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Management of hip fracture patients on direct oral anticoagulants: a survey of orthopaedic trauma surgeons, systematic review, and meta-analysis

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Abstract

Objectives: This systematic review examined the literature regarding management of fracture patients who take direct oral anticoagulant (DOAC) medications, with a focus on delay in surgical treatment, and need for transfusions. In addition, a survey of orthopaedic trauma surgeons was conducted to gain insight on current practices.

Data Sources: A review of PubMed, Cochrane, Embase, and Scopus databases was performed from inception through March 2024, including English language publications.

Study Selection: Studies were included if they reported time to surgery and transfusion rates among fracture patents who were taking DOAC medications. Additional data points were collected on an "if-reported" basis, including mortality, venous thromboembolism, and bleeding complications.

Data Extraction: In all, 4546 abstracts were screened. Full-text review was conducted on 86 publications, and 25 articles were included in the final analysis. Each article was independently screened by 2 reviewers, with disputes settled by a third reviewer. Study quality was assessed using the Methodological Index for Non-Randomized Studies (MINORS) tool.

Data Synthesis: Descriptive statistics are reported for overall study findings. Meta-analysis was performed for the variables "time to surgery" and "transfusion rate."

Conclusions: Our findings indicate that fracture patients taking DOACs experience longer delays before surgery but have equivalent transfusion rates compared with nonanticoagulated patients. Survey results indicate that surgeons do not delay operating on emergent or percutaneous cases, regardless of anticoagulant medications. In circumstances when they do delay, they are more likely to do so for patients taking DOAC medications.

Level of Evidence: Level III, systematic review and meta-analysis of Level II and III articles.

Keywords: anticoagulation, hip fracture, delay, trauma, transfusion

1. Introduction

Hip fractures are common injuries among older adults. The per-capita incidence of hip fractures has reportedly decreased.[1] However, this has been outpaced by the growing population of older adults, resulting in an overall increase in the number of these injuries each year.[2] It is estimated that by 2050, hip fractures will have a global incidence of 4.5 million per year.[3] Hip fractures carry a high disease burden, including prolonged hospital stays, rehabilitation challenges, mobility limitations, along with a significant economic cost.[4,5]

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Members of the Orthopaedic Trauma Association's Evidence-Based Quality Value and Safety Committee are included in an Appendix at the end of the article.

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Mortality after hip fracture remains a significant problem, with a reported 30-day mortality rate of 7%[6] and a 1-year mortality reported between 14% and 58%.[7] The timing of surgical treatment of hip fracture is important, with earlier surgery being associated with improved outcomes, including a lower mortality rate.[6,8–10]

The population most at risk of hip fracture, older adults, are also likely to have comorbid conditions. Jantzen et al[1] reported that the incidence of cardiovascular disease has increased among hip fracture patients. This has been accompanied by an increase in the percentage of patients with atrial fibrillation treated with direct oral anticoagulants (DOACs).[11] In addition, an overall increase in the rate of oral anticoagulant (OAC) use, including vitamin K agonists (VKAs), among hip fracture patients has been reported.[12] Studies report 14%–40% of hip fracture patients are on OACs at the time of admission.[13,14]

Hip fracture patients on OACs are often faced with surgery delayed beyond the 48-hour guideline.[15,16] Delays are often imposed to allow for anticoagulant washout to mitigate the theoretical increased risk of bleeding. Despite this being a common practice, previous studies found no benefit to delaying surgical care in anticoagulated hip fracture patients.[13,17,18] A review published by You et al[19] in 2021 reported delays in time to surgery and higher mortality in patients with hip fractures on OACs. In 2023, these authors reported VKA-reversal protocols decrease time to hip fracture surgery without an increased bleeding risk.[20] They reported hip fracture surgery within 48 hours in DOAC-treated patients is safe, with a small increase in blood transfusion risk. However, no widely agreed-upon guidelines exist to guide the management of hip fracture patients on OACs.

The aim of this study was to perform a systematic review and meta-analysis to evaluate the effect of DOAC use on time to surgery (TTS), transfusion rate, mortality, and venous thromboembolism (VTE) in adults with hip fracture. In addition, this study reports survey results of Orthopaedic Trauma Association members regarding common practices in the management of anticoagulated fracture patients to compare current practices with current evidence. It is hypothesized that delaying surgery in hip fracture patients taking DOACs is common practice but yields minimal benefit and worse postoperative outcomes.

