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Comparing aspirin, enoxaparin, and rivaroxaban post primary total knee replacement: A prospective study from Saudi Arabia

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Abstract

Background: Patients undergoing major orthopedic surgery are at significantly high risk for venous thromboembolism (VTE), and therefore the routine use of thromboprophylaxis has been standard-of-care for several years. The aim of this study is to compare the clinical outcomes for aspirin, enoxaparin, and rivaroxaban post primary total knee replacement surgery.

Method: This is a prospective observational study that is done in two medical centers in Saudi Arabia. A prospective data collection sheet was used to follow up each patient for 35 days post-surgery.

Results: In this study, 242 patients were included with a response rate of 87.86% (242/276), according to the type of Extended VTE Prophylaxis medications patients were divided on 3 groups; Enoxaparin 85/242 (35.1 %), Rivaroxaban 128/242 (52.9 %), Aspirin 29/242 (12.0 %).

Conclusion: In this study, rivaroxaban has the worst profile, in both having the highest number of DVT cases, as well as 2 minor bleeding cases. Aspirin group patients have the best profile in terms of complications and recovery measures post-surgery.

Keywords: Aspirin, enoxaparin, rivaroxaban, total knee replacement, compare, clinical outcomes**,** thromboprophylaxis, venous thromboembolism

1. Introduction

Patients undergoing major orthopedic surgery or with major lower extremity injuries are at significantly high risk for VTE, and therefore the routine use of thromboprophylaxis has been standard-of-care for several years [1]. Before thromboprophylaxis was widely used, deep vein thrombosis (DVT), that is usually clinically silent [2], occurred in 40-60% of these patients, pulmonary embolism (PE) occurred in 5-10% of patients, and fatal embolism was one among the foremost common causes of death [3]. The use of evidence-based thromboprophylaxis has been shown to scale back the risk of DVT by a minimum of fiftieth and, as a result, major and fatal VTE are currently terribly uncommon [1]. Actually, huge numbers of clinical trials have evaluated many various thromboprophylaxis modalities for VTE prophylaxis post major orthopedic surgeries [4]. Several oral options are available and approved to be used as VTE prophylaxis post major orthopedic surgeries [1]. A recent study that was done in Saudi Arabia stated that the incidence of symptomatic VTE is 1.9% [5]. One research was performed in seven major hospitals in Saudi Arabia and found that thromboprophylaxis was underused in major Saudi hospitals., Denote a discrepancy between actions and guidelines [6]. The aim of this study is to compare the clinical outcomes for aspirin, enoxaparin, and rivaroxaban post primary total knee replacement surgery.

Method

This is a prospective observational study that is done in two medical centers in Saudi Arabia. Prince Sultan Military Medical City (PSMMC) located in Riyadh, which is considered as one of the most advanced medical centers in the Middle East with a capacity of about 1200 beds, accredited by the International Joint Commission. And King Abd Allah University Hospital (KAAUH) which is located in the southern area of Princess Noura University (PNU) Campus, a 300-bed teaching hospital serving PNU faculty. All patients who underwent primary TKR surgery in the included medical centers between the period of October 2018 till July 2019 were eligible for this study. A prospective data collection sheet was used to follow up each patient for 35 days post-surgery. Type of extended VTE prophylaxis post-surgery for each patient was dependent on surgeons' experience and patients' specific risks. Enoxaparin 40mg, Rivaroxaban 10mg, and Aspirin 160 mg were used in this study. The study was approved by the Institutional Review Board (IRB) in both centers with Reference numbers (HP-01-R-079) and (H-01-R-059) for PSMMC and KAAUH respectively. Inclusion criteria (patients who m*et al*l criteria will be

included) were: Male or Female patients who are planned for elective TKR surgery (primary only), Agreed to sign the Informed consent form (ICF) and aged older than 18 years. Exclusion criteria were Patients receiving anticoagulant for treatment, Patients with a history of DVT or PE, Patients with renal or hepatic failure, renal failure is defined as end-stage kidney disease (on dialysis); hepatic failure is defined as complete liver cirrhosis, pregnant woman, and revision surgeries. During the follow up period all complications were recorded, symptomatic DVT or PE, Bleeding (was defined to include oozing, minor or major bleeding), surgical site infection (SSI), readmission, and sudden death.

