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Perioperative Medicine



Comparing the post-operative complications following surgery for hip fracture of patients who were on warfarin versus patients who were on novel oral anticoagulants: a meta-analysis

Yuxi Wei^{1†}, Chi Chen^{1†}, Zhihong Yu¹ and Jun Guo^{1*}

Abstract

Background Hip fracture in the elderly is considered a significant public health burden due to a high rate of mortality and this is globally being seen as a serious concern. However, comorbidities requiring anticoagulants are of particular concern in the post-operative setting. In this analysis, we aimed to systematically compare the post-operative complications following surgery for hip fracture of patients who were on warfarin versus patients who were on novel oral anticoagulants (NOACs).

Methods Web of Science, EMBASE, Google Scholar, the Cochrane databases, MEDLINE, and http://www.ClinicalTr ials.gov were searched for relevant studies from January to February 2024. The post-operative complications were considered the endpoints in this study. Risk ratios (RR) with 95% confidence intervals (CIs) were used to represent the data following statistical analysis. Weighted mean difference (WMD) calculated with mean and standard deviation, with 95% CIs, was used to represent the result for mean length of hospital stay.

Results A total number of 15,019 participants with hip fracture were included in this analysis. Eleven thousand two hundred and fifteen (11,215) participants were on warfarin therapy prior to fracture and surgery, whereas 3804 participants were on NOACs. Results of this analysis showed that the risks of post-operative mortality (RR, 1.03; 95% CI, 0.92–1.16; P=0.57), deep vein thrombosis (RR, 1.10; 95% CI, 0.41–2.98; P=0.84), pulmonary embolism (RR, 1.17; 95% CI, 0.44–3.10; P=0.75), stroke (RR, 1.25; 95% CI, 0.23–6.71; P=0.80) and myocardial infarction (RR, 0.42; 95% CI, 0.03–6.98; P=0.55) were not significantly different in patients who underwent surgery for hip fracture and who were on warfarin versus on NOACs. The risks of infection (RR, 0.90; 95% CI, 0.28–2.93; P=0.87) and blood transfusion (RR, 1.08; 95% CI, 0.80–1.45; P=0.62) were also similarly manifested.

However, the length of hospital stay [WMD, -0.93; 95% CI, -1.83 to 0.03; P = 0.04] was significantly less in patients who were on NOACs in comparison to those who were on warfarin.

Conclusions The post-operative complications following surgery for hip fracture of patients who were on warfarin versus patients who were on NOACs were similar. However, those patients who were on warfarin had a significantly longer length of hospital stay.

Keywords Novel oral anticoagulants, Warfarin, Hip fracture, Post-operative complications

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Introduction

Hip fracture in the elderly is considered a significant public health burden due to a high rate of mortality (Roche et al. 2005), and this is globally being seen as a serious concern at both the individual level and the population level. Admissions for hip fracture among the elderly have increased with an estimated current value over 300,000 annual cases which could reach up to 650,000 cases per annum by the year 2050 in the USA (Cooper et al. 1992), and this significant rise has been predicted due to the aging population (Ottesen et al. 2022). In the UK, the incidence of hip fracture has increased from 91,500 cases in the year 2020 (BOA 2018), and is consistently increasing due to this aging population.

With this aging population, non-communicable diseases (NCDs) are also on the rise and several patients suffer from conditions such as diabetes mellitus (DM), cardiovascular diseases (CVDs), atrial fibrillation (AF), cerebro-vascular diseases, cancers, valvular heart diseases, and peripheral vascular diseases (Marengoni et al. 2011) requiring the lifelong use of anticoagulants to reduce the risk of thrombo-embolic events (Henderson and White 2001). Thromboprophylaxis significantly reduces the risk of venous thromboembolism in the elderly (Falck-Ytter et al. 2012). In Canada, there were over 7 million prescriptions for oral anticoagulants in 2013, representing an increase of above 3 million prescriptions over the past 5 years, and those oral anticoagulants were often used by elderly above 50 years old (Weitz et al. 2015). Previously, warfarin, a vitamin-k antagonist, has been used as the most common oral anticoagulant (Ridker et al. 2003). Nevertheless, recent scientific reports have shown novel direct oral anticoagulants to be more effective in preventing thrombo-embolic events without increasing bleeding risks (Chen and Patel 2018).

