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Research Article

The Likelihood of Wound Complications Following the Use of Rivaroxaban as a Thrombo-Prophylactic Agent in Patients Undergoing Spinal Canal Stenosis Surgery: A Case Series

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Abstract

Background: Wound complications are major morbidities after orthopedic surgery, and thrombo-prophylactic drugs may increase the likelihood of such complications. In this regard, our study has evaluated the possible effects of rivaroxaban on wound complication issues following spinal canal stenosis surgery.
Methods: This prospective cohort study was conducted on 40 patients suffering from spinal canal stenosis secondary to degenerative lumbar spine changes. The eligible patients included those patients receiving rivaroxaban to prevent thrombo-emboli post-operatively. The patients were followed up for three months and assessed for postoperative wound-related complications.
Results: None of the patients suffered vascular and thromboembolic complications. Regarding wound complications, these events are mostly limited to the first week post-operatively, including wound dehiscence in 5.0%, serosanguineous discharge in 25.0%, erythema in 35.0%, superficial infection in 10.0%, requiring surgical debridement in 5.0%, cellulitis in 10.0%, and wound induration in 30.0%. Deep infection or hematoma was not reported in our patients. Erythema and wound induration remained 10.0% and 15.0% within the second week, respectively. The hypertrophic scar was a delayed complication that appeared in 15.0% of patients within 1 to 3 months post-operatively.
Conclusion: The main risk profiles related to wound complications, especially infections, were a history of hypertension (HTN), uncontrolled diabetes mellitus (DM), and renal insufficiency. The use of rivaroxaban may be accompanied by temporary and minor wound complications and not with potentially debilitating morbidity in patients undergoing spinal canal stenosis surgery. Therefore, its prescription as a safe thrombo-prophylactic drug in patients undergoing spinal canal stenosis surgery is confidently recommended.

Keywords: Cohort Studies; Postoperative Complication; Spine; Surgery; Wounds

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Background

Venous thromboembolism (VTE) is one of the main and life-threatening problems in orthopedic surgeries; therefore, the method of prophylaxis and drug of choice for this complication has always been a challenge for surgeons (1). For the past 20 years, low-molecular-weight heparin (LMWH) has been recommended for the prophylaxis of major thrombosis (2), but the method of prescribing the drug, the need for subcutaneous injection, and patient compliance are some of the problems with this drug (2, 3).

Xarelto (rivaroxaban) is a direct oral active factor Xa inhibitor medication (3) that received the United States Food and Drug Administration (FDA) approval in 2011 for thromboembolic prophylaxis in the knee and hip arthroplasty procedures (4). Other main indications for using this drug include secondary prevention of recurrent VTE as well as reducing the risk for brain stroke in the field of arrhythmic events (5, 6). Due to the advantages of this drug, including easy administration, no need for monitoring, no risk of thrombocytopenia, no need for dose adjustment, larger therapeutic index, and fewer drug interactions than other oral anticoagulants (5, 7), this medication has been proposed as a thrombo-prophylactic agent recently.

Following comprehensive studies on rivaroxaban in the field of orthopedic surgery as a postoperative prophylactic agent and its hopeful outcomes in this field, such as a reduced risk of bleeding, several physicians and numerous studies have paid attention to its potential effects on other procedural-related sequels, such as wound sequels (8). Considering the results of increasing wound complications in using this drug in hip and knee replacement surgeries (9), this study is the first research project to evaluate wound complications in patients who have undergone spinal surgery and have not received enoxaparin for thrombo-prophylaxis.

Methods

This prospective cohort study was conducted on 40 patients suffering from spinal canal stenosis secondary to degenerative changes of the lumbar spine without spondylolisthesis who have undergone laminectomy without the need for elective fusion at Sina Hospital, Tehran, Iran, from 2017 to 2019. This study has been firstly approved by the Ethics Committee of Tehran University of

Medical Sciences (code: IR.TUMS.MEDICINE.REC.1396.3376).

The eligible patients included those patients receiving rivaroxaban to prevent thromboembolism events. In this regard, those without indications for thromboembolism prophylaxis or without conscious satisfaction to participate in the study were not included in our study. Besides, those who received anticoagulants in the last three months, had evidence of active bleeding or high risk for bleeding, had not been referred for follow-up, or had not taken their medication were all excluded from the study.