Results

In this study, 242 patients were included with a response rate of 87.86% (242/276), according to the type of Extended VTE Prophylaxis medications patients were divided on 3 groups; Enoxaparin 85/242 (35.1 %), Rivaroxaban 128/242 (52.9 %), Aspirin 29/242 (12.0 %). Table 1 shows Patients' demographic characteristics, the mean age for all participants was 65.86±8.96 and most of them were females 137/242 (56.6 %). Body mass index (BMI) population mean was 32.46±5.51. There were statistically significant differences between the extended VTE prophylaxis postoperatively after discharge in age, diseases (RA, osteoarthritis, benign prostatic hyperplasia (BPH), diabetes mellitus (DM), hypertension (HTN), ischemic heart disease (IHD) and gout). For medications (H2 blocker, diabetes' medication, HTN-medication, IHD-medication, gout-medication, proton pump inhibitors (PPIs) and antiplatelet). The mean age of VTE extended analysis among the three groups of enoxaparin, rivaroxaban and aspirin was the highest for enoxaparin group. Seven diseases out of 11 were significantly associated with VTE extended analysis, these seven diseases were rivaroxaban 5 (2.1 %) was highest among the VTE extended analysis that associated with RA then aspirin 4 (1.7 %) and Enoxaparin 2 (0.8 %), respectively. Rivaroxaban 123 (50.8 %) was highest among the VTE extended analysis that associated with osteoarthritis then enoxaparin 83 (34.3 %) and aspirin 25 (10.3 %), respectively. Enoxaparin 7 (2.9 %) and rivaroxaban 1 (0.4 %) were among the VTE extended analysis that associated with BPH, respectively. Rivaroxaban 83 (34.3 %) was the highest among the VTE extended analysis that associated with DM then Enoxaparin 45 (18.6 %) and aspirin 12 (5.0 %), respectively. Rivaroxaban 81 (33.5 %) was the highest among the VTE extended analysis that associated with HTN then Enoxaparin 68 (28.1 %) and aspirin 15 (6.2 %), respectively. Rivaroxaban 81 (33.5 %) was the highest among the VTE extended analysis that associated with IHD then Enoxaparin 68 (28.1 %) and aspirin 15 (6.2 %), respectively. Rivaroxaban and aspirin were equally 2 (0.8 %) among the VTE extended analysis which associated with gout. Among the medicines that used in study area, there were seven out of 13 medications that significantly associated with VTE extended analysis. However, these three drugs were; Rivaroxaban 21 (8.7 %) was the highest among the VTE extended analysis that associated with H2 blocker then aspirin 12 (5.0 %) and Enoxaparin 11 (4.5 %), respectively. Rivaroxaban 83 (34.3 %) was the highest among the VTE extended analysis that associated with diabetic medications then Enoxaparin 45 (18.6 %) and aspirin 12 (5.0 %), respectively. Rivaroxaban 81 (33.5 %) was the highest among the VTE extended analysis that associated with HTN medication, then Enoxaparin 68 (28.1 %) and aspirin 15 (6.2 %), respectively. Enoxaparin 16 (6.6 %) was the highest among the VTE extended analysis that associated with IHD-medications, then rivaroxaban 6 (2.5 %) and aspirin 5 (2.1 %), respectively. Rivaroxaban and aspirin were equally 2 (0.8 %) among the VTE extended analysis that associated with gout medications. Rivaroxaban 97 (40.1 %) was the highest among the VTE extended analysis that associated with PPIs, then Enoxaparin 47 (19.4 %) and aspirin 17 (7.0 %), respectively. Enoxaparin 9 (3.7 %) was the highest among the VTE extended analysis that associated with antiplatelet, then aspirin 4 (1.7 %) and rivaroxaban 3 (1.2 %), respectively.