Comorbidities requiring anticoagulants are of particular concern in the post-operative setting. The rise in the use of potential novel oral anticoagulants (NOACs) has raised concerns due to the reported risk of bleeding post-operatively in several patients (Brekelmans et al. 2017). Therefore, those patients with hip fracture requiring surgery and who are on anticoagulants are at risk of post-operative bleeding, forcing clinicians to stop anticoagulants prior to surgery (Lai et al. 2014). However, due to the lack of consensus on surgical timing in patients on oral anticoagulants, surgeries on such patients have often been delayed, potentially contributing to worse postoperative outcomes (Franklin et al. 2018).

In this analysis, we aimed to systematically compare the post-operative complications following surgery for hip fracture of patients who were on warfarin therapy versus patients who were on NOACs.

Methods

Search databases

The search databases included Web of Science, EMBASE, Google Scholar, the Cochrane databases, MEDLINE (subset PubMed), and http://www.ClinicalTrials.gov.

Search strategies

The above-mentioned electronic databases were carefully searched (from January to February 2024) for publications comparing the post-operative outcomes observed in patients who underwent surgery for hip fracture and who were previously on warfarin versus on NOACs.

The following search terms were used:

- Hip fracture and warfarin
- Hip fracture and novel oral anticoagulants
- Hip fracture and direct oral anticoagulants
- Hip fracture and anticoagulants
- Hip fracture and surgery and warfarin
- Hip fracture and surgery and direct oral anticoagulants
- Hip fracture and surgery and novel oral anticoagulants
- Hip fracture, post-operative outcomes and warfarin
- Hip fracture, post-operative outcomes and novel oral anticoagulants

Reference lists of relevant papers were also searched for publications.

Inclusion and exclusion criteria

The inclusion criteria were:

- (a) Studies that were based on patients with hip fracture who were previously on warfarin versus on NOACs
- (b) Studies that were mentioned above whereby the post-operative outcomes were reported
- (c) Studies that were published in English

The criteria for exclusion included:

- (a) Studies that were literature reviews, systematic reviews or meta-analyses, or any other narrative reviews
- (b) Studies that did not report length of hospital stay or post-operative outcomes
- (c) Studies that did not involve the comparison between warfarin and NOACs
- (d) Studies that were published in another language apart from English

(e) Duplicated studies

Outcomes

The following endpoints were assessed in this analysis:

- (a) Length of hospital stay
- (b) Mortality
- (c) Deep venous thrombosis (DVT)
- (d) Pulmonary embolism (PE)
- (e) Stroke
- (f) Myocardial infarction (MI)
- (g) Infection
- (h) Blood transfusion

The outcomes which were reported in each original study have been listed in Table 1.

All the outcomes were of the same level. We did not differentiate between primary or secondary. All were primary outcomes that we assessed.

Data extraction and quality assessment

All the authors independently extracted data from the selected original studies. Important details including the total number of participants who were on warfarin and NOAC therapy respectively, the post-operative outcomes which were reported in each study, the number of events associated with respective outcomes, the baseline features, the methodological features, and the percentage of participants with early or delayed surgery were all carefully extracted. Any disagreement which occurred at the time of data extraction was carefully discussed among the authors and a consensus was reached.

The quality assessment of the studies was carried out with the recommendations from the Newcastle Ottawa Scale (NOS) (Stang 2010). Grades (A, B or C) were given to denote low, intermediate, or a high risk of bias.

