Periprocedural Anticoagulation Management of Patients receiving Warfarin in Qatar: A Prospective Cohort Study

Islam Eljilany, MSc[a], Mohamed Elarref, MD[b],
Nabil Shallik, MD[b,c],
Abdel-Naser Elzouki, MBChB, DTM&H, MSc, MD, PhD,
FRCP (UK)[c,d,e],
AbdulMoqeeth Mohammed, CCT (UK), MRCGP (UK),
PG Med Edu (UK)[d], Bassam Shoman, MD[f],
Sami Ibrahim, MD, DPHE, CIPS, FIPP[g,h],
Cornelia Carr, MD[e,f], Daoud Al-Badriyeh, PhD[a],
Larisa H. Cavallari, PhD[i], and
Hazem Elewa, RPh, PhD, BCPS[a,i]

From the [a] College of Pharmacy, QU Health, Qatar University, Doha, Qatar, [b] Department of anesthesia, Hamad General Hospital, Hamad Medical corporation, Doha, Qatar, [c] Weill Cornell Medical College, Doha, Qatar, [d] Department of Medicine, Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar, [e] College of Medicine, Qatar University, Doha, Qatar, [f] Department of Cardiothoracic Surgery, Heart Hospital, Hamad Medical corporation, Doha, Qatar, [g] Department of anesthesia, Al Wakra Hospital, Hamad Medical corporation, Doha, Qatar, [h] Faculty of Medicine, Zagazig University, Zagazig, Egypt, [i] Department of Pharmacotherapy and Translation Research, Center for Pharmacogenomics and Precision Medicine, College of Pharmacy, University of Florida, Gainesville, Florida, USA and [j] Biomedical and Pharmaceutical Research Unit, QU Health, Qatar University, Doha, Qatar.

Abstract: *Background:* **The use of anticoagulant bridging remains controversial. This study was conducted to evaluate our warfarin periprocedural management in Qatar and investigate the associated clinical outcomes with such management.** *Methods:* **A prospective cohort study was designed to describe the periprocedural clinical practice in warfarin patients**

in Qatar and to compare clinical safety and efficacy outcomes between anticoagulant bridging and non-bridging. *Results:* 103 patients were recruited. Bridging occurred in 82% of the participants. No thromboembolic events were observed, while 39.1% of patients experienced bleeding events during the study period. The incidence of overall bleeding and major bleeding were numerically higher for bridging group compared to nonbridging but did not reach statistical significance ([30.6% vs 22.2%, $P = 0.478$] and [12.9% vs 5.6%, $P = 0.375$], respectively). *Conclusion:* Warfarin interruption and bridging are overwhelmingly used in warfarin-treated patients in Qatar. While bridging was numerically associated with increased bleeding events, there is no statistical difference in reported clinical events between bridging and nonbridging strategies. (Curr Probl Cardiol 2021;46:100816.)

Introduction

Need for warfarin interruption prior to elective procedures affects about 250,000 patients annually in the United States of America and Canada alone.[1] Managing warfarin, particularly in the periprocedural period, raises many concerns, primarily how to achieve balance between thromboembolic and bleeding risks. The discontinuation of warfarin may elevate the risk of thromboembolism (TE), while its continuation can boost the risk of bleeding during and/or after the procedure.[2,3] Another concern is the potential risk of TE when warfarin is interrupted periprocedurally.[4] To balance these risks and overcome these concerns, standard clinical guidance has been put in place when a procedure is scheduled for warfarin patients. Warfarin treatment is typically discontinued if the procedure has more than minimal risk of bleeding. Warfarin is paused 5-7 days prior to the elective procedure to let its anticoagulant effect diminish.[5,6] The choice of bridging with parenteral anticoagulation therapy (typically with intravenous unfractionated heparin (UFH) or subcutaneous low molecular-weight heparin (LMWH)), for the period of the interruption of warfarin treatment is made if the risk of TE is significant and exceeds the risk of bleeding. The objective of this step is to allow the continuation of the anticoagulation during the transient holding of warfarin. Finally, when hemostasis is secured after the procedure, warfarin is

resumed (with bridging if the risk of TE is significant and exceeds the risk of bleeding). The resumption of warfarin needs 5-10 days of treatment to achieve therapeutic anticoagulation.[7,8]