The required information was evaluated and collected by the examiner in the form of a questionnaire, which was prepared for information at the time of admission and information about referrals to the clinic after the operation, in the first and second weeks, as well as at the end of the first and third months of surgery. At the time of admission, patients' data including age, weight and height, risk profiles related to the risk for hypercoagulopathy [history of hypertension (HTN), hyperlipidemia, previous history of VTE, smoking, and diabetes mellitus (DM)], history of steroid use, history of receiving antibiotics in the last ten days, history of renal failure, serum hemoglobin level, prophylactic antibiotics received, the volume of intraoperative bleeding, and type of suture used were all collected. Contact information for patients was also obtained for access and more information if necessary.

Prior to discharge, the patient received the necessary training and advice on the need for dressing at the earliest opportunity and the correct method of dressing and taking care of the wound.

The duration of hospitalization post-operatively in all patients was one day, and they received the first dose of the drug during this period. The surgery technique, incision, approach, and final wound dressing were the same for all the patients who entered the study. A single spine surgeon performed all surgeries. The only difference was the number of stenotic surfaces that had undergone surgery. The drug prescribed to all patients was provided by a single pharmaceutical company (Abidi Pharmaceutical Company) and prescribed with the same dose of 20 mg daily with food for 14 days.

The primary endpoints assessed were would-related complications, including superficial hematoma, serosanguineous discharge, erythema, superficial infection, deep infection, need for surgical debridement, cellulitis wound induration, and hypertrophic scar. The secondary endpoints were related to VTE-related sequels, including deep vein thrombosis (DVT), pulmonary thromboembolism, epidural hematoma, subdural hematoma, and other sources of bleeding, as well as reducing serum hemoglobin levels within the first week of operation.

Throughout the study, the researcher was in contact with the patients. Before each visit to the clinic, the patients were contacted and reminded to refer and follow up on their condition. Following the patients to evaluate the complications of the wound, the researcher visited the patinets after the operation, in the first and second weeks, and at the end of the first and third months.

For statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using a t-test or Mann-Whitney test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. The categorical variables were compared using the chi-square test or Fisher's exact test if required. P-values of ≤0.05 were considered statistically significant. The SPSS statistical software (version 23.0, IBM Corporation, Armonk, NY, USA) was used for the statistical analysis.

Sample size calculation: According to the results of the study by Banat et al., the prevalence rate of thromboembolism event in the group receiving rivaroxaban was found to be 2.7% (10). Considering the reliability coefficient of 0.05 and the accuracy limit of 0.05, the minimum sample size required for the study was estimated to be 40 people:

$$N = P \times (1 - P) \times Z_{1-\frac{\alpha}{2}}^2 / d^2$$

$$P = 0.027, \alpha = 0.05, Z_{1-\frac{\alpha}{2}} = 1.96, d = 0.05$$

$$N = 40$$

N: Number; P: Prevalence; d: Accuracy limit; Z: Z score for reliability coefficient of 0.05

Results

Initially, access was provided to 43 patients, 3 of whom were excluded from the study due to exclusion criteria, one due to a documented history of epidural bleeding, and the other two due to the lack of regular visits to the clinic; thus, 40 patients were entered into the final analysis. The following variables have not been checked due to being the same in all cases: 1) intraoperative prophylaxis antibiotics administered to all patients as cefazolin (1 to 2 g intravenously), 30 to 60 minutes before surgery, which was repeated every 8 hours until 24 hours post-operatively, and 2) the type of suture performed, which silk thread was used in all the patients to repair the subcutaneous tissue and nylon thread to repair the skin tissue under the same conditions and the same technique. During telephone calls with the patients, none of them complained of any side effects such as constipation, diarrhea, nausea and vomiting, arthralgia, limb pain, dizziness, headache, and itching following oral administration of this drug.

As shown in table 1, the average age of patients was 57.00 ± 12.32 years, and 30.0% were men. Regarding underlying risk profiles, 30.0% were hypertensive, 30.0% were diabetics, 20.0% were smokers, and 55.0% had a history of dyslipidemia. None of them had a history of thromboembolism.

Table 1. Baseline characteristics of the study population (n = 40)

Item	Value
Male gender	12 (30.0)
Mean age (year)	57.00 ± 12.32
Mean BMI (kg/m²)	28.41 ± 2.56
History of thromboembolism	0 (0)
History of hypertension	12 (30.0)
History of diabetes mellitus	12 (30.0)
History of smoking	8 (20.0)
History of hyperlipidemia	22 (55.0)
History of smoking	1 (2.5)
History of antibiotic use	6 (15.0)
Mean serum HbA1c level (%)	5.90 ± 0.89
Serum urea level (mg/dl)	37.65 ± 12.23
Serum creatinine level (mg/dl)	1.08 ± 0.17
Volume of intraoperative bleeding (ml)	360.00 ± 166.87
Serum hemoglobin level (mg/dl)	13.36 ± 1.72
Serum hematocrit level (mg/dl)	39.81 ± 4.78

