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Use and Outcomes Associated With Bridging During Anticoagulation Interruptions in Patients With Atrial Fibrillation

Findings From the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF)

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Background**—**Temporary interruption of oral anticoagulation for procedures is often required, and some propose using bridging anticoagulation. However, the use and outcomes of bridging during oral anticoagulation interruptions in clinical practice are unknown.

Methods and Results**—**The Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) registry is a prospective, observational registry study of US outpatients with atrial fibrillation. We recorded incident temporary interruptions of oral anticoagulation for a procedure, including the use and type of bridging therapy. Outcomes included multivariable-adjusted rates of myocardial infarction, stroke or systemic embolism, major bleeding, cause-specific hospitalization, and death within 30 days. Of 7372 patients treated with oral anticoagulation, 2803 overall interruption events occurred in 2200 patients (30%) at a median follow-up of 2 years. Bridging anticoagulants were used in 24% (n=665), predominantly low-molecular-weight heparin (73%, n=487) and unfractionated heparin (15%, n=97). Bridged patients were more likely to have had prior cerebrovascular events (22% versus 15%; *P*=0.0003) and mechanical valve replacements (9.6% versus 2.4%; *P*<0.0001); however, there was no difference in CHA_2DS_2-VASc scores (scores ≥2 in 94% versus 95%; *P*=0.5). Bleeding events were more common in bridged than nonbridged patients (5.0% versus 1.3%; adjusted odds ratio, 3.84; *P*<0.0001). The incidence of myocardial infarction, stroke or systemic embolism, major bleeding, hospitalization, or death within 30 days was also significantly higher in patients receiving bridging (13% versus 6.3%; adjusted odds ratio, 1.94; *P*=0.0001).

Conclusions**—**Bridging anticoagulation is used in one quarter of anticoagulation interruptions and is associated with higher risk for bleeding and adverse events. These data do not support the use of routine bridging, and additional data are needed to identify best practices concerning anticoagulation interruptions.

Clinical Trial Registration**—**URL: http://www.clinicaltrials.gov. Unique identifier: NCT01165710.

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Oral anticoagulation (OAC) significantly reduces the risk of stroke in patients with atrial fibrillation (AF). However, many AF patients on long-term anticoagulation undergo procedures that require temporary interruption of OAC.[1,2] Some have advocated that patients receive short-acting anticoagulants during these temporary interruptions to “bridge” the patient and to potentially reduce the risk

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of embolic events during the interruption.[3] Although guidelines have been published on when and how to initiate bridging therapy,[4] they are based on limited data. Thus, it remains unclear whether patients who temporarily interrupt their anticoagulation should receive bridging anticoagulation.

We assessed the incidence of temporary interruption of OAC for procedures among a national outpatient AF registry. We specifically examined causes for the interruption of anticoagulation, the patterns of use of bridging anticoagulation agents (relative to underlying risk and current guidelines), and the outcomes among patients who were bridged compared with patients who were not bridged.

Methods

The Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORIBT-AF) is a national, community-based registry of outpatients with AF. Eligible patients were enrolled by a nationally representative sample of primary care, cardiology, or electrophysiology sites. An adaptive design was used to ensure heterogeneity of practice type and geography. Study coordination was managed by the Duke Clinical Research Institute. Major inclusion criteria were age of ≥18 years and ECG-documented AF that was not attributable to a reversible cause, and follow-up was to a maximum of 3 years. The ORBIT-AF registry has been described in detail previously.[5] The present analysis includes patient data out to 2 years of follow-up.

Data collection was derived primarily from the patients' medical records and included demographics, medical history, and AF history at baseline. Additionally, at baseline and every 6 months, investigators recorded medical and surgical therapies, vital signs, laboratory measurements, and echocardiographic data. The collection of medication data included the use and monitoring of OAC therapies. Sites were also instructed to enter which OAC treatment was used, as well as values for international normalized ratio monitoring when applicable. At each follow-up, investigators were queried as to whether the patient temporarily interrupted OAC to undergo a procedure. Only interruptions for procedures were recorded; interruptions as a result of bleeding or other reasons are not captured. All medical management around the procedure was guided entirely by the patient's treatment team. For such interruptions, we collected the date and type of procedure, use of bridging anticoagulant (defined as an anticoagulant temporarily administered in place of long-term therapy for the purpose of stroke prevention before, during, or after the periprocedural period), and adverse events occurring during the interruption (bleeding event, thrombotic event, or other event; no further specification was reported). Type of procedure was categorized as cardiac catheterization, catheter ablation, endoscopy (gastrointestinal, bronchoscopic, or genitourinary), cardiac surgery, noncardiac surgery (not further specified), device implantation, dental procedures, or other (not further specified). Bridging anticoagulant was categorized as low-molecular-weight heparin (LMWH), unfractionated heparin (UFH), fondaparinux, or other (not further specified).