2. Methods

2.1. Search Strategy and Study Selection

This study was approved by the IRB at the University of Alabama at Birmingham (IRB-300011753). This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards.[21] A search of PubMed, EMBASE, Cochrane Library, and Scopus databases was performed from inception to 3/8/24. The full search criteria can be found in Appendix A, http://links.lww.com/OTAI/A101. Duplicate articles were removed before the screening process. Four authors screened abstracts, with 2 authors independently screening each title, abstract, and full text (R.R., Z.M., M.M., M.Y.). Disagreements were resolved by a third reviewer. Randomized controlled trials, observational cohort studies, or case-control studies (including meeting abstracts) reporting postoperative outcomes of patients treated with DOACs (dabigatran, rivaroxaban, apixaban, edoxaban, or betrixaban) before hip fracture were included. Studies only reporting data on other forms of anticoagulation were not included in this analysis. This was supplemented by searching Clinicaltrials.gov and clinicalstudyresults.org, contacting study authors for unavailable articles, and forward and backward reference searching of the bibliographies from publications. Only human studies available in English were included. Case reports, reviews, letters to the editor, and commentaries were excluded.

2.2. Data

Two authors independently extracted the following from each article: methodology of the study, average age of patients, type of fracture treated, ratio of male to female patients, total number of patients included, number of patients in the DOAC and control groups, TTS, transfusion rates, mortality, length of stay, rates of VTE, and bleeding complications. All results compatible with each outcome domain in each study were sought. Missing data were not altered. VTE complication was defined as pulmonary embolism or deep vein thrombosis, and bleeding complications were defined as a hematoma at the surgical site, excessive bleeding during or after surgery at the surgical site, or internal bleeding at other sites (eg, intracranial bleed).

2.3. Methodological Quality

Two authors independently used the Methodological Index for Non-Randomized Studies (MINORS) tool to assess risk of bias.[22] This tool evaluated nonrandomized comparative studies on 12 criteria evaluating study design and methodology. Noncomparative studies are evaluated based on 8 criteria. Each criterion is ranked from 0 to 2, with comparative studies having a maximum score of 24. Comparative studies with a score of 17 or higher were considered to have low risk of bias, scores 13–16 were considered medium risk, and 12 or below was considered high risk. Noncomparative studies have a maximum score of 16, with risk of bias being considered a score of 13 or higher, scores of 9–12 being considered medium risk, and 8 or below high risk.

2.4. Survey

A survey was designed to learn about orthopaedic trauma surgeons' current practice regarding management of patients taking anticoagulation medications. The survey was sent to Orthopaedic Trauma Association members and captured surgeon opinions on whether they delay emergent surgery, urgent surgery, percutaneous surgery, open pelvic/acetabular surgery, and time-sensitive but not urgent fracture surgery for patients on oral anticoagulants. For each case, we asked questions regarding which medications cause them to choose to delay surgery and whether they use time or laboratory test results to determine delay. We also asked questions regarding use of intravenous reversal agents. The survey was distributed online to members of the Orthopaedic Trauma Association and was available from November 2023 to April 2024.

2.5. Analysis

Details for each included study are presented in Table 1. Results are synthesized and described. For the time-to-surgery and transfusion rate outcomes, there were enough studies with adequate data reporting to conduct a meta-analysis.

Forest plots were used to describe the difference in time to surgery and transfusion rate for each study, as well as the combined effects between the DOAC and control groups. Initial

Table 1

Summary of included studies of surgically treated hip fracture patients taking direct oral anticoagulants (DOACs) before injury.

Author (y)	Study design	Control group	DOAC medications included	Mean age (y)	% Female	Patients, n			Time to surgery, (h)		Transfusions		MINORS Score
						Total (15,075)	DOAC (1,831)	Control (13,244)	DOAC	Controls	% transfusions DOAC	% transfusions Control	
Schermann (CRIF) (2019)[23]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran	83	78.0%	1037	60	977	40.2	31.2	9.0%	7.7%	15
Schermann (Hemiarthroplasty) (2019)[23]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran	83	68.0%	518	29	489	42.3	36.6			
Franklin (2018)[24]	Retrospective observational	Control group	Not Defined	78	42.0%	95	19	76	28.9	21.4	37.5%	37.5%	17
Rostagno (2021)[25]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran, endoxaban	84	74.0%	280	74	206	86.4	51.6	46.0%	41.0%	17
Tarrant (2020)[26]	Retrospective observational	Matched controls	Rivaroxaban, apixaban, dabigatran	84	68.0%	224	112	112	52.8	28.8	27%		18
Hofer (2023)[27]	Retrospective observational	No control group	Rivaroxaban, apixaban, dabigatran, endoxaban	86	67.0%	155	155		24.8		45.8%		10/16
King (<48 h) (2020)[28]	Retrospective observational	Matched controls	Rivaroxaban, apixaban, dabigatran	84	83.6%	73	17	56	49.7	26.0	11.8%	30.4%	13
King (>48 h) (2020)[28]	Retrospective observational	Matched controls	Rivaroxaban, apixaban, dabigatran	82	45.5%	11	11		76.7		9.1		
Leer-Salvesen (2020)[29]	Retrospective observational	Control group	Not Defined	82	70.0%	314	47	267	28.9	26.1	45.0%	42.0%	15
Goh (2022)[30]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran, endoxaban	83.4	71.7%	755	81	674	22.1	20.3	25.2%	24.9%	17
Fenwick (2023)[31]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran, endoxaban	79.8	68.9%	921	180	741	32.3	22.1	37.2%	30.0%	18
Frenkel (2018)[2]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran	83	66.7%	693	47	646	55.3	28.7			16
Hourston (2020)[32]	Retrospective observational	Control group	Not Defined	85	73.0%	761	32	729	29	22			16
Tran (2015)[16]	Retrospective observational	Matched controls	Rivaroxaban, apixaban, dabigatran	86	62.3%	287	27	260	66.9	26.2	37.0%	39.3%	18
Gosch (2021)[33]	Retrospective observational	Control group	Not Defined	—	—	87	26	61	42.7	30	69.2%	49.2%	16
Bruckbauer (2019)[34]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran, endoxaban	83	69.4%	261	54	207	30	12	53.7%	38.0%	12
Lott (2018)[35]	Retrospective observational	Control group	Rivaroxaban, apixaban	83	—	391	24	367	40.8	38.4			17
Saliba (2020)[36]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran	82	68.7%	3255	247	3008	31.8	24.6	37.4%	41.2%	15
Rostagno (2023)[37]	Prospective observational	Control group	Rivaroxaban, apixaban, endoxaban	86	76.5%	365	82	283	67.2	43.2		44.0%	18

