

# Timing and safety of hip fracture surgery in patients on direct-acting oral anticoagulants



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## ABSTRACT

**Background:** Many geriatric patients presenting for emergency hip fracture surgery are on direct oral anticoagulants (DOACs) most of which are not easily reversible. A safe policy was required to reduce delays to surgery. Prior to institution of our hospital's protocol in January 2021, most of these patients had surgery after 48 h following the last dose of DOAC due to concerns about increased perioperative blood loss.

**Methods:** This was a prospective closed loop audit of the protocol-surgery within 24 h from last dose of DOAC (if creatinine clearance >50 ml/min) with administration of 1-g of tranexamic acid at anesthesia induction. 131 eligible patients (DOAC, n = 22; no anticoagulation, n = 109) between January–June 2021 who had emergency hip fracture surgery were identified. Primary outcome measures were peri-operative blood loss, transfusion requirements and policy compliance. Secondary outcome measures were 30-day mortality, thrombotic complications and wound bleeding.

**Results:** Compliance with surgical timing and tranexamic acid administration were 55% and 81% respectively after the second audit cycle. The mean estimated blood loss (EBL) in the DOAC group versus the non-anticoagulated control group was 500 ml and 330 ml respectively. The difference between these groups was statistically significant at an alpha level of 5% (P = 0.0115, 95% CI 38.48–299.16). The difference for intra-operative (RR 3.43; 95% CI 1.68–7.01) and post-operative blood transfusion (RR 2.10; 95% CI 1.23–3.58) for the 2 groups was also statistically significant. However, there was no case of massive blood transfusion in both groups. The DOAC group had a lower risk for 30-day mortality (RR 0.71; 95% CI 0.09–5.46). There was no major thrombotic complication in the DOAC group.

**Conclusion:** This audit has shown that this protocol is safe although clinicians should anticipate some degree of increased intra-operative blood loss. We will recommend continuation of this policy with sustained safety monitoring in order to reduce delays to surgery.

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## 1. Introduction

Hip fractures account for an estimated 1% of the United Kingdom (UK) National Health Service (NHS) expenditure with 76,000 cases per year.<sup>1</sup> Many geriatric patients presenting for emergency hip fracture surgery are on direct oral anticoagulants (DOACs) some of which cannot be reversed quickly prior to emergency surgery. In the United Kingdom, 2% of patients presenting for

hip fracture surgery are on direct oral anticoagulants pre-operatively.<sup>2</sup> The direct oral anticoagulants include the factor X inhibitors like rivaroxaban, edoxaban and apixaban. The second group of direct oral anticoagulants are the direct thrombin inhibitors which include dabigatran, melagatran and argatroban.<sup>3</sup>

A safe policy was required to comply with the United Kingdom best-practice tariff for hip fracture surgery (surgery within 36 h of admission) in order to reduce the risks of delayed surgery in these patients who are mostly elderly. This will help reduce perioperative mortality, the associated financial costs of delayed surgery and avoid prolonged hospital stay. Most U.K. centers strive for a delay of no more than 24 h for patients on DOAC (if there is no renal compromise) while many European countries have policies

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recommending a 48-h delay or anticoagulation reversal prior to surgery.<sup>4</sup>

A multidisciplinary team-based approach between the Orthopedic surgeons, Orthogeriatricians, anesthetists, emergency department clinicians, theatre operating room nurses/practitioners and hematologists was employed in order to come up with the new hospital protocol. Prior to the institution of this new policy in January 2021, most of these patients had surgery after 48 h from the last dose of DOAC due to concerns about increased perioperative blood loss. Triaging these patients based on type of oral anticoagulant being used, renal function, type of anesthesia planned, and complexity of the surgery was required in order to improve perioperative safety. Despite the importance of accelerated surgical protocols, the need to avoid exposing patients to unnecessary risks from increased perioperative blood loss and thrombotic complications was acknowledged. Thus, a closed loop audit for this new policy was completed with the aim of improving compliance to the policy and monitoring for potential complications that could arise as a result of adherence to the policy.