Separately at each follow-up, investigators recorded the incidence and dates of any adverse events, including death, cause-specific hospitalization (cardiovascular, bleeding, or other, as determined by the investigator), incident heart failure, myocardial infarction, stroke or systemic embolism (adjudicated by the coordinating center from primary source documentation), or major bleeding as defined by the International Society of Thrombosis and Haemostasis criteria.[6]

Analyzing Temporary Interruptions

The present analysis included only patients on OAC at baseline who had at least 1 follow-up visit. The study population was subsequently divided by incidence of interruption during follow-up: none versus any (≥1). The baseline characteristics of these patients were compared.

Subsequently, all interruption events were queried for the type of procedure requiring interruption and the use of bridging anticoagulant. Additionally, the use of bridging anticoagulation was compared among high-risk subgroups. Among patients using warfarin, time to resumption of therapeutic international normalized ratio (≥2) was calculated. The use of bridging anticoagulation in the subgroup of patients receiving dabigatran was also described.

Adverse events occurring during the interruption of long-term anticoagulation (bleeding, thrombotic, or other [not further detailed]) are described and stratified by the use of any bridging anticoagulant versus none. The incidence and timing of adverse events occurring within 30 days after the date of the procedure for which there was an interruption are also described (and may overlap with those occurring during interruption); these include cause-specific hospitalization and the composite of myocardial infarction, stroke, major bleeding, hospitalization, or death. The association of bridging with adverse events was assessed in a multivariable model of the composite outcome.

Statistical Methods

Comparisons between groups with no interruption and groups with any interruption are performed at the patient level. Comparisons between procedure types, bridging anticoagulant, and adverse events are performed at the interruption level (a patient may have had >1 interruption during follow-up). In univariate analyses, categorical variables are presented as frequencies and percentages, and differences between 2 groups are assessed by the χ^2 test. Continuous variables are presented as median (quartiles 1–3) or mean (standard deviation), and differences between 2 groups are assessed by the Wilcoxon rank-sum test.

In analysis of adverse events within 30 days after interruption, multiple interruption events from the same patient were included unless the interruptions occurred within 30 days of a prior interruption. However, interruption events were excluded if the date was missing. To identify the association between the use of any bridging anticoagulant and adverse events, a multivariable model was developed. Covariates included age, estimated glomerular filtration rate, sex, prior cerebrovascular events, the presence of significant valvular disease or prior mechanical valve replacement, prior gastrointestinal bleeding, the presence of congestive heart failure, type of AF at baseline (new onset, paroxysmal, persistent, longstanding persistent), left atrial diameter size, patient level of education, $CHADS_2$ score, the procedure requiring interruption (with noncardiac surgery as the referent), and type of OAC at baseline (warfarin versus dabigatran; neither rivaroxaban nor apixaban was used in this cohort). The outcomes examined included any bleeding events (major bleeding or bleeding hospitalization); cardiovascular events (stroke, systemic embolism, myocardial infarction, or cardiovascular hospitalization); and the composite of any myocardial infarction, stroke or systemic embolism, any hospitalization, or death, all within 30 days after the date of the procedure requiring interruption. Adjusted odds ratios (ORs) were calculated from logistic regression with the generalized estimating equation, which also accounted for correlations within the same patient.

The ORBIT-AF registry was approved by the institutional review board of Duke University, and each site received institutional review board approval subject to local requirements. All patients signed written, informed consent, and analyses of the aggregate, deidentified data were performed by the Duke Clinical Research Institute using SAS software (version 9.3, SAS Institute, Cary, NC).