(*continued on next page*)

Table 1 (*continued*)

Author (y)	Study design	Control group	DOAC medications included	Mean age (y)	% Female	Patients, n			Time to surgery, (h)		Transfusions		MINORS Score
						Total (15,075)	DOAC (1,831)	Control (13,244)	DOAC	Controls	% transfusions DOAC	% transfusions Control	
Noll (2023)[38]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran	81.6	72.4%	3429	217	3212	64.8	34.7	58.5%	57.7%	15
Meinig (2023)[39]	Retrospective observational	Matched controls	Rivaroxaban, apixaban, dabigatran, endoxaban	81	65.0%	31	31		43		13.0%		15
Wang (2023)[40]	Retrospective observational	No control group	Rivaroxaban, apixaban	84.4	79.4%	68	68		44.8		36.8%		12/16
Mayor (2023)[41]	Retrospective observational	Matched controls	Rivaroxaban, apixaban, dabigatran, endoxaban	83.4	70.0%	160	80	80	26	22.4	52.5%	57.5%	16
Shamsuri (2023)[42]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran, endoxaban	80.8	71.5%	291	12	279	117	62			17
Cafaro (2019)[43]	Retrospective observational	Control group	Rivaroxaban, apixaban, dabigatran	84.1	72.5%	444	31	413	61	44	58.0%	30.8%	17
Sabo (2018)[44]	Prospective observational	Control group	Apixaban	79.3	74.5%	46	5	41	66	25			20
Mullins (2018)[17]	Retrospective observational	Matched controls	Rivaroxaban, apixaban, dabigatran	85	75.0%	123	63	60	19	19	17.5%	10.0%	15

multivariable meta-regressions including 3 moderator variables (type of control group, percentage of female patients, and average patient age) were run to identify significant moderators for the time to surgery and transfusion rate outcomes. Meta-regressions were then rerun to include only significant moderators and intercept for the effect size. Finally, funnel plots were used to assess publication bias. All meta-analysis were performed using R-Studio 1.2.5042 2009–2020 RStudio, Inc (Boston, MA).

2.6. Synthesis Methods

A table describing the characteristics of all studies was created. Tables for each outcome were created, and all studies that reported the given outcome were included. To decide study eligibility for each synthesis, study characteristics were tabulated and compared against the planned groups for each synthesis. The eyeball test was used to test for homogeneity by the presence of overlaps of the confidence intervals of studies and the summary estimate on a forest plot.[45] For each outcome, homogeneous studies were weighed by number of patients, and individual study results were plotted on a forest plot. Subgroup analysis and meta-regression were used to explore possible sources of heterogeneity among study results. Risk of bias due to missing results in a synthesis was assessed by funnel plots.

3. Results

3.1. Study Characteristics

The search identified 4546 nonduplicate records. After title and abstract screening, 4460 studies were excluded. Eighty-six studies underwent full-text review and 25 were included (Fig. 1). Two studies grouped anticoagulated patients based on either fixation method[23] or time to surgery.[28] Data were collected separately for the groupings, and thus each study was considered as 2 separate studies in the analysis, yielding 27 groups of patients in the analysis. Together, these studies included 15,075 patients, of which 1831 (12%) were taking DOACs before their injury and 13,244 (88%) were not taking DOACs. Publication dates of the studies ranged from 2015 to 2023. Two studies were prospective observational, with the remaining studies being retrospective observational. The mean age of patients included was 83 years and ranged from 78 to 86. Female patients made up 69% of those included and ranged from 42% to 79%. Seventeen studies (68%) reported the ratio of female to male patients between groups, with the DOAC group having an average of 68.2% female, ranging from 42% to 83%, and the control group having an average of 70.4% female, ranging from 42% to 84%. Thirteen studies (52%) reported comorbidity status in the form of American Society of Anesthesiologists Physical Status Classification, although the methodology of reporting varied widely and prevented any meaningful analysis. Only 2 studies did not include a comparison group, with only data on DOAC-treated patients available. Two additional studies included control groups but did not report data on the control group in a fashion that could be used for this analysis. Study characteristics are presented in Table 1.