Statistical analysis

This is a meta-analysis based on the post-operative complications following surgery for hip fracture in patients who were previously on warfarin versus those who were on NOACs. The RevMan software (version 5.4) was used to analyze the data. Heterogeneity is common in metaanalyses (Langan 2022). Therefore, in order to assess for heterogeneity, first of all, the Q statistic test was used whereby a subgroup with a P value less or equal to 0.05 was considered statistically significant, whereas a subgroup with a P value greater than 0.05 was considered statistically insignificant. Secondly, the I^2 statistic test was used to assess for heterogeneity. A subgroup analysis with an I^2 percentage above 50% was considered to have a high heterogeneity indicating the use of a random effect statistical model during analysis, whereas a subgroup analysis with an I^2 percentage below 50% was considered to have a low heterogeneity indicating the use of a fixed effect statistical model during analysis.

Risk ratios (RR) with 95% confidence intervals (CIs) were used to represent the data following statistical analysis.

Weighted mean difference (WMD) calculated with mean and standard deviation, with 95% CIs was used to represent the result for mean length of hospital stay.

Sensitivity analysis was also carried out in order to ensure that the results of this meta-analysis were not

Table 1 Post-operative complications reported

Studies	Complications reported	Type of participants
Aigner 2022	Surgical complications, soft tissue complications, length of hospital stay, mortality	Geriatrics hip fracture patients
Bruckbauer 2019	Mortality, blood loss, blood transfusion, length of hospital stay	Patients with hip fractures
Cafaro 2019	Mean length of hospital stay, venous thromboembolism, deep vein thrombosis, pulmonary embolism, pre-operative major bleeding, stroke, mortality, blood transfusion	Patients with hip fractures
Creeper 2022	Blood transfusion	Elderly with hip fracture
Daugaard 2019	Mortality, blood transfusion	Patients with hip fracture
Elete 2023	Length of hospital stay, mortality, overall complication, stroke, infection in hospital	Patients with hip fracture
Lott 2018	Length of hospital stay, blood loss, number of complications	Patients with hip fracture
Mahmood 2021	Mortality, blood transfusion, infection, re-operation	Patients with hip fracture
Noll 2023	Mortality, pulmonary embolism, deep vein thrombosis, infection, stroke, blood transfusion, myocardial infarction	Patients with hip fracture
Rostagno 2023	Length of hospital stay, atrial fibrillation, deep vein thrombosis and pulmonary embolism	Elderly patients with hip fracture
Rutenberg 2018	Length of hospital stay, infection, deep vein thrombosis, atrial fibrillation, myocardial infarction, stroke	Patients with hip fracture
Saliba 2020	Mortality	Elderly patients with hip fracture
Tran 2015	Venous thromboembolism, mortality, stroke, pulmonary embolism	Patients with hip fracture

influenced by any particular study. This sensitivity analysis was carried out by a method of exclusion whereas each of the study which has been selected for this metaanalysis was excluded one by one, by turn, and a new analysis was carried out each time one particular study was excluded, in order to observe for any significant difference in the main results of this analysis.

Publication bias was also carried out. This publication bias was carried out by visually observing the funnel plot which was generated through RevMan.

Ethical approval

An ethical or board review approval was not required for this study. In this study, the authors have used data which were published from previous studies. No experiments from humans or animals have been carried out by any of the authors.

Results

Search outcomes

The preferred reporting items for systematic reviews and meta-analyes (PRISMA) guideline was followed (Page et al. 2020). A total number of 106 publications were obtained through the search process. A first round of elimination was carried out following a thorough assessment of the titles and abstracts. Thereafter, 64 full-text articles were assessed for eligibility. A second round of elimination was carried out after considering the criteria for inclusion and exclusion. The reasons for this second round of elimination were due to:

- (a) Systematic review/meta-analyses/literature reviews(6)
- (b) Letter to editors (5)
- (c) Absence of a control group (4)
- (d) The data could not be used (2)
- (e) The post-operative outcomes were not reported (2)
- (f) Repeated studies (32)

Finally, only 13 studies (Aigner et al. 2022; Bruckbauer et al. 2019; Cafaro et al. 2019; Creeper et al. 2022; Daugaard et al. 2019; Elete et al. 2023; Lott et al. 2018; Mahmood et al. 2021; Noll et al. 2023; Rostagno et al. 2023; Rutenberg et al. 2018; Saliba et al. 2020; Tran et al. 2015) were selected for this meta-analysis. The flow diagram for this study selection has been demonstrated in Fig. 1.