Results

The overall ORBIT-AF population included 10 132 patients from 176 sites; 9642 patients had at least 1 follow-up visit. Excluding patients not on OAC at baseline (n=2270) yielded a final study cohort of 7372 patients. The median follow-up duration was 24 months. Overall, there were 2803 reported interruptions, the majority in noncardiac surgery (n=746, 27%), other procedures (n=712, 25%), and endoscopy (n=504 18%). Overall, 2138 interruptions (76%) did not use bridging anticoagulation, whereas 665 (24%) did. Distribution of bridging use by procedure is shown in the Figure.

Among the 665 interruption events that involved bridging anticoagulation, LMWH was used in 487 (73%), UFH in 97 (15%), fondaparinux in 7 (1.1%), and another anticoagulant in

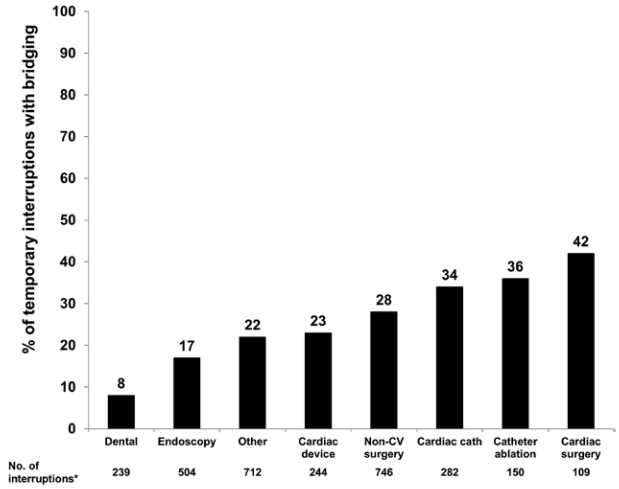

Figure. Proportion of interruptions involving anticoagulant bridging by procedure. Endoscopy includes gastrointestinal, genitourinary, or bronchoscopic. cath indicates catheterization; and CV, cardiovascular.

76 (11%). Twenty-three interruptions involving bridging were in patients treated with dabigatran at baseline: 12 used LMWH, 6 used UFH, and 5 used other agents (none used fondaparinux).

A comparison of baseline characteristics between patients with no interruption (n=5172, 70%) and those with ≥1 interruption during follow-up (n=2200, 30%) stratified by bridging use is shown in Table 1. Compared with patients who did not have any interruption, those experiencing at least 1 interruption were slightly younger (median age, 75 versus 76 years; *P*=0.0002), more likely white (92% versus 89%; *P*=0.005), and less likely to have new-onset AF (2.6% versus 4.3%; *P*=0.0001) and had higher median calculated creatinine clearance (71 versus 69 $mL \cdot min^{-1} \cdot 1.72\ m^{-2}$; *P*=0.002).[7] Rates of prior coronary vascular or cerebrovascular disease, as well as mean $CHADS_2$ scores, were all similar (*P*=NS for each). Of patients with at least 1 interruption, patients with any bridging interruption were statistically younger (median age, 74 versus 75 years; *P*=0.009) and were more likely to have congestive heart failure (44% versus 34%; *P*<0.0001), prior cerebrovascular events (22% versus 15%; *P*=0.0003), any valve disease (34% versus 27%; *P*=0.0006), and prior mechanical valve (9.6% versus 2.4%; *P*<0.0001) compared with patients who had at least 1 interruption but none with bridging. Baseline OAC also differed significantly (dabigatran in 3.7% versus 6.8%; *P*=0.02). Although mean $CHADS_2$ (2.53 versus 2.34; *P*=0.004) and CHA_2DS_2-VASc (4.25 versus 4.03; *P*=0.01) scores were higher in bridged patients, there were no differences in rates of $CHADS_2$ score ≥2 (78% versus 76%; *P*=0.4) or CHA_2DS_2-VASc score ≥2 (94% versus 95%; *P*=0.5). Use of additional antiplatelet therapy was similar for concomitant single antiplatelet (39% versus 36%) and dual antiplatelet therapy (3.0% versus 2.2%; *P*=0.2 across antiplatelet categories).