In 2015, 2 major trials reported the clinical outcomes associated with bridging. The Outcomes Registry for Better Informed Treatment of Atrial Fibrillation study (ORBIT-AF)[9] revealed that anticoagulation disruptions is associated with higher risk for bleeding (Adjusted odds ratio [OR], 3.84 for major bleeding; 95% confidence interval [CI], 2.07-7.14; P < 0.0001) and higher risk of adverse events including the composite of myocardial infarction, bleeding, stroke or systemic embolism (Adjusted OR, 1.94; 95% CI, 1.38-2.71; P = 0.07). The Bridging Anticoagulation in Patients who Require Temporary Interruption of Warfarin Therapy for an Elective Invasive Procedure or Surgery (BRIDGE) trial,[10] on the other hand was a large double-blind randomized clinical trial (RCT), comparing bridging anticoagulation versus nonbridging in patients with atrial fibrillation (AF) who interrupted warfarin. The study showed that nonbridging was associated with a significant reduction in major bleeding compared to bridging (relative risk [RR], 0.41; 95% CI, 0.20-0.78; P = 0.005). Furthermore, there was no statistical difference in terms of TE events between groups. Unfortunately, these results could not be generalized as the study included AF patients only and predominantly those with low to moderate stroke risk (CHA_2DS_2 score < 3). Both studies compound the uncertainty of the necessity of bridging during the warfarin interruption period.

Current guidelines such as the American College of Chest Physicians (ACCP) endorse an individualized approach to define the need for warfarin bridging based on the patient's anticipated periprocedural bleeding and thromboembolic risk.[11] Nevertheless, these recommendations have weak level of evidence (Level 2C), indicating the absence of high-quality evidence. All the above shows the uncertainty linked with ideal periprocedural warfarin management and the usefulness of bridging therapy, which creates different practices among health care providers (HCPs). The decision of warfarin interruption according to patient's and procedure's bleeding risks is considered another debate.

Our group recently surveyed practitioners in Qatar on their knowledge and practices during the periprocedural management of warfarin and revealed wide variation in the responders' practice.[12] Consequently, this study was designed to evaluate the real-world clinical practice of warfarin periprocedural management and investigate the clinical outcomes associated with warfarin bridging versus nonbridging in Qatar.

Methods

Study Design

The current study is part of an ongoing prospective cohort study that investigates the effect of genetic and nongenetic factors on international normalization ratio (INR) decline in Arabs undergoing warfarin interruption prior to elective surgery. We hereby report the clinical practice of warfarin interruption and the associated clinical outcomes and compare the clinical events in patients undergoing warfarin bridging and those without bridging. The study was performed over 24 months from September 2018 till September 2020.

Study Setting and Ethics Approval

The study was conducted at Al Wakra Hospital (AWH), Hamad General Hospital (HGH), and the Heart Hospital (HH). These 3 sites are part of Hamad Medical Corporation (HMC), the major medical institution in Qatar. Patients were recruited from anticoagulation, cardiology, anesthesia, or surgery clinics. Ethical approval was obtained from the Institutional Review Board (IRB) of HMC (Protocol# MRC-16415/16) and Qatar University (QU-IRB 1296-FBA/20).

Population

A sample of convenience was used in this study. Inclusion criteria included patients of Arab descent (as confirmed by the reported patient nationality) undergoing elective surgery that requires warfarin discontinuation as per planned clinical decision for 3 days or more; age $\geq$ 18 years old, and treatment with warfarin for at least one month with a stable INR for the last 2 consecutive visits with a minimum one-week interval. A stable INR was defined as INR within $\pm$ 0.2 units of the target therapeutic range.[13] Patients were excluded if they had an emergency procedure or minor procedure that required warfarin interruption for 1-2 days; were scheduled for a procedure but did not stop warfarin, received vitamin K, fresh frozen plasma, or Prothrombin complex concentrates (PCC) during the preoperative period; or had major bleeding (MB) within the previous month. The definition of major bleeding was summarized in Appendix 1.

Data Collection

Following subjects' screening and consent, data on patient's demographics, characteristics, and relevant clinical information were collected.