Fig. 1 Flow diagram representing the study selection

General features of the studies

A total number of 15,019 participants with hip fracture were included in this analysis. Eleven thousand two hundred and fifteen (11,215) participants were on warfarin therapy prior to surgery, whereas 3804 participants were on NOACs as shown in Table 2. All the studies were observational studies including a higher number of retrospective cohorts followed by prospective and case-control studies. Studies with the highest number of participants included Daugaard 2019, Aigner 2022, and

Table 2 General features of the studies

Noll 2023, whereas studies with the lowest number of participants included Cafaro 2019, Elete 2023, Lott 2018, and Bruckbauer 2019.

Baseline features of the participants

The baseline features of the participants have been listed in Table 3. The mean age of the participants ranged from 81.4 to 90.0 years, and the percentage of male participants ranged from 24.6 to 46.4%. Majority of the participants were female patients. The mean percentage

Studies	No. of participants using	No. of participants using	Type of study	Bias risk grade
	warfarin (<i>n</i>)	NUACS (<i>n</i>)		
Aigner 2022	1325	1361+234	Retrospective	В
Bruckbauer 2019	59	54	Retrospective	В
Cafaro 2019	28	31	Retrospective	В
Creeper 2022	63	82	Retrospective	В
Daugaard 2019	1681+4162	221 + 1063	Population-based cohort study	В
Elete 2023	21	41	Retrospective cohort study	В
Lott 2018	37	28	Retrospective study	В
Mahmood 2021	92	69	Retrospective study	В
Noll 2023	3212	217	Retrospective study	В
Rostagno 2023	36	82	Prospective cohort study	В
Rutenberg 2018	103	47	Retrospective cohort study	В
Saliba 2020	163	247	Retrospective cohort study	В
Tran 2015	233	27	Case control study	В
Total no of participants (n)	11,215	3804		

Abbreviations: NOACs novel oral anticoagulants

Table 3 Baseline features of the participants

Studies	Age (years)	Males (%)	HBP (%)	DM (%)	HF surgery within 24 h (%)	HF surgery after 24 h (%)
	W/NOAC	W/NOAC	W/NOAC	W/NOAC	W/NOAC	W/NOAC
Aigner 2022	85.0/85.0	28.1/28.1	-	-	-	-
Bruckbauer 2019	83.0/87.0	45.8/35.2	-	-	50.8/37.0	8.50/13.0
Cafaro 2019	90.0/86.0	46.4/22.6	-	-	-	-
Creeper 2022	83.0/83.0	28.7/28.7	-	-	53.0/53.0	87.7/87.7
Daugaard 2019	-	38.2/37.6	-	-	41.6/49.2	29.1/25.4
Elete 2023	85.0/86.0	29.0/29.0	-	-	-	-
Lott 2018	83.8/83.8	-	-	-	-	-
Mahmood 2021	83.8/84.3	46.0/30.0	-	-	-	-
Noll 2023	81.4/83.2	27.5/29.0	48.9/59.5	17.1/19.8	72.6/37.8	27.4/62.2
Rostagno 2023	87.3/86.7	25.0/24.6	-	-	-	-
Rutenberg 2018	82.2/82.9	30.7/35.6	-	-	-	-
Saliba 2020	81.4/83.4	40.5/35.2	93.9/91.9	39.9/42.1	-	-
Tran 2015	86.0/86.0	37.0/37.0	-	-	-	-

Abbreviations: HBP hypertension, DM diabetes mellitus, CVD cardiovascular diseases, W warfarin, NOACs novel oral anticoagulants, HF hip fracture