Venous thromboembolism was reported in 9 studies. The rate ranged from 0% to 6% for DOAC-treated patients and 0.7% to 9% for control patients. Bleeding complications were reported in 7 studies. The rate ranged from 0% to 80% for DOAC-treated patients and 1% to 85% for control patients.

Mortality was not consistently reported or was reported at different time points across studies. Mortality during admission (n = 10 studies) ranged from 0% to 9% for DOAC-treated patients and 1% to 7% for control patients. Thirty-day mortality

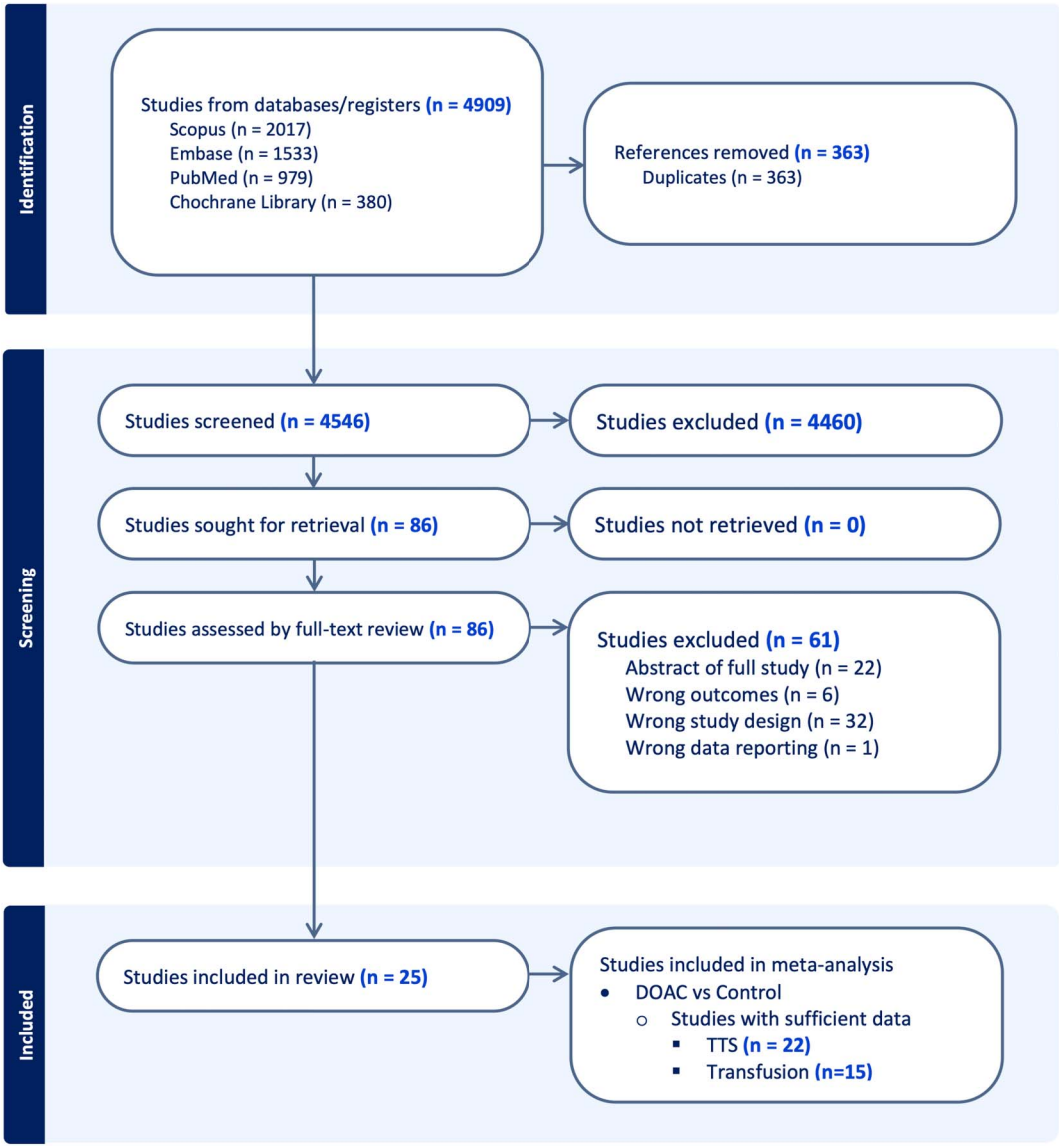

Figure 1. Preferred Reporting Items for Systematic-Reviews and Meta-Analyses (PRISMA) flowchart of study screening.