Table 2 shows Surgical procedure, treatment, risk factors, and recovery measures during hospitalization. There are significant differences in Caprini score, length of hospital stay, length of surgery, pain score, type of analgesia, duration for extended VTE prophylaxis, cost for the extended VTE prophylaxis, mobility within hours post operation (D0), fully mobilized no later than D1, day for start walking post operation, day of achieving full mobilization post operation. The mean (SD) Caprini score was the highest in Enoxaparin 8.07 (0.94) then rivaroxaban 7.84 (0.81) and aspirin 7.10 (0.77). The mean (SD) for duration of hospital stay for Enoxaparin 6.15 (1.37) was the most drug prescribed among the VTE extended analysis which is associated with the length of hospital stay then rivaroxaban 5.57 (1.20) and aspirin 4.79 (1.24), respectively. Similarly, the mean (SD) of length of surgery for Enoxaparin 2.30 (0.60) was the most drug prescribed among the VTE extended analysis which associated with the length of surgery then rivaroxaban 2.15 (0.64) and aspirin 1.72 (0.31), respectively. The frequency of the pain score was highest in severe pain then moderate and mild pain, respectively. However, among the pain score the rivaroxaban 102 (42.1 %), 19 (7.9 %) and 7 (2.9 %) was the most prescribed among the VTE extended analysis, then Enoxaparin 60 (24.8 %), 17 (7.0 %) and 8 (3.3 %), and aspirin 8 (3.3 %), 16 (6.6 %) and 5 (2.1 %) among severe, moderate and mild pain score, respectively. The frequency of type of analgesia (non-opioid, weak opioid and strong opioid) was associated with prescribed among the VTE extended analysis (rivaroxaban 1 (0.4 %), 10 (4.1 %) and 117 (48.3 %), Enoxaparin 4 (1.7 %), 21 (8.7 %) and 60 (24.8 %), and aspirin 1 (0.4 %), 15 (6.2 %) and 13 (5.4 %), respectively). The mean (SD) duration for extended VTE prophylaxis was associated with aspirin 28.48 (1.81), Enoxaparin 19.54 (6.74) and rivaroxaban 18.22 (7.41). The mean (SD) for the cost of the extended VTE prophylaxis medications was associated with Enoxaparin $104.04 (35.06), rivaroxaban $ 58.22 (24.33) and aspirin $ 7.87 (22.20). The frequency of the mobilized patients within hours post-operatively was associated with Enoxaparin 1 (0.4 %) and aspirin 2 (0.8 %). The frequency of patients being fully mobilized no later than on the day after surgery (Day 1) was associated with Enoxaparin 3 (1.2 %), rivaroxaban 5 (2.1 %) and aspirin 9 (3.7 %). The mean (SD) for days needed to start walking post operation was associated with Enoxaparin 2.65 (1.06), rivaroxaban 2.56 (1.03) and aspirin 1.79 (1.15). The mean (SD) for days needed to achieve fully mobilization post operation was associated with Enoxaparin 4.67 (1.60), rivaroxaban 4.09 (1.23) and aspirin 2.72 (1.62).

Table 3 shows Frequencies for all complications post surgeries during follow up period. From all complications deep vein thrombosis cases were associated with rivaroxaban 14 (5.8 %) and Enoxaparin 1 (0.4 %), while aspirin has zero DVT cases. Regarding bleeding, there were 2 cases of minor bleeding in rivaroxaban group, without a significant difference. Moreover, there were 4 cases of readmission in enoxaparin group versus 2 cases in

rivaroxaban group and zero readmission cases in aspirin group without significant differences.