	DOAC	s	Warfa	irin		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I M-H, Fixed, 95% Cl
1.1.1 Mortality							
Aigner2022	125	1595	86	1325	18.6%	1.21 [0.93, 1.57]	+ = -
Bruckbauer2019	2	54	5	59	0.9%	0.44 [0.09, 2.16]	
Cafaro2019	2	31	2	28	0.4%	0.90 [0.14, 5.99]	
Daugaard2018	145	1284	637	5843	45.5%	1.04 [0.87, 1.23]	•
Elete2023	4	41	4	21	1.0%	0.51 [0.14, 1.85]	
Mahmood2021	6	69	6	92	1.0%	1 33 [0 45 3 96]	
Noll2023	74	217	1134	3212	28.4%	0.97 [0.80, 1.17]	÷
Tran2015	0	27	16	233	0.7%	0.25 [0.02, 4.11]	
Subtotal (95% CI)	0	3318	10	10813	96.7%	1.03 [0.92, 1.16]	•
Total events	358	0010	1800	10010	0011 /0	1100 [0102, 1110]	
Heterogeneity: $Chi^2 = P$	5 20 df = '	7 (P = (1631.15	0%			
Test for overall effect:	7 – 0 57 (I	P = 0.5	7) 7)	070			
	z = 0.37 (i	0.5	,)				
1 1 2 Deen Venous Th	rombosi	e					
Orfere 2010	II UIIIDUSI	5	0	00	0.40/	0 70 10 40 04 441	
Cataro2019	1	31	0	28	0.1%	2.72 [0.12, 64.14]	
Noli2023	0	217	9	3212	0.2%	0.78 [0.05, 13.28]	
Rostagno2023	5	82	3	36	0.8%	0.73 [0.18, 2.90]	-
Rutenberg2018	0	47	0	103		Not estimable	
Tran2015	1	27	3	233	0.1%	2.88 [0.31, 26.69]	
Subtotal (95% CI)		404		3612	1.3%	1.10 [0.41, 2.98]	
Total events	7		15				
Heterogeneity: Chi ² = 7	1.42, df = 3	3 (P = 0	0.70); l² =	0%			
Test for overall effect: 2	Z = 0.20 (I	P = 0.84	4)				
1.1.3 Pulmonary Emb	olism						
Cafaro2019	0	31	0	28		Not estimable	
Noll2023	2	217	13	3212	0.3%	2.28 [0.52, 10.03]	
Rostagno2023	5	82	3	36	0.8%	0.73 [0.18, 2.90]	
Tran2015	0	27	0	233		Not estimable	
Subtotal (95% CI)		357		3509	1.2%	1.17 [0.44, 3.10]	\bullet
Total events	7		16				
Heterogeneity: Chi ² = ²	1.22. df =	1 (P = 0).27): ² =	18%			
Test for overall effect:	Z = 0.31 (I	P = 0.7	5)				
			-,				
1.1.4 Stroke							
Cafaro2019	0	31	0	28		Not estimable	
Noll2023	1	217	15	3212	0.4%	0 99 [0 13 7 44]	
Rutenberg2018	0	87		103	0.770	Not estimable	
Tran2015	0	27	1	222	0 1%	2 70 10 12 66 751	
Subtotal (95% CI)	0	362		3576	0.1%	1 25 [0 23 6 71]	
Tatal aventa	1	302	16	5570	0.470	1.25 [0.25, 0.71]	
	1 200 -15 - 1	4 (D – C		00/			
Heterogeneity: Chi ² = 0	J.30, at =	T(P = 0)).59); I ² =	0%			
lest for overall effect:	Z = 0.26 (I	P = 0.80	0)				
4.4.5.14							
1.1.5 Myocardial Infai	rction						
Noll2023	0	217	17	3212	0.4%	0.42 [0.03, 6.98]	
Rutenberg2018	0	87	0	103		Not estimable	
Subtotal (95% CI)		304		3315	0.4%	0.42 [0.03, 6.98]	
Total events	0		17				
Heterogeneity: Not app	olicable						
Test for overall effect:	Z = 0.60 (I	P = 0.5	5)				
Total (95% CI)		4745		24825	100.0%	1.03 [0.92, 1.16]	•
Total events	373		1954				
Heterogeneity: Chi ² = 8	3.84, df =	16 (P =	0.92); l²	= 0%			
Test for overall effect:	Z = 0.59 (I	P = 0.5	5)				UUI U.I I 10 100
Test for subaroup diffe	rences: C	hi² = 0.	52, df = 4	(P = 0.9	97), l² = 09	%	ravours [DOACS] Favours [vvariarin]
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Fig. 2 Post-operative complications in patients who underwent surgery for hip fracture and who were on warfarin versus NOACs