A clinical investigator from each facility was responsible for patient recruitment and data collection. All data was then sent to the principal investigator, who was responsible for the maintenance of the study database, data validation, and analyses.

Periprocedural Management of Warfarin

Periprocedural management of warfarin was according to the treating HCP's decision as there was no unified protocol among the 3 facilities to instruct on when stop and resume warfarin perioperatively and whether bridging should be applied. The most common practice was to pause warfarin for 5 days before the procedure, then bridge with UFH or LMWH when INR < 2 (typically 3 days prior to the procedure with the last dose 24 hours prior to the procedure for LMWH and 6 hours prior to the procedure for UFH). Following the procedure, warfarin, at the preoperative dose, and UF or LMWH were restarted 12-24 hours postprocedure provided that the patient has normal hemostasis and was stable. Bridging medication was stopped when the INR became therapeutic. Bridging anticoagulation was defined as perioperative use of a therapeutic dose of LMWH (e. g. enoxaparin 1 mg/kg subcutaneously [SC] twice daily, dalteparin sodium 100 IU/Kg SC twice daily) or I.V UFH 18 IU/Kg/hr. before and/or after the procedure.

Categorization of Procedures

Procedures were categorized into minor or major according to the same classification used in BRIDGE[10] and RELY- trials.[14] Minor or low-bleeding risk surgery was any surgery lasting for less than 1 hour, otherwise, it was classified as major or high-bleeding risk surgery. Some examples are shown in Appendix 2.

Study Outcome

Study outcomes from the time of warfarin interruption until 30 days after the procedure were recorded, with an average total period of 35 ± 2 days. The clinical outcomes were reported through electronic health records and confirmed via follow-up phone calls with the patients. The study outcomes include any major or minor hemorrhage, or TE event like ischemic stroke (IS), systemic embolism (SE), myocardial infarction (MI), deep vein thrombosis (DVT), or pulmonary embolism (PE). The definitions of clinical outcomes were summarized in Appendix 1.

Statistical Analyses

For baseline and patient characteristics, continuous data was presented as mean ± SD or median and interquartile range (IQR). Independent Student's t-test and Mann-Whitney U tests were used for comparing means and medians, respectively. Categorical variables were reported as counts and frequencies. Comparison between categorical data of both bridging and nonbridging groups was performed using the Chi-Square test.

For clinical outcomes and adverse events at 30 days postprocedure, data was expressed as count and frequency. Differences in clinical outcomes between the 2 groups were tested using univariate analysis. Significant differences were further evaluated through multivariate analysis (logistic regression). Logistic regression was also used to determine other factors [body mass index (BMI) ($\leq$25 or >25 kg/m^2), CHF, dyslipidemia, hypertension, and AF conditions, CHA$_2$DS$_2$-Vasc score ($\leq$4 or >4 points) as low and moderate/ high, HAS-BLED score ($\leq$ 2 or > 2 points) as low and moderate/high, procedure type (minor or major), vitamin_K intake as low and medium/high and taking high bleeding risk medications] associated with clinical outcomes and was expressed as odds ratio (OR) and 95 % confidence interval (CI). IBM Statistical Package for Social Science (IBM SPSS 26 software; IBM, New York) was used to carry out the statistical analysis. A two-tailed p-value of <0.05 was considered significant.