Among patients treated with warfarin who had at least 1 follow-up international normalized ratio after the procedure (n=1452), time to the achievement of the therapeutic range (first international normalized ratio ≥2) after the procedure was significantly shorter for interruptions with bridging compared with those without bridging (median, 17 versus 23 days; *P*<0.001).[8]

Outcomes

Unadjusted rates of individual outcomes during and after interruption are shown in Table 2. Events during interruption were relatively infrequent overall. Event rates were higher for interruptions in which bridging anticoagulation was used, including any adverse event during interruption (5.3% versus 2.8%; *P*=0.01), major bleeding (3.6% versus 1.2%; *P*=0.0007), bleeding hospitalization (2.2% versus 0.7%; *P*=0.006), and cardiovascular hospitalization (4.2% versus 2.2%; *P*=0.02). Event counts and rates across different procedure types stratified by bridging are shown in Table 3.

The association between bridging and adverse events persisted in multivariate-adjusted analysis (Table 4): The use of bridging anticoagulation during interruption was significantly associated with an increase in bleeding events (adjusted OR, 3.84 for major bleeding or bleeding hospitalization; 95% confidence interval, 2.07–7.14; *P*<0.0001) and showed a trend toward increased cardiovascular events (adjusted OR, 1.62; 95% confidence interval, 0.95–2.78; *P*=0.07). Overall, bridging was associated with an increased risk of adverse events, including the composite of myocardial infarction, bleeding, stroke or systemic embolism, hospitalization, or death within 30 days (adjusted OR 1.94; 95% confidence interval, 1.38–2.71; *P*=0.0001). The procedure for which the patient required interruption appeared to minimally influence composite adverse outcomes (*P*=0.2 across all procedures); however, adverse events were significantly less common for dental procedures (adjusted OR, 0.19 versus noncardiac surgery; 95% confidence interval, 0.06–0.63, $P_{pairwise}$=0.0063). Baseline anticoagulant (warfarin versus dabigatran) was not significantly associated with outcomes after temporary interruption in the adjusted model.

In a sensitivity analysis that included baseline concomitant antiplatelet use (none, single, double), a consistent, significant association remained between bridging and adverse outcome.

Discussion

There are 3 major findings from this study. First, interruptions of OAC are common in contemporary patients with AF in clinical practice, often for cardiac procedures and noncardiac surgery, as well as for minimally invasive procedures. Second, in those temporary interruptions, bridging anticoagulation was used in approximately one quarter of patients, and the decision to use bridging appears to be guided by patient factors related to bleeding or thromboembolic risk. Finally, we found that the use of bridging anticoagulation was significantly associated with higher overall bleeding and adverse event rates.

The rate of bridging anticoagulation was higher than that reported in contemporary trials.[9] Patients with prior cerebrovascular events, those with mechanical valves, and patients receiving warfarin (compared with dabigatran) were more likely to receive bridging anticoagulation, as would be expected. Additionally, bridging varied by type of procedure. These data generally reflect the limited guideline support for bridging, specifically that the decision for bridging in moderate- or high-risk patients should be patient and procedure specific and that bridging in patients at low risk of thromboembolism should be avoided.[4] Furthermore, the guidelines recommend more conservative management of bridging medications and call attention to scenarios in which OAC could be continued without

Table 1. Baseline Demographics, Medical History, and Laboratory Studies by Incidence of Temporary Interruption

	No Temporary Interruption (n=5172)	≥1 Temporary Interruptions (n=2200)		
		Patients With ≥1 Interruptions, None With Bridging (n=1608)	Patients With ≥1 Interruptions With Bridging (n=592)	*P* Value, No Bridging Versus Bridging
Age, y	76 (68–82)	75 (68–81)	74 (67–80)	0.009
Female, %	43	41	42	0.7
Race/ethnicity, %				0.1
White	89	92	91	
Black	5.0	3.5	5	
Hispanic	4.6	3.7	2.7	
Other	1.5	1.2	0.5	
AF type, %				0.5
New onset	4.3	2.7	2.2	
Paroxysmal	46	46	48	
Persistent	19	16	17	
Long-standing persistent	31	35	32	
$CHADS_2$ score, mean (SD)	2.4 (1.3)	2.34 (1.21)	2.53 (1.31)	0.004
CHA_2DS_2-VASc score, mean (SD)	4.0 (1.7)	4.03 (1.62)	4.25 (1.74)	0.01
ATRIA score, mean (SD)	2.78 (1.89)	2.74 (1.94)	2.72 (1.95)	0.9
Prior cerebrovascular event, %	17	15	22	0.0003
Coronary artery disease, %	36	36	41	0.05
Congestive heart failure, %	34	34	44	<0.0001
Significant valve disease, %	27	27	34	0.0006
Moderate/severe mitral stenosis, %	1.7	1.1	2.5	0.01
Prior mechanical valve replacement, %	3.6	2.4	9.6	<0.0001
Prior GI bleeding, %				0.97
Never	92	91	91	
>6 mo prior	6.9	1.4	1.5	
≤6 mo prior	0.8	7.3	7.1	
Baseline oral anticoagulant, %				0.02
Warfarin	93	93	96	
Dabigatran	6.5	6.8	3.7	
Most recent INR before the procedure, mean (SD)	…	2.34 (0.76)	2.28 (0.71)	0.3
Percentage of time with INR 2–3 before the procedure, %*	…	67	62	0.0002
Concomitant antiplatelet, %†				
Aspirin	36	36	38	0.4
Clopidogrel	4.5	4.2	6.9	0.01
Prasugrel	0.03	0.06	0	0.5
Calculated creatinine clearance, $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$‡	69 (49–95)	71 (54–97)	70 (51–96)	0.3
LVEF, %	55 (50–60)	55 (50–60)	55 (45–60)	<0.001

