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The Impact of Anticoagulant Medications on Fragility Femur Fracture Care: The Hip and Femoral Fracture Anticoagulation Surgical Timing Evaluation (Haste) Study

MM Farhan-Alanie , R Chinweze , R Walker , WGP Eardley , On behalf of HASTE collaborators

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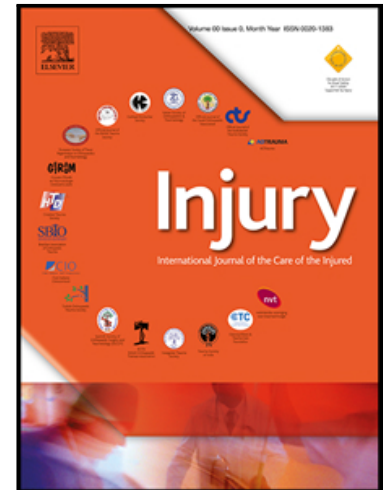
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Highlights

- Approximately one in five femoral fragility fracture patients take an anticoagulant medication, primarily DOACs
- Anticoagulated patients differ in several demographic and comorbidity characteristics
- Time to surgery was longer for anticoagulated patients and fewer received surgery within 36 hours of admission
- Differences in time to surgery were similar between countries however there was some variation between hospitals
- Adjusted 30-day and overall mortality from admission was higher in anticoagulated patients

The Impact of Anticoagulant Medications on Fragility Femur Fracture Care: The Hip and Femoral Fracture Anticoagulation Surgical Timing Evaluation (Haste) Study

Farhan-Alanie MM[1]*, Chinweze R[2], Walker R[3], Eardley WGP[3,4,5], On behalf of HASTE collaborators[6]

1. Warwick Medical School, University of Warwick, Coventry, CV4 7AL, UK.
2. North Cumbria Integrated Care NHS Foundation Trust, Carlisle, CA2 7HY, UK.
3. South Tees Hospitals NHS Foundation Trust, Middlesbrough, TS4 3BY, UK.
4. University of Teesside, Middlesbrough, TS1 3BX, UK.
5. University of York, York, YO10 5DD, UK.
6. Supplementary material (table S1)

* corresponding author (email address: u1874544@live.warwick.ac.uk). ORCID ID 0000-0002-9209-0108

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Funding

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Ethical approval

Research and Ethics Committee approval was not required. Institutional information governance approval was obtained by the project management team at the lead site (South Tees Hospitals NHS Trust). Moreover, all collaborators obtained local approval from their respective institutions and registered the study as service evaluation prior to data collection.

The Impact of Anticoagulant Medications on Fragility Femur Fracture Care: The Hip and Femoral Fracture Anticoagulation Surgical Timing Evaluation (Haste) Study

Abstract

Introduction: Due to their hypocoagulable state on presentation, anticoagulated patients with femoral fragility fractures typically experience delays to surgery. There are no large, multicentre studies previously carried out within the United Kingdom (UK) evaluating the impact of anticoagulant use in this patient population. This study aimed to evaluate the current epidemiology and compare the perioperative management of anticoagulated and non-anticoagulated femoral fragility fracture patients.

Methods: Data was prospectively collected through a collaborative, multicentre approach involving hospitals across the United Kingdom. Femoral fragility fracture patients aged ≥ 60 years and admitted to hospital between 1st May to 31st July 2023 were included. Main outcomes under investigation included time to surgery, receipt of blood transfusion between admission and 48 hours following surgery, length of stay, and 30-day mortality. These were assessed using multivariable linear and logistic regression, and Cox proportional hazards models. Only data from hospitals $\geq 90\%$ case ascertainment with reference to figures from the National Hip Fracture Database (NHFD) were analysed.

Results: Data on 10,197 patients from 78 hospitals were analysed. 18.5% of patients were taking anticoagulants. Compared to non-anticoagulated patients, time to surgery was longer by 7.59 hours (95%CI 4.83–10.36; $p < 0.001$). 42.41% of anticoagulated patients received surgery within 36 hours (OR 0.54, 95%CI 0.48–0.60, $p < 0.001$). Differences in time to surgery were similar between countries however there was some variation across units. There were no differences in blood transfusion and length of stay between groups (OR 1.03, 95%CI 0.88–1.22, $p = 0.646$ and 0.22 days, 95%CI -4.48–

0.887; $p=0.887$ respectively). Mortality within 30 days of admission was higher in anticoagulated patients (HR 1.27, 95%CI 1.03–1.57, $p=0.026$).

Conclusions: Anticoagulated femoral fragility fracture patients comprise a substantial number of patients, and experience relatively longer delays to surgery with less than half receiving surgery within 36 hours of admission. This may have resulted in their comparatively higher mortality rate. Inclusion of anticoagulation status in the minimum data set for the NHFD to enable routine auditing of performance, and development of a national guideline on the management of this growing and emerging patient group is likely to help standardise practice in this area and improve outcomes.

Keywords: hip, femoral, periprosthetic, fracture, delay, timing, surgery, anticoagulant, length of stay, blood transfusion, mortality

Introduction

The benefits of expedited surgery to patients with fragility femoral fractures is established and underpins guidelines for their care [1, 2]. Despite this, patients who take anticoagulant medications such as Vitamin K antagonists (VKA) and Direct Oral AntiCoagulants (DOAC) typically experience longer surgical delay greater than those that don't [3]. Anecdotally, delay is driven by concerns of complications despite the fact that prompt surgery is both safe and feasible [4-9] and evidence for increased complications is scarce.

As the proportion of anticoagulated patients within the femoral fragility fracture population rises, addressing this issue grows in importance. Approximately 20% of the fragility femoral fracture population in the United Kingdom (UK) take anticoagulants [10, 11] and in other countries the prevalence is even higher [3, 10-14]. Numbers of anticoagulated patients with fracture to the hip or the rest of the femur being exposed to the risks associated with delayed surgery is therefore both substantial and avoidable.

To help standardise and improve care, the British Orthopaedic Association (BOA) and National Institute for Clinical Excellence (NICE) have published guidelines [15, 16] for fragility femur fracture management. The BOA state that surgery should be performed within 36 hours of admission and protocols for anticoagulation reversal must be available. Similarly, NICE state that surgery should be performed on the day of, or day following, admission to hospital and that surgery should not be delayed by anticoagulation.

