






# Factors associated with bleeding complications in hernia repair of warfarin users

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## SUMMARY

**OBJECTIVE:** In this retrospective study, we aimed to determine factors associated with bleeding complications in patients on long-term warfarin, undergoing inguinal hernia repair using low-molecular-weight heparin (LMWH) bridging.

**METHODS:** Two-year hospital records yielded 44 inguinal hernia repair patients on long-term warfarin (26 men, 4 women, aged 57.4 [38–72] years). All patients were managed with LMWH bridging. Patient and operative characteristics, LMWH bridging characteristics, and international normalized ratio (INR) values were compared between patients with and without postoperative bleeding complications.

**RESULTS:** Indication for warfarin use was heart valve disease (n=15), atrial fibrillation (n=7), deep venous thrombosis (n=3), cerebrovascular event (n=3), and pulmonary embolism (n=2). Four of the operations were urgent, while the remaining were elective. There were four ecchymosis cases and three hematoma cases in a total of seven patients. Baseline (2.94±0.26 versus 2.16±0.38, p<0.001) and preoperative INR values (1.69±0.67 versus 1.31±0.35, p=0.027) were significantly higher, while postoperative INR values (1.04±0.09 versus 1.2±0.13, p=0.004) were significantly lower in patients having bleeding complications.

**CONCLUSIONS:** Baseline, preoperative INR, and postoperative INR were the only variables associated with postoperative bleeding complications in patients undergoing LMWH-bridged inguinal hernia repair. We suggest close monitoring of INR levels in long-term warfarin users, even for relatively low-bleeding risk operations such as inguinal hernia repair.

**KEYWORDS:** Inguinal hernia. Anticoagulants. Warfarin. Low-molecular-weight heparin.

## INTRODUCTION

Inguinal hernia repair is the most common operation in general surgery, with more than 20 million hernia repair operations conducted worldwide, every year<sup>1</sup>. The lifetime risk of having inguinal hernia repair is 27% for men and 3% for women<sup>2</sup>. Patients at increased risk of arterial thromboembolism due to conditions, such as atrial fibrillation or prosthetic heart valve, and patients with a history of venous thromboembolism require long-term anticoagulation treatment<sup>3</sup>.

Vitamin K antagonist warfarin is a commonly used oral anticoagulation agent; however, it may pose a bleeding risk in

patients requiring surgery. Warfarin therapy is interrupted in most types of major surgery in order to minimize blood loss. Patients at high risk of a thromboembolic event are recommended to discontinue warfarin and bridge the perioperative period by switching to a short-acting anticoagulant such as subcutaneous low-molecular-weight heparin (LMWH) or intravenous unfractionated heparin<sup>4</sup>. However, guidelines are less clear in patients at moderate risk of bleeding and/or moderate risk of a thromboembolic event. As common as hernia repair may be, the number of studies investigating postoperative complications following LMWH-bridged hernia repair surgery is few.

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Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.

Received on August 23, 2021. Accepted on August 29, 2021.

In this study, we aimed to determine the incidence of bleeding complications and investigate factors related to bleeding complications in long-term warfarin users undergoing inguinal hernia repair via LMWH bridging protocol.

## METHODS

This was a retrospective study of LMWH bridging of patients on long-term warfarin treatment, undergoing inguinal hernia repair. We reviewed files of patients having inguinal hernia repair within the past 2 years and identified 30 patients who had been on long-term warfarin therapy prior to the operation. All patients were managed with LMWH bridging. Patient characteristics, reason for warfarin use, operative characteristics, timing of warfarin discontinuation and reinitiation, timing of LMWH bridging, preoperative and postoperative international normalized ratio (INR) values, and postoperative complications were recorded.

Factors related to complications were investigated. The design of this study has been approved by local Ethics Committees. Due to the retrospective nature of this study, the Ethics Committee did not require written consent from the participants.