Data are presented as mean ± standard deviation (SD) or number (%)
BMI: Body mass index; HbA1c: Hemoglobin A1c

Regarding wound-related complications (Table 2), most sequels were reported within the first week of postoperative assessment as wound dehiscence in 5.0%, serosanguineous discharge in 25.0%, erythema in 35.0%, superficial infection in 10.0%, requiring surgical debridement in 5.0%, cellulitis in 10.0%, and wound induration in 30.0%. In addition, erythema and wound induration remained within the second week in 10.0% and 15.0% of the patients, respectively. The hypertrophic scar was found to be a delayed complication that appeared in 15.0% of patients within the first month and remained within the third month of assessment.

Table 2. Wound-related complications

Complication	1st week	2nd week	1st month	3rd month
Dehiscence	2 (5.0)	0 (0)	0 (0)	0 (0)
Superficial hematoma	0 (0)	0 (0)	0 (0)	0 (0)
Serosanguineous discharge	10 (25.0)	0 (0)	0 (0)	0 (0)
Erythema	14 (35.0)	4 (10.0)	0 (0)	0 (0)
Superficial infection	4 (10.0)	0 (0)	0 (0)	0 (0)
Deep infection	0 (0)	0 (0)	0 (0)	0 (0)
Need for surgical debridement	2 (5.0)	0 (0)	0 (0)	0 (0)
Cellulitis	4 (10.0)	0 (0)	0 (0)	0 (0)
Wound induration	12 (30.0)	6 (15.0)	0 (0)	0 (0)
Hypertrophic scar	0 (0)	0 (0)	6 (15.0)	6 (15.0)

Data are presented as number (%)

None of the patients suffered vascular complications, including DVT, pulmonary emboli, epidural or subdural hematoma, or documented bleeding source. Reducing hemoglobin level within the first week of assessment was 0.75 ± 0.39 g/dl.

Comparing baseline parameters between the two groups with and without wound-related complications (Table 3) showed significantly higher rates of HTN and DM, higher level of hemoglobin A1c (HbA1c), as well as lower levels of serum hematocrit.

Table 3. Comparing baseline characteristics between those with and without wound complications

Parameter	With wound complication	Without wound complication	P-value
Male gender	4 (25.0)	8 (33.0)	0.729
Mean age (year)	57.38 ± 11.27	56.75 ± 13.20	0.924
Mean BMI (kg/m2)	28.68 ± 3.29	28.22 ± 1.99	0.672
History of thromboembolism	0 (0)	0 (0)	-
History of hypertension	12 (75.0)	0 (0)	< 0.001
History of diabetes mellitus	10 (62.5)	2 (8.3)	< 0.001
History of smoking	2 (12.5)	6 (25.0)	0.439
History of hyperlipidemia	12 (75.0)	10 (41.7)	0.054
History of smoking	1 (6.2)	0 (0)	0.400
History of antibiotic use	4 (25.0)	2 (8.3)	0.195
Mean serum HbA1c level (%)	6.55 ± 0.92	5.46 ± 0.54	< 0.001
Serum urea level (mg/dl)	42.13 ± 15.88	34.67 ± 8.11	0.141
Serum creatinine level (mg/dl)	1.15 ± 0.21	1.03 ± 0.12	0.113
Volume of intraoperative bleeding (ml)	375.00 ± 187.97	350.00 ± 154.63	0.279
Serum hemoglobin level (mg/dl)	12.67 ± 1.80	13.82 ± 1.54	0.070
Serum hematocrit level (mg/dl)	37.41 ± 4.84	41.40 ± 4.10	0.023

Data are presented as mean ± standard deviation (SD) or number (%)
BMI: Body mass index; HbA1c: Hemoglobin A1c

Moreover, comparing the subgroups with and without wound infection (Table 4) showed higher rates of HTN and DM, higher level of HbA1c, and higher mean of serum urea in the former group.

