Int Surg 2015;**100**:225–232
DOI: 10.9738/INTSURG-D-14-00139.1

Results of Surgery in General Surgical Patients Receiving Warfarin: Retrospective Analysis of 61 Patients

Sedat Belli, Huseyin Ozgur Aytac, Hakan Yabanoglu, Erdal Karagulle, Alper Parlakgumus, Tarik Zafer Nursal, Sedat Yildirim

Department of Surgery, Baskent University Faculty of Medicine, Ankara, Turkey

The aim of this study is to investigate postoperative complications, mortality rates, and to determine the factors affecting mortality on the patients receiving warfarin therapy preoperatively, as well as comparing the results obtained from emergency and elective surgeries. Surgical outcomes of 61 patients on long-term oral anticoagulation with warfarin who underwent surgery in our center were retrospectively reviewed over an 8-year period. Thirty-three (54.1%) patients were female, with a mean age of 53 years. Mitral valve replacement (62.3%) was the most frequent indication for chronic anticoagulation therapy. Twelve out of 61 (19.2%) patients underwent emergency surgery; 59 (96.7%) operations were classified as major surgery. We did not observe any thromboembolic events on patients receiving our bridging therapy protocol. Cardiopulmonary dysfunction (CPD; 19.7%) and hemorrhage (16.4%) were the most encountered postoperative complications. Presence of CPD, bleeding, endocarditis, and mortality were statistically significant for emergency surgeries when compared with the results obtained from elective surgeries. There were 5 (8.2%) deaths observed during follow-up. It was found that advanced age, prolonged duration of operations, and presence of CPD had a statistically significant effect on mortality ($P < 0.05$). The patients receiving oral anticoagulant had high postoperative complication and mortality rates. This case was more evident in emergency surgeries. It is recommendable that as mortality is more apparent in the patients who undergo emergency surgeries—being older, having long duration of operations as well as CPD. Therefore during the postoperative follow-up process, the patients should be closely monitored.

Key words: Emergency – Postoperative complications – Morbidity – Mortality – Warfarin

---

Corresponding Author: Sedat Belli, MD, Department of Surgery, Adana Baskent Medical and Research Center, 01250, Adana, Turkey.
Tel.: +90 3223272727; Fax: +90 3223271276; E-mail: bellisedat@gmail.com

Thromboembolism is a major global health concern contributing to more than 0.5 million deaths in Europe and up to 300,000 deaths in the United States each year.[1] Versatile arrays of anticoagulant and/or anti-aggregant agents are available. They are used to treat and prevent thrombosis occurring as a result of venous stasis, valvular heart disease, prosthetic valves, atrial fibrillation, or myocardial infarction. After using these medications, patients who require elective or emergency surgery represent a specific population; moreover, they are prone to developing either excessive bleeding or thrombosis.

The annual incidence of major bleeding as a result of oral anticoagulant (OAC) use is reported between 2 and 5%.[2] Patients on OAC may require elective or sometimes emergency surgical or invasive procedures. There is no consensus on standard protocol to follow for those who require perioperative management.[3]

In the current literature, there are limited numbers of studies regarding the discussions about the operations in general surgery patient population receiving warfarin treatments. In this retrospective study, our aim was to document the complications and outcomes of general surgical procedures implemented on patients receiving warfarin. Along with the comparison of the emergency and elective surgeries performed, we also aimed to determine the factors affecting mortality.

Patients and Methods

Data collection

The study was conducted according to the tenets of the Declaration of Helsinki on Biomedical Research involving Human Subjects. This retrospective clinical study was performed at Baskent University, Department of General Surgery after obtaining the approval of the university ethical committee (KA13/129). This is a retrospective review of patients on long-term anticoagulation with warfarin who underwent surgery in our department over a period of 8 years: from January 2006 to December 2013. Demographic data, mode of presentation, American Society of Anesthesiologists (ASA) score, indication and duration of OAC therapy, comorbidities, international normalized ratio (INR), prothrombin time (PT) and activated partial thromboplastin time (aPTT) values, surgical technique, and duration of procedures were collected retrospectively from charts and computerized medical records. Treatment outcomes, mortality rates, thromboembolic or bleeding events observed, and length of hospital stay were also recorded.