Discussions

In this study, the total symptomatic VTE within 35 days post operation was 4.95% (12/242), which is within the international range for VTE incidence rate. According to the literature, the symptomatic VTE rate during the first 3 months post orthopedic surgery is within the range of 1.3% to 10% [7]. Actually, huge numbers of clinical trials have evaluated many various thromboprophylaxis modalities for VTE prophylaxis post major orthopedic surgeries. Several oral options are available and approved to be used as VTE prophylaxis post major orthopedic surgeries [1], vitamin K antagonists (Warfarin) factor Xa inhibitors like rivaroxaban and apixaban, and direct thrombin inhibitors like dabigatran. A recent meta-analysis done by Lu & Lin, 2018 [8], up to the author knowledge, this is the first meta-analysis that evaluates the overall relative efficacy of LMWH compared with placebo control, factor Xa inhibitors, and direct thrombin inhibitor to be used as prophylactic post-TKR and THR surgeries. Results showed that the prophylactic treatment with LMWH significantly reduces the rate of VTE events when compared to placebo, while factor Xa inhibitors have a better profile in reducing VTE events. However, LMWH has similar VTE incidence rate with direct thrombin inhibitors, but with a lower incidence rate of major bleeding [8]. In this study, rivaroxaban has the worst profile, in both having the highest number of DVT cases, as well as 2 minor bleeding cases. Aspirin group patients have the best profile in terms of complications and recovery measures post-surgery, and this agrees with the literature [9]. Several studies compared the clinical profile for novel oral anticoagulant (NOAC), a recent meta-analysis was done by Cohen, *et al*., 2016 [10], they were comparing rivaroxaban, apixaban, and dabigatran, the author concluded that all NOAC have comparable efficacy in preventing VTE events, but they differ in bleeding risk profile, apixaban is shown to have the most favorable profile between the studied options. This is an observational study without any intervention or randomization, so selection bias could affect the results for this study. Moreover, the assessment of medication compliance relied solely on patients' recall.

Table 1: Comparing Demographic and Clinical Data according to Type of Extended VTE Prophylaxis.

Demographics/ Clinical data		**Enoxaparin 40 mg 85 (35.1 %)**	**Rivaroxaban 10 mg 128 (52.9 %)**	**Aspirin 160 mg 29 (12.0 %)**	**All (N, %)**	***p***
Age	Mean (SD)	67.71 (9.65)	66.02 (8.07)	59.72 (8.18)	65.86 (8.96)	0.000
Gender	Male (N, %)	36 (14.9 %)	51 (21.1 %)	18 (7.4 %)	105 (43.4 %)	0.090
	Female (N, %)	49 (20.2 %)	77 (31.8 %)	11 (4.5 %)	137 (56.6 %)	
BMI	Mean (SD)	32.86 (4.40)	32.52 (6.02)	30.98 (6.02)	32.46 (5.51)	0.282
Lifestyle*	Restricted (N, %)	48 (19.8 %)	61 (25.2 %)	12 (5.0 %)	121 (50.0 %)	0.277
	Normally Active (N, %)	37 (15.3 %)	67 (27.7 %)	17 (7.0 %)	121 (50.0 %)	
	Highly Active (N, %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
Diseases	RA (N, %)	2 (0.8 %)	5 (2.1 %)	4 (1.7 %)	11 (4.5 %)	0.034
	Dyslipidemia (N, %)	24 (9.9 %)	34 (14.0 %)	4 (1.7 %)	62 (25.6 %)	0.287
	Osteoarthritis (N, %)	83 (34.3 %)	123 (50.8 %)	25 (10.3 %)	231 (95.5 %)	0.034
	BPH (N, %)	7 (2.9 %)	1 (0.4 %)	0 (0.0 %)	8 (3.3 %)	0.007
	Asthma (N, %)	4 (1.7 %)	5 (2.1 %)	0 (0.0 %)	9 (3.7 %)	0.506
	DM (N, %)	45 (18.6 %)	83 (34.3 %)	12 (5.0 %)	140 (57.9 %)	0.036
	CKD (N, %)	1 (0.4 %)	1 (0.4 %)	0 (0.0 %)	2 (0.8 %)	0.830
	HTN (N, %)	68 (28.1 %)	81 (33.5 %)	15 (6.2 %)	164 (67.8 %)	0.005
	IHD (N, %)	16 (6.6 %)	6 (2.5 %)	5 (2.1 %)	27 (11.2 %)	0.003
	Gout (N, %)	0 (0.0 %)	2 (0.8 %)	2 (0.8 %)	4 (1.7 %)	0.042
	Hypothyroidism (N, %)	17 (7.0 %)	31 (12.8 %)	5 (2.1 %)	53 (21.9 %)	0.622
Medications	H2 blocker	11 (4.5 %)	21 (8.7 %)	12 (5.0 %)	44 (18.2 %)	0.002
	Analgesic	85 (35.1 %)	128 (52.9 %)	29 (12.0 %)	242 (100.0 %)	-
	A.B	85 (35.1 %)	128 (52.9 %)	29 (12.0 %)	242 (100.0 %)	-
	VTE-Prophylaxis	85 (35.1 %)	128 (52.9 %)	29 (12.0 %)	242 (100.0 %)	-
	Anti-DM	45 (18.6 %)	83 (34.3 %)	12 (5.0 %)	140 (57.9 %)	0.036
	Anti-HTN	68 (28.1 %)	81 (33.5 %)	15 (6.2 %)	164 (67.8 %)	0.005
	Anti-IHD	16 (6.6 %)	6 (2.5 %)	5 (2.1 %)	27 (11.2 %)	0.003
	Anti-gout	0 (0.0 %)	2 (0.8 %)	2 (0.8 %)	4 (1.7 %)	0.042
	PPIs	47 (19.4 %)	97 (40.1 %)	17 (7.0 %)	161 (66.5 %)	0.005
	Antiemetic	85 (35.1 %)	128 (52.9 %)	29 (12.0 %)	242 (100.0 %)	-
	Levothyroxine	15 (6.2 %)	31 (12.8 %)	5 (2.1 %)	51 (21.1 %)	0.445
	Statins	29 (9.5 %)	30 (12.4 %)	4 (1.7 %)	57 (23.6 %)	0.347
	Antiplatelet	9 (3.7 %)	3 (1.2 %)	4 (1.7 %)	16 (6.6 %)	0.015