## 2. Methods

A closed loop audit was conducted involving all patients with hip fractures undergoing emergency hip fracture surgery between January 15, 2021 to June 30, 2021. The audit was a single-center study performed at the Royal Berkshire hospital, Reading, United Kingdom. The patient inclusion and exclusion criteria for this audit are as set out in Table 1.

This was a prospective audit study involving a complete audit cycle. The audit standard was the new trust policy (see Fig. 1) on timing of surgery in patients with hip fractures who were on the direct-acting oral anticoagulants (DOAC) preoperatively (The “DOAC” group). In the hospital, all patients on DOAC included in the study were either on apixaban or rivaroxaban. Patients on coumarin derivatives, unfractionated heparin, low molecular weight heparins and anti-platelets were not included as established and audited protocols/guidelines for these already existed in the hospital trust. Data was also collected for patients undergoing hip fracture surgery who were on no routine anticoagulants preoperatively (The “non-anticoagulated” group). This cohort of patients was used to compare safety data against the DOAC group. Thus, this audit was not just aimed at assessing compliance with the trust policy but also focused on monitoring for major problems that could arise with adherence to this policy so that useful recommendations could be proffered towards improving patient safety.

The primary outcome measures for the study were intra-operative blood loss, intraoperative/postoperative blood transfusion requirement, compliance with the policy in terms of adherence to the stated time frames for surgery and with tranexamic acid (TXA) administration at induction of anesthesia. The

secondary outcome measures were 30-day mortality, 30-day postoperative thrombotic complications and 30-day postoperative complications related to bleeding from surgical wounds.

There was no patient randomization, change to routine patient surgical pathways outside the aforementioned trust protocol or administration of novel surgical interventions or medications. No patient identifiable information was collected. Postoperatively, all patients had venous thromboembolism (VTE) prophylaxis (both mechanical and/or chemical) based on risk assessment using the trust VTE prevention policy. The audit was registered with the hospital's clinical audit department and the orthopedics clinical governance team. Appropriate approval was obtained prior to commencement of this study. Results and recommendations for each audit cycle were presented and discussed at the Trauma and Orthopedics Clinical governance meeting in the hospital and feedback provided to the Clinical audit team. Data was collected on a Microsoft excel sheet and verified by 2 authors (FA and AK) prior to analysis. Statistical testing was performed using Medcalc<sup>R</sup> (Medcalc software Ltd., Belgium).

## 3. Results

A total of 171 consecutive patients admitted with hip fractures were screened during this period. 3 patients who were treated non-operatively, 18 patients who had incomplete data recorded in the medical notes and 5 patients who had surgery for periprosthetic hip fractures were all excluded. 14 patients who were on non-DOAC anticoagulants or anti-platelet drugs were also excluded.

A total of 131 patients comprising 22 patients for the DOAC hip fracture group and 109 patients for the non-anticoagulated hip fracture group met the inclusion criteria for final analysis. The mean age for all patients in the DOAC group was 84.5 years while it was 81 years for the non-anticoagulated group. 100% of the DOAC patients were above 60 years of age compared to 97% for the non-anticoagulated group. The mean age for all 131 patients included in the study was 81.5 years with a male to female ratio of 1:1.2.

50% of the DOAC hip fracture patients had intracapsular femoral neck fractures while 60.5% of the non-anticoagulated group sustained intracapsular femoral neck fractures. The rest of the patients sustained extracapsular femoral neck fractures. For the type of surgery for the DOAC group, 10 (45.5%) patients had hip hemiarthroplasty surgery; 4 (18.2%) patients had intramedullary nail (IM) fixation; 7 (31.8%) patients had dynamic hip screw (DHS) fixation; and 1 (4.5%) patient had fixation with cannulated hip screws. For the non-anticoagulated group, 43 (39.4%) patients had a hip hemiarthroplasty; 17 (15.6%) patients had a total hip replacement; 14 (12.8%) patients had an IM nail fixation; 30 (27.5%) patients had DHS fixation; and 5 (4.6%) patients had cannulated hip screw fixation.