Values are presented as median (interquartile range) when appropriate. AF indicates atrial fibrillation; ATRIA, Anticoagulation and Risk Factors in Atrial Fibrillation; GI, gastrointestinal; INR, international normalized ratio; and LVEF, left ventricular ejection fraction.

*As calculated using the Rosendaal et al[8] method.

†Including aspirin, clopidogrel, or prasugrel; no patient was on ticagrelor.

‡As calculated by the Cockcroft-Gault[7] formula.

interruption (eg, dental procedures). Although this appears to demonstrate improvement in the previously described practice variability,[10] room for further improvement remains, as indicated by the data in this study. Bridging anticoagulation appeared to be used more commonly than the guidelines would suggest. For example, we observed that a significant number of OAC interruptions were for dental procedures (n=239, 9% of all interruptions), and 8% of these temporary interruptions

Table 2. Unadjusted Outcomes During and After Temporary Interruption of OAC

	Overall (n=2280), % (n)	No Bridging (n=1766), % (n)	Bridging (n=514), % (n)	*P* Value
Any adverse event during interruption	3.4 (77)	2.8 (50)	5.3 (27)	0.01
Bleeding event	2.2 (50)	1.8 (31)	3.7 (19)	0.02
Thrombotic event	0.6 (13)	0.5 (9)	0.8 (4)	0.5
Other adverse event	0.6 (14)	0.6 (10)	0.8 (4)	0.6
Events within 30 d after the procedure requiring interruption*				
Myocardial infarction	0.2 (5)	0.2 (4)	0.2 (1)	0.9
Stroke or systemic embolism	0.4 (8)	0.3 (5)	0.6 (3)	0.3
Major bleeding	1.7 (38)	1.2 (20)	3.6 (18)	0.0007
Hospitalization				
Cardiovascular	2.7 (59)	2.2 (38)	4.2 (21)	0.02
Bleeding	1.0 (23)	0.7 (12)	2.2 (11)	0.006
Other	3.1 (69)	2.8 (49)	4.0 (20)	0.2
Death	0.2 (4)	0.2 (3)	0.2 (1)	0.9

OAC indicates oral anticoagulation.

*Denominators exclude interruptions missing date or those that occurred within 30 days of a previous interruption (n=2227 overall, 1724 without bridging, 503 with bridging). Events within 30 days of the procedure requiring interruption may overlap with those during interruption.

involved the use of a bridging anticoagulant. Furthermore, there were excess adverse events in bridged patients undergoing specific procedures (eg, catheter ablation, endoscopy), indicating particularly unfavorable risk in these cases. Such management may contribute to worse clinical outcomes overall, and our data do not support the routine use of bridging in AF patients requiring temporary interruption of anticoagulation.

