A Bridge Too Far?
Findings of Bridging Anticoagulation Use and Outcomes in the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF)

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In the current issue of Circulation, Steinberg et al describe the use and outcomes associated with bridging anticoagulation (AC) in patients with atrial fibrillation (AF) in the contemporary Outcomes Registry for Better Informed Treatment of AF (ORBIT-AF). Chronic oral anticoagulation (OAC) significantly reduces the risk of stroke or thromboembolism in patients with AF. Despite the growing population burden of AF, the increasing use of OAC, and the frequent need for cardiac and noncardiac procedures in this population, remarkably little contemporary data exist to help guide the clinician with respect to periprocedural AC decision making. Although guidelines exist on the topic, they are based on limited and largely observational data. Current guideline-supported periprocedural AC management supports the discontinuation of OAC and the use of short-acting AC, most commonly low-molecular-weight heparin or unfractionated heparin, to bridge AF patients at high risk for thromboembolic complications during the immediate pre- and postprocedure period (American College of Chest Physicians grade 2C; American Heart Association grade 1C).3,4

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“To bridge or not to bridge,” is a question often asked in clinical practice, with an estimated 250,000 patients on OAC undergoing cardiac and noncardiac procedures annually in North America. The authors are therefore to be congratulated for examining the topic of use and outcomes of bridging AC in an effort to better inform us and enhance the safety of our AF patients. Currently, the periprocedural management of patients who are receiving OAC is often informed by a clinician’s (1) assessment of patient risk for thromboembolism, (2) assessment of risk for perioperative bleeding, and (3) the type of procedure. Although CHADS2, CHA2DS2-VASc, HAS-BLED, and ATRIA scores are used in clinical practice to assess the risks of thromboembolism and bleeding, respectively, there are no validated risk stratification schemes specific to periprocedural AC decision making. Hence, the management of periprocedural AC among AF patients varies widely, as is evidenced by the findings of the present investigation. Further complicating the situation is the fact that the timing of OAC discontinuation, the timing of resumption of OAC, and the differences in type of short-acting AC agent used for bridging are areas where considerable uncertainty and practice variation remain.

Recent data, including from clinical trials of AF patients undergoing catheter ablation and cardiac device implantation, suggest that uninterrupted OAC therapies may be associated with a lower likelihood of bleeding than discontinuation of OAC with bridging. Consistent with the findings of these smaller studies, a recent meta-analysis including >12,000 patients undergoing an elective invasive procedure or surgery in 34 studies (however, only 1 randomized, controlled trial) showed that bridging therapy in patients with AF using OACs increased the risk of bleeding events with a similar risk of thromboembolic events. Nevertheless, few studies have examined current practices in periprocedural AC management in a large, contemporary cohort of real-world AF patients treated with novel and traditional OAC agents and undergoing a diverse array of cardiovascular and noncardiovascular procedures. Therefore, the findings of the present analysis, although consistent with previous studies, are of great importance and provide valuable new insights to the field.

Among ORBIT-AF participants, a bridging strategy was used in 1 of 4 AF patients who had interruption of OAC for a procedure. Not surprisingly, given the fact that clinicians often use stroke risk prediction instruments to guide periprocedural AC management, bridged AF patients generally had higher average CHADS2 and CHA2DS2-VASc scores or had a history of mechanical heart valve replacement. Despite their higher predicted risk for stroke based on prediction instruments, bridged patients in ORBIT-AF did not have a higher risk for thromboembolism over the 30 days following their procedure. This finding suggests that traditional thromboembolic risk prediction scores validated in ambulatory AF populations may not have merit as predictors of short-term periprocedural stroke/thromboembolism risk.

In contrast to thromboembolic events, bleeding events were much more common among ORBIT-AF participants who were bridged with a short-acting AC than among patients who were not bridged (5.0% versus 1.3%), even after the adjustment for factors affecting risk for bleeding (odds ratio, 3.8; P<0.0001). Although one might have expected higher bleeding risks among patients undergoing more invasive surgeries,
in a stratified analysis, procedure type did not significantly influence risk for bleeding. It is notable, however, that a significant minority (=1 in 10) of patients in ORBIT-AF were bridged for low-risk procedures (eg, dental procedures) not recommended for bridging based on current American College of Chest Physicians guidelines. This emphasizes that opportunities exist for improved education around current periprocedural AC guidelines.