Not only were the patients receiving no warfarin prior to their procedure excluded, but we also excluded those who were to have their warfarin discontinued immediately postoperatively. We also excluded patients who received anticoagulant agents other than warfarin. Besides assuring the conditions stated above, the patients having deep venous thrombosis and pulmonary embolism were also excluded.

Perioperative bridging anticoagulation therapy

In patients who were undergoing elective surgical procedures, warfarin was discontinued 5 days prior to surgery (that is, the last dose was given 6 days prior to the day of surgery). Patients were admitted to an inpatient clinic 3 days before surgery. Bridging therapy with unfractionated heparin (UFH) was started when INR levels dropped below 2.0. A level of INR of 1.5 or below was considered suitable for surgery. A final PT and INR level was obtained for every patient on the morning of surgery. If the patient still had an increased INR (1.8 or above) after 3 days, vitamin K (oral preparation of 1–2.5 mg) was given. Unfractionated heparin was stopped 6 hours before surgery. However, if the patient required emergency surgery, the bridging process had to be expedited by holding the warfarin and administering 10 mg of vitamin K via intravenous infusion over 15 to 30 minutes. The next step was to administer 15 mL of fresh-frozen plasma (FFP) per kilogram of patient body weight.

If no bleeding was suspected or observed, UFH was started again 6 hours after surgery. Complete blood count and INR levels were obtained daily during the postoperative period. Follow-up INR levels were obtained once every 3 days after the target level of INR was reached. When oral intake was allowed, OAC was started along with UFH until the target level of INR was reached. Unfractionated heparin was then discontinued and patients were discharged when their general medical condition was satisfactory. Levels of INR were obtained monthly (28 $\pm$ 4 days) when there were no additional problems. For the patients with a history of previous heart valve replacement, antibiotic prophylaxis was provided with sulbactam + ampicillin (4 g) and gentamycin sulfate (120 mg) during the induction of anesthesia.

Outcome variables

For the purposes of the study, major hemorrhage was defined as: overt bleeding leading to a more than 3 g dL^{-1} drop in hemoglobin levels; transfusion of more than 2 units of packed red blood cells or whole blood; or any intracranial, retroperitoneal, or intraocular bleeding that required surgical intervention or resulted in death. All other bleeding events that did not meet the criteria for major bleeding were classified as minor in accordance with previous literature.[4]

Major surgery was described as intervention lasting longer than 45 minutes or orthopedic, cardiothoracic, vascular surgical procedures. All other surgical procedures were defined as minor surgery, similar with the earlier publications.[5] Emergency surgery was defined as nonelective surgery performed when the patients' life or well-being was in direct jeopardy.

Subgroup analysis was performed to determine the incidence of major bleeding by the extent of the procedure (minor or major surgery). Cardiopulmonary and thromboembolic events were taken into consideration when they occurred at any time during the study period (from the cessation of warfarin therapy 5 days prior to surgery until 28 days after the INR value was within the therapeutic range).

We define "cardiopulmonary dysfunction" in accordance with previous studies and with the European Association for Cardio-thoracic Surgery/ European Society of Thoracic Surgeons thoracic surgery database as postoperative pneumonia; postoperative respiratory failure (requiring mechanical ventilation for more than 48 hours); pulmonary edema, atelectasis or hypoxemia, serious postoperative arrhythmias; acute coronary syndromes and cardiac failure.[6–8] Postoperative morbidity and mortality were considered as those occurring within 30 days postoperatively or for a longer period when the patient was still in hospital follow-up.[6–8]

Statistical analysis

Data were collected and analyzed digitally using a program for statistics (SPSS, version 17.0; SPSS, Inc., Chicago, IL, USA). For each continuous variable, normality was checked by Kolmogorov Smirnov and Shapiro-Wilk tests and by histograms. Comparisons between groups were applied using Mann Whitney *U* test when the data were not normally distributed. The categorical variables between the groups were analyzed by using the χ^2 test or Fisher's exact test. Factors associated with a *P* value of less than 0.05 in univariate analysis were further evaluated in a multiple regression analysis. A multiple logistic regression analysis was used to determine the associations between mortality or morbidity and other measurements that were classified as dependent variables. Values of $P < 0.05$ were considered statistically significant.