Our data show that the risks associated with interruptions and the risk of bridging during them are not limited to the periprocedural period. Adverse events in patients interrupting OAC persist as late as 30 days and include bleeding events, thrombotic events, and recurrent hospitalizations. Although the use of bridging has been shown to be safe in closely controlled clinical trials,[3,11] outcomes in the community, where protocols are often absent or inconsistent, have been more limited. They included heterogeneous patient cohorts anticoagulated for a variety of indications, and only bleeding and thromboembolic outcomes were reported.[1,2]

Table 3. Adverse Events Within 30 Days by Procedure Type and Bridging Anticoagulation

	Cardiovascular Events, n (%)*		Bleeding Events, n (%)†	
	No Bridging (n=1724)	Bridging (n=503)	No Bridging (n=1724)	Bridging (n=503)
Catheterization/PCI	9/139 (6.5)	3/65 (4.6)	2/139 (1.4)	1/65 (1.5)
Catheter ablation	1/66 (1.5)	5/41 (12.2)	1/66 (1.5)	0/41 (0)
Endoscopic procedure	9/343 (2.6)	2/64 (3.1)	5/343 (1.5)	5/64 (7.8)
Cardiac surgery	3/48 (6.3)	2/28 (7.1)	2/48 (4.2)	2/28 (7.1)
Noncardiac surgery	6/410 (1.5)	2/149 (1.3)	5/410 (1.2)	12/149 (8.1)
Device implantation	9/139 (6.5)	2/38 (5.3)	0/139 (0)	0/38 (0)
Dental work	1/166 (0.6)	0/16 (0)	0/166 (0)	0/16 (0)
Other	5/413 (1.2)	7/102 (6.9)	7/413 (1.7)	5/102 (4.9)

Excluding interruptions missing a date or those that occurred within 30 days of a previous interruption. PCI indicates percutaneous coronary intervention.

*Includes stroke, systemic embolism, myocardial infarction, or cardiovascular hospitalization within 30 days of the procedure requiring interruption.

†Includes major bleeding or bleeding hospitalization within 30 days of the procedure requiring interruption.

Table 4. Adjusted 30-Day Outcomes by Use of Bridging Anticoagulation

	Unadjusted, % (n)			Adjusted*	
	No Bridging (n=1724)	Bridging (n=503)	*P* Value	Adjusted OR (95% CI), Bridging Versus No Bridging	*P* Value
Cardiovascular events†	2.5 (43)	4.6 (23)	0.02	1.62 (0.95–2.78)	0.07
Bleeding events‡	1.3 (22)	5.0 (25)	<0.0001	3.84 (2.07–7.14)	<0.0001
Overall composite§	6.3 (108)	13 (64)	<0.0001	1.94 (1.38–2.71)	0.0001

Denominators exclude interruptions missing a date or those that occurred within 30 days of a previous interruption. Events within 30 days of the procedure requiring interruption may overlap with those during interruption. CI indicates confidence interval; and OR, odds ratio.

*Adjustment model covariates included age, estimated glomerular filtration rate, sex, prior cerebrovascular events, the presence of significant valvular disease or prior mechanical valve replacement, prior gastrointestinal bleeding, the presence of congestive heart failure, type of atrial fibrillation at baseline (new onset, paroxysmal, persistent, long-standing persistent), left atrial diameter size, patient level of education, $CHADS_2$ score, procedure requiring interruption (with noncardiac surgery as the referent), and type of oral anticoagulation at baseline (warfarin versus dabigatran; neither rivaroxaban nor apixaban was used in this cohort).

†Includes stroke, systemic embolism, myocardial infarction, or cardiovascular hospitalization within 30 days of the procedure requiring interruption.

‡Includes major bleeding or bleeding hospitalization within 30 days of the procedure requiring interruption.

§Includes the composite of stroke, myocardial infarction, major bleeding, hospitalization, or death within 30 days of the procedure requiring interruption.

The most recent US national guidelines highlight the dearth of evidence for the practice[12]; furthermore, there is mounting evidence that certain procedures may be performed more safely with anticoagulation uninterrupted.[13,14] Importantly, there is less experience with uninterrupted, direct-acting OACs in this setting.[15,16] The risks of bridging likely highlight the challenges in managing patients on OAC in the periprocedural period. In the patient receiving bridging agents, both of the most common drugs (UFH and LMWH) require attention to dosing to prevent bleeding and to provide anticoagulant effect (UFH on a continuous basis; LMWH with changes in weight, kidney function, or in pregnancy). Additionally, many patients require transitions in anticoagulants at the same time they are experiencing a transition in care (eg, on admission, from the intensive care unit to the floor, or during discharge to another facility or home). Such circumstances likely contribute to an increased risk associated with the use of short-term anticoagulants. Close attention to anticoagulant transitions and dosing is vital to minimizing risk.[17] Properly identifying the group of patients, if any, in whom the risk of these pitfalls is outweighed by the benefit of OAC interruption and bridging remains a challenge. They are likely to include patients at extremely high risk of periprocedural thromboembolic events (eg, those with mechanical mitral valve prostheses) undergoing procedures for which uninterrupted, periprocedural anticoagulation is prohibitively dangerous (eg, neurological procedures).