Results

Patient Demographics

One hundred and ninety-eight patients underwent at least one procedure during the study period, but 48% of them were excluded for different reasons (Fig 1). One hundred and three patients were recruited from the 3 healthcare facilities over 2 years, with an average of 1 patient/week. Bridging was performed in 85 patients (82.5%) while the remaining 18 subjects (17.5%) were in the nonbridging group. Table 1 summarizes the patient characteristics. Patients' mean age was 58.7±14.5 years, with a median (IQR) BMI 31.6 (34.5) Kg/m^2; BMI was significantly higher in the bridging compared to the nonbridging group (32.2 vs 30.1, P= 0.036). About half (56, 53.3%) of the participants were males. The local population (Qatari citizens) represented 40% of the total participants. Fifty-eight patients (56.3%) had AF as their main indication for warfarin. One out of 5 (20%) of the patients were taking aspirin alone or in combination with clopidogrel. The median (IQR) of CHA$_2$DS$_2$-VASc and HAS-BLED
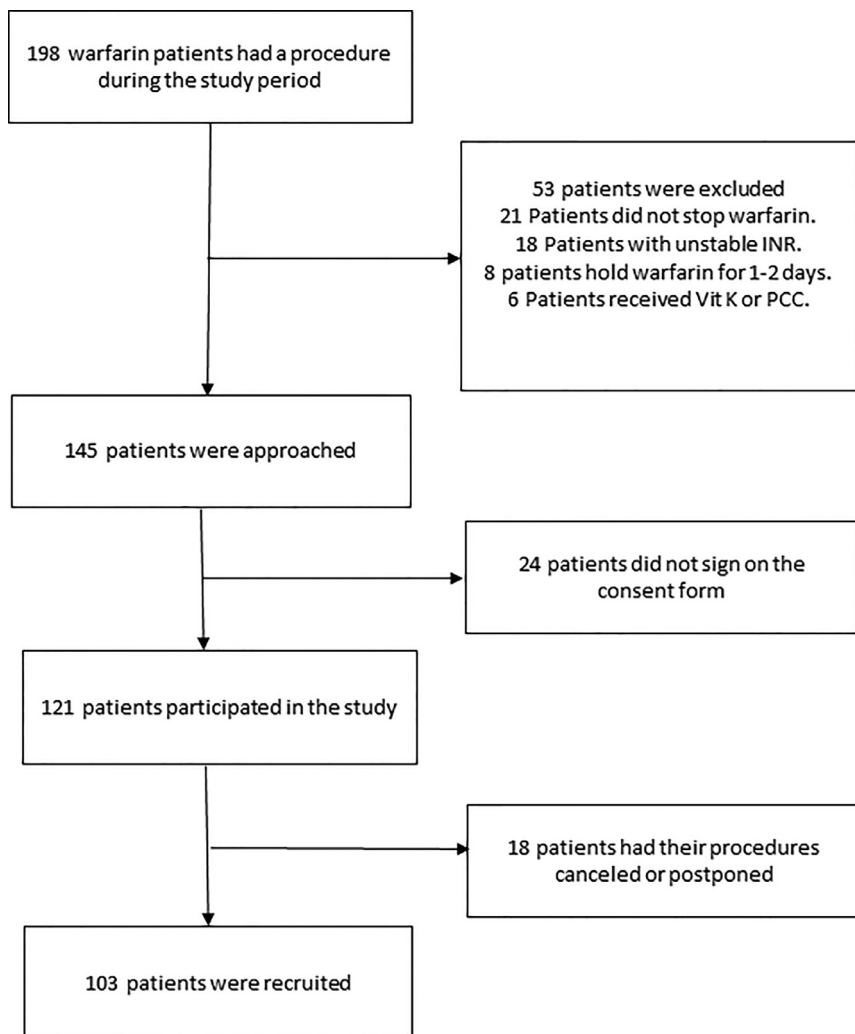
FIG 1. Diagram of eligible patients' inclusion. INR; international normalization ratio, PCC; prothrombin complex concentrates.

were 4 (2) and 2 (2), respectively, and values were not different among the 2 study groups.

Periprocedural Warfarin Management and the Classifications of Performed Procedures

One hundred and three patients went for a procedure and had warfarin interruption for more than 2 days; the list of complete procedures is