The current prevalence of anticoagulated femoral fragility fracture patients and their peri-operative management is unknown. Although studies have addressed this topic, most are limited by small sample sizes and are single centre, and focussed on a limited number of variables. Most importantly,

these studies are exclusively restricted to hip fracture patients only [10, 11, 17-21] and do not include patients with injury to the rest of the femur and periprosthetic fractures. It is unknown if prior work on this topic has influenced practice or whether disparity between these patient groups continues to exist. Also, the consistent findings of these prior studies suggests there is a mismatch between awareness and clinical practice on this topic [3]. Further work is needed to highlight other factors influencing this discrepancy. Although the National Hip Fracture Database (NHFD) captures and includes a high volume of cases across hospitals in England, Wales and Northern Ireland, it does not routinely collect information on delays relating to anticoagulation [22].

Using a multinational collaborative approach, this study comprehensively describes the management of anticoagulated femoral fragility fracture patients compared to non-anticoagulated patients. It will assess whether perioperative care including time to surgery differs between fracture groups both within units and across four countries.

Methods

Study design and eligibility criteria

A collaborative, multicentre, prospective observational study evaluating service received by femoral fragility fracture patients across England, Scotland, Wales, and Northern Ireland was performed. This study adhered to an *a priori* protocol [23] peer reviewed by the BOA Surgical Specialty Leads for Clinical Trials [24]. All consecutive patients aged 60 years and older presenting to hospital with a native or periprosthetic hip or femoral fracture over a three-month period (1st May to 31st July 2023 inclusive) were included and followed up to 31st August 2023. All UK hospitals were eligible to enrol in the study until 14th June 2023 in order to capture a minimum six weeks data. Patients undergoing revision procedures were not eligible for inclusion.

Data sources and quality assurance

Data collection was performed by collaborators at participating sites (table S1). Data was submitted via a standardised electronic data collection proforma developed using REDCap (REDCap; Vanderbilt University, USA). This was refined based on an external pilot study between 1st and 30th April 2023 across two sites (James Cook University Hospital, Middlesbrough; University Hospital Coventry, Coventry).

Quality assurance checks were conducted every two weeks throughout the study period. These evaluated both case ascertainment and data completeness metrics at each individual participating site. Case ascertainment was established by comparing the number of records submitted on REDCap to that expected based on data available from the National Hip Fracture Database [25]. This was not possible to conduct for participating hospitals in Scotland due to the absence of publicly available data on the volume of eligible cases treated at individual sites. The data completeness evaluation involved identifying missing or anomalous data field submissions for submitted records on REDCap. Participating collaborators at each site were contacted and sent the results for both these metrics following each round of quality assurance to allow the opportunity to address any issues. Records with at least one missing data field by the end of the study period were considered incomplete and discarded. A minimum adjusted case ascertainment level of 90% was required, allowing a buffer to account for the possibility of relatively fewer presentations during the study period. Only data from sites which met this criteria were included for analysis.

Statistical analysis

Categorical variables are summarised as frequencies and percentages, and analysed using Chi-squared or Fisher's exact tests. Parametric data was reported using mean and standard deviation (SD), and analysed using two-sided unpaired t-tests. Non-parametric data was reported as median and interquartile range (IQR), and analysed using independent samples Mann–Whitney U test. Median differences were calculated using Hodges–Lehmann technique and presented alongside robust confidence intervals. Outcomes time to surgery, surgery within 36 hours of admission, and

surgery on the day or day following admission were assessed using multivariable linear and logistic regression models, adjusting for American Society of Anaesthesiologists (ASA) score, additional injuries (yes/no), operation performed, and type of fracture. Multivariable linear regression was also used to assess the association between hospital length of stay and anticoagulant use adjusting for age (continuous), sex, non-operative management (yes/no), operation performed, type of fracture, pre-operative abbreviated mental test score (AMTS), ASA score, and Rockwood clinical frailty score. Multivariable logistic regression was used to assess the association between need for blood transfusion from admission to 48 hours post-operatively and anticoagulant use adjusting for antiplatelet use, operation performed, type of fracture, other associated injuries (yes/no), admission haemoglobin level (continuous), tranexamic acid use, and ASA score. Mortality outcomes were assessed using 1 – Kaplan-Meier estimates and a Cox proportional hazards model was used for comparison between groups adjusting for age (continuous), sex, ASA score, AMTS score, admission haemoglobin level (continuous), additional injuries (yes/no), non-operative management (yes/no), operation performed, type of fracture, residence status, active malignancy in last 20 years, receipt of blood transfusion (continuous), and method of presentation to hospital. Robust standard errors were used in the linear regression models. 95% confidence intervals (CI) are presented, and statistical significance was set at $p < 0.05$. Analyses were performed using Stata software (version 18.0, StataCorp LLC, College Station, Texas, USA, 1985–2023).

Results

Case ascertainment and quality assurance

84 hospitals (73 in England, 7 in Scotland, 2 in Wales, and 2 in Northern Ireland) participated. Following the final quality assurance check and data cleaning, records from six hospitals in England were excluded from the analysis due to case ascertainment volume not meeting the eligibility criteria. A further 183 records were excluded due to containing at least one missing data field. This

resulted in the inclusion of data from 10,197 complete records submitted by 354 collaborators over 78 hospitals for the analysis. Figure S1 illustrates the geographical distribution of the participating hospitals over the study period. Median number of submitted records per site was 126.5 (IQR 92 - 153). The median data collection period among all included sites was 83 days (IQR 68 - 92). Median case ascertainment was estimated to be 100% (IQR 100-100).

Patient demographics

Figure 1 illustrates the femoral fragility fracture patient population included in the study. There were 8,309 non-anticoagulated and 1,888 anticoagulated patients who sustained a femoral fragility fracture over the study period. Anticoagulated patients represented 18.5% of the total population with warfarin and DOACs comprising 2.16% and 16.17% respectively. There were differences in multiple characteristics observed between the two patient groups (Tables 1 and S2). The most commonly used anticoagulant was apixaban (45.95%) and arrhythmia was the most common indication for anticoagulant use (73.7%). Table S3 provides a breakdown of the different anticoagulant medications taken by patients and the indications for their use.

Non-operative management

The minority of patients were managed non-operatively although a relatively higher proportion were anticoagulated patients (4.45% versus 3.32%; $p=0.017$). Reasons for non-operative management differed between patient groups, with a higher proportion of anticoagulated patients being deemed unfit for surgery ($p=0.011$). Tables 2 and S4 provide further details on non-operative management between groups.