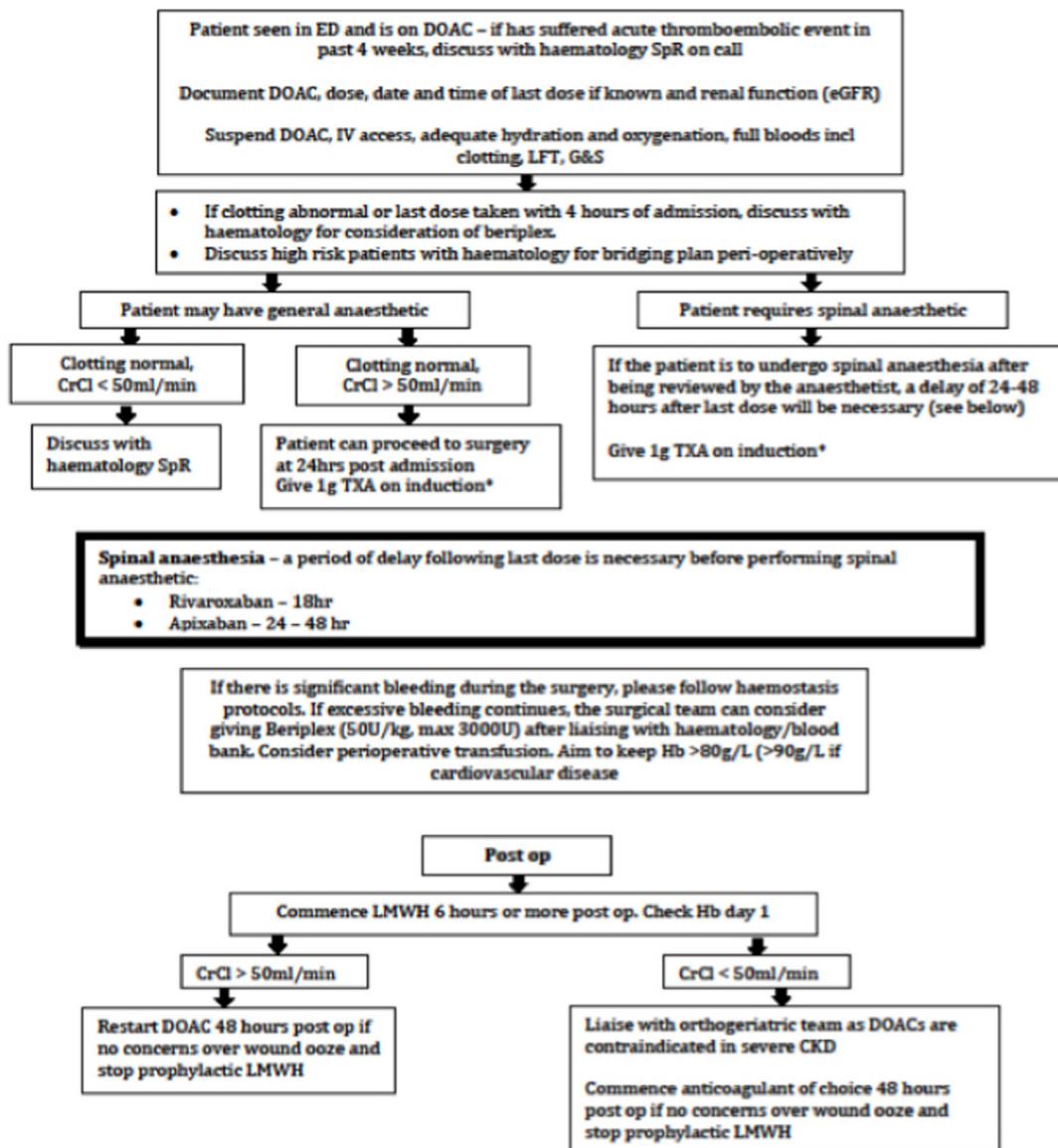
The mean intra-operative estimated blood loss was 500 ml for the DOAC group and 331 ml for the non-anticoagulated group. At an

**Table 1**

A summary of the inclusion and exclusion criteria for patients in this study. LMWH = low molecular weight heparin; UFH = unfractionated heparin.