Table 4. Comparing baseline characteristics between those with and without wound infection

Parameter	With wound infection	Without wound infection	P-value
Male gender	2 (50.0)	10 (27.8)	0.570
Mean age (year)	66.00 ± 8.08	56.00 ± 13.38	0.074
Mean BMI (kg/m2)	29.32 ± 3.63	28.30 ± 2.46	0.499
History of thromboembolism	0 (0)	0 (0)	-
History of hypertension	4 (100)	8 (22.2)	0.005
History of diabetes mellitus	4 (100)	8 (22.2)	0.005
History of smoking	0 (0)	8 (22.2)	0.566
History of hyperlipidemia	12 (75.0)	18 (50.0)	0.114
History of smoking	0 (0)	1 (2.8)	0.114
History of antibiotic use	2 (50.0)	4 (11.1)	0.100
Mean serum HbA1c level (%)	6.77 ± 0.37	5.80 ± 0.88	0.008
Serum urea level (mg/dl)	55.50 ± 6.35	35.67 ± 11.07	0.003
Serum creatinine level (mg/dl)	1.34 ± 0.29	1.05 ± 0.13	0.060
Volume of intraoperative bleeding (ml)	300.00 ± 230.94	366.67 ± 161.24	0.811
Serum hemoglobin level (mg/dl)	13.10 ± 1.96	13.39 ± 1.72	0.879
Serum hematocrit level (mg/dl)	37.85 ± 0.06	40.02 ± 4.92	0.346

Data are presented as mean ± standard deviation (SD) or number (%)
BMI: Body mass index; HbA1c: Hemoglobin A1c

Discussion

As expected, rivaroxaban successfully prevented thromboembolic complications after spinal canal stenosis surgery, and none of these complications occurred after surgery in our patients.

We have shown that wound complications following the administration of this drug in patients undergoing spinal canal stenosis surgery are mostly minor and temporary, and basically heal completely within the first week after surgery without potentially prolonged morbidities. In fact, among the common complications that can be seen after spinal canal stenosis surgery, only a limited number of complications, including erythema and wound induration (in one-third of patients within the first week) and hypertrophic scar (as a delayed sequel in 15% of patients within 1 to 3 months after surgery) were reported. As shown in different studies, wound complications are one of the prominent disturbing events after a spinal canal stenosis operation. As indicated by Deyo et al., superficial and deep infections occurred in 1.9% and 1.2%, respectively, and wound disruption in 0.3% of patients (11).

In Nahhas et al. study, 4.2% of cases undergoing thoracolumbar spinal fusions had at least one wound complication, especially those with obesity, preoperative transfusion, preoperative wound infection, and prolonged operation (12).

Wang et al. also indicated wound complications following lumbar spinal stenosis surgery in 24 out of 88 patients older than 75 years (13). Therefore, the fact that in our study, the significant complications of the wound that can lead to the patients' morbidity were reduced to zero is a very important finding of the safety of rivaroxaban.

Surgical site sequels after spinal canal stenosis surgery can potentially result in morbidity, prolonged hospitalization, and thus increased cost burden. The common precautions used to prevent these complications include controlling preoperative risk profiles, wound debridement, meticulous aseptic techniques, long-term antibiotic use, and wound closure (14-16).

In some cases, even removing instrumentation is also indicated (14). Due to the prevalence of wound infection resulting from the multi-microbial origin, especially Staphylococcus aureus-related wound infection after spinal surgery, broad-spectrum antibiotics may be considered. In the present study, it seems that the provision of initial measures for wound prevention despite administrating rivaroxaban has been very successful in preventing wound infection without additional considerations. Based on our findings, the main risk profiles related to wound complications, especially infections, were history of HTN, uncontrolled DM state, and renal insufficiency. Therefore, along with prophylactic medications and perioperative precautions, controlling the modifiable risk factors is also essential to prevent such complications.

Our study shows its potential importance when, based on a review of literature by the researchers, it is the first to evaluate the effect of rivaroxaban on postoperative wound complications in patients undergoing spinal stenosis surgery. However, our study has also had potential limitations; first, it is not enough to judge only cross-sectional studies to prove the effectiveness of drugs in preventing complications, and it is necessary to design clinical trial studies with greater power. We know this fact and plan to perform more reliable studies to re-evaluate the mentioned results. Besides, the sample size of our

study is small, and therefore, comparative studies with this number of samples cannot provide an accurate picture of the significance of the resulting relationships.

Conclusion

It seems that the use of rivaroxaban may be accompanied by temporary and minor wound complications and not by potentially disturbing morbidities in patients undergoing spinal canal stenosis surgery. Therefore, its use as a safe thrombo-prophylactic drug in patients undergoing spinal canal surgery is confidently recommended. The promising results in the prevention of the discussed complications and minor wound-related problems are the good news of our study. However, since this is the first study of its kind, a detailed assessment of the pathophysiological mechanisms and efficacy of the drug should be extensively studied.

Conflict of Interest

The authors had no conflict of interest.

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