Operative management

Anticoagulated patients were less likely to receive a spinal anaesthetic and a peripheral nerve block compared to non-anticoagulated patients ($p=0.010$ and $p<0.001$ respectively). Time from admission to surgery was relatively longer for anticoagulated patients; median 39.72 hours (IQR 25.85 – 56.81)

versus 31.15 hours (IQR 20.68 - 48), $p < 0.001$. The difference in time to surgery persisted in the multivariable linear regression model (table 4). Fewer anticoagulated patients received surgery within 36 hours of admission, and on the day of or day after admission; adjusted OR 0.54 (95% CI 0.48 – 0.60, $p < 0.001$) and 0.53 (95% CI 0.48 to 0.59, $p < 0.001$) respectively. Causes of surgical delay outwith 36 hours following admission in anticoagulated patients were reported to be due to solely anticoagulation status and **insufficient list space** in 24.86% and **52.19%** cases ($p < 0.001$) **respectively**. Figure 2 and S2 illustrate time to surgery between the patient groups.

Mean estimated glomerular filtration rate (eGFR) among anticoagulated patients taking DOACs was 59.01 ± 20.15 ml/min/1.73 m². There was very low correlation between eGFR level on admission and time to surgery in anticoagulated patients taking DOACs (Spearman's rank correlation coefficient $\rho = -0.0452$; $p = 0.073$). There were no differences in weight bearing status between patient groups ($p = 0.353$). There were also no differences in receipt of blood transfusion from admission to 48 hours post-operatively between the patient groups in the multivariable logistic regression model (adjusted OR 1.03, 95% CI 0.88 to 1.22; $p = 0.646$).

Tables 3 and S6 summarise anaesthetic and operative level characteristics.

Clinical practice between different countries and units

There were differences in the median time to surgery between anticoagulant and non-anticoagulated patients in most of the participating countries (table 5). The overlapping confidence intervals in the observed median differences suggests similar disparities in clinical practice between most of the four countries. Variations in clinical practice were observed on a unit level (Figure 3).

Length of stay and mortality

Unadjusted median length of stay was longer for anticoagulated patients ($p < 0.001$) however multivariable linear regression found no difference between groups (0.22 days, 95% CI -4.48 to 0.887; $p = 0.887$). Anticoagulated patients had a relatively higher mortality within 30 days of

admission (HR 1.272, 95% CI 1.030 to 1.572, $p=0.026$, figure 4) and over the entire study period (HR 1.294, 95% CI 1.066 to 1.570, $p=0.009$; supplementary figure 3). Nottingham Hip Fracture Scores were higher in anticoagulated patients ($p<0.001$). Also, anticoagulated patients had a relatively higher Charlson Comorbidity Index ($p<0.001$) and lower estimated 10 year survival compared to non-anticoagulated patients (median 2%, IQR 0-21, and 21%, IQR 2-53 respectively; $p<0.001$). Table 6 provides additional results on post-operative outcomes.

Discussion

This is the largest and most comprehensive study investigating the epidemiology and management of anticoagulated femoral fragility fracture patients. We have provided, for the first time, a multi-centre, multi-national assessment of this patient group. This approach has helped ensure that the results are generalisable and contemporary. In addition we provide evidence, at scale, for injury groups previously under reported such as patients with periprosthetic and native femoral diaphyseal and distal fractures.

Our study found that approximately one in five patients presenting with a femoral fragility fracture take an anticoagulant medication, the majority being DOACs, primarily apixaban. Furthermore, anticoagulated patients differ to non-anticoagulated patients in several patient level characteristics. A greater proportion of anticoagulated patients were male, more frail, and comorbid with a higher ASA grade. Despite injury patterns and procedures being similar between groups, anticoagulated patients were less likely to receive a regional block, spinal anaesthetic, and prompt surgery. Similar disparities in clinical practice were observed between most of the countries and there was variation in time to surgery between the different hospitals. There was no correlation observed between eGFR levels and time to surgery among DOAC patients. The receipt of a blood transfusion from admission to 48 hours post-operatively was similar between groups. Both patient groups remained in hospital for comparable periods of time however 30-day mortality was higher in anticoagulated patients.

Previous studies on this topic carried out in the United Kingdom align with our results. Hourston et al. performed a single-centre study of 845 patients [10]. They found approximately one third fewer patients taking anticoagulants compared to our study, and the majority used warfarin rather than DOAC (10% versus 4%). Similar to our study, their multivariable regression analysis identified anticoagulation as being a significant factor affecting time to surgery ($p=0.028$). Another single centre study by Eardley et al. compared 1024 non-anticoagulant and warfarin-coagulated femoral fragility fracture patients [20]. They also demonstrated that time to theatre was significantly longer in the latter patient group (mean 53.71 versus 32.09 hours; $p<0.001$). Mahmood et al. analysed 1,038 femoral fragility fracture patients, and found a similar proportion of patients taking an anticoagulant medication to our study however more were taking warfarin than DOAC (9% versus 7%). Nonetheless, their study also found similar differences in patient characteristics with regards to age, gender, and ASA grade [11]. Although a greater proportion of anticoagulated patients experienced relatively delayed surgery in their study, this unadjusted result was just shy of being considered statistically significant (mean 23.5 versus 29.0 hours; $p=0.077$). Differences in the findings of the proportion of anticoagulated patients and time to theatre compared to our study are likely due to a variety of reasons including regional variation in practice, single centre studies, and differences in study time periods. These studies, several of which are now up to around ten years old, are not reflective of current prescribing practices and suffer from limitations that prevent generalisation to the broader more contemporary patient group – an issue we have addressed.

Work performed out with the UK has also found similar results to our study [3, 26, 27]. Aigner et al. analysed 15,099 patients (hip fractures alone) in the combined Germany, Switzerland and Austria Registry for Geriatric Trauma (ATR-DGU) [12]. They demonstrated an increasing trend in the proportion of anticoagulated patients using DOAC rather than VKA over time, and in the final year of the study period there were relatively more anticoagulated patients using DOAC which is consistent with our study results. In contrast to our study, there were no differences in the type of anaesthetic

received by between the patient groups. However, time to theatre was also delayed for anticoagulated patients ($p < 0.001$).

