

November 2015 Tucson Critical Care Journal Club: Atrial Fibrillation in Sepsis

Walkey AJ, Evans SR, Winter MR, Benjamin EJ. Practice patterns and outcomes of treatments for atrial fibrillation during sepsis: A propensity-matched cohort study. *Chest*. 2015 Aug 13. [\[CrossRef\]](#)

Sepsis is a major public health concern in the United States (1). Nearly one-third of in-hospital deaths are the result of sepsis (2). Atrial fibrillation (A-fib) is the most common arrhythmia in sepsis and its development portends worse outcomes (3). Current guidelines recommend cardioversion in hemodynamically unstable patients with sepsis; however, there is scant evidence to guide the choice between amiodarone, beta-blockers, calcium-channel blockers, and digoxin (4). In patients with decompensated heart failure, digoxin and amiodarone are preferred over beta-blockers and calcium channel blockers (4). In patients with multiple organ failure there is no evidence to suggest any one agent is superior to the others. This study by Walkey *et al.* sought to identify current practice patterns in the pharmacologic treatment of A-fib among hospitalized patients with sepsis and to compare outcomes after controlling for potential confounding variables.

This retrospective cohort study used a nationally representative source of hospital billing data from 2010-2013 to examine outcomes among patients admitted with sepsis who received antibiotics on the first day of hospitalization and had either pre-existing or new-onset A-fib. Use of intravenous beta-blockers, calcium channel blockers, cardiac glycosides, and amiodarone within 14 days of admission was also examined. Those who received oral medications or those who received multiple agents on the same day were excluded. Patient- and hospital-level characteristics were also obtained from billing data. The primary outcome was in-hospital mortality.

Propensity scoring was used to adjust for measured confounding and an instrumental variable approach was used to account for unmeasured confounding. Outcomes among those treated with beta-blockers were then compared to those treated with other classes of medication.

Approximately 540,000 patients were hospitalized with sepsis and 113,511 had sepsis and A-fib. Approximately 40,000 received intravenous therapy and comprised the analytic sample. Of those patients included, 49% were women and 76% were white; the average age was 77 years. Calcium channel blockers were the most frequently used initial therapy (36%), followed by beta-blockers (28%), digoxin (20%), and amiodarone (16%).

In comparison to patients treated initially with beta-blockers, those receiving calcium channel blockers were more likely to be younger, female, and white; they also had fewer comorbid conditions. Patients initially treated with beta-blockers were less likely to experience in-hospital mortality as compared to those initially treated with calcium channel blockers, 18.3% versus 20.0%, respectively (RR 0.92, 0.86-0.97). There was no effect modification based on pre-existing or new-onset A-fib or the presence of heart

failure; however, outcomes were better among patients treated with a vasopressor as compared to those not similarly treated ($p=0.02$).

Patients receiving digoxin were typically older and more likely to have heart failure, COPD, malignancy, or shock than those receiving beta-blockers. Beta-blocker use was associated with lower in-hospital mortality than digoxin use, 20.5% versus 25.7%, respectively (RR 0.79, 0.75-0.84). There was no effect modification by A-fib onset, vasopressor use, or heart failure.

Patients receiving amiodarone were more likely to be critically ill or have heart failure, new onset A-fib, malignancy, or acute organ failure. Beta-blocker use was associated with lower mortality as compared to amiodarone use, 27% versus 42%, respectively (RR 0.65, 0.61, 0.69). There was no effect modification based on onset of A-fib or presence of heart failure; however, outcomes were better among those with concomitant treatment with vasopressors ($p=0.003$).

Overall, greater hospital-level use of beta-blockers was associated with reduced individual mortality (RR 0.67, 0.58- 0.79). These data support the conclusion that beta-blocker use among patient with sepsis and A-fib was associated with statistically and clinically significant reductions in in-hospital mortality irrespective of vasopressor use, timing of A-fib, or presence of heart failure.

Nevertheless, the study relied on an observational design which is subject to bias and confounding. However, the analytic approach used two rigorous methodologies, propensity scoring and instrumental variable, to account for measured and unmeasured confounding, respectively. More rigorous data will only come from a large, multi-center, randomized controlled trial. Unfortunately, such a trial will be expensive and will take many years to yield results. How should today's clinicians respond given at least some risk that these results may turn out to be spurious? In situations when beta-blockers are not clearly contraindicated, it seems reasonable to recommend using beta-blockers first realizing that doing so does not preclude subsequently using another agent to achieve the desired therapeutic goal. While observational data would not be sufficient to overturn evidence from randomized controlled trials, in this case, no such data exist. Given the consistency of the findings, it is reasonable to ask whether greater use of beta-blockers in the treatment of severe sepsis might be warranted even in the absence of A-fib.

Ryan R. Nahapetian MD, Joe Gerald PhD
Pulmonary, Allergy, Critical Care, & Sleep Medicine
University of Arizona
Tucson, AZ

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