Results

A total of 61 patients on long-term warfarin were included in the study. The demographics, perioperative clinical features, and distribution of indications for OAC use of 61 anticoagulated patients are detailed in Table 1. A history of mitral valve replacement (MVR) was the most common indication for using warfarin preoperatively, followed by aortic valve replacement (Table 1). At least more than 1 disease state requiring OAC use was present in 36 patients (59%). Comorbidities other than reason for OAC use—including diabetes mellitus and hypertension—were present in 63.9% of patients (Table 1). Four of the patients (6.5%) received vitamin K (INR $\geq$ 1.8) pre-operatively.

Cholecystectomy was the most frequently performed primary procedure (n = 36; 59%). Twelve patients had also synchronous secondary operations that were all elective. Among all operations performed, 49 (80.3%) were elective and 12 (19.7%) were emergency (Table 2). The patients receiving emergency operations were not optional. Fifty nine (96.7%) operations were classified as major and 2 (3.3%) were as minor. Intraoperatively drains were placed in 35 (57.4%) patients as a part of surgical procedures.

Cardiopulmonary dysfunction (CPD) and bleeding were the most frequently encountered postoperative complications more pronounced in emergency cases (Table 3). Major bleeding was encountered in 7 (11.5%) patients while 3 (4.9%) of the patients had minor bleeding. In the analysis of the patients having postoperative bleeding, it was found that there was statistically significant differences regarding the duration of operations ($P = 0.012$). Moreover, it was also found that the difference regarding the length of hospital stay was statistically significant ($P = 0.001$). Seven patients with CPD had also bleeding. Five of these bleeding events were major and 2 were minor.

Mortality was observed in 5 patients (Table 3). All these patients who died developed major bleeding

Table 1 Perioperative demographics, clinical features, and distribution of indications for OAC use among patients

Variable	Total, n = 61 (%) or mean ± SD
Mean age, y	55 ± 13
Sex	
Female	33 (54.1)
Male	28 (45.9)
Mean body mass index	27 ± 5
Indications for taking warfarin	
Mitral valve replacement	38 (62.3)
Aortic valve replacement	15 (24.6)
Atrial fibrillation	7 (11.5)
Coronary bypass grafting	1 (1.6)
Comorbidities	
Present	39 (63.9)
Absent	22 (36.1)
ASA classification	
II	20 (32.8)
III	41 (67.2)
Preoperative INR value	1.3 ± 0.5
Preoperative aPTT value	38 ± 13
Preoperative PT	16 ± 5
Mean duration of procedure, min	97 ± 67
Length of stay, days	9 ± 6
Pre-operative	4 ± 3
Postoperative	6 ± 4

and CPD. It was determined that the high preoperative INR levels ($P = 0.003$), PT levels ($P = 0.004$), and the duration of operations ($P = 0.004$) were individually significant risk factors affecting CPD in analysis of univariate. As for in analysis of multivariate, it was also determined that the duration of operations was an individually significant risk factor affecting CPD (1.1%; 95% CI, 1.01–1.02; $P = 0.033$). All the bleeding episodes were encountered before patients were discharged. The rate of blood transfusion was 16.4%. After all, we did not observe any thromboembolic events.

Five out of 7 patients who had major bleeding were managed conservatively (erythrocyte suspension, fresh frozen plasma and vitamin K replacement). The remaining 2 patients were re-operated on for hemostasis. These patients were initially operated for pancreas carcinoma (pancreaticoduodenectomy) and sigmoid colon perforation (Colon resection and Hartmann's procedure). Although hemostasis was restored during the revision surgery, both patients died.