The main strength of our study is the large number of prospectively collected cases from numerous, widespread hospitals. This enables the findings to be representative of practice and generalisable across the broader injury population. In greatest contrast to other studies, this work includes not just fractures around the intracapsular and trochanteric region of the femur, on which current knowledge is based. We have provided for the first time an assessment of the entire patient group, having a fracture at any level. This includes all proximal femur, diaphyseal and distal (including articular) fractures. In addition we have captured the important group in which there is perhaps the greatest variation in overall practice, the periprosthetic femur fracture patient [28-30]. This study is also unique in allowing an understanding of clinical practice both between units and across nations. All different types of hospitals in four countries having similar but differing care systems were included. We collected information on a comprehensive range of data fields including causes for the surgical delay. The use of an *a priori* protocol and validation of case ascertainment levels ensured transparency and limited the risk of selection bias respectively [23] [25].

Equally, there are limitations of this work that must be appreciated when interpreting the results and recommendations. With approximately 10,500 patients and many data fields analysed, this work carries the inherent issues and limitations of big data sets [31]. Misclassification, confounders, lumping and proxy outcomes cannot be eliminated. We have addressed the majority of these issues through ensuring as many variables impacting on the patient pathway are identified. We have supplemented the often criticised ASA comparator with frailty assessment. We have used the NHFS to stratify groups. We have identified differing fracture types accurately as this is established practice within NHFD and not unique or novel to this study. Utilising NHFD data fields that are routinely collected and embedded within hospital processes at nearly all of the sites again ensures that our

study can limit big data effects especially in terms of incorrect coding or misclassification through lack of familiarity.

Another limitation of this study relates to the unknown factors influencing the voluntary decision of hospitals to participate in this study. It is possible that performance between participating and non-participating sites may be differential. However, this is an uncontrollable source of potential bias which has been mitigated through participation of many centres and covering a wide geographical area, achieved by promoting and allowing all units to participate in the study. Also, the prospective study design may have increased the risk of performance bias although it is unlikely that local practice was influenced by knowledge of the study due to the variety and volume of surgeons carrying out these operations at each unit. **It is also worth mentioning there may be variations in the differences for timing of surgery between patient groups based on the type of procedure being performed. This may be due to reasons relating to differences in blood loss and transfusion requirements between different procedures however performing this subanalysis was outside the scope of this study [32].**

There are many factors which can affect the orthopaedic trauma theatre list order and influence the timing of patients' surgeries [33]. In the context of this topic, the 'golden patient' [34] is generally considered by surgeons to be non-anticoagulated and is typically prioritised on the trauma theatre list over an anticoagulated patient if both were admitted to hospital at the same time. Moreover, delays in surgery for anticoagulated patients awaiting an operation in hospital may be exacerbated by subsequent admissions of other patients requiring surgery for various high priority indications and who are then given precedence on the theatre list [33]. These factors are likely to have contributed to the reasons for insufficient list space for operating on anticoagulated femoral fragility fracture patients within 36 hours of their admission. This may also have contributed to the reason why the Kaplan-Meier plot curves (figure 2) illustrating time to surgery between patient groups do not cross until approximately 80 hours following patient admission.

Despite previous work on this subject [3], disparity persists between these two patient groups, and equal priority and access to surgery should be being provided for anticoagulated patients.

Over half of all orthopaedic trauma operations are performed on patients over 60 years of age [35]. In addition, looking more globally at the injured of the UK, the average age of patients with significant injury burden, the Major Trauma group, has doubled over recent years [36, 37]. The importance of understanding and assessing pathways of care for this injury group is transparent. Large numbers of older patients are being injured and cared for within national trauma systems [38]. The impact of variation in this care and improvements gained through standardisation and eliminating delay and excessive bed occupation are key determinants of any future healthcare policy.

Conclusion

Older patients with a broken femur have been closely studied and subject to assessment and care guidance for a considerable period of time [39]. This injury group are more closely monitored and have been the subject of many trials and guidance iterations to improve care [40]. The inception of the NHFD and then payment by results based on specific Key Performance Indicators has had a hugely beneficial effect on care and has decreased mortality [40-42]. With increasing numbers of older patients [38] and within a closely monitored injury population, we have shown that there still remains areas of considerable variation and inexplicable practice. The perioperative management of anticoagulation in the older patient with a femoral fracture unfortunately remains one such area. This is despite extensive evidence supporting the safety of expedited surgery in this patient population [4, 6, 7] and delayed surgery being associated with increased mortality [3]. Our own study has also highlighted the existence of some variation in practice between different units. The inclusion of anticoagulation status as part of the minimum data set for the NHFD to enable routine auditing of performance, and development of a national guideline on the management of this growing and emerging patient group is likely to help standardise practice in this area and improve outcomes.

Conflicts of interest

WE is the Surgical lead of the National Hip Fracture Database of England and Wales. The other authors declare no conflicts of interest.

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	Total (n=10,197)	Anticoagulated patients (n=1888)			Non- anticoagulated patients (n=8309)	p-value [^]
		All (n=1888)	Warfarin (n=220)	DOAC (n=1647)		
Median age, yrs (IQR)	83 (76 - 88)	85 (79 - 90)	84.5 (78-89)	86 (79-90)	82 (76 – 88)	<0.0001
Sex, n (%)						
Male	3,093 (30.33)	719 (38.12)	80 (36.36)	632 (38.41)	2,373 (28.56)	<0.001
Female	7,104 (69.67)	1,169 (61.88)	140 (63.64)	1,015 (61.59)	5,936 (71.44)	
Ethnicity, n (%)						
Asian or Asian British	148 (1.45)	15 (0.79)	1 (0.45)	14 (0.85)	133 (1.60)	0.044
Black, African, Caribbean, or Black British	29 (0.28)	5 (0.26)	0 (0)	5 (0.30)	24 (0.29)	
White	9,920 (97.28)	1,855 (98.25)	218 (99.09)	1,617 (98.18)	8,065 (97.06)	
Mixed or Multiple Ethnic Groups	42 (0.41)	7 (0.37)	1 (0.45)	5 (0.30)	35 (0.42)	
Other	58 (0.57)	6 (0.32)	0 (0)	6 (0.36)	52 (0.63)	
Mean ASA grade (SD)	2.97 (0.66)	3.21 (0.55)	3.26 (0.54)	3.21 (0.55)	2.92 (0.67)	<0.0001
Injury type, n (%)						
Hip fracture	9,050 (88.75)	1,671 (96.26)	204 (97.61)	1,449 (96.03)	7,379 (95.23)	0.024
Native femoral fracture	435 (4.27)	65 (3.74)	5 (2.40)	60 (3.97)	370 (4.78)	
Periprosthetic femoral fracture	712 (6.98)	152 (8.05)	11 (5)	138 (8.37)	560 (6.74)	
Pre-admission residence, n (%)						
Own Home/Sheltered Housing	8,383 (82.21)	1,539 (81.52)	201 (91.36)	1,320 (80.16)	6,844 (82.37)	0.639
Residential Care	779 (7.64)	153 (8.10)	5 (2.27)	146 (8.86)	626 (7.53)	
Nursing care	1,035 (10.15)	196 (10.38)	14 (6.36)	181 (10.98)	839 (10.10)	
Median pre-operative AMTS (IQR)	9 (5-10)	9 (6-10)	10 (8-10)	9 (5-10)	9 (5-10)	0.212