INCLUSION CRITERIA	EXCLUSION CRITERIA
All adult patients (age >16 years)	Pediatric patients (<16 years of age)
COVID-19 negative at time of surgery	COVID-19 positive at time of surgery
Closed intracapsular or extracapsular hip fractures	Patients with periprosthetic proximal femoral fractures, polytrauma patients, gunshot injuries, open fractures
Treated operatively either via fixation or an arthroplasty procedure	Treated non-operatively due to being deemed unfit for anesthesia or urgent surgery not indicated
On direct-acting oral anticoagulants or no anticoagulation prior to emergency admission	Patients on other anticoagulants prior to admission including warfarin, anti-platelets, UFH, LMWH. For patients on no anticoagulation prior to admission, starting prophylactic LMWH for the index emergency admission does not fit the exclusion criteria.
Surgery performed on an emergency admission	Surgery performed via a non-emergency admission for example delayed surgery following a trial of non-operative treatment for non-displaced intracapsular femoral neck fractures

**Perioperative Management of DOACs in Fracture Neck of Femur Patients:  
Protocol. NOT FOR USE FOR DABIGATRAN (See separate protocol)**



**Fig. 1.** Flow chart summarizing our new hospital trust protocol for patients on factor X-inhibiting direct-acting oral anticoagulants (DOAC) undergoing emergency surgery for femoral neck fractures. ED = emergency department; IV = intravenous; LFT = liver function test; G&S = group and save blood; CrCl = creatinine clearance; TXA = tranexamic acid; eGFR = estimated glomerular filtration rate; CKD = chronic kidney disease; SpR = specialty registrar/senior registrar.

alpha level of 0.05, the mean blood loss between the groups was statistically significant using the unpaired T-test ( $p = 0.0115$ ; 95% confidence interval 38.48–299.16). 40.9% of the DOAC group and 11.9% of the non-anticoagulated group received intra-operative blood transfusion. This was statistically significant (RR 3.43; 95% CI 1.68–7.01). For post-operative blood transfusion within 48 h of surgery, the incidence was 33.3% for the DOAC group and 29.9% for the non-anticoagulated group. The difference between the groups was also statistically significant (RR 2.10; 95% CI 1.23–3.58). However, none of the patients in the DOAC group had massive blood transfusion either intra-operatively or post-operatively.

Compliance with administration of TXA for the DOAC group improved from 72% in the first audit cycle to 81.8% in the second cycle. Compliance with performance of surgery within 24 h (for

DOAC patients with creatinine clearance >50 ml/min) showed slight improvement from 50% for the first cycle to 55% for the second cycle. There was no observed increase in 30-day mortality for the DOAC group who had a 4.5% mortality rate compared to the non-anticoagulated group with a 6.4% mortality rate (RR 0.71; 95% CI 0.09–5.46).

For postoperative bloody wound ooze (as a result of reactionary or secondary hemorrhage), 27.3% of the DOAC group had this problem compared to 9.2% for the non-anticoagulated group. Although this difference was statistically significant (RR 2.97; 95% CI 1.21–7.33), none of the DOAC hip fracture patients required a secondary procedure like image-guided aspiration or wound washout in theatre to address this problem. One patient for the non-anticoagulated group required an ultrasound-guided

aspiration for a non-infected wound hematoma. None of the DOAC group patients had a thrombotic complication within 30 days post-operatively. On the other hand, one patient in the non-anticoagulated group had a pulmonary embolism within 30 days post-operatively.

#### 4. Discussion

There were more female patients with hip fractures in this audit study. This is similar to the literature evidence in most countries showing hip fractures in the elderly population as being more common in women.<sup>5–7</sup> These fragility fractures are mainly due to the higher incidence of osteoporosis in post-menopausal women. The mean age in this audit study conforms to published literature that shows a preponderance of hip fractures in the elderly population compared to younger patients.<sup>5,7</sup>

There is mixed evidence in the literature on significant differences in blood loss and transfusion requirements in DOAC patients compared with non-anticoagulated patients. A single-center study from a U.K. hospital performed by Hoerlyck et al. found no difference in intra-operative or post-operative blood transfusion requirements for the DOAC and non-anticoagulated groups.<sup>8</sup> On the other hand, a systematic review by Xu et al. found an increased risk of intra-operative bleeding and perioperative blood transfusion in patients on oral anticoagulants with the time interval between the last dose and surgery ranging from 21 to 82 h.<sup>9</sup> A Danish registry-based study found a slightly increased risk of blood transfusion in DOAC patients.<sup>10</sup> It can be seen that use of anticoagulants prior to surgery especially for accelerated surgical protocols can lead to increased blood loss. However, the key focus of most policies is to balance the benefits against the risks of post-operative mortality and bleeding-related morbidity.