Two patients who were operated in emergency settings developed major bleeding. These 2 patients also developed endocarditis following surgery. One patient died due to severe sepsis on postoperative day 13. This patient had received 18 units of erythrocyte suspension prior to surgery to treat upper gastrointestinal bleeding and an additional 7 units after the surgery. The second patient also died due to sepsis on day 12 after the surgery. It was found that in the analysis of univariate, demographic and clinical data were not determined as a risk factor regarding the development of endocarditis.

Two of the emergency procedures were appendectomy (Table 2) and these patients' INR values were 1.9 and 1.6. When decision for surgical

Table 2 Surgical treatment procedures in patients receiving warfarin

All patients (n = 61)	Types of surgical procedure, (n = 61)	Synchronous secondary operations, (n = 12)
Elective surgery, 49 (80.3%)	Hepatobiliary pancreatic surgery (35)	Hernia (4)
	• Cholecystectomy (34)*	Breast surgery (3)
	• Pancreaticoduodenectomy (1)	Upper gastrointestinal system surgery (2)
	Hernia (7)	Hepatobiliary pancreatic surgery (2)
	Thyroid and parathyroid (3)	• Choledocotomy (1)
	Proctological surgery (2)	• Cholecystectomy (1)
	Colorectal surgery (2)	Thyroid and parathyroid surgery (1)
Emergency surgery, 12 (19.7%)	Upper gastrointestinal system (5)	
	• Truncal vagotomy and pyloroplasty (2)	
	• Subtotal small bowel resection (2)	
	• Primary repair for bleeding ulcer (1)	
	Colorectal surgery (3)	
	• Appendectomy (2)	
	• Sigmoid colon resection and colostomy (1)	
	Hernia (3)	
	• Strangulated incisional hernia (2)	
	• Strangulated femoral hernia (1)	
	Hepatobiliary pancreatic surgery (1)	
	• Cholecystectomy (1)	

* Laparoscopic cholecystectomy (n = 24).

Table 3 Summary of outcome events of follow-up and comparison of variable subgroups for emergency versus elective surgery

Postoperative complications and variable	Emergency, n (%) or mean ± SD	Elective, n (%) or mean ± SD	*P* value
Mean age, y*	63.2 ± 13.9	53.1 ± 13.3	0.023
Preoperative INR*	1.77 ± 0.8	1.2 ± 0.1	0.004
Preoperative PT*	20.7 ± 9.8	15 ± 2.1	0.006
Duration of procedure, min	125 ± 97	90 ± 57.7	0.11
Cardiopulmonary dysfunction*	7/12 (58.3)	5/49 (10.2)	0.001
Bleeding*	5/12 (41.7)	5/49 (10.2)	0.008
Endocarditis*	2/12 (16.6)	0	0.004
Mortality*	3/12 (25)	2/49 (4.1)	0.018
Length of stay, d	14.8 ± 10.3	8.6 ± 4.5	0.085
Postoperative length of stay, d*	10.2 ± 6.4	4.8 ± 3.6	0.004

* Statistically significant factors ($P < 0.05$).

operation was given, average 3.5 hours passed from decision until operation time for bridging therapy. The first patient received 2 units of FFP and the other patient received 1 unit of FFP; and in the postoperative period, none of the patients bled.

In terms of bleeding rates, comparing the elective group with the emergency treatment group, whom were prepared quickly and treated, the rate of the emergency treatment group was higher and statistically more significant ($P = 0.008$). Therefore, the emergency group was compared again. Twelve patients in the emergency group were given a median of 2 units of FFP (range: 1–3 units) and they were operated after a median of 2 hours (range: 1–6 hours). Five of these patients (41.7%) bled. The effect of the amount FFP administered and the delay for the decision until operation time to perform bridging therapy on postoperative bleeding complications were compared as subgroups, the result of which was not statistically significant ($P > 0.05$).

Median level of INR before the operation was 1.5 (range: 1.1–4.1) for the patients who bled. Two of those patients were operated on again. The patient who underwent a Whipple procedure was operated on due to major vessel injury. The other patient for whom ostomy was performed after sigmoid colon perforation, there was not a significant source of bleeding and we interpreted the situation as it was related to impaired coagulation parameters because of sepsis. In 5 out of 8 patients who were not reoperated were found to have disorder of coagulation parameters because of sepsis, and the other 3 patients were seen to have postoperative hemorrhage because of gastrointestinal bleeding.

