition that this is a very strict end-point and may underestimate the true clinical benefit of AF ablation. For this reason, the Consensus Document encourages clinical trials to also define, and report, "clinical success" as a secondary end-point of AF ablation trials. Important factors to consider when defining "successful" SR restoration are (1) the AF treatment setting (controlled clinical trial, observational study); (2) the arrhythmia monitoring technology (noncontinuous or continuous ECG, Holter monitor, implantable loop recorder, pacemaker, or defibrillator); (3) the hospital-specific follow-up protocol for clinical care; and (4) patient follow-up protocol adherence. When "success" is defined as the freedom from AF (FFAF) at prespecified timepoints, such as yearly marks or the last follow-up, the overall temporal dynamics of "success" are only partially conveyed, and the true clinical benefit is likely to be underestimated. The likelihood of AF detection is directly proportional to the duration and frequency of arrhythmia monitoring. Hence, "success" comparisons among groups might be difficult in the absence of a standardized rhythm monitoring protocol and/or strict adherence. Furthermore, it is not straightforward to summarize "success" when patients experience intermittent AF episodes before SR restoration.[3]

Instead, we focus on a surrogate measure of "success"—freedom from late reinterventions, such as CA or CV.[6,10,11] Unless permanent AF has been accepted, the absence of a reintervention might be equated, to some degree, with SR restoration. Reintervention data provide "hard" end-points in contrast to FFAF-type end-points. Currently used "success" reporting metrics do not facilitate a comprehensive temporal characterization of the SR "success" risk after the index AF surgical ablation. Nor do they permit characterization of the subsequent risk of reintervention. For example, the Kaplan–Meier curve is not designed to summarize events that are recurrent in nature, such as AF episodes or CV/CA reinterventions. As such, the 2012 HRSA/EHRA/ECAS expert consensus statement on CA and SA of AF identifies areas that would benefit from adequate outcome reporting statistical methodology.[3] Question 12 (p. 56) states the need for *"…useful,* ***robust*** *performance measures characterizing outcomes of ablation…"* since "*…Kaplan-Meier analyses… may underestimate the true effectiveness of AF ablation.*" Furthermore, "*another endpoint that should be considered in clinical trials is an assessment of 'AF burden' at various points in time during follow-up.*"

To address post-SA "success" reporting, we present robust and intuitive methods that are applicable to CV/CA reporting, thus facilitating the visualization and analysis of postindex AF treatment outcomes. First, we present the *SMART plot* (*S*ummary of *M*ortality *A*nd Outcomes *R*eported Over *T*ime). It simultaneously displays patient-level late reintervention(s) type and timing, together with the most recent vital status. Second, to summarize the average number of reinterventions per patient *at any time,* not only yearly or at last follow-up, we propose using the *mean cumulative function (MCF).*[12] Unlike the Kaplan–Meier estimator, the MCF was designed to analyze recurrent events. Being cumulative over time, the MCF might serve as a good indicator of "AF burden," both in terms of late reinterventions and AF recurrences. The derivative function of the *MCF* represents the *reintervention rate*. Third, one may adjust for confounders when comparing MCFs. Therefore, we propose the use of the *proportional means model (PMM)* and the *proportional rates model (PRM).*[13] These models mimic the well-known Cox proportional hazards model yet are specifically designed for recurrent events.

Patient population

Data for this project were obtained from the Cardiovascular Research Database (CARD) in the Clinical Trial Unit of the Bluhm Cardiovascular Institute at Northwestern Memorial Hospital. CARD is approved by the Institutional Review Board at Northwestern University (Project No. STU00012288). Any subjects who refused participation in the project were not included in the analysis. In total, 1082 patients underwent SA of AF, in either isolated (8.3%) or concomitant (91.7%) fashion between April 2004 and December 2013. The surgical indication for all patients was preoperative AF, and 135 (12.5%) had a prior CA.

Postoperative rhythm monitoring and management

Patients were prospectively followed since January 2006 when a dedicated clinical/research nurse was hired. A standardized postoperative AF management protocol was developed in collaboration with cardiac electrophysiologists. Standard definitions for types and classification of AF were used.[3] Patients and cardiologists were given copies for reference. The protocol advised discharge on antiarrhythmic medications, unless contraindicated, for the first 3 months. For patients with persistent AFL or AF past 1 month, CV was recommended. Extended monitoring, at the minimum being a Holter monitor, was recommended at 3 months. Patients with dual-chamber implanted defibrillators or pacemakers had mode-switch parameters activated. Rhythm data were obtained from cardiac rehabilitation sessions. If no AF was observed during monitoring, antiarrhythmic medications were discontinued at the discretion of the cardiologist. Patients with persistent AFL, AF, or AT were offered referral to a cardiac electrophysiologist for further management. Rhythm monitoring was repeated at 6 months, and anticoagulation was discontinued for patients maintaining SR off antiarrhythmic medications at the discretion of the cardiologist. Patients participating in CARD were sent surveys at 6 and 12 months and annually thereafter. Copies of medical records were obtained for any