TABLE 1. Clinical and demographics characteristics of patients

Characteristic (N = 103)	Bridging (N = 85)	Nonbridging (N = 18)	P-Value
Age in years, mean $\pm$ SD[†]	58.0 $\pm$ 14.7	61.6 $\pm$ 13.6	0.344
BMI in kg/m, median (IQR)[¥]	32.2 (34.5)	30.1 (16.0)	*0.036
Male sex, no. (%)	46 (54.1)	10 (55.5)	0.911
Country of origin, no. (%)	33 (38.8)	9 (50.0)	0.381
Qatari	52 (61.2)	9 (50.0)	
Non-Qatari			
Comorbid conditions, no. (%)	12 (14.1)	1 (5.5)	0.353
Congestive heart failure (CHF)	40 (47.0)	12 (66.6)	0.131
Diabetes mellitus	49 (57.6)	15 (83.3)	* 0.041
Hypertension	37 (43.5)	10 (55.5)	0.352
Dyslipidemia			
Vitamin-K food intake/week no. (%)			0.907
Low	16 (18.8)	3 (16.6)	
Medium	66 (77.6)	14 (77.7)	
High	3 (3.5)	1 (5.5)	
Warfarin indication, no. (%)			
AF	44 (51.7)	14 (77.7)	* 0.043
Heart valve replacement	37 (43.5)	4 (22.2)	0.093
VTE	11 (12.9)	4 (22.2)	0.311
Thrombophilia	7 (8.2)	0	0.207
Others (LVT, Stroke)	9 (10.5)	1 (5.5)	0.521
Concomitant high bleeding-risk medications, no. (%)	26 (30.6%)	5 (27.8%)	0.83
Antiplatelet	5 (5.9%)	3 (16.7%)	0.120
NSAIDs			
Risk assessment for AF patients (N = 58)[¥]	**Bridging** (N = 44)	**Nonbridging** (N = 14)	0.669
CHA$_2$DS$_2$-Vasc, median (IQR)	4 (2)	4 (2)	0.805
CHA$_2$DS$_2$-Vasc $\leq$ 4, no. (%)	32 (72.7%)	10 (71.4%)	0.953
HAS-BLED, median (IQR)	2 (2)	2 (2)	0.605
HAS-BLED $\leq$ 2, no. (%)	27 (61.4%)	10 (71.4%)	

All P-value < 0.05 was tested using Chi-square test except †; independent-samples t-test AF, ¥Mann-Whitney U test. *Significantly different between bridged and nonbridged groups. Atrial fibrillation, BMI; body mass index, IQR; interquartile range, LVT; left ventricular thrombosis, NSAIDs; nonsteroidal anti-inflammatory drugs, SD; standard deviation. CHA$_2$DS$_2$Vasc refers to congestive heart failure, hypertension, age > 75 years, diabetes and prior stroke or transient ischemic attack, vascular disease, age 65-74 and female sex. HAS-BLED refers to hypertension, abnormal liver or renal function, stroke, bleeding, liable INR, elderly (Age >65), drugs (NSAIDs or aspirin) or alcohol. Vitamin-K was categorized according to the number of portions of vitamin-k food intake/week as low (1-2 time), medium (3-4 times) and high (5-7 times), one portion equal to one bowl containing approximately 100 gm of food.

categorized and summarized in Table 2. Three quarters (75%) of recruited patients had minor or low-bleeding risk procedures. As expected, minor procedures were more frequent in nonbridging (83.4%) than in the bridging group (75.6%), but the difference was not statistically

TABLE 2. List of performed procedures

Procedure	Bridging (N = 85)	Nonbridging (N = 18)
Minor no. (%)	**64 (75.6%)**	**15 (83.4%)**
Dental procedure no. (%)	24 (28.2%)	6 (33.3%)
Endoscopy no. (%)	13 (15.3%)	5 (27.8%)
Ophthalmology procedure no. (%)	12 (14.1%)	2 (11%)
Valvuloplasty no. (%)	3 (3.6%)	1 (5.6%)
Others no. (%)	12 (12.1%)	1 (5.6%)
Major no. (%)	**21 (24.7%)**	**3 (16.6%)**
Resection no. (%)	6 (7.0%)	1 (5.6%)
CABG no. (%)	5 (5.8%)	2 (11%)
Knee replacement no. (%)	2 (2.3%)	0
MVR no. (%)	2 (2.3%)	0
Gastric sleeve, no. (%)	2 (2.3%)	0
Others, no. (%)	4 (4.6%)	0

CABG; coronary artery bypass grafting, MVR; mitral valve replacement.

significant ($P = 0.178$). Dental procedures were the most common (29%) type of minor procedure among bridging and nonbridging groups, whereas resection procedures were the most common major procedure (6.5%).

Periprocedural management variables such as 1st INR reading after warfarin interruption; last INR reading before the procedure; incidence of INR ≥ 1.5 at the time of procedure; and number of preprocedural warfarin discontinuation days are presented in Table 3. There were no statistical differences between bridging and nonbridging groups in these variables.