We found a statistically significant result as to the comparison of the complications of the patients undergoing emergency and elective surgeries; CPD, bleeding, and endocarditis rates were higher in the patients undergoing emergency surgeries (Table 3). Seven out of 10 patients (58.3%) who had bleeding had CPD. In a similar way, the mortality rate was higher in a statistically significant manner for the patients undergoing emergency surgeries (Table 3). Mean age, preoperative INR, and PT values were significantly higher in the patients who underwent emergency surgery as well as experienced a longer postoperative hospital stay (Table 3).

Patients who underwent synchronous surgery were compared with those patients having no synchronous operation in terms of bleeding, mortality, and CPD. There were no statistically significant differences between the 2 groups, in terms of bleeding, mortality, and CPD (respectively, $P = 0.67$, 0.69, 0.25). When all complications were evaluated, there was no statistical difference ($P = 0.49$).

In the analysis of the patients with mortality, age ($P = 0.003$), and the duration of operations ($P = 0.003$) were statistically significant (Table 4). In analysis of multivariate, it was determined that there was not any individual risk factors regarding the mortality rates. However, when it comes to the individual analysis of the complications affecting the mortality rates, CPD ($P = 0.001$) had a significant effect on the mortality. It was also found that endocarditis ($P = 0.158$) and postoperative bleeding ($P = 0.185$) had no significant effect on mortality.

Discussion

Patients who are on oral anticoagulants because they have atrial fibrillation, mechanical heart valves, myocardial infarction, and pulmonary embolism are at a high risk for arterial or venous thromboembolism.[9] Cessation of OAC therapy may be required in patients who are in need of elective or emergency surgery and other invasive procedures. These patients need some sort of bridging anticoagulant therapy and may require hospitalization prior to

Table 4 Analysis of factors that may have an effect on mortality

	Mortality		
	n (%) or mean ± SD		
Variable	Yes, (n = 5)	No, (n = 56)	*P* value
Mean age,* y	72 ± 6	53 ± 13	0.003
Sex			1
Female	3 (60)	30 (53.6)	
Male	2 (40)	26 (46.4)	
Mean body mass index	28 ± 5	27 ± 5	0.733
Indications for taking warfarin			0.922
Mitral valve replacement	3 (60)	35 (62.5)	
Aortic valve replacement	1 (20)	14 (25)	
Atrial fibrillation	1 (20)	6 (10.7)	
Coronary bypass grafting	0 (0)	1 (1.8)	
Comorbidities			0.645
Present	4 (80)	35 (62.5)	
Absent	1 (20)	21 (37.5)	
ASA classification			0.162
II	0 (0)	20 (32.8)	
III	5 (12.2)	36 (67.2)	
Preoperative INR value	1.7 ± 0.6	1.3 ± 0.4	0.077
Preoperative aPTT value	34 ± 4	38 ± 14	0.482
Preoperative PT	19 ± 5	16 ± 5	0.168
Mean duration of procedure,* min	180 ± 118	90 ± 56	0.003
Length of stay, d	14 ± 13	9 ± 5	0.136
Pre-operative	6 ± 9	4 ± 3	0.125
Postoperative	9 ± 6	9 ± 6	0.42
Postoperative complications			
CPD* (12)	5 (100)	7 (12.5)	0.001
Bleeding (10)	2 (40)	8 (14.3)	0.185
Endocarditis (2)	1 (20)	1 (1.8)	0.158

* Statistically significant factors ($P < 0.05$).

their planned procedure. In Europe and North America, it is reported that nearly 4 million patients use OAC and each year 10% of these require cessation of OAC therapy for various reasons.[10] Unfortunately, there is no consensus regarding the protocol on how to conduct bridging anticoagulation for these patients.[11] Major reasons for this lack of standardization are the large span of indications, comorbidities, procedures, and different heparin types available. It is the physician's responsibility to balance risk of bleeding against risk of thromboembolic complications for each individual patient.