Extracapsular hip fractures have been shown to have a higher intraoperative blood loss and transfusion requirements compared to intracapsular fractures.<sup>11</sup> The slightly lower percentage of extracapsular fractures in the non-anticoagulated group compared to the DOAC group in this study might also contribute to the observed differences. Nevertheless, despite the fact that this study showed an increased need for perioperative blood transfusion and an increased estimated blood loss in the DOAC group, the aforementioned safety concerns were not prevalent especially if the creatinine clearance is greater than 50 ml/min at the time of surgery.

Evidence in the literature also points to the absence of a significant difference in 30-day mortality between the DOAC and non-anticoagulated patient groups undergoing hip fracture surgery.<sup>12,13</sup> The baseline overall 30-day mortality in the United Kingdom for hip fracture surgery prior to the COVID-19 pandemic was 6.4%.<sup>14</sup> These findings are similar to the results from this audit with 6.4% mortality rate for the non-anticoagulated group and 4.5% for the DOAC group.

For post-operative wound bleeding, the result from this study (27.3% incidence) is comparable to that from the study by Lee-Salvesen et al. who found a 26% incidence of wound bleeding for the DOAC group compared with 5.6% for the non-anticoagulated group.<sup>15</sup> This conforms to the fact that patients on anticoagulants are at increased risk of bloody wound ooze post-operatively. However, in this audit study, none of them required any further procedure to address this and most resolved following temporary suspension of anticoagulant use and application of pressure dressings.

This study had certain strengths. This was a closed loop audit performed prospectively. The study led to improved compliance with the use of TXA in the DOAC patients following completion of the audit cycle. This study also demonstrated that the new hospital

protocol for these patients was relatively safe in terms of perioperative mortality, hemorrhagic complications and thrombotic complications when compared to non-anticoagulated patients.

Some of the limitations observed in this audit study include the fact that 41% of patients on DOAC who had spinal or general anesthesia still had their surgery later than 48 h despite attempts at improving this with the new policy. However, it is to be noted that there are other perioperative confounding factors that can lead to surgical delays in these patients including associated comorbidities requiring optimization and availability of theatre space. Also, only 9 of the 22 DOAC patients had a creatinine clearance >50 ml/min at the time of surgery which meant they had to be delayed further by the anesthetist in order to achieve safe surgery. There is also a possibility of inter and intra-observer error in calculating estimated blood loss among operating room personnel. This can be a source of measurement bias. Other confounding factors like complexity of surgery, American society of anesthesiologist (ASA) grade, age, presence of malignancy, peri-operative delirium, post-operative COVID-19 infection and cardiac risk index can contribute to perioperative mortality and complications.<sup>16–18</sup> This study did not incorporate any statistical analysis to adjust for these as it was focused on protocol adherence and safety profile monitoring within the realm of an audit cycle.

#### 5. Conclusion

This closed loop audit has led to some improvement in compliance with the hospital policy on improving timing of surgery in hip fracture patients on direct-acting oral anticoagulants. The study has shown that this policy is safe for patients despite the fact that there is a statistically increased bleeding risk and need for blood transfusion. If tailored suitably to each individual patient, this type of policy has the potential to counter other risks associated with delayed surgery especially in elderly patients with hip fractures. It can also potentially reduce healthcare costs associated with unnecessary surgical delays.

Patient safety remains the key concern for any perioperative policy. Evidence-based practice means we must balance literature evidence with our local setting exigencies and the peculiarities of the individual patient. Despite the mixed evidence in the literature relating to perioperative blood loss and transfusion requirements, this study has shown that such a policy is relatively safe and we recommend that hospitals with similar DOAC protocols for hip fracture surgery need to continue active surveillance to monitor for perioperative blood loss, transfusion requirements and complications through regular audits. The goal of achieving best practice accelerated surgery must be balanced against the anticipated risks to each patient.

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