Warfarin Periprocedural Management Clinical Outcome

During the 30-day follow-up period following the procedure, there were no thromboembolic events, while 30 (39 %) participants had bleeding

TABLE 3. Periprocedural warfarin management

Variable	Bridging (N = 85)	Nonbridging (N = 18)	P-Value
1st INR reading after the interruption median (IQR)	2.1 (0.7)	2.4 (0.8)	0.142
lastINR reading before the procedure median (IQR)	1.2 (0.9)	1.4 (0.2)	0.59
Incidence of INR ≥ 1.5 at the time of procedure, number (%)	9 (10.5%)	3 (16.6%)	*0.465
No. of preprocedural warfarin discontinuation days, median (IQR)	3 (2)	3 (2)	0.947

*Chi-square test was used, P-value < 0.05 was tested using the Mann-Whitney U test. 1st INR reading was checked on the first day of warfarin discontinuation, last INR was examined on the day or one day before the procedure. INR; international normalization ratio, IQR; interquartile range.
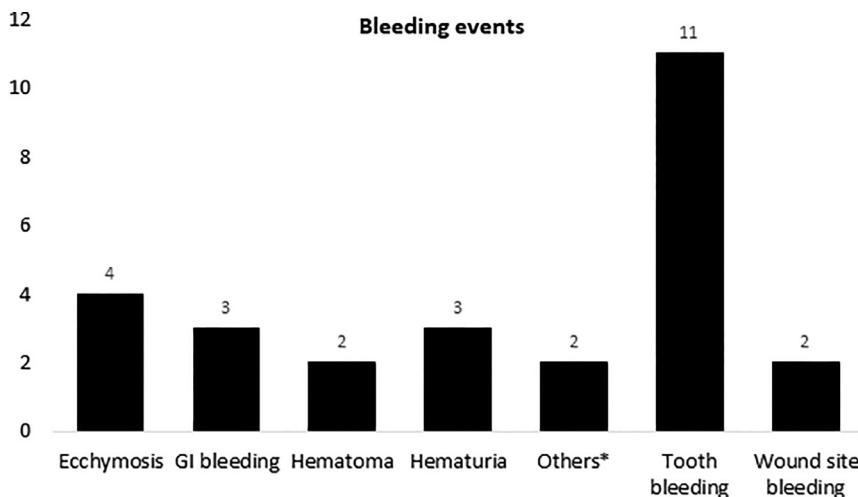
FIG 2. Reported hemorrhagic events during periprocedural warfarin management. *others (thoracic bleeding and hemarthrosis), GI; gastrointestinal.

events (Fig 2). Eighteen of these events were minor (60%) while the remaining 12 were major (40%). The incidence of overall bleeding was numerically higher in bridging compared to the nonbridging group but did not reach statistical significance (30.6% vs 22.2%, *P* = 0.48). Similarly, postoperative bleeding in the bridging group was more than two-fold higher than bleeding in the nonbridging group (27.1% vs 11.1% %, *P* = 0.241). The difference did not reach statistical significance likely due to the small sample size. Moreover, bridging was not associated with bleeding events when tested in multivariate analysis after adjustment for other baseline characteristics. Multiple logistic regression however showed low vitamin-K intake to be associated with lower bleeding risk compared to higher vitamin K intake (adjusted OR, 0.1; 95% CI, 0.012−0.882; *P* = 0.038), and the use of antiplatelet medications to be associated with MB (OR, 3.7; 95%CI, 1.16−12.15, *P* = 0.027). The use of antiplatelet agents also tended to increase overall bleeding, but results were not statistically significant (OR, 2.3; 95%CI, 0.95−5.73, *P* = 0.064). One death was reported among the participants in the bridging group (Table 4).