Median Rockwood clinical frailty score (IQR)	5 (3-6)	5 (4-6)	5 (4-6)	5 (4-6)	5 (3-6)	<0.0001
Median Charlson Comorbidity Index score (IQR)	5 (4-6)	6 (5-7)	6 (4.5 – 7)	6 (5-7)	5 (4-6)	<0.0001
Additional injuries, n (%)						
Yes	774 (7.59)	167 (8.84)	25 (11.36)	142 (8.62)	607 (7.31)	0.023
No	9,423 (92.41)	1,721 (91.16)	195 (88.64)	1,505 (91.38)	7,702 (92.69)	
Median pre-operative Hb#, g/L (IQR)	123 (111-133)	121 (109 - 132)	121 (110-131)	121 (109-132)	123 (111-133)	<0.0001
Antiplatelet medication use, n (%)						
Yes	2,238 (21.95)	219 (11.59)	20 (9.09)	193 (11.71)	2,019 (24.30)	<0.001
No	7,959 (78.05)	1,669 (88.41)	200 (90.91)	1,454 (88.29)	6,290 (75.70)	

Table 1: Characteristics of anticoagulated and non-anticoagulated patient groups.

#Haemoglobin, Hb; ^comparison between all anticoagulated and non-anticoagulated groups

	Total (n=360)	Anticoagulated patients			Non- anticoagulated patients (n=276)	p-value [^]
		All (n=84)	Warfarin (n=14)	DOAC (n=69)		
Non-operative treatment, n (%) \$						
No immobilisation	295 (81.94)	69 (82.14)	14 (100)	54 (78.26)	226 (81.88)	0.029
Brace – ROM prohibited first 6 weeks	20 (5.55)	7 (8.33)	0 (0)	7 (10.14)	13 (4.71)	0.057
Brace – ROM allowed	9 (2.50)	1 (1.19)	0 (0)	1 (1.45)	8 (2.90)	0.567
Cast	34 (9.44)	7 (8.33)	0 (0)	7 (10.14)	27 (9.78)	0.755
Other	8 (2.22)	1 (1.19)	0 (0)	1 (1.45)	7 (2.54)	0.661
Reason for non-operative management, n (%)						
Surgeon preference	183 (50.83)	33 (39.29)	5 (35.71)	27 (39.13)	150 (54.35)	0.011
Patient preference	24 (6.67)	6 (7.14)	1 (7.14)	5 (7.25)	18 (6.52)	
Poor soft tissues	6 (1.67)	3 (3.57)	0 (0)	3 (4.35)	3 (1.09)	
Patient non- mobile prior to injury	17 (4.72)	1 (1.19)	0 (0)	1 (1.45)	16 (5.80)	
Not fit for surgery \$	130 (36.11)	41 (48.81)	8 (57.14)	33 (47.83)	89 (32.25)	

Table 2 – Summary of non-operative management among patient groups. [^]comparison between all anticoagulated and non-anticoagulated groups \$Further details on specialty making this decision in table S4

	Total (n=9,837)	Anticoagulated patients			Non- anticoagulated patients (n=8,033)	p- value [^]
		All (n=1,804)	Warfarin (n=206)	DOAC (n=1,578)		
Anaesthetic, n (%)						
General anaesthetic	5,630 (57.23)	1,090 (60.42)	135 (65.53)	942 (59.70)	4,540 (56.52)	0.010
Spinal anaesthetic	3,774 (38.37)	638 (35.37)	64 (31.07)	567 (35.93)	3,136 (39.04)	
General and spinal anaesthetic	433 (4.40)	76 (4.21)	7 (3.40)	69 (4.37)	357 (4.44)	
Block, n (%)						
No	953 (9.69)	256 (14.19)	47 (22.82)	204 (12.93)	697 (8.68)	<0.001
Yes	8,884 (90.31)	1,548 (85.81)	159 (77.18)	1,374 (87.07)	7,336 (91.32)	
Median time to surgery, hours (IQR)	33.42 (21.32 – 49.29)	39.72 (25.85 – 56.81)	43.06 (27.22 – 61.07)	39.17 (25.50 – 55.99)	31.15 (20.68 - 48)	<0.0001
Surgery within 36 hours, n (%)	5,328 (54.16)	765 (42.41)	77 (37.38)	683 (43.28)	4,563 (56.80)	<0.001
Reason for delay if surgery outwith 36 hours, n (%) \$						
Solely due to Anti-Coagulation	272 (5.85)	272 (24.86)	60 (38.22)	212 (22.62)	0 (0)	<0.001
Due to Insufficient List Space	3,384 (72.77)	571 (52.19)	55 (35.03)	516 (55.07)	2,813 (79.11)	
Due to Medical Reasons	994 (21.38)	251 (22.94)	42 (26.75)	209 (22.31)	743 (20.89)	
Surgery on day or day after admission, n (%)	5,215 (53.01)	743 (41.19)	77 (37.38)	661 (41.89)	4,472 (55.67)	<0.001
Procedure, n (%)						
Sliding Hip Screw or Similar Device	2,355 (23.94)	413 (22.89)	55 (26.70)	355 (22.50)	1,942 (24.18)	0.395
Hip Hemi-Arthroplasty	4,390 (44.63)	845 (46.84)	101 (49.03)	737 (46.70)	3,545 (44.13)	
Total Hip Replacement	600 (6.10)	43 (2.38)	5 (2.43)	38 (2.41)	557 (6.93)	
Short IM Nail	570 (5.79)	114 (6.32)	10 (4.85)	102 (6.46)	456 (5.68)	