of participants with high blood pressure and diabetes mellitus ranged from 48.9 to 93.9%, and 17.1 to 42.1% respectively as shown in Table 3. The percentage of participants with surgery for hip fracture carried out within 24 h ranged from 37.0 to 72.6%, whereas the percentage of participants with surgery after 24 h ranged from 8.50 to 87.7% as shown in Table 3.

Main results of this analysis

Results of this analysis showed that the risks of postoperative mortality (RR, 1.03; 95% CI, 0.92–1.16; P=0.57), deep vein thrombosis (RR, 1.10; 95% CI, 0.41– 2.98; P=0.84), pulmonary embolism (RR, 1.17; 95% CI, 0.44–3.10; P=0.75), stroke (RR, 1.25; 95% CI, 0.23–6.71; P=0.80), and myocardial infarction (RR, 0.42; 95% CI, 0.03–6.98; P=0.55) were not significantly different in patients who underwent surgery for hip fracture and who were on warfarin versus on NOACs as shown in Fig. 2. The risks of infection (RR, 0.90; 95% CI, 0.28–2.93; P=0.87) and blood transfusion (RR, 1.08; 95% CI, 0.80– 1.45; P=0.62) were also similarly manifested as shown in Fig. 3.

However, the length of hospital stay [WMD, -0.93; 95% CI, -1.83 to 0.03); P=0.04] was significantly less in patients who were on NOACs in comparison to those who were on warfarin as shown in Fig. 4. The main results of this analysis have been represented in Table 4.

Sensitivity analysis resulted in consistent results throughout. There was low evidence of publication bias across all the studies that were involved during data analysis in this study as shown in Figs. 5 and 6.

Sensitivity analysis and publication bias

Sensitivity analysis was carried out, and based on the findings which were obtained, the results for sensitivity analysis were consistent when compared to the main results of this analysis. There was no influence of any particular study during the analysis. Consistent results were obtained throughout.

Publication bias was also carried out, and based on this visual inspection of the funnel plot, there was only little evidence of publication bias across all the studies that were considered when analyzing the data.

Discussion

In this analysis, the post-operative complications were assessed in patients who underwent surgery for hip fracture and who were pre-operatively on either warfarin or NOACs. Our current results showed that there were no significant difference in mortality, deep vein thrombosis, pulmonary embolism, stroke, blood transfusion, infection, and myocardial infarction. However, the mean length of hospital stay was significantly longer in those patients who were on warfarin compared to those patients who were on NOACs.