Discussion

This study provides insights into the clinical practice of warfarin periprocedural management as well as the procedural characteristics and consequent clinical outcomes in a Qatari healthcare setting. One of our main findings is that warfarin was interrupted in 90% of patients who had

TABLE 4. Bleeding events from the time of warfarin interruption till 30 days after the procedure

Clinical outcome	Overall (N = 103)	Bridging (N = 85)	Nonbridging (N = 18)	P-value*
Preoperative				
Overall bleeding, no. (%)	5 (4.9%)	3 (3.5%)	2 (11.1%)	0.235
Major bleeding, no. (%)	1 (1.0%)	1 (1.2%)	0	0.644
Minor bleeding, no. (%)	4 (3.9%)	2 (2.4%)	2 (11.1%)	0.081
Death, no. (%)	0	0	0	
Postoperative				
Overall bleeding, no. (%)	25 (24.3%)	23 (27.1%)	2 (11.1%)	0.241
Major bleeding, no. (%)	11 (10.7%)	10 (11.8%)	1 (5.6%)	0.338
Minor bleeding, no. (%)	14 (13.6%)	13 (15.3%)	1 (5.6%)	0.198
Death, no. (%)	1 (0.97%)	1 (1.1%)	0	
Total observation period				
Overall bleeding, no. (%)	30 (39.1%)	26 (30.6%)	4 (22.2%)	0.478
Major bleeding, no. (%)	12 (11.7%)	11 (12.9%)	1 (5.6%)	0.375
Minor bleeding, no. (%)	18 (17.5%)	15 (17.6%)	3 (16.7%)	0.921
Death, no. (%)	1 (0.97%)	1 (1.1%)	0	0.644

*P-value < 0.05 was tested using Chi-square test to compare the overall bleeding between 2 groups of bridging and nonbridging.

undergone elective surgery. This was consistent with our earlier observation, which showed that HCPs had been interrupting warfarin for more than 75% of cases.[12] This rate of warfarin interruption is even higher than that previously reported in sub-study of the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE)[15] (63%) and in the ORBIT-AF study[9] (30%). We believe that these results reflect the personal preference of local surgeons, which tends to be more cautious towards intraoperative hemorrhage.

Additionally, the present study underscores the significant use of bridging, which was employed in 82.5% of patients in whom warfarin had been interrupted. This outcome is in line with our previous survey for the HCPs in Qatar who formerly reported the use heparin bridging with an average of 50%-75% of their patients. The proportion of bridging in this study is also significantly higher than those reported in the ORBIT-AF[9] and RE-LY[14] trials (25% and 30%, respectively).

According to the current report, about 25% of performed procedures were major surgeries. This was similar to the finding of Fingar et al,[16] who demonstrated that 29% of procedures performed in the USA in 2003-2012 for warfarin patients were major procedures. Likewise, in the BRIDGE trial,[10] major surgeries represented 30% of all the performed operations. Given that more than 75% of the performed procedures in this report were minor, it was surprising to see that warfarin was still

interrupted. It was also surprising that bridging was used in more than 80% of patients with major surgery or surgeries with high bleeding risk and despite that TE risk in the cohort was mostly low-moderate based on the CHA_2DS_2-Vasc score (71% had a score ≤4). It was noted however, that the frequency of some higher risk TE conditions such as valvular replacement, thrombophilia and stroke were higher (but not statistically significant) in the bridging arm which justifies the use of bridging in these conditions.

In this study, the median (IQR) of warfarin discontinuation days was 3 (2) days, which was lower than the reported mean $\pm$ SD days of interruption in the BRIDGE trial (5.2 $\pm$ 1.4).[10] This could be attributable to the high number of minor operations, which might have required shorter periods to achieve a target INR of <2

The current study did not show any difference in the incidence of clinical outcomes between bridging and nonbridging groups which is apparently due to the small sample size especially in the nonbridging group (n = 18). However, there was a numerical tendency towards increased bleeding risk in majority of bleeding categories in the bridging compared to nonbridging arm. There were also no TE events reported in the study. Increased risk of bleeding with bridging was confirmed in previous studies. In the RE-LY trial,[14] the risk of major bleeding among bridged patients was significantly higher than that in nonbridged patients (6.8% vs 1.6%, $P < 0.001$), and there was no significant impact on ATE (0.5% vs 0.2%, $P = 0.32$). The ORBIT-AF trial[9] also revealed a higher bleeding rate when bridging anticoagulation therapy had been implemented during periprocedural warfarin interruption. In the BRIDGE study,[10] bridging was correlated with increased bleeding risk, while no additional benefits for ATE prevention could be concluded.