Long IM Nail	1,295 (13.16)	259 (14.36)	28 (13.59)	226 (14.32)	1,036 (12.90)	
Fixation with Single Plate	359 (3.65)	73 (4.05)	3 (1.46)	69 (4.37)	286 (3.56)	
Fixation with Dual Plate	44 (0.45)	8 (0.44)	1 (0.49)	7 (0.44)	36 (0.45)	
IM Nail and Plate Fixation	56 (0.57)	9 (0.50)	1 (0.49)	7 (0.44)	47 (0.59)	
Proximal Femoral Replacement	13 (0.13)	1 (0.06)	0 (0)	1 (0.06)	12 (0.15)	
Distal Femoral Replacement	35 (0.36)	11 (0.61)	0 (0)	11 (0.70)	24 (0.30)	
Revision Arthroplasty	115 (1.17)	26 (1.44)	1 (0.49)	24 (1.52)	89 (1.11)	
Monolateral External Fixator	1 (0.01)	0 (0)	0 (0)	0 (0)	1 (0.01)	
Girdlestone	3 (0.03)	2 (0.11)	1 (0.49)	1 (0.06)	1 (0.01)	
Above knee amputation	1 (0.01)	0 (0)	0 (0)	0 (0)	1 (0.01)	
Weight bearing status, n (%)						
Weight bear as tolerated	9,533 (96.91)	1,751 (97.06)	201 (97.57)	1,532 (97.08)	7,782 (96.88)	0.353
Partial weight bearing or less	223 (2.27)	43 (2.38)	4 (1.94)	37 (2.34)	180 (2.24)	
Non weight bearing	81 (0.82)	10 (0.55)	1 (0.49)	9 (0.57)	71 (0.88)	
Blood transfusion from admission to ≤ 48 hours post-operatively, n (%)						
Yes	1,662 (16.90)	341 (18.90)	37 (82.04)	297 (18.82)	1,321 (16.44)	0.012
No	8,175 (83.10)	1,463 (81.10)	169 (82.04)	1,281 (81.18)	6,712 (83.56)	

Table 3: Detailed summary of operative management of patient groups. ^comparison between all anticoagulated and non-anticoagulated groups \$selection of multiple options permitted

Patient group	Difference relative to non-anticoagulated patients (hours)	95% CI	p-value
Anticoagulated patients	7.59	4.83 to 10.36	<0.001
Warfarin	7.33	2.88 – 11.78	0.001
DOAC	7.42	4.40 – 10.45	<0.001

Table 4: Multivariable linear regression analysis results for time to surgery

Country	Non-anticoagulated patients median time to surgery, hours (IQR)	Anticoagulated patients median time to surgery, hours (IQR)	Median difference, hours (95% CI)	p-value
England (n=8,063)	29.79 (20.38 – 46.96)	39.13 (25.43 – 55)	6.22 (5.11 - 7.33)	<0.001
Scotland (n=1,185)	31.10 (20.84 – 47.33)	38.35 (26.76 – 50.01)	5.95 (2.87 – 9.04)	<0.001
Wales (n=349)	38.01 (23.74 – 58.21)	40.4 (26.23 – 62.50)	2.25 (-3.23 – 7.70)	0.400
Northern Ireland (n=240)	67.01 (46.18 – 92.81)	79.52 (58.33 – 104.88)	13.02 (2.56 – 23.77)	0.016

Table 5: Comparison of difference in time to surgery between anticoagulant and non-anticoagulated patients among the different countries

	Total (n=10,197)	Anticoagulated patients			Non- anticoagulated patients (n=8,309)	P value*
		All (n=1,888)	Warfarin (n=220)	DOAC (n=1,647)		
Median length of stay, days (IQR)	14 (9 - 22)	15 (10-23)	16 (11-16)	15 (10-23)	13 (8-21)	<0.0001
Status at discharge, n (%)						<0.001
Alive	9,307 (91.27)	1,660 (87.92)	188 (85.45)	1,455 (88.34)	7,647 (92.03)	
Deceased	545 (5.34)	151 (8.00)	20 (9.09)	128 (7.77)	394 (4.74)	
Inpatient	345 (3.38)	77 (4.08)	12 (5.45)	64 (3.89)	268 (3.23)	
Median NHFS* (IQR)	6 (5-7)	6 (6-7)	6 (6-7)	6 (6-7)	6 (5-7)	<0.0001
Median predicted 10 year survival using CCI^ score, % (IQR)	21 (2-53)	2 (0-21)	2 (0-53)	2 (0-21)	21 (2-53)	<0.0001

Table 6: Results of length of stay and mortality outcomes between groups. *Nottingham Hip Fracture Score, NHFS; ^Charlson comorbidity index *comparison between all anticoagulated and non-anticoagulated groups

