Thrombosis Research 136 (2015) 962–965

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

The impact of oral anticoagulation on time to surgery in patients hospitalized with hip fracture☆

Thomas Tran [a], Aurélien Delluc [b], Carine de Wit [c], William Petrcich [c], Grégoire Le Gal [a,b,c], Marc Carrier [a,c,*]

[a] Department of Medicine, University of Ottawa at The Ottawa Hospital, 501 Smyth Road, Box 201A, Ottawa, Ontario K1H 8L6, Canada
[b] Département de Médecine Interne, Brest University Hospital, EA3878, bd Tanguy Prigent, 29609 Brest Cedex Brest, France
[c] The Ottawa Hospital Research Institute, 725 Parkdale Avenue, Ottawa, Ontario K1Y 4E9, Canada

ARTICLE INFO

Article history:
Received 10 July 2015
Accepted 22 September 2015
Available online 25 September 2015

Keywords:
Anticoagulants
Arthroplasty
Hip fractures
Surgery
Warfarin

ABSTRACT

Introduction: Current clinical guidelines recommend expedited repair of hip fracture to reduce morbidity and mortality. A significant number of hip fracture patients have concomitant cardiovascular disease requiring anticoagulation. Vitamin K antagonists (VKAs), which have been traditionally used, might be associated with an increased time to surgery (TTS) and it remains unknown what effect direct oral anticoagulants (DOACs) have on this metric. Our objective is to determine how anticoagulation with a VKA or DOAC affects TTS.
Materials and methods: This is a case control study comparing TTS in consecutively admitted hip fracture patients receiving either a DOAC or VKA with age- and gender-matched controls between January 1, 2010 and March 24, 2014. The primary end point is TTS, which is defined as the time elapsed from admission to surgery. Secondary end points include the rate of stroke, death, bleeding and VTE during admission.
Results: Of 2258 patients, 233 were on a VKA while 27 were on a DOAC. Median TTS seems to be longer in patients receiving a DOAC or a VKA when compared to controls. (40 h vs. 26.2 h). The DOAC group tended to have longer median TTS when compared to the VKA groups (66.9 h vs. 39.4 h) There was no difference in the rate of stroke, death, bleeding and VTE during admission.
Conclusions: Patients on anticoagulation prior to admission for hip fracture experienced longer delays in surgery when compared to patients not receiving anticoagulation. Patients on a DOAC experienced the longest surgical delay.

1. Introduction

Hip fracture is a major public health problem with an estimated incidence in the United States of 957.3 per 100,000 (95% confidence intervals (CI): 921.7 to 992.9) for women and 414.4 per 100,000 (95% CI: 401.6 to 427.3) in men [1] and a case fatality rate greater than 30% at one year [2].

Current guidelines recommend repair within 48 h in order to reduce mortality, morbidity and length of hospital stay [3–5]. However, patients with hip fracture frequently have cardiovascular conditions necessitating anticoagulation, which may increase the time to surgery (TTS).

Vitamin K antagonists (VKAs) are rapidly reversible with vitamin K in combination with frozen plasma or prothrombin complex concentrates (PCC), and thus should not significantly increase length of TTS. By contrast, direct oral anticoagulants (DOACs), an increasingly popular treatment option in non-valvular atrial fibrillation and venous thromboembolism (VTE), do not currently have a specific antidote. To safely undergo surgery, it is suggested to postpone repair and await clearance of the drug [6].

Therefore, the aim of this study is to determine whether the TTS for hip fracture is different in patients receiving DOACs compared with those receiving VKAs or no anticoagulants. Secondary outcomes include death, VTE, bleeding, and stroke during admission.

2. Methods

We conducted a case–control study among all hip fracture patients admitted to The Ottawa Hospital between January 1, 2010 and March 24, 2014 for surgical repair. Cases were defined as patients on oral anticoagulation (VKA or DOAC) at the time of admission to hospital. For each case, an age- and gender-matched control was selected from the same cohort of patients. Exclusion criteria included: (i) pre-existing

☆ An abstract of this presentation was presented at the XXV Congress of the International Society on Thrombosis and Haemostasis (ISTH) in Toronto, Canada on June 24, 2015.