	DOAC	s	Warfa	rin		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.1.1 Infection							
Mahmood2021	2	69	0	92	0.8%	6.64 [0.32, 136.19]	
Noll2023	12	217	149	3212	10.8%	1.19 [0.67, 2.11]	- - -
Rutenberg2018	4	87	14	103	4.9%	0.34 [0.12, 0.99]	
Subtotal (95% CI)		373		3407	16.6%	0.90 [0.28, 2.93]	
Total events	18		163				
Heterogeneity: Tau ² = (0.64; Chi²	= 5.76	df = 2 (F	P = 0.06	5); l² = 65%)	
Test for overall effect: 2	Z = 0.17 (F	P = 0.8	7)				
1.1.2 Blood Transfusi	on						
Bruckbauer2019	29	54	32	59	15.6%	0.99 [0.70, 1.39]	
Cafaro2019	18	31	8	28	9.4%	2.03 [1.05, 3.92]	
Creeper2022	15	82	19	63	10.5%	0.61 [0.34, 1.10]	
Mahmood2021	32	69	20	92	12.9%	2.13 [1.34, 3.39]	
Noll2023	127	217	1854	3212	19.8%	1.01 [0.90, 1.14]	T
Saliba2020	37	99	30	58	15.2%	0.72 [0.51, 1.03]	
Subtotal (95% CI)		552		3512	83.4%	1.08 [0.80, 1.45]	₹
Total events	258		1963				
Heterogeneity: Tau ² = 0	0.09; Chi²	= 20.6	3, df = 5 ((P = 0.0)	010); l² = 1	76%	
Test for overall effect: 2	Z = 0.50 (F	P = 0.6	2)				
Total (95% CI)		925		6919	100.0%	1.05 [0.79, 1.38]	
Total events	276		2126				
Heterogeneity: Tau ² = (0 10 [.] Chi ²	= 26.4	df = 8	P = 0.0	$(009) \cdot 1^2 = 3$	70%	· · · · · · · · · · · · · · · · · · ·
Test for overall effect: 7	7 = 0.32 (F	P = 0.7	5)	. 0.0	,		0.01 0.1 1 10 100
Tost for subgroup diffor	rancas: Ch	$ni^2 = 0.1$) 38 df = 1	$(\mathbf{P} = 0)$	77) $I^2 = 0^6$	0/2	Favours [DOACs] Favours [Warfarin]

Fig. 3 Post-operative complications in patients who underwent surgery for hip fracture and who were on warfarin versus NOACs

	DOACs		Wa	arfarin			Mean Difference		Mear	I Differe	nce		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% C		IV, F	<u>ixed, 95°</u>	% CI	
1.2.1 Length of Hospi	tal Stay	/											
Cafaro2019	16.1	10.8	31	15.6	7.1	28	3.8%	0.50 [-4.12, 5.12]			+		
Lott2018	7.8	3.9	28	8.8	4.8	37	18.2%	-1.00 [-3.12, 1.12]			4		
Rostagno2023	12.1	4.3	82	13.2	2.9	36	46.1%	-1.10 [-2.43, 0.23]					
Rutenberg2018	9.6	5.6	47	10.3	5.4	103	22.3%	-0.70 [-2.61, 1.21]			•		
Saliba2020	10.6	18.2	247	11.7	11.9	163	9.6%	-1.10 [-4.01, 1.81]			1		
Subtotal (95% CI)			435			367	100.0%	-0.93 [-1.83, -0.03]					
Heterogeneity: Chi ² = ().50, df :	= 4 (P	= 0.97)	; l ² = 0%	6								
Test for overall effect: 2	Z = 2.02	? (P = (0.04)										
Total (95% CI)			435			367	100.0%	-0.93 [-1.83, -0.03]					
Heterogeneity: Chi ² = ().50. df :	= 4 (P	= 0.97)	$ ^{2} = 0$	6				H		<u> </u>	+	<u> </u>
Test for overall effect: $7 = 2.02$ (P = 0.04)						-100	-50	0	50	100			
Tost for subgroup differences: Not applicable								Favours [DOA	Jsj Favo	ours [Warfarin]			

Fig. 4 Mean length of hospital stay in patients who underwent surgery for hip fracture and who were on warfarin versus NOACs

In a systematic review and meta-analysis (You et al. 2021) based on the effect of oral anticoagulant use on surgical delay and mortality in hip fracture with a total number of 34 studies including 39,446 patients, the authors concluded that those patients experienced a delay in time to surgery and higher mortality than patients who were not on any anticoagulant. However, our analysis was based on patients who underwent surgery for hip fracture and who were pre-operatively on warfarin versus NOACs. The comparison was not with a group without anticoagulant.