### Statistical analysis

SPSS version 17.0 was used in the statistical analysis. Descriptive statistics were used to summarize data: continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as number and percentage. Dependent group comparisons were performed using repeated-measures analysis of variance and paired-sample *t* test. Independent group comparisons were performed using Mann-Whitney *U* test. Comparison of categorical variables was performed using chi-square or Fisher's exact test. The limit of statistical significance was set at  $p < 0.05$ .

## RESULTS

A review of hospital records from the past 2 years revealed 30 inguinal hernia repair patients (4 women and 26 men) who had been on long-term warfarin treatment. The mean age of the patients was 57.4 years, ranging between 38 and 72 years. Indication for warfarin use was heart valve disease ( $n=15$ ), atrial fibrillation ( $n=7$ ), deep venous thrombosis (DVT) ( $n=3$ ), cerebrovascular event ( $n=3$ ), and pulmonary embolism ( $n=2$ ) (Table 1). The majority of patients had a primary hernia (90%), and most patients were diagnosed with indirect inguinal hernia (70%) (Table 1).

Surgical characteristics are summarized in Table 2. Elective surgery was performed on 26 patients, while emergency surgery

was performed on 4 patients. In total, 7 (23.3%) patients had postoperative bleeding complications, with 4 (13.3%) patients having ecchymosis and 3 (10%) developing hematoma. All cases with hematoma resolved naturally without surgical intervention. No venous thromboembolic events were recorded in the postoperative follow-up of patients. There was no significant

**Table 1.** Patient characteristics.

	n (%)
Male/female	26/4 (86.7/13.3)
Indication for warfarin use	
Heart valve disease	15 (50)
Arterial fibrillation	7 (23.3)
Deep venous thrombosis	3 (10)
Cerebrovascular event	3 (10)
Pulmonary embolism	2 (6.7)
Hernia type	
Primary/secondary	27/3 (90/10)
Direct	6 (20)
Indirect	21 (70)
Femoral	2 (6.7)
Pantaloon	1 (3.3)
Hernia location	
Right	19 (63.4)
Left	9 (30)
Bilateral	2 (6.6)

**Table 2.** Surgical characteristics.

	n (%)
Elective surgery	26 (86.7)
Emergency surgery	4 (13.3)
Type of anesthesia	
Local	1 (3.3)
Regional	22 (73.3)
General	7 (23.4)
Surgical drain present	
<24 h	5 (71.4)
24–48 h	1 (14.2)
48–72 h	1 (14.2)
Bleeding complications	
Hematoma	4 (13.3)
Ecchymosis	3 (10)

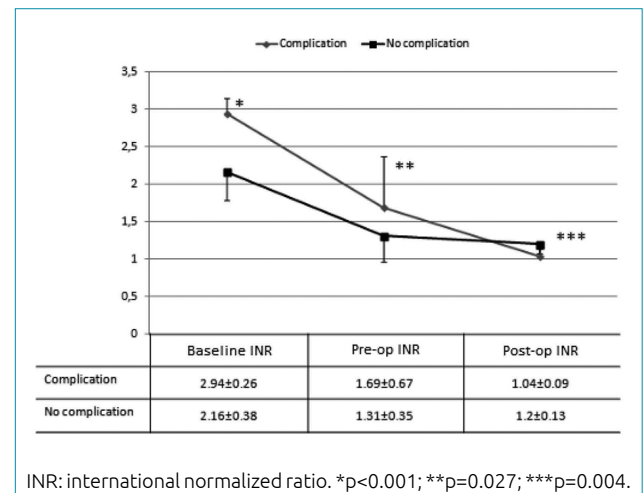
difference between patients with and without complications in terms of patient or surgical characteristics (Table 3). In addition, the timing of the LMWH bridging protocol was not significantly different between the groups (Table 4). INR readings were taken on the day of warfarin discontinuation (baseline INR), preoperatively on the morning of surgery (pre-op INR), and on the day of warfarin reinitiation (post-op INR).