* Corresponding author at: Ottawa Hospital Research Institute, University of Ottawa, The Ottawa Hospital, General Campus, 501 Smyth Road, Box 201A, Ottawa, Ontario, Canada.
E-mail addresses: ttran@toh.on.ca (T. Tran), aurelien.delluc@chu-brest.fr (A. Delluc), cdewit@toh.on.ca (C. de Wit), wpetrcich@ohri.ca (W. Petrcich), glegal@toh.on.ca (G. Le Gal), mcarrier@toh.on.ca (M. Carrier).

http://dx.doi.org/10.1016/j.thromres.2015.09.017
0049-3848/

Table 1
Baseline characteristics of patients.

Characteristic	VKA (N = 233)	DOAC (N = 27)	No anticoagulation (N = 260)
Median age — years (range)	86 (44.0–102.0)	86 (61.0–97.0)	86.0 (44.0–99.0)
Gender — N (%)			
Female sex	147 (63.0)	17 (63.0)	160 (61.5)
Male sex	86 (37.0)	10 (37.0)	100 (38.5)
Surgery type			
Arthroplasty — N (%)	106 (45.5)	11 (40.7)	109 (41.9)
Subtrochanteric repair — N (%)	125 (53.6)	16 (59.3)	150 (57.7)
Both — N (%)	2 (0.9)	0 (0.0)	1 (0.4)
Admission Hgb g/L (SD)	122.8 (17.0)	122.0 (20.1)	123.8 (16.6)
Admission Plt × 10^9/L (SD)	216.3 (84.4)	200.4 (54.1)	226.9 (74.7)
Creatinine μmol/L (SD)	133.0 (128.3)	98.5 (52.5)	94.4 (66.7)
Indication for anticoagulation*			
Atrial fibrillation — N (%)	187 (81.3)	25 (92.6)	0 (0.0)
VTE — N (%)	28 (12.2)	1 (3.7)	0 (0.0)
Mechanical valve — N (%)	10 (4.4)	1(3.7)	0 (0.0)
Other	5 (2.2)	0 (0.0)	0 (0.0)
Median CHADS2 score —	3	3	–
score (range)	(0–6)	(0–6)	–
Cancer			
Active — N (%)	28 (12.0)	3 (11.1)	30 (11.5)
History — N (%)	33 (14.2)	2 (7.4)	38 (14.6)
EBL mL (SD)	317.4 (214.0)	295.5 (244.9)	300.9 (161.4)
PCC — N (%)	73 (31.3)	0 (0.0)	0 (0.0)
Transfusion — N (%)	104 (44.6)	10 (37.0)	102 (39.3)

Abbreviations: VKA, vitamin K antagonist; DOAC, direct oral anticoagulant; Hgb, hemoglobin; SD, standard deviation; Plt, platelets; EBL, estimated blood loss; PCC, prothrombin concentrate complex.
* In three cases, an indication was not found.

need for regular blood transfusions; (ii) non-surgical candidates or those who ultimately did not have surgery; (iii) patients for whom hip fracture was not the primary admitting diagnosis; (iv) patients prescribed anticoagulation but who were not taking them at the time of admission, or (v) patients requiring other surgery in addition to hip repair. Research Ethics Board approval was obtained.

The following variables were extracted and analyzed: (i) patient demographics; (ii) laboratory values; (iii) estimated intraoperative blood loss (EBL) as reported in the anesthesia record; (iv) blood transfusion requirements; (v) use of PCC; (vi) bleeding events (as defined as per the ISTH criteria); (vii) occurrence of pulmonary embolism (PE) or deep vein thrombosis (DVT) during admission; (viii) type of surgical repair (arthroplasty vs. subtrochanteric repair vs. both); (ix) stroke during admission; (x) indication for anticoagulation; (xi) CHADS2 score; (xii) active or past cancer history; (xiii) death during admission; (xiv) date and time of admission; and (xv) date and time of surgical repair according to the anesthesia record.