AB=antibiotics, BMI= Body Mass Index, CKD = chronic kidney disease, DM = diabetes mellitus, HTN = Hypertension, IHD = ischemic heart disease, N= number or frequency of patients, OA = osteoarthritis, PPIs= Proton pump inhibitors, RA = rheumatoid arthritis, SD = standard deviation, TKR = total knee replacement, VTE = venous thromboembolism. To test the difference between continuous variables, compare means ANOVA test was used. Chi square was conducted to test discrete variables (frequencies). * Lifestyle: restricted means always sitting, normal means everyday life activity and highly active means exercising on daily basis.

Table 2: Surgical procedure, treatment, risk factors, and recovery measures during hospitalization.

Demographics/ Clinical data		Enoxaparin 40 mg 85 (35.1 %)	Rivaroxaban 10 mg 128 (52.9 %)	Aspirin 160 mg 29 (12.0 %)	All (N, %)	*p*
Caprini Score	Mean (SD)	8.07 (0.94)	7.84 (0.81)	7.10 (0.77)	7.83 (0.90)	0.000
Risk for bleeding	(N, %)	5 (2.1 %)	4 (1.7 %)	2 (0.8 %)	11 (4.5 %)	0.518
Length of hospital stay	Mean (SD)	6.15 (1.37)	5.57 (1.20)	4.79 (1.24)	5.68 (1.32)	0.000
Type of metal implants	Cemented (N, %)	85 (35.1 %)	128 (52.9 %)	29 (12.0 %)	242 (100.0 %)	-
	Cementless (N, %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
	Others (N, %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
Length of surgery	Mean (SD)	2.30 (0.60)	2.15 (0.64)	1.72 (0.31)	2.15 (0.62)	0.000
Pain Score	No pain (N, %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0.000
	Mild pain (N, %)	8 (3.3 %)	7 (2.9 %)	5 (2.1 %)	20 (8.3 %)	
	Moderate pain (N, %)	17 (7.0 %)	19 (7.9 %)	16 (6.6 %)	52 (21.5 %)	
	Sever pain (N, %)	60 (24.8 %)	102 (42.1 %)	8 (3.3 %)	170 (70.2 %)	
Type of analgesia	No analgesia (N, %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0.000
	Non-opioid (N, %)	4 (1.7 %)	1 (0.4 %)	1 (0.4 %)	6 (2.5 %)	
	Weak opioid (N, %)	21 (8.7 %)	10 (4.1 %)	15 (6.2 %)	46 (19.0 %)	
	Strong opioid (N, %)	60 (24.8 %)	117 (48.3 %)	13 (5.4 %)	190 (78.5 %)	
Extended VTE prophylaxis medications' Cost	Mean (SD)	104.04 (35.6)	58.22 (24.33)	7.87 (22.20)	68.28 (41.88)	0.000
Mobility within hours post operation (D0)	Yes (N, %)	1 (0.4 %)	0 (0.0 %)	2 (0.8 %)	3 (1.2 %)	0.010
	No (N, %)	84 (34.7 %)	128 (52.9 %)	27 (11.2 %)	239 (98.8 %)	
Fully mobilized no later than D1	Yes (N, %)	3 (1.2 %)	5 (2.1 %)	9 (3.7 %)	17 (7.0 %)	0.000
	No (N, %)	82 (33.9 %)	123 (50.8 %)	20 (8.3 %)	225 (93.0 %)	