This study by Steinberg et al is well positioned to examine the safety and efficacy of contemporary perioperative PC bridging practices and guidelines, but it does have several limitations that warrant consideration when interpreting its findings. Besides the fact that the observational study design precludes causal inference and introduces the possibility that unmeasured confounding may explain the observed differences between study groups, the study does not provide important information about why a decision was made to interrupt AC in some cases and not in others. Although this question was not the primary focus of the present investigation (which instead compared bridging versus not among those with interrupted OAC), the question as to whether or not uninterrupted OAC is superior to interrupted OAC without bridging with respect to thromboembolic and bleeding complications in patients undergoing cardiac and noncardiac procedures remains a critical unanswered question. Many cardiac electrophysiologists have already shifted practice away from OAC interruption for catheter-based procedures, including AF ablation, in the light of recent data showing fewer bleeding complications with uninterrupted OAC. Further study in this area is needed.

Another limitation of Steinberg's analysis is that it does not indicate whether or not OAC reversal agents (eg, vitamin K, fresh-frozen plasma) were used for the reversal of the AC effect, nor do the authors present data on the timing of the initiation and discontinuation of bridging AC agents, factors known to contribute to periprocedural bleeding complications. Moreover, the absolute number of ORBIT-AF participants with interrupted OAC, when grouped by procedure type, was relatively small (eg, cardiac surgery, n=109). Therefore, the results of secondary analyses showing similar rates of adverse events across all procedure types (eg, dental procedures and cardiac surgery) should be interpreted with some caution. We do not believe this analysis is adequately powered and suggest that providers should, until data from larger samples are available, continue to use the 3-tier risk stratification system proposed by the American College of Chest Physicians, which includes procedure type and duration as important contributors to periprocedural bleeding risk.

The time to achievement of therapeutic OAC after procedure was significantly shorter among patients bridged with a short-acting AC in comparison with those who were not bridged. Whether earlier achievement of a therapeutic international normalized ratio led to higher risk for bleeding in the bridged group remains unclear, especially because the timing of bridging AC discontinuation is not reported. One can imagine that patients on both bridging agents and therapeutic OAC would be at considerably higher risk than other patient subgroups.

Although this analysis would be of considerable importance, the authors were unable to compare the rates of bleeding complications by type of OAC (novel versus warfarin) based on the limited number of patients treated with dabigatran who had OAC interrupted. In contrast, a recent Randomized Evaluation of Long-term Anticoagulation Therapy (RE-LY) trial secondary data analysis was able to examine the topic and concluded that dabigatran-treated AF patients had increased risk of major bleeding without any significant difference for the risk of thromboembolism when a bridging strategy was used in comparison with patients who were not bridged. A recent multicenter study of 290 AF patients undergoing catheter ablation showed that periprocedural dabigatran use without interruption was associated with a higher risk of adverse events in comparison with uninterrupted warfarin therapy. In light of the increasing number of AF patients treated with novel OACs, further study is clearly needed to compare the risks for bleeding among AF patients treated with novel OAC versus warfarin who undergo a procedure, further stratified by whether or not a bridging strategy is used.

In this important study, Steinberg et al show that (1) OAC interruption was common (approximately half of AF patients over a 2-year follow-up), (2) a bridging strategy was used in a significant minority (1 in 4) of ORBIT-AF participants with interrupted OAC, and (3) bridging was associated with higher rates of bleeding and overall adverse event rates. These findings fly somewhat in the face of conventional dogma and may begin a paradigm shift away from the routine use of a bridging strategy for AF patients undergoing procedures.

We agree strongly with Steinberg et al that the results of randomized studies are needed to build on their foundational work. Randomized studies should not only examine whether or not AC is discontinued and bridging AC used, but should also examine whether or not outcomes differ by type of short-acting AC (heparin versus low-molecular-weight heparin), type of OAC (novel versus warfarin), or timing of initiation and discontinuation of bridging AC. Fortunately, 2 large randomized, placebo-controlled trials (Effectiveness of Bridging Anticoagulation for Surgery [BRIDGE] and A Safety and Effectiveness Study of LMWH Bridging Therapy Versus Placebo Bridging Therapy for Patients on Long Term Warfarin and Require Temporary Interruption of Their Warfarin [PERIOP-2]) are underway to better inform periprocedural AC decision making. For the time being, however, this investigation calls into serious question whether or not, in our efforts to reduce periprocedural thromboembolic complications from AF, we are in fact exposing patients to increased risk for harm from bleeding. To borrow the words of the British Lieutenant General Frederick Browning before the overreaching and unsuccessful Allied Market Garden campaign, “I think we may be going a bridge too far.”

**Disclosures**

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**References**


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