(n = 8 studies) ranged from 2% to 14% for DOAC-treated patients and 5% to 16% for control patients. Six-month mortality (n = 5 studies) ranged from 6% to 34% for DOAC-treated patients and 4% to 35% for control patients. One-year mortality (n = 4 studies) ranged from 11% to 71% for DOAC-treated patients and 4% to 59% for control patients.

3.2. Methodological Quality and Bias

Using the MINORS tool, 11 studies were categorized as low risk of bias, 13 were considered medium risk, and 1 was considered high risk. Bias results are included in Table 1. Funnel plots demonstrate minimal skew, indicating a low risk of bias regarding study selection.

3.3. Time to Surgery

Time to surgery was reported in all included studies. Overall, the average time to surgery was 46.7 hours for DOAC-treated patients and 30.3 hours for control patients. One study reported equivalent time to surgery in both groups.[17] All others reported an increased TTS for DOAC-treated patients, ranging from 6% increase[35] to 164% increase in time to surgery.[44] Univariate analysis of TTS demonstrated a significantly longer time to surgery among DOAC-treated patients compared with control patients ($P < 0.001$).

3.4. Transfusion

Nineteen studies reported percentage of patients who received transfusion. For DOAC-treated patients, the percentage requiring transfusion ranged from 9.0% to 69%. For control patients, the percentage requiring transfusion ranged from 8% to 58%. Five studies (n = 5/19, 26%) found lower or equivalent rates of transfusion among DOAC-treated patients.[16,24,28,36,41] All others found increased rates of transfusion among DOAC-treated patients, ranging from a 1% increased rate of transfusion to an 88% increased rate of transfusion. The mean rate of

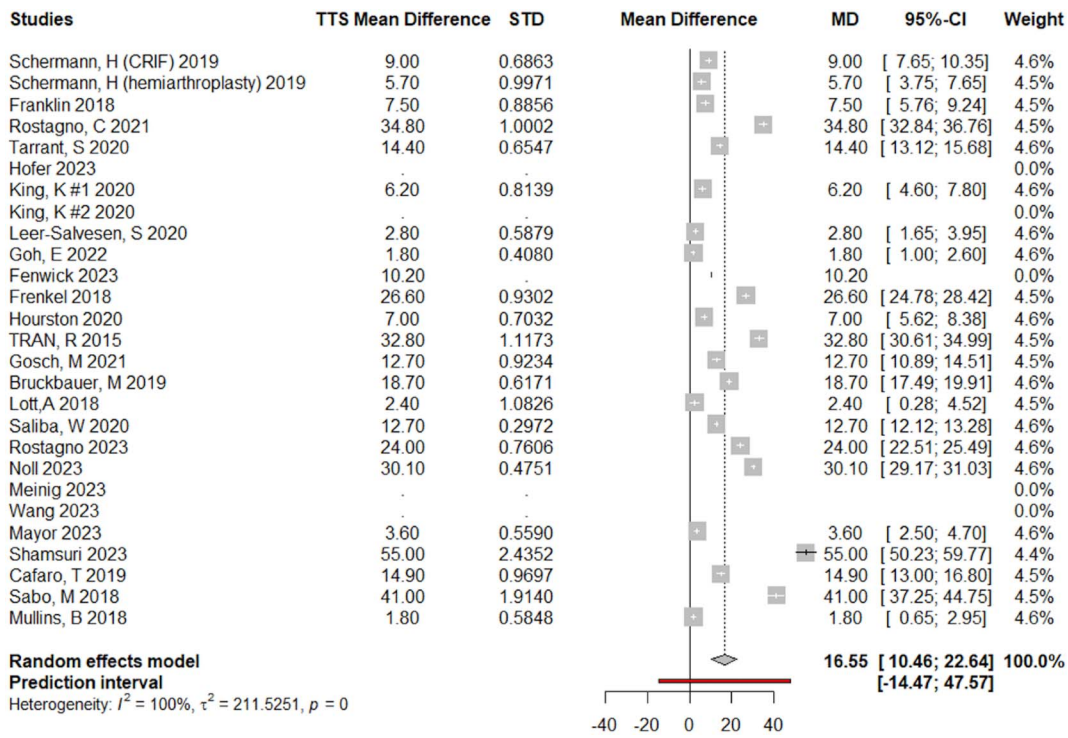

Figure 2. Forest plot of time-to-surgery difference between DOAC and control groups.

transfusions among the DOAC group was 36.4%, versus 36.3% in the control group. Univariate analysis by paired-samples *t* test included 15 studies due to case-wise exclusion of studies that did not report values for both groups but found that transfusion rate was not significantly different between DOAC-treated patients and control patients (mean 39.7% ± 17.8% vs. 35.8% ± 14.4%; $P = 0.193$). Two studies report the number of units transfused per patient, both of which report lower volumes transfused to DOAC-treated patients (0.65 and 0.63 units per patient) compared with control patients (0.72 and 0.87 units per patient).[24,36]

3.5. Other Outcomes

Venous thromboembolism was reported in 9 studies. The rate ranged from 0% to 6% for DOAC-treated patients and 0.7% to 9% for control patients. Bleeding complications were reported for 7 studies. The rate ranged from 0% to 80% for DOAC-treated patients and 1% to 85% for control patients.