As warfarin is the most commonly used OAC, bridging anticoagulation is usually conducted by discontinuing warfarin and administering UFH or low molecular weight heparin (LMWH).[12–18] Both agents have advantages and disadvantages.[4,5,14,15,19–22] There are several studies stating that LMWH is safer and more efficient than UFH. On the other hand, a comparative study enrolling 901 patients found no difference between UFH and LMWH in terms of thromboembolism, major bleeding, and death ratios.[5] At our center, UFH is preferred for bridging anticoagulation therapy since, it has a shorter half-life than LMWH, and its effects may be monitored and reversed much easier.

Many of our patients were treated with OAC due to previous MVR and aortic valve replacement, in a similar manner with the literature.[23] Again, most of our patients were in the category of ASA III and had comorbid diseases. Of the surgical procedures, 96.7% were in major surgical categories. In our experience, laparoscopic cholecystectomy was the most common surgical procedure (n = 24; 39.3%). Bleeding was encountered in only 2 of the patients who had laparoscopic cholecystectomy (18.3%). The largest series involving laparoscopic cholecystectomy in this group of anticoagulated patients included 44 patients.[24] Enoxaparin was used for bridge anticoagulation in that study. Postoperative bleeding was observed in 11 (25%) of 44 patients.[24] Thromboembolism cases have not been reported in the same study. Again, bleeding was not reported in 33 patients on warfarin undergoing elective laparoscopic cholecystectomy and was given bridging therapy with LMWH.[24] In our study, the likelihood of bleeding seems to be quite high in patients on warfarin undergoing elective laparoscopic cholecystectomy compared with mentioned former series. We did not find thromboembolism in these patients. There are few related studies and consensus in the literature in this ratio. Again, bridging therapy protocol to be applied in these patients is still unclear. Larger prospective clinical studies are needed for this condition to be set forth more clearly. Different rates of major hemorrhage were reported when the series of different branches of surgical operations were evaluated.[21–24] These rates vary over a wide range of 0.7 to 27.5%.[21–25] In the same study, thromboembolism was reported in a ratio of 0.4 to 3.6%.[21–25] Although none of our patients developed thromboembolism, the major bleeding rate was 11.5% in our study.

Comorbid pathologies and presence of major surgery are reported to be the independent risk factors for bleeding.[21–25] In our experience, major bleeding was observed in 16.9% of 59 patients who had major surgery and no bleeding was observed in patients having minor surgery. However, our study did not determine the effects of comorbid diseases on bleeding. Unlike some other studies, absence of different branches of surgical operations (especially orthopedic and cardiac surgery) and usage of heparin for bridging therapy may have been the reason that thromboembolism was not seen in our series.[19–25] However, as we noted earlier, larger prospective clinical studies are needed for this situation to be demonstrated more clearly. Duration of the surgery which was not specified in previous studies was seen to be an independent risk factor for bleeding in our study. In addition, the duration of hospital stay in these patients was found to be longer, as reported in previous studies.[23]

Bleeding, endocarditis, CPD, and mortality was found to be significantly higher in patients who were operated on urgently. Again, levels of PT/INR were significantly higher and hospital stay was significantly longer for the emergency operation group than the group undergoing elective surgery. These conditions were not evaluated in previous studies. In a recent study, it has been advised that in order to reduce the risk of bleeding, warfarin needs to be stopped 5 days prior to surgery and an INR level of 1.5 is desirable.[26] However, the condition of the patient may not permit optimization of the INR level as observed in our emergency patients (n = 12) in whom 5 (41.7%) had a bleeding episode postoperatively. Contrary to our usual practice, we placed drains in many patients (57.4%) in this series. Although drains are not advised for standard intra-abdominal procedures, in this group they may have important practical value as we have detected postoperative bleeding by monitoring the discharge from the drains. As a practical measure, we recommend that drains be placed in most patients in this category for the early detection and management of postoperative bleeding. Endocarditis was detected in only two patients those who had emergency surgery. We did not find any independent risk factors for endocarditis. Also, there were no data in previous studies regarding endocarditis.