Baseline ( $2.94 \pm 0.26$  versus  $2.16 \pm 0.38$ ,  $p < 0.001$ ) and pre-op INR values ( $1.69 \pm 0.67$  versus  $1.31 \pm 0.35$ ,  $p = 0.027$ ) were significantly higher, while post-op INR values ( $1.04 \pm 0.09$  versus  $1.2 \pm 0.13$ ,  $p = 0.004$ ) were significantly lower in patients having bleeding complications (Figure 1).

## DISCUSSION

In this retrospective study, we found the incidence of all bleeding complications was 23.3%, while the incidence of hematoma development was 10%. Baseline, pre-op INR, and post-op INR were the only variables associated with postoperative bleeding complications following LMWH-bridged inguinal hernia repair surgery. Mean INR on the day of surgery was 1.69 in patients developing complications and 1.31 in patients without complications.

Perioperative management of patients on long-term anticoagulation therapy depends on the patient's risk of having a thromboembolic event and the risk of bleeding. However, there are no clear-cut recommendations on perioperative



**Figure 1.** Comparison of international normalized ratio on the day of warfarin discontinuation (baseline INR), on the day of surgery (pre-op INR), and on the day of warfarin reinitiation (post-op INR) in patients with and without bleeding complications.

**Table 3.** Comparison of patient and surgical characteristics according to complication.

	Complication, n=7	No complication, n=23	p
Gender			
Male/female	6/1 (85/15)	20/3 (87/13)	1.000
Hernia location			
Right/left/bilateral	5/2/0 (70/30/0)	14/7/2 (60/30/10)	0.667
Hernia type			
Primary/secondary	6/1 (85/15)	21/2 (91/9)	1.000
Surgery			
Emergency/elective	0/7 (0/100)	4/19 (18/82)	0.559
Anesthesia			
Local/regional/general	0/4/3 (0/50/50)	2/16/5 (8/70/22)	0.057
Surgical drain			
Yes/no	3/4 (43/57)	4/19 (18/82)	0.971

**Table 4.** Comparison of low-molecular-weight heparin bridging periods according to complication.

	Complication, n=7	No complication, n=23	p
Warfarin discontinuation and LMWH initiation*	$6.00 \pm 2.61$	$6.29 \pm 1.71$	0.926
Warfarin reinitiation†	$2.67 \pm 0.82$	$3.14 \pm 0.67$	0.138
LMWH discontinuation†	$5.34 \pm 0.52$	$5.45 \pm 0.61$	0.562

LMWH: low-molecular-weight heparin. \*Number of days before surgery; †Number of days after surgery.

anticoagulation management for the majority of patients with a mechanical heart valve, atrial fibrillation, or DVT, who have a moderate risk of thromboembolism and a low/moderate risk of bleeding<sup>4</sup>.

Our standard perioperative anticoagulation management protocol in hernia repair surgery involves warfarin interruption and LMWH bridging. LMWH bridging was shown to be a safe and effective method to manage anticoagulation during the perioperative period of a variety of surgeries, in patients with mechanical heart valves, atrial fibrillation, or DVT in retrospective observational studies and prospective registries<sup>5-7</sup>. LMWH is preferred to unfractionated heparin as it can be safely delivered at fixed doses in an outpatient setting, minimizing hospital stay and its related costs<sup>8</sup>.

The incidence of bleeding complications found in this study was similar to the rates reported by Bombuy et al.<sup>9</sup>, who employed the same standard LMWH bridging protocol for patients on long-term warfarin therapy undergoing elective hernia repair. In their study, among 47 patients bridged with LMWH in the perioperative period, 6 (13%) had surgical-site hematoma and 1 patient had major bleeding, necessitating surgical intervention<sup>9</sup>. No thromboembolic events or deaths were seen in either study.

