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All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Clinical Electrophysiology* author instructions page.

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Limitations of Administrative Data for Examining Secondary Atrial Fibrillation

The management of "secondary" atrial fibrillation (AF) is unclear (1). When AF is detected as a secondary diagnosis during hospitalization for another condition, it may be a temporary phenomenon that does not recur after the precipitating stressor is removed. Alternatively, it may be the first diagnosis of paroxysmal AF. A better understanding of "secondary" AF is necessary to determine whether clinicians should prescribe oral anticoagulation (OAC) for stroke prevention.

On the basis of their analysis of administrative data, Quon et al. (2) suggest that there is no clear benefit to using OAC in patients with "secondary" AF. However, there are several limitations with their analysis. The ascertainment of AF prevalence using administrative data has low sensitivity, even when validated algorithms are used (3). More specifically, the detection by Quon et al. (2) of "secondary" AF during hospitalization also appears insensitive because they identify 102 patients with sepsis and secondary AF over a 17-year period in Quebec (~8 million residents). This number is much lower than would be expected based on prior studies (4). Finally, the assessment of the effects of OAC on patients with "secondary" AF is subject to many confounders. Patient- and physician-related factors that determine the risk of stroke and other adverse outcomes are also associated with the decision to prescribe OAC after "secondary" AF. Multivariable adjustment can only partially correct for imbalances in these factors, and such correction is never complete. Considering these limitations, one should be cautious in assuming that OAC does not afford benefit in this setting. Randomized controlled trials (RCTs) have demonstrated marked benefit from OAC, and another observational study in this "secondary" AF group demonstrated benefit from OAC (adjusted hazard ratio: 0.59; 95% confidence interval: 0.40 to 0.86) (5).

Our group has proposed atrial fibrillation occurring transiently with stress (AFOTS) as a more accurate term for describing "secondary" AF (1). The term "secondary" implies clinical certainty that AF will not return once the stressor (e.g., sepsis, acute lung disease) is removed. An RCT of OAC in these patients would be the most definitive way to address the management of AFOTS. Without such an RCT, the demonstration of AF recurrence after hospitalization in a high proportion of patients with AFOTS would suggest that AFOTS may simply represent the first detection of typical clinical AF. In retrospective studies with low-sensitivity detection methods (i.e., 12-lead electrocardiograms and short-duration ambulatory monitors), up to 50% of patients with AFOTS have AF recurrence within 1 year (1). Our ongoing multicenter study (AFOTS [Atrial Fibrillation Occurring Transiently With Stress]; NCT03221777) is designed to demonstrate this finding with a high-sensitivity detection method and will be the first step in defining an optimal management strategy for AFOTS.

We agree with Quon et al. (2) that in the absence of RCT data, clinicians must carefully evaluate the risks and benefits of OAC for "secondary" AF. In fact, the risks and benefits may be partly stressor dependent. The increased bleeding risk in post-acute coronary syndrome patients who require antiplatelet therapy may outweigh any potential benefit in stroke prophylaxis. Conversely, in septic patients with multiple

comorbidities not requiring antiplatelet therapy, stroke prophylaxis benefit may significantly outweigh the increased bleeding risk.

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REPLY: Limitations of Administrative Data for Examining Secondary Atrial Fibrillation

The clinical benefit of anticoagulation in secondary atrial fibrillation (AF) remains unclear. In our study (1), we did not demonstrate benefit of oral anticoagulation (OAC) therapy in stroke reduction in patients who develop secondary AF associated with acute coronary syndromes, acute pulmonary disease, or sepsis. We agree with Mr. Um and colleagues that one should be cautious in assuming that OAC does not offer benefit in these patients. While awaiting more data on the incidence of recurrent AF in patients with acute medical illnesses and noncardiac surgery and a randomized clinical trial on the benefits of OAC, our study provides much needed information. Dr. Um and colleagues raise issues regarding: 1) ascertainment of AF prevalence; 2) residual confounding; and 3) estimates of benefit of OAC and recurrence of AF.

Dr. Um and colleagues are concerned with ascertainment of AF prevalence because of low sensitivity for detection of secondary AF using administrative databases. Our study was not aimed at measuring prevalence, which we agree would require high sensitivity, but at identifying patients with secondary AF; therefore high specificity rather than high sensitivity was privileged. To ensure true secondary AF (i.e., optimize specificity), our study criteria were designed to exclude both pre-existing primary AF and persistent AF. Unlike the retrospective study cited (2), we included only AF that was coded as a complication of the hospitalization and then additionally excluded patients who had received OAC in the prior year. We also excluded patients who had a previous hospital admission or physician visit with documented AF within the prior year. Thus we believe the patients included in our various cohorts had secondary AF, but we recognize we may not have identified all such patients.

The evidence for benefit of OAC in secondary AF associated with acute medical illness is limited in published reports and is further detailed in our study. Although residual confounding can always be cited to explain results in observational studies, the use of OAC in our study patients was associated with higher bleeding with little evidence of benefit on stroke prevention. The null findings may be more a problem of power than of confounding. The study by Fauchier and colleagues (3), which Dr. Um and colleagues quote, cannot be used as an example of benefit from OAC because this study included patients with primary AF. In fact, 551 of 2,009 (27.4%) of their study patients were reported to have permanent AF. It is unclear how this particular study specifically relates to determining possible benefit of OAC in patients with secondary AF.

Although our study was designed to look at stroke and bleeding risk, we look forward to the results of the ongoing multicenter study (AFOTS [Atrial Fibrillation Occurring Transiently With Stress]; NCT03221777) to determine rates of AF recurrence among patients who experienced transient AF following noncardiac surgery and medical illness. Indeed, little is known about the true risk of recurrence of AF in these patients. We support any further studies that can help define an optimal management strategy for secondary AF.