In our analysis, mortality was found to be higher in elderly patients and in patients with longer duration of surgery. In our study we did not find any independent risk factors for mortality. However, we found that although CPD had an effect on mortality rate, endocarditis, and bleeding did not. We were unable to find any reviews about this situation in previous studies. According to our results, advanced patient age, prolonged operation time and limitation in cardiopulmonary reserve were shown to be effective on the increased mortality. Although bleeding is common with 40% since the result is not statistically significant with P value of 0.185, it does not seem that it has an effect on mortality whatsoever. Under the strength of these results, we assume that the mortality and morbidity of urgent operations are higher due to the inability to correct coagulation parameters adequately and appropriately.

The largest restriction of our study is its retrospective nature. Most of the studies in literature deal with heterogeneous patient series in terms of various surgical specialties. In these studies, more bleeding and thromboembolic complications were evaluated as the most outstanding ones. However, in our study CPD was observed as the most common complication which is the only factor having an effect on mortality rates. Although our study still lacks patient homogeneity, to some extent, is more specific than other studies in the literature evaluating only general surgical operations. This situation is the second major restriction of our study. We believe that this case can be specified by means of additional multicenter prospective trials.

Conclusion

As a result, invasive procedures performed in patients on oral anticoagulants are always risky. Surgery in patients on anticoagulation therapy increases the risk of bleeding and mortality especially on emergent cases. Although bleeding is common, we determined that it had no effects on mortality. Mortality is high especially with advanced age, prolonged surgical procedures, and the presence of CPD for patients on warfarin. It is recommended that there should be a close and strict follow-up with these patients.

Acknowledgments

The authors thank Cagla Sariturk, the statistician of Adana Baskent Medical and Research Center, who performed the statistical analysis of this article.

This study was approved by the Research Fund of Baskent University (KA13/129). The authors alone are responsible for the content and writing of the paper.

Author contributions: surgical procedure (BS, AHO, YH, YS); article writing and literature review in a comprehensive literature search (BS, KE, NTZ, PA); manuscript design and preparation (BS, YS).