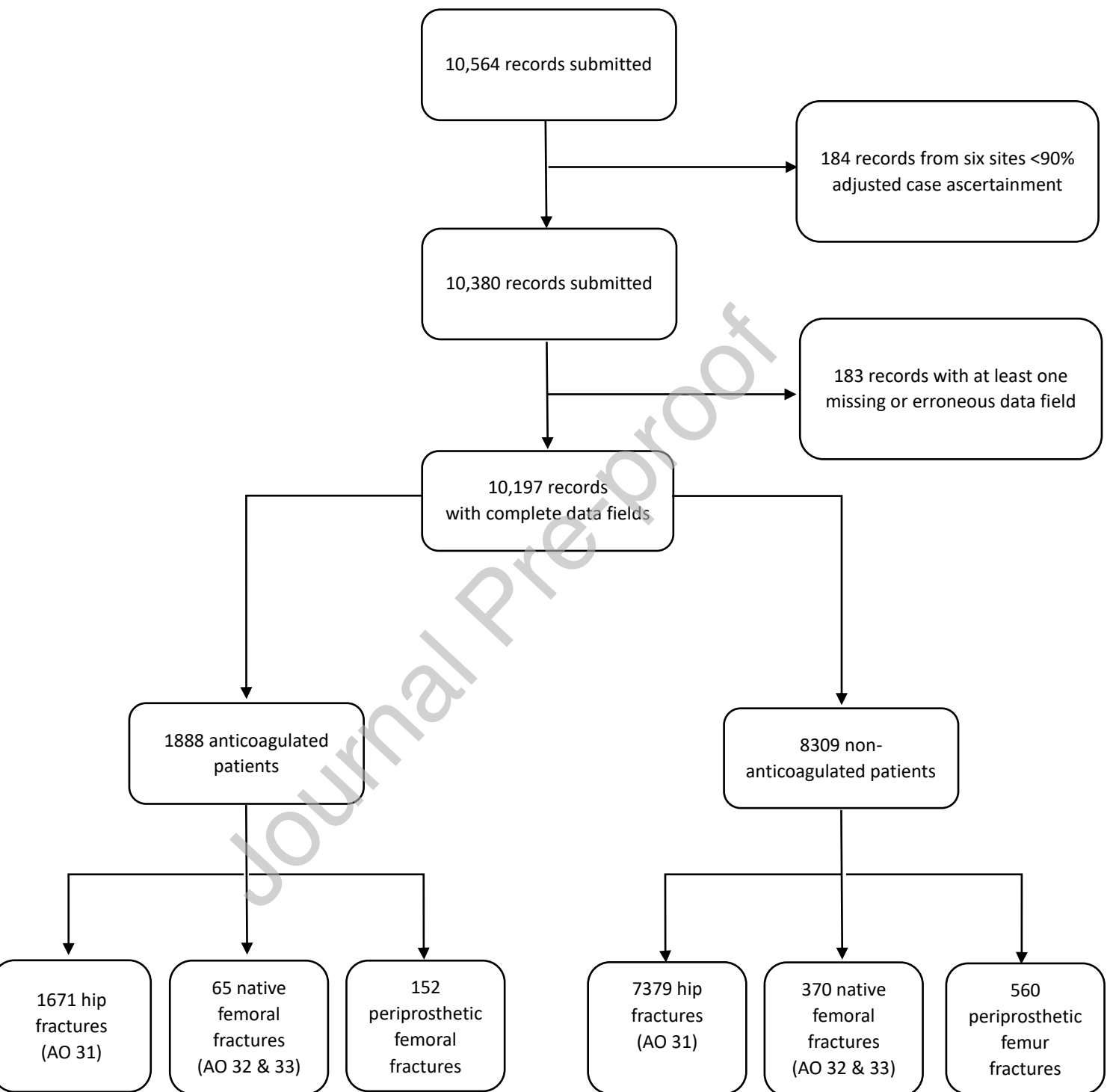


Figure 1: Flow diagram of patients included over the study period

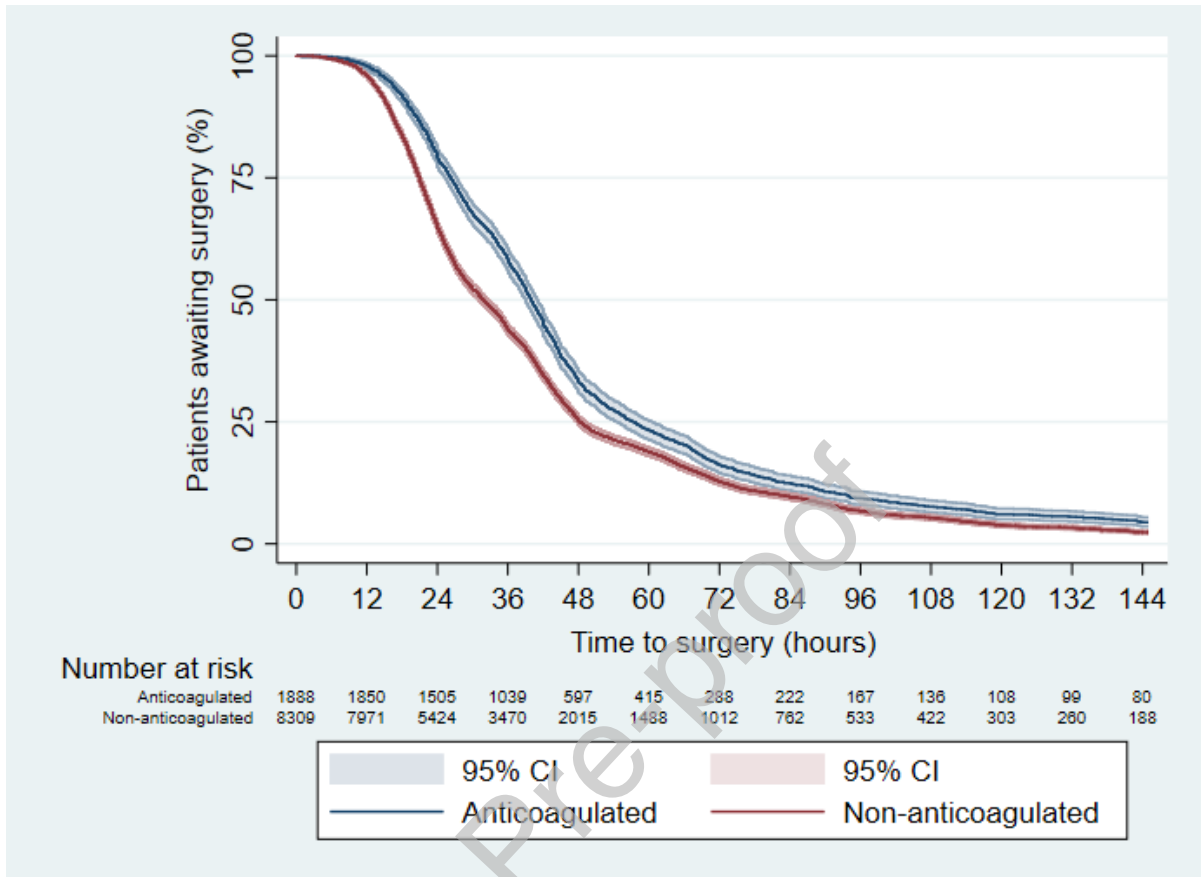


Figure 2: Kaplan-Meier plot of time to surgery following admission for the patient groups. Non-operative patients censored at 24 hours post-admission to reflect clinical decision making process.