Mortality was not consistently reported or was reported at different time points across studies. Mortality during admission (n = 10 studies) ranged from 0% to 9% for DOAC-treated patients and 1% to 7% for control patients. 30-day mortality (n = 8 studies) ranged from 2% to 14% for DOAC-treated patients and 5% to 16% for control patients. 6-month mortality (n = 5 studies) ranged from 6% to 34% for DOAC-treated patients and 4% to 35% for control patients. One-year mortality (n = 4 studies) ranged from 11% to 71% for DOAC-treated patients and 4% to 59% for control patients.

Table 2

Meta-regression models for time to surgery and transfusion rate.

	Mixed-effects model	
	Estimate (95% CI)	***P***
Time to surgery		
Intercept	3.13 (2.22, 4.05)	**<0.01**
Transfusion rate		
Intercept	−0.046 (−0.15, 0.067)	0.39
Type of control group	0.12 (−0.0082, 0.25)	0.064

Bold denotes statistically significant.

4. Results: Meta-Analysis

For the time-to-surgery outcome, Figure 2 displays the forest plot of all available studies. All studies had a positive mean difference, indicating the DOAC group had a longer time to surgery. The overall weighted mean difference was 16.55 (95% CI: 10.46–22.64), demonstrating a statistically significant increased time to surgery for the DOAC group as compared with control. For time to surgery, no moderators were statistically significant; therefore, the final meta-regression model included only the intercept. This model also identified a statistically significant association between DOAC use and longer time to surgery ($P < 0.01$) (Table 2).

For the transfusion rate outcome, Figure 3 displays the forest plot of all available studies. The mean differences were minimal in all studies, ranging from 0 to 0.20 percent difference. The overall weighted mean difference was 0.07 (95% CI: −0.01, 0.16), demonstrating no statistically significant difference in transfusion rate between the DOAC and control groups. For transfusion rate, the type of control group was a statistically significant moderator; therefore, it was included in the final model. The final model (Table 2) found no statistically significant differences between the groups.

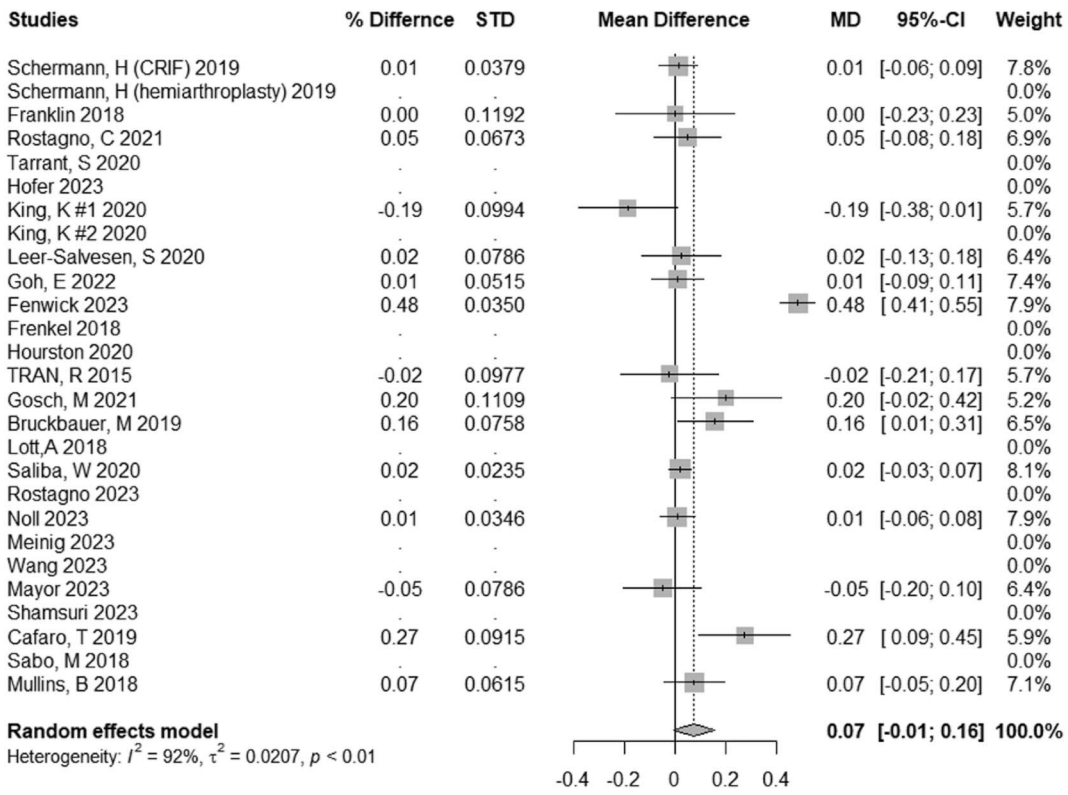

Figure 3. Forest plot of transfusion rate difference between DOAC and control groups.