Another meta-analysis (Abatzis-Papadopoulos et al. 2023) compared the effectiveness and safety of direct oral anticoagulants versus conventional pharmacologic thromboprophylaxis including low molecular weight heparin in patients with hip fracture. Data from two randomized trials were included in the analysis with a total number of 279 patients. Results of the meta-analysis showed that there was no significant difference post-operatively in patients who were on NOACs versus those on low-molecular-weight heparin. Nevertheless, our current analysis focused on warfarin versus NOACs.

Table 4 Results of this analysis

Post-operative complications	RR/WMD with 95% CI	P value	l ² (%)
Mortality	1.03 [0.92–1.16]	0.57	0
Deep venous thrombosis (DVT)	1.10 [0.41–2.98]	0.84	0
Pulmonary embolism (PE)	1.17 [0.44–3.10]	0.75	18
Stroke	1.25 [0.23–6.71]	0.80	0
Myocardial infarction (MI)	0.42 [0.03-6.98]	0.55	-
Infection	0.90 [0.28–2.93]	0.87	65
Blood transfusion	1.08 [0.80–1.45]	0.62	76
Mean length of hospital stay	-0.93 [-1.83 to -0.03]	0.04	0

Abbreviations: RR risk ratio, Cl confidence intervals, WMD weighted mean difference

Those patients who were on warfarin prior to surgery for hip fracture had a significantly longer mean length of hospital stay following surgery. The reason for this longer hospital stay was patients' INR (Nelson et al. 2015). After that warfarin was stopped, it could take days for the INR to return to its normal range. Moreover, post-operatively, when warfarin was resumed, it again takes a few days for the INR to return to the therapeutic range in order that the patient could be discharged from the hospital owing to the lengthy hospital stay (Roumeliotis et al. 2019).

In a retrospective study, the authors demonstrated that in geriatric patients who underwent surgery for hip fracture and who were previously on NOACs, those patients required less blood transfusion and the length of hospital stay was shorter and other complication rates were similar (Brameier et al. 2024). However, in our analysis, even though the length of hospital stay was shorter with NOACs, the number of patients who required blood transfusion was similar.

Nevertheless, even when patients who underwent early surgery were compared with patients who underwent delayed surgery after hip fracture, the type of anticoagulation did not make any difference in blood transfusion requirement, and blood loss (A Lott et al. 2019). The number of complications including death following surgery was also similar.

Limitations

This study also has limitations. First of all, data were extracted only from observational studies. Data from observational studies are believed to be highly heterogeneous. However, there was no randomized trial based on such comparison. This inclusion of data from observational studies could be one limitation of this analysis. Another limitation could be the fact that several studies did not record important data such as



Fig. 5 Funnel plot showing publication bias

the international normalized ratio (INR) of patients who were on warfarin at the time of operation. This data was missing in several original studies. In addition, several important post-operative outcomes such as major and minor bleedings were not reported in the original studies, and therefore those complications could not be assessed in our current analysis. In addition, important features such as the degree of fracture and the amount of blood loss pre-operatively were not given. However, patients who required blood transfusion post-operatively were reported.



Fig. 6 Funnel plot showing publication bias

Conclusions

The post-operative complications following surgery for hip fracture of patients who were on warfarin versus patients who were on NOACs were similar. However, those patients who were on warfarin had a significantly longer length of hospital stay compared to patients who were on NOACs.

Abbreviations

NOACs	Novel oral anticoagulants
HF	Hip fracture
VKA	Vitamin K antagonists
RR	Risk ratio

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Authors' contributions

The authors Yuxi Wei, Chi Chen, Zhihong Yu, and Jun Guo were responsible for the conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the initial manuscript, and revising it critically for important intellectual content. The final draft was written by the authors Yuxi Wei and Chi Chen. All the authors gave their approval to the final manuscript as it has been written.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Ethical approval and consent to participate were not applicable for this systematic review and meta-analysis.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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