As hernia repair is considered a low-bleeding risk surgery, some groups investigated the possibility of continuing therapeutic dose warfarin in the perioperative period. In a retrospective study, Sanders et al.<sup>10</sup> investigated the outcome of inguinal repair surgery in 49 patients while using full-dose warfarin. The rate of small hematomas requiring no intervention was 14.2%, while the rate of large hematomas requiring surgical or medical intervention was 8.2%. They found a significantly higher risk of hematoma in patients with INR $>3$  and suggested that patients may undergo inguinal repair while on warfarin therapy, as long as INR is  $<3$ . In another study, McLemore et al.<sup>11</sup> reported a similar rate of postsurgical hematoma in inguinal hernia repair patients who continued warfarin (2/19) and those who had heparin bridging (2/15), even though most patients continuing warfarin had an INR $>3$  and those with heparin bridge had INR $<1.5$ . However, they indicated that due to a limited number of patients, their study may lack statistical power to detect a significant difference between surgical-site hematomas. Although these studies appear to undermine the importance of having INR $<1.5$  preoperatively, there could be inherent biases in the selection of patients, as warfarin continuation was not their standard protocol.

The American Academy of Neurology published a recent guideline on periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular

disease<sup>12</sup>, where inguinal herniorrhaphy was listed among procedures that possibly do not increase bleeding risk. Thus, they had a Level C recommendation to continue warfarin in patients undergoing hernia repair. In contrast, we preferred to exercise caution against the continuation of warfarin during hernia repair, since INR was the only significant factor associated with bleeding in our study. As far as we know there is no increased risk of thromboembolism associated with the use of LMWH bridging, warfarin continuation would only serve to simplify the perioperative management protocol. Warfarin continuation during hernia repair would necessarily mean having INR $>2$  or even  $>3$  and may yet show an increased risk of bleeding when practiced in larger numbers.

Smoot et al.<sup>13</sup> recommended meticulous management of patients requiring warfarin, as chronic warfarin may be a risk factor for postoperative hematoma development in inguinal hernia repair. The recommended current procedure is for warfarin interruption that is omitted for 3 days before elective surgery and then used bridging LMWH for patients with the low/moderate bleeding risk category concomitant high-risk thromboembolism<sup>14</sup>. The biological half-life of warfarin is 36–42 h, which is based on this timing of warfarin interruption. In this process, the INR falls below 2<sup>15</sup>. Postprocedure INR $>3$  significantly increases the risk of major bleeding (associated decrease in hemoglobin $\geq 20$  g/L) in patients on long-term warfarin<sup>16</sup>. Although the value of INR is more clearly defined for major bleeding, it is difficult to estimate the value for minor bleeding. Although the surgeon feels safe to prevent postoperative bleeding with an INR of  $<1.5$  preoperatively, INR $<2$  is acceptable in patients at high risk of thromboembolism. In this study, the difference between the values in this INR range seems to be significant for minor bleeding.

## CONCLUSIONS

This study has limitations. Due to the insufficient number of patients included in this study, we could not obtain a significant INR cutoff value for minor bleeding. Since warfarin continuation during inguinal hernia repair is being discussed as a possibility, studies focused on perioperative management of hernia repair are needed. On the other hand, the strength of this study is the investigation of LMWH bridging in a homogeneous group of hernia repair patients, while the less number of such patients is a limitation. Future studies with large-scale patient series may be useful to determine the appropriate INR range to prevent minor bleeding in low/moderate-risk groups on long-term warfarin.

INR was the only factor associated with bleeding complications in patients receiving long-term warfarin therapy, undergoing LMWH-bridged inguinal hernia repair. We suggest close monitoring of INR levels in long-term warfarin users, even for relatively low bleeding risk operations such as inguinal hernia repair.

## AUTHORS' CONTRIBUTIONS

**EGD:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **IK:** Data curation. Software. **ÖP:** Formal analysis. **MÖ:** Project administration. **MK:** Investigation, Supervision.

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