5. Results: Survey

A total of 80 participants responded to the surgeon survey. No surgeons report delaying emergent surgery or percutaneous fracture surgery (Table 3). There was more variation for the other types of surgeries. Most (52.5%) would delay open pelvis/acetabular surgery, 38.8% delay for time-sensitive but not urgent fracture surgery, and 14% delay for urgent open surgery. Only 1 respondent chose to delay for patients taking aspirin and only for the time-sensitive but not urgent population. Surgeons who delay surgery most often delay for warfarin, Factor IIa inhibitors, or Factor Xa inhibitors. For those who delay for warfarin, the median INR threshold used is 2, with a range of 1.2–3, depending on the type of surgery. For those who delay for DOACs, almost all delay based on time. For all types of surgeries, the most common length of time to wait is 24 hours; however, some surgeons report waiting up to 72 hours. For the few surgeons who reported using laboratory test results to track coagulability of DOAC-treated patients, the most common value used is prothrombin time.

Reported use of reversal agents is high for emergent cases, regardless of anticoagulant and/or INR value (all >85%). Use of intravenous reversal agents is also high for urgent cases for patients on warfarin (~75%), but not as high for patients on DOACs (58%). These agents are sometimes used for semi-elective cases (9% for DOAC; 15%–20% for warfarin). They are rarely used for elective cases (all <10%) (Table 4). Some surgeons left free-text comments. Several of these noted that their decisions are based more on the medical state of the patient, comorbidities, and/or expected time of surgery or estimated blood loss than simply the medication and time/laboratory test results.

6. Discussion

There are 15,075 patients across 25 studies included in this meta-analysis; hip fracture patients on DOACs had longer TTS and similar transfusion rates to nonanticoagulated hip fracture patients. The survey demonstrated 14% of surgeons delay urgent surgery such as hip fracture repair for patients on DOACs for 12–48 hours. Seventy-seven percent of surgeons reported using preoperative reversal agents in patients whose INR is in the therapeutic range, and 76% reported use of reversal for supra-therapeutic INR before urgent surgery. Fifty-eight percent report routine DOAC reversal for urgent surgery.

In this study, patients on DOACs had a 46.7-hour mean TTS compared with 30.3 hours for nonanticoagulated hip fracture patients. A systematic review by You et al[19] reported that patients on VKAs or DOACs had longer TTS, independent of comorbidities. Meinig et al[39] reported in a geriatric cohort, anticoagulation management caused 38% of operative delays, while medical optimization caused 17% of delays. Understanding factors that affect the optimal timing of repair among hip fracture surgery patients is important as the use of anticoagulants and DOACs continues to rise. Twenty percent of patients are on DOACs when they sustain a hip fracture, yet there are no guidelines from major societies for optimal timing in this patient population.[34,46,47] Evidence-based guidelines would help surgeons manage the opposing risks of surgical delay and bleeding and would help reduce the high mortality rates after this injury. The European Heart Rhythm Association recommends delaying urgent surgery in patients on DOACs with normal renal function to 24 hours after the last dose to ensure 80% reduction in the therapeutic effect.[48] The use of regional anesthesia may require a longer delay and requires further investigation on hip fracture patients on

Table 3

Survey results of orthopaedic trauma surgeons regarding management of anticoagulated trauma patients, n (%).

Total respondents = 80	Emergent surgery*	Urgent surgery†	Percutaneous fracture surgery‡	Open pelvic/acetabular surgery	Time-sensitive but not urgent fracture surgery§
Would delay surgery in anticoagulated patient	0 (0%)	11 (13.8%)	0 (0%)	42 (52.5%)	31 (38.8%)
Would delay surgery for:					
Warfarin	—	5 (45.5%)	—	35 (83.3%)	25 (80.6%)
Aspirin	—	0 (0%)	—	0 (0%)	1 (3.2%)
ADP receptor inhibitor‖	—	0 (0%)	—	10 (23.8%)	12 (38.7%)
Factor IIa inhibitor¶	—	5 (45.5%)	—	29 (69.0%)	24 (77.4%)
Factor Xa inhibitor#	—	9 (81.8%)	—	39 (92.9%)	30 (96.8%)
If delay for warfarin, over what INR? Median (min, max)	—	2 (1.5, 2.5)	—	2 (1.3, 3.0)	1.7 (1.2, 3.0)
If delay for DOAC, delay based on:					
Time	—	9 (100%)	—	35 (94.6%)	26 (89.7%)
Laboratory test results	—	0 (0%)	—	3 (8.1%)	4 (13.8%)
How long after the last dose?					
12 h	—	2 (22.2%)	—	1 (2.9%)	1 (3.8%)
24 h	—	4 (44.4%)	—	14 (40.0%)	8 (30.8%)
36 h	—	1 (11.1%)	—	6 (17.1%)	5 (19.2%)
48 h	—	2 (22.2%)	—	12 (34.3%)	8 (30.8%)
60 h	—	0 (0%)	—	0 (0%)	2 (7.7%)
72 h	—	0 (0%)	—	2 (5.7%)	2 (7.7%)
Which laboratory value is used?					
Prothrombin time	—	—	—	2 (100%)	4 (100%)
Partial thromboplastin time	—	—	—	0 (0%)	2 (50.0%)
Anti Xa assay	—	—	—	0 (0%)	0 (0%)
Thrombin time	—	—	—	0 (0%)	1 (25.0%)
Other	—	—	—	0 (0%)	0 (0%)