Some have speculated that, in patients at lower risk of bleeding, bridging may be worthwhile.[11] However, in our cohort of AF patients, most of whom had low-risk Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) bleeding scores, we found that bridging anticoagulation was still significantly associated with worse clinical events at 30 days, particularly bleeding and bleeding hospitalizations. This said, the results here are observational, and we cannot rule out the beneficial role of bridging in select circumstances. The ongoing Effectiveness of Bridging Anticoagulation for Surgery (BRIDGE) study, which randomized nearly 2500 warfarin-treated patients undergoing surgery to either LMWH or placebo during the perioperative period, will provide additional insight (http://www.clinicaltrials.gov; NCT00786474).

Importantly, we also observed the use of bridging anticoagulation in patients receiving the oral direct thrombin inhibitor dabigatran. Although guidelines on the use of novel OACs in the setting of procedures are limited,[18] their pharmacokinetics are such that bridging is likely redundant (although this remains to be proven in patients at high risk of thromboembolic events). In contrast to warfarin, which requires several days both to take effect and to wash out, direct-acting anticoagulants demonstrate short time to onset and are cleared relatively quickly, similar to LMWHs. Thus, the use of bridging anticoagulants in such patients has been cautioned; however, additional studies are needed.[9]

Limitations

This analysis is derived from the ORBIT-AF registry, which is an observational study of real-world patients in community, clinical practice. Limitations of such a study include enrollment or sampling biases and reporting bias. Because patients were not randomized either to the occurrence of an interruption or to the use of bridging, a causal relationship between these events and adverse outcomes cannot be confirmed. Furthermore, it is possible that postprocedure parenteral anticoagulation is a requirement of the procedure; thus, use of such an agent would occur regardless of whether a patient is on long-term OAC. Data for patients who undergo procedures without interruption and for those who interrupt anticoagulation for reasons other than procedures are not available; thus, we cannot comment on the implications of our findings for these groups. Finally, despite statistical methods aimed at adjusting for baseline differences in the population, we cannot exclude residual or unmeasured confounding of the results.

Conclusions

Temporary interruptions are common in patients receiving OAC for AF and occur even for minimally invasive procedures. Many patients receive bridging anticoagulation, and its use varies by procedure type and certain patient characteristics. Use of bridging anticoagulation was associated with an increased risk of bleeding and adverse events after interruption. These data do not support the use of routine bridging in anticoagulated patients with AF, and additional data are needed to identify best practices concerning anticoagulation interruptions.

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CLINICAL PERSPECTIVE

Patients receiving oral anticoagulation often require temporary interruption of such therapy for invasive procedures. Often, bridging with short-acting anticoagulants is used; however, the safety and effectiveness of such an approach have not been proven. We assessed the association between bridging anticoagulation and clinical outcomes in patients with atrial fibrillation receiving anticoagulation that was temporarily interrupted for a procedure. Among 7372 community outpatients in the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) registry treated with oral anticoagulation at baseline, 2803 overall interruption events occurred in 2200 patients (30%) at a median follow-up of 2 years. Bridging anticoagulants were used in 24% (n=665), most commonly with low-molecular-weight heparin (73%, n=487) and unfractionated heparin (15%, n=97). After adjustment for known confounders, bleeding events were more common in bridged than nonbridged patients (5.0% versus 1.3%; adjusted odds ratio, 3.84; $P<0.0001$). The incidence of myocardial infarction, stroke or systemic embolism, major bleeding, hospitalization, or death within 30 days was also significantly higher in patients receiving bridging (13% versus 6.3%; adjusted odds ratio, 1.94; $P=0.0001$). These data call into question the safety of routinely bridging patients on oral anticoagulation who require temporary interruption for a procedure. Additional prospective trials are necessary to identify in which patients, if any, the benefit of bridging outweighs the risk.

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