Day for Start walking post operation	Mean (SD)	2.65 (1.06)	2.56 (1.03)	1.79 (1.15)	2.50 (1.08)	0.001
Day of achieving Fully mobilization post operation	Mean (SD)	4.67 (1.60)	4.09 (1.23)	2.72 (1.62)	4.13 (1.5)	0.000

D0= same operation day, D1= after 24 hours post operation, SD=standard deviation, UFH= unfractionated heparin, VTE= venous thromboembolism. To test the difference between continuous variables, compare means ANOVA test was used. Chi square was conducted to test discrete variables (frequencies)

Table 3: Frequencies for all complications post surgeries during follow up period

Demographics/ Clinical data		Enoxaparin 40 mg 85 (35.1 %)	Rivaroxaban 10mg 128 (52.9 %)	Aspirin 160 mg 29 (12.0 %)	All (N, %)	*p*
Pulmonary embolism event	Yes (N, %)	1 (0.4 %)	0 (0.0 %)	0 (0.0 %)	1 (0.4 %)	0.391
	No (N, %)	83 (34.4 %)	128 (53.1 %)	29 (12.0 %)	240 (99.6 %)	
Sudden death	Yes (N, %)	1 (0.4 %)	0 (0.0 %)	0 (0.0 %)	1 (0.4 %)	0.391
	No (N, %)	83 (34.4 %)	128 (53.1 %)	29 (12.0 %)	240 (99.6 %)	
Deep vein Thrombosis Symptoms	Yes (N, %)	1 (0.4 %)	14 (5.8 %)	0 (0.0 %)	15 (6.2 %)	0.005
	No (N, %)	83 (34.4 %)	114 (47.3 %)	29 (12.0 %)	226 (93.8 %)	
Confirm diagnosis (PE or DVT)	None (N, %)	82 (34.0 %)	114 (47.3 %)	29 (12.0 %)	225 (93.4 %)	0.068
	Confirmed (N, %)	2 (0.8 %)	10 (4.2 %)	0 (0.0 %)	12 (5.0 %)	
	Not confirmed (N, %)	0 (0.0 %)	4 (1.7 %)	0 (0.0 %)	4 (1.7 %)	
Bleeding	No (N, %)	84 (34.9 %)	126 (52.3 %)	29 (12.0 %)	239 (99.2 %)	0.411
	Yes, minor (N, %)	0 (0.0 %)	2 (0.8 %)	0 (0.0 %)	2 (0.8 %)	
	Yes, major (N, %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
Surgical site	Yes (N, %)	0 (0.0 %)	2 (0.8 %)	0 (0.0 %)	2 (0.8 %)	0.411
	No (N, %)	84 (34.9 %)	126 (52.3 %)	29 (12.0 %)	239 (99.2 %)	
Readmission	Yes (N, %)	4 (1.7 %)	2 (0.8 %)	0 (0.0 %)	6 (2.5 %)	0.225
	No (N, %)	80 (33.2 %)	126 (52.3 %)	29 (12.0 %)	235 (97.5 %)	
Did you take the VTE prophylactic medication as prescribed for you?	Yes (N, %)	84 (34.9 %)	125 (51.9 %)	29 (12.0 %)	238 (98.8 %)	0.262
	No (N, %)	0 (0.0 %)	3 (1.2 %)	0 (0.0 %)	3 (1.2 %)	
Tell its name, dose, and schedule	Can tell	56 (23.2 %)	89 (36.9 %)	26 (10.8 %)	171 (71.0 %)	0.055
	Cannot tell	28 (11.6 %)	39 (16.2 %)	3 (1.2 %)	70 (29.0 %)	
Duration for extended VTE-prophylaxis till day 14	Mean (SD)	14 (0.0)	14 (0.0)	14 (0.0)	14 (0.0)	-
Duration for extended VTE Prophylaxis till	Mean (SD)	19.54 (6.74)	18.22 (7.41)	28.48 (1.81)	19.91 (7.45)	0.0