* For example, compartment syndrome, irreducible dislocation, and fracture with vascular injury.
† For example, hip fracture surgery and open fracture debridement.
‡ For example, percutaneous pelvic surgery and external fixation.
§ For example, ankle fracture, plateau fracture, and upper extremity fracture.
‖ For example, clopidogrel (Plavix) and ticagrelor (Brilinta).
¶ Dabigatran (Pradaxa).
# For example, apixaban (Eliquis), rivaroxaban (Xarelto), and endoxaban (Lixiana).

DOACs.[49] Observational studies have reported general anesthesia alters cerebral autoregulation and results in higher rates of postoperative delirium and mortality in hospitalized patients after hip fracture surgery compared with regional anesthesia. However, a 2016 systematic review and two 2021 and 2022 randomized trials reported similar or worse outcomes with regional compared with general anesthesia in hip fracture surgery.[50–52] The need to minimize bleeding risk and other DOAC-related complications must be balanced by the well-reported mortality benefit from early fixation.[6,9] The HIP ATTACK trial reported that patients with longer time from injury to presentation benefitted more from accelerated surgery.[53] Recent studies reported surgery in the first 24 or 48 hours of admission for patients on DOACs did not lead to increased OR time, transfusion requirements, or mortality.[17,24,35]

In this study, patients on DOACs had similar risk of transfusion compared with nonanticoagulated hip fracture patients. A 2023 meta-analysis reported higher rates of transfusion in hip fracture patients on DOACs treated within 48 hours compared with patients not on anticoagulants. However, the study with the most significant increase in transfusion rate in that review included only peritrochanteric fractures and no arthroplasty.[54] The increased risk of blood loss previously reported in hip fracture fixation compared with arthroplasty may explain the difference in findings and should be investigated further to help define optimal management of different fracture patterns of the proximal femur.[55] In the only available published study analyzing the effect of reversal, patients who did not receive DOAC reversal had shorter TTS and length of stay and similar mortality and transfusion rates compared with patients who received reversal.[56]

Table 4

Survey results of orthopaedic trauma surgeons regarding anticoagulation reversal.

Would use intravenous reversal agent	Patients on warfarin with therapeutic INR (eg, 2–3) N = *69 responses*	Patients on warfarin with supratherapeutic INR (eg, 5) N = *79 responses*	Patients on DOACs N = 52 *responses*
Emergent surgery	59 (85.5%)	75 (94.9%)	51 (98.1%)
Urgent surgery	53 (76.8%)	60 (75.9%)	30 (57.7%)
Semielective surgery	11 (15.9%)	16 (20.3%)	5 (9.6%)
Elective surgery	5 (7.2%)	8 (10.1%)	3 (5.8%)

Strengths of this study include the comprehensive literature search reporting the effect of DOACs on TTS and transfusion risk in hip fracture patients. The inclusion of the survey results demonstrated orthopaedic trauma surgeons' common practice of delaying surgery for DOAC-treated patients, which may be unnecessary given the findings of this study.

Limitations of this study include a lack of analysis of the confounding effect of comorbidity due to wide variance in reporting among the studies. Significant heterogeneity of all outcomes existed in the studies because of variety in patient demographics, years of study, hospital protocols, and surgeons. Most studies were retrospective and affected by selection bias. More prospective trials would help to delineate optimal protocols to manage patients with hip fractures on DOACs.

7. Conclusion

Hip fracture patients taking DOAC medications are likely to experience longer delays to surgery compared with their non-anticoagulated counterparts, despite the finding that DOAC-treated patients do not require transfusions at an increased rate. Equivalent transfusion rates are even seen in several studies which practiced an expedited surgical protocol for hip fracture patients taking DOACs. Survey results indicate that surgeons do not delay operating on emergent or percutaneous cases based on anti-coagulation status and rarely delay operating on urgent cases. When performing emergent surgery on patients taking DOACs, a majority would elect to use reversal agents.

Appendix 1. Contributors

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