The primary outcome was the TTS as measured by the time elapsed between when the admission order was written and the start time of surgical repair. The secondary outcomes were the rates of major bleeding events (as per ISTH definition), strokes, VTEs, and deaths during admission [7]. Venous thromboembolism was defined as proximal lower limb (popliteal vein or more proximal) DVT on ultrasonography or pulmonary embolism on computed tomographic pulmonary angiography or ventilation perfusion scan.

Baseline summary statistics are reported as mean and standard deviation (SD) for continuous variables with the exception of age and CHADS2 score, which are reported as median and range. Categorical variable are reported as number and percentages (%). The comparison of median time to surgery was made by Wilcoxon two sample testing. The TTS was analyzed using Kaplan–Meier curves and differences between groups tested using the log-rank test. The Chi-squared and Fisher exact test were used for comparison of qualitative variables as appropriate. Analyses were performed using SAS version 9.3.

3. Results

Over the study period, 2258 patients were admitted for hip fracture. A total of 278 (12.3%) of these patients were taking anticoagulation at the time of admission. Eighteen patients were excluded (surgery not performed (n = 11). The remaining 260 patients were included as cases, 233 were on VKAs while 27 were on DOACs (dabigatran (n = 22), rivaroxaban (n = 4), and apixaban (n = 1)). Two hundred sixty non-anticoagulated age- and gender-matched controls were sampled from the cohort. Baseline characteristics of the patients are depicted in Table 1. There was no difference between the three groups with respect to age, gender distribution, type of hip repair, admission hemoglobin or platelet count. A large majority of patients were anticoagulated for atrial fibrillation (92.6% of DOACs and 81.3% of VKA) (Table 1).

Wilcoxon two sample testing demonstrated that median TTS were longer in patients on DOAC or VKA (40.1 h; IQR: 28.6 to 50.3) when

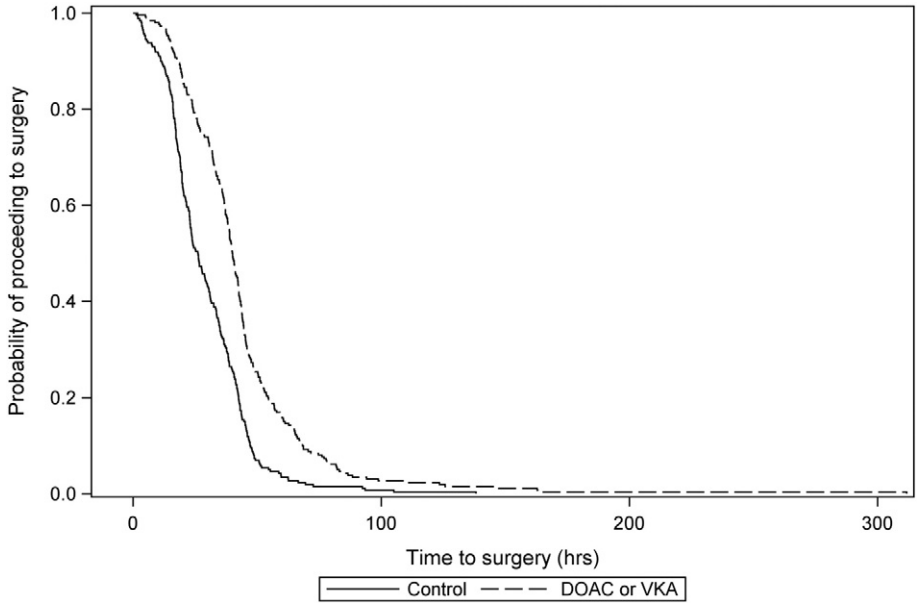

Fig. 1. Kaplan–Meier curves of the probability of proceeding to surgery, according to anticoagulation status. VKA and DOAC vs. Control Log Rank p < 0.001.