day 35						00

DVT= Deep vein Thrombosis**,** PE=Pulmonary embolism**,** SD=standard deviation, VTE= venous thromboembolism. To test the difference between continuous variables, compare means ANOVA test was used. Chi square was conducted to test discrete variables (frequencies).

Conclusion

This is a prospective observational study that is done in two medical centers in Saudi Arabia to compare the clinical outcomes for aspirin, enoxaparin, and rivaroxaban post primary total knee replacement surgery. In this study, rivaroxaban has the worst profile, in both having the highest number of DVT cases, as well as 2 minor bleeding cases. Aspirin group patients have the best profile in terms of complications and recovery measures post-surgery.

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List of abbreviations

VTE	venous thromboembolism
TKR	Total Knee Replacement
DVT	deep vein thrombosis.
PE	pulmonary embolism
ICF	Informed consent form
PSMMC	Prince Sultan Military Medical City
KAAUH	King Abd Allah University Hospital
PNU	Princess Noura University
IRB	Institutional Review Board
BMI	Body Mass Index
HTN	Hypertension
DM	Diabetes Mellitus
IHD	Ischemic Heart Disease
US	United States
LOS	length of stay
SSI	surgical site infection
PPI	Proton pump inhibitors
D1	day one
ACCP	American Collage of Chest Physicians.

Declarations

-Ethics approval and consent to participate

The study was approved by the Institutional Review Board (IRB) in both centres, first IRB was obtained from Research Ethics Committee, Scientific Research Center, Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia-11149, with a reference number (HP-01-R-079). Second IRB was obtained from Institutional Review Board (IRB)OV 2018, Princess Nourah bin Abdulrahman University, Riyadh, Kingdom of Saudi Arabia, with a reference number (H-01-R-059). Consent forms were stacked to the survey (written consent forms were used).

-Consent for publication

All authors confirm that the manuscript has been read and approved by all named authors. The order of authors listed in the manuscript has been approved by all named authors.

-Availability of data and material

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

-Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All listed authors meet the International Committee of Medical Journal Editors criteria. We attest that all authors contributed significantly to the creation of this manuscript. 'MA' and 'SAS' have contributed in the idea creation for this research, they have designed methodology. 'MA' wrote the manuscript after the analysis and study findings have been discussed by all contributed authors. Moreover, all authors have been involved in revising this manuscript critically. 'AA' and 'MFA' have been involved in the implementation of this research and adjusting the methodology to suit the relevant guidelines and regulation. 'MA' 'AA' and 'MFA' have been involved in data collection and follow up records for all patients through the study period. Finally, all authors reviewed the manuscript.

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