References

1. Cohen AT, Agnelli G, Anderson FA, Arcelus JI, Bergqvist D, Brecht JG. Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. *Thromb Haemost* 2007;**98**(4):756–764
2. Rubboli A, Becattini C, Verheugt FW. Incidence, clinical impact and risk of bleeding during oral anticoagulation therapy. *World J Cardiol* 2011;**3**(11):351–358
3. Martin MT, Kuchta AM, Nutescu EA. A clinician's guide to perioperative bridging for patients on oral anticoagulation. *J Pharm Pract* 2010;**23**(4):303–312
4. Dunn AS, Spyropoulos AC, Turpie AG. Bridging therapy in patients on long-term oral anticoagulants who require surgery: the Prospective Peri-operative Enoxaparin Cohort Trial (PROSPECT). *J Thromb Haemost* 2007;**5**(11):2211–2218
5. Spyropoulos AC, Turpie AG, Dunn AS, Spandorfer J, Douketis J, Jacobson A. Clinical outcomes with unfractionated heparin or low-molecular-weight heparin as bridging therapy in patients on long-term oral anticoagulants: the REGIMEN registry. *J Thromb Haemost* 2006;**4**(6):1246–1252
6. Sachdev G, Napolitano LM. Postoperative pulmonary complications: pneumonia and acute respiratory failure. *Surg Clin North Am* 2012;**92**(2):321–344
7. Brunelli A, Xiumé F, Al Refai M, Salati M, Marasco R, Sabbatini A. Risk-adjusted morbidity, mortality and failure-to-rescue models for internal provider profiling after major lung resection. *Interact Cardiovasc Thorac Surg* 2006;**5**(2):92–96
8. Berrisford R, Brunelli A, Rocco G, Treasure T, Utley M. The European Thoracic Surgery Database project: modelling the risk of in-hospital death following lung resection. *Eur J Cardiothorac Surg* 2005;**28**(2):306–311
9. Singer DE, Albers GW, Dalen JE, Go AS, Halperin JL, Manning WJ. Antithrombotic therapy in atrial fibrillation: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;**126**(3 suppl):429S–456S
10. Mannucci C, Douketis JD. The management of patients who require temporary reversal of vitamin K antagonists for surgery: a practical guide for clinicians. *Intern Emerg Med* 2006;**1**(2):96–104
11. Dunn AS, Turpie AG. Perioperative management of patients receiving oral anticoagulants: a systematic review. *Arch Intern Med* 2003;**163**(8):901–908
12. Douketis JD, Crowther MA, Cherian SS. Perioperative anticoagulation in patients with chronic atrial fibrillation who are undergoing elective surgery: results of a physician survey. *Can J Cardiol* 2000;**16**(3):326–330
13. Douketis JD, Crowther MA, Cherian SS, Kearon CB. Physician preferences for perioperative anticoagulation in patients with a mechanical heart valve who are undergoing elective noncardiac surgery. *Chest* 1999;**116**(5):1240–1246
14. Douketis JD, Johnson JA, Turpie AG. Low-molecular-weight heparin as bridging anticoagulation during interruption of warfarin: assessment of a standardized periprocedural anticoagulation regimen. *Arch Intern Med* 2004;**164**(12): 1319–1326
15. Spandorfer JM, Lynch S, Weitz HH, Fertel S, Merli GJ. Use of enoxaparin for the chronically anticoagulated patient before and after procedures. *Am J Cardiol* 1999;**84**(4):478–480
16. Ansell JE. The perioperative management of warfarin therapy. *Arch Intern Med* 2003;**163**(8):881–883
17. Ickx BE, Steib A. Perioperative management of patients receiving vitamin K antagonists. *Can J Anaesth* 2006;**53**(6 suppl):S113–S122
18. Douketis JD. Perioperative anticoagulation management in patients who are receiving oral anticoagulant therapy: a practical guide for clinicians. *Thromb Res* 2002;**108**(1):3–13
19. Tinmouth AH, Morrow BH, Cruickshank MK, Moore PM, Kovacs MJ. Dalteparin as periprocedure anticoagulation for patients on warfarin and at high risk of thrombosis. *Ann Pharmacother* 2001;**35**(6):669–674
20. Ferreira I, Dos L, Tornos P, Nicolau I, Permanyer-Miralda G, Soler-Soler J. Experience with enoxaparin in patients with mechanical heart valves who must withhold acenocumarol. *Heart* 2003;**89**(5):527–530
21. Spyropoulos AC, Jenkins P, Bornikova L. A disease management protocol for outpatient perioperative bridge therapy with enoxaparin in patients requiring temporary interruption of long-term oral anticoagulation. *Pharmacotherapy* 2004;**24**(5): 649–658
22. Kovacs MJ, Kearon C, Rodger M, Anderson DR, Turpie AG, Bates SM. Single-arm study of bridging therapy with low-molecular-weight heparin for patients at risk of arterial embolism who require temporary interruption of warfarin. *Circulation* 2004;**110**(12):1658–1663
23. Ercan M, Bostanci EB, Ozer I, Ulas M, Ozogul YB, Teke Z. Postoperative hemorrhagic complications after elective laparoscopic cholecystectomy in patients receiving long-term anticoagulant therapy. *Langenbecks Arch Surg* 2010;**395**(3):247–253
24. Leandros E, Gomatos IP, Mami P, Kastellanos E, Albanopoulos K, Konstadoulakis MM. Elective laparoscopic cholecystectomy for symptomatic gallstone disease in patients receiving anticoagulant therapy. *J Laparoendosc Adv Surg Tech A* 2005; **15**(4):357–360
25. Dunn AS, Spyropoulos AC, Turpie AG. Bridging therapy in patients on long-term oral anticoagulants who require surgery: the Prospective Peri-operative Enoxaparin Cohort Trial (PROSPECT). *J Thromb Haemost* 2007;**5**(11):2211–2218
26. White RH, McKittrick T, Hutchinson R, Twitchell J. Temporary discontinuation of warfarin therapy: changes in the international normalized ratio. *Ann Intern Med* 1995;**122**(1):40–42