The only deceased case in the present analysis was a 52-year-old female patient using warfarin for stroke prevention status post mitral valve replacement. She underwent a hysteroscopy and polypectomy, and she was bridged. She developed gastrointestinal bleeding 12 days after surgery while she was on postoperative bridging along with warfarin. She died 4 days after the postoperative hemorrhage.

An overall observation from this study is that the practice followed for warfarin patients undergoing surgical procedures in Qatar are not in accordance with the most recent clinical evidence guidelines.[7,17] According to the 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular AF guidelines published by the American College of Cardiology, warfarin should

not be discontinued in patients undergoing procedures with minimal to low bleeding risk when these patients don't have risk factors to increase the risk of bleeding.[7] Additionally, the use of bridging in patients with low TE risk (CHA_2DS_2-Vasc score ≤ 4) is not recommended. Similar recommendation is endorsed by the American Society of Hematology 2018 guidelines for patients with VTE that have low to moderate TE risk.[17] These recommendations are based primarily on the overwhelming recent evidence that showed increased bleeding and net harm in patients undergoing bridging with no justifiable reduction in the risk of TE.[9,14,18,19]

A significant strength of the current research is that it prospectively evaluated the local practice of HCPs and the adverse events of warfarin interruption among patients undergoing surgeries for various warfarin indications and with variable thromboembolic and bleeding risks. However, the study was not without limitations. Importantly, our study lacked the necessary power to detect significant difference between both groups due to the small sample size, particularly in the nonbridging group. Although our study was conducted over a relatively long period (2 years) in 3 hospitals, the slow flow of eligible patients might have contributed to the small sample size. Moreover, patient recruitment might have been affected by the unprecedented situation of the Coronavirus disease 2019 (COVID-19) pandemic, which has resulted in suspending elective surgeries for 6 months. Accordingly, this might have caused a lack of significant differences between bridged and nonbridged patients in clinical outcomes. The small number of major surgeries in our study may partly explain the lack of TE events, which might be associated with the procedure type and blood pressure variation during the procedure.[20,21] Lastly, there is a potential for sampling bias since patients were neither randomized to interruption nor to bridging. Based on the mentioned observations, future studies with larger sample sizes are needed to evaluate the clinical benefits of warfarin interruption and bridging in periprocedural management in Qatar. Furthermore, economic analysis may help determining the cost-effectiveness of stopping versus continuing warfarin and bridging against nonbridging in periprocedural management.

In conclusion, the present study revealed that warfarin is mostly interrupted among patients who undergo elective surgery, and bridging was the primary strategy used by many clinicians. While bridging was numerically associated with increased bleeding events, there is no statistical difference in reported clinical events between bridging and nonbridging strategies.

APPENDIX 1. Clinical events definitions

Clinical event	Definition	Ref.
Death	All-cause of death	[1]
Major bleeding	At least one of the following must be satisfied	[1,2]
	1- Symptomatic or clinically overt bleeding that is associated with one or more of:	
	- Transfusion of ≥ 2 units heterologous packed red blood cells or whole blood	
	- Decrease in hemoglobin level of >20 g/L (>2 g/dL).	
	- Need for reoperation or invasive intervention (e.g., evacuation of wound hematoma).	
	2- Symptomatic or clinically overt bleeding at a critical anatomic site; bleeding that is intracranial, intraspinal, intraocular (retro-orbital, vitreous, choroidal, or retinal hemorrhage), retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome	
	3- Fatal bleeding	
	Bleeding directly contributes to death (e.g., intracranial bleed) or causes clinical deterioration leading to death (e.g., bleeding associated with sepsis or major organ failure).	
Minor bleeding	Symptomatic or clinically overt bleeding that does not satisfy the criteria for major bleeding	[1]

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APPENDIX 2. Examples of minor and major procedures

Minor or low-bleeding risk procedure	Major or high-bleeding risk procedure
Diagnostic test	Intra-abdominal surgery
Endoscopy	Intrathoracic surgery
Ophthalmic procedure	Internal defibrillator insertion
Dental extraction or procedure	Orthopedic surgery
Dermatological procedure	Resection surgery
Cardiac catheterization procedure	Arterial revascularization

Declarations of Competing Interest

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Ethics Approval

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