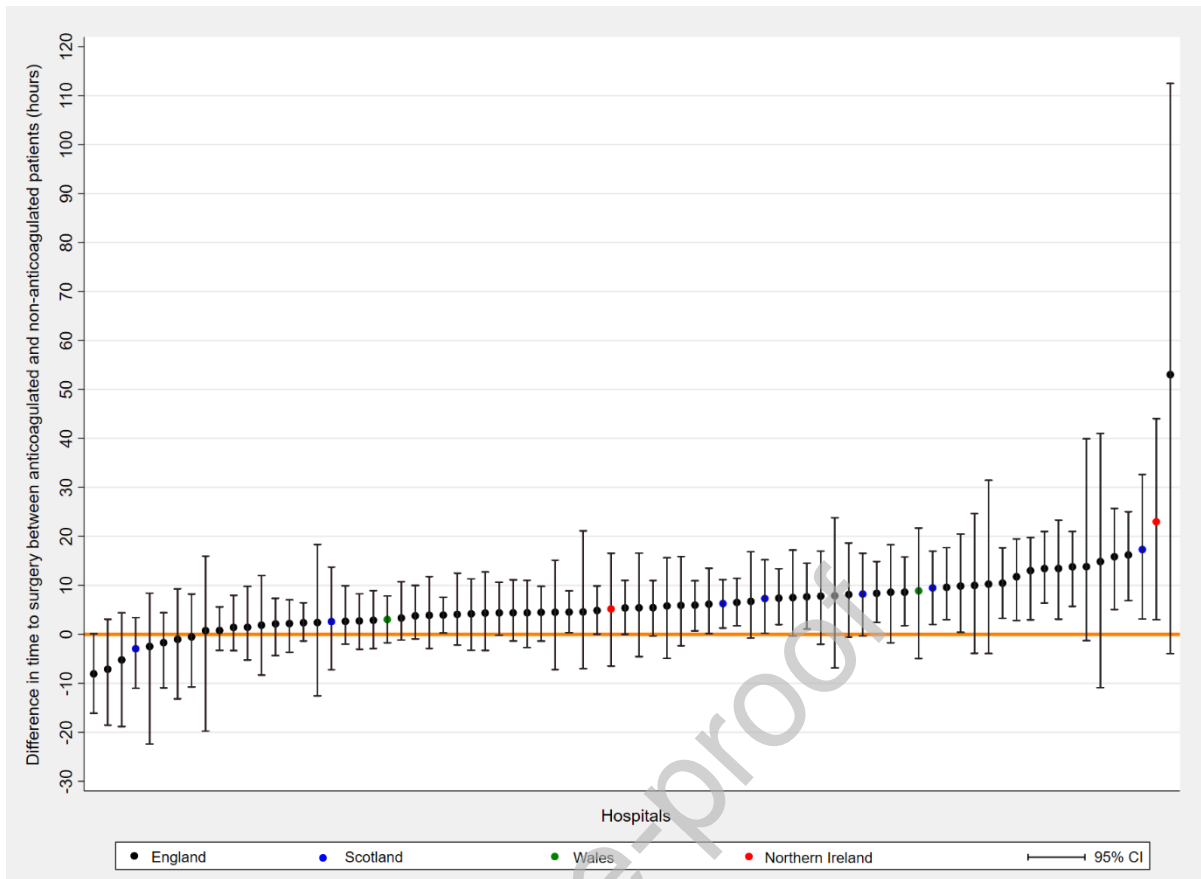


Figure 3: Point estimates and 95% CI of median differences in time to surgery between anticoagulant and non-anticoagulated patients among the different hospitals

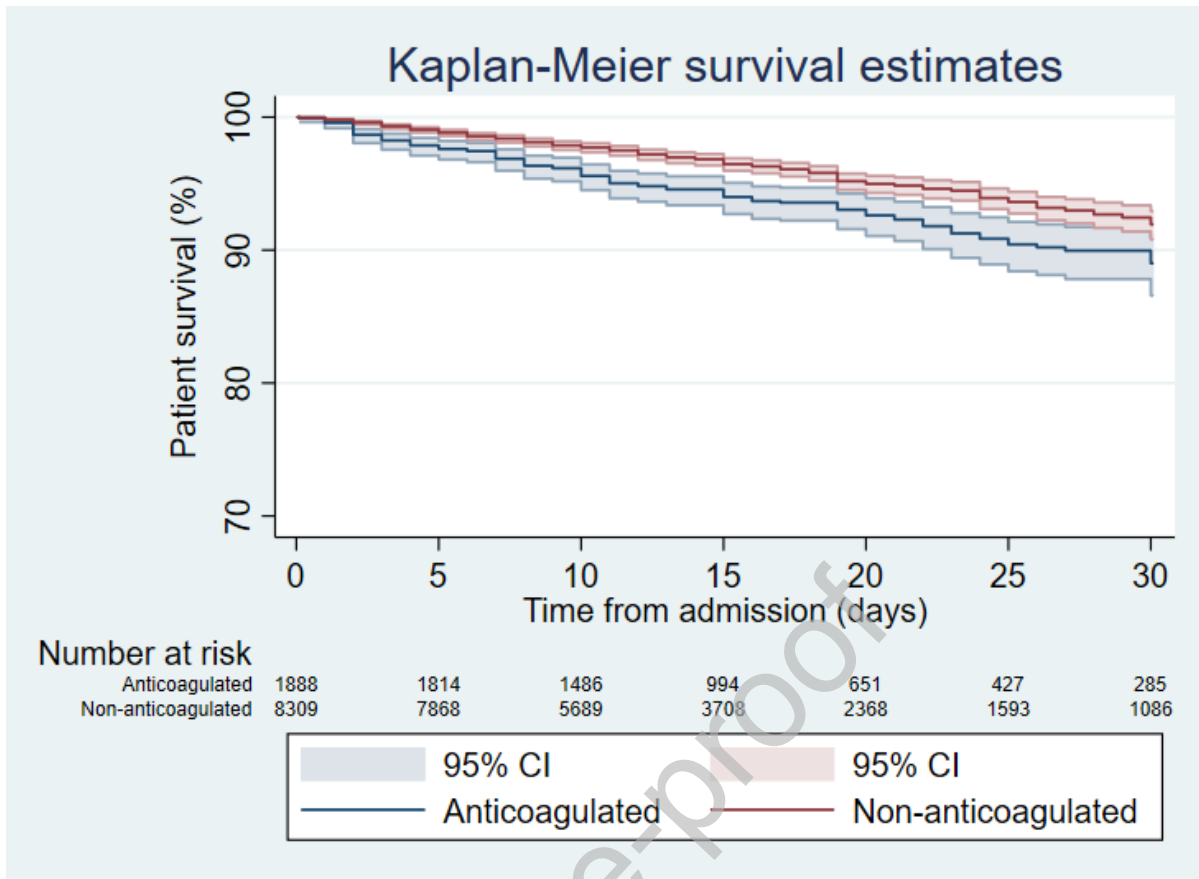


Figure 4: 30-day Kaplan-Meier survival curve of patients by anticoagulation status

Declarations of competing interest: Will Eardley is the Surgical lead of the National Hip Fracture Database of England and Wales. The other authors declare no conflicts of interest.