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Jørgensen, Christoffer Calov; Kehlet, Henrik; Kjærsgaard-Andersen, Per

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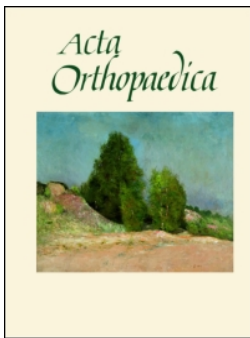
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# Thromboembolic and major bleeding events in relation to perioperative bridging of vitamin K antagonists in 649 fast-track total hip and knee arthroplasties

Christoffer C JØRGENSEN<sup>1,2</sup> and Henrik KEHLET<sup>1,2</sup> on behalf of the Lundbeck Foundation Center for Fast-Track Hip and Knee Replacement Collaborative Group<sup>3</sup>

<sup>1</sup> Section for Surgical Pathophysiology and <sup>2</sup> the Lundbeck Foundation Center for Fast-track Hip and Knee Replacement, Rigshospitalet, Copenhagen University, Copenhagen, Denmark.

Correspondence: christoffer.calov.joergensen@regionh.dk

<sup>3</sup> Members of the Lundbeck Foundation Center for Fast-track Hip and Knee Collaborative Group:

Kjeld Søballe, Department of Orthopedics, Aarhus University Hospital, Aarhus; Torben B Hansen, Department of Orthopedics, Regional Hospital Holstebro and University of Aarhus, Holstebro; Henrik Husted, Department of Orthopedics, Hvidovre Hospital, Hvidovre; Mogens B Laursen, Northern Orthopaedic Division, Aalborg University Hospital, Aalborg; Lars T Hansen, Department of Orthopedics, Sydvestjysk Hospital Esbjerg/Grindsted, Grindsted; Per Kjærsgaard-Andersen, Department of Orthopedics, Vejle Hospital, Vejle; Soren Solgaard, Department of Orthopedics, Gentofte University Hospital, Copenhagen; Lars-Peter Jørn, Department of Orthopedics, Viborg Hospital, Viborg, Denmark.

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**Background** — The benefit of preoperative bridging in surgical patients with continuous anticoagulant therapy is debatable, and drawing of meaningful conclusions may have been limited by mixed procedures with different thromboembolic and bleeding risks in most published studies.

**Patients and methods** — This was an observational cohort treatment study in consecutive primary unilateral total hip and knee arthroplasty patients between January 2010 and November 2013 in 8 Danish fast-track departments. Data were collected prospectively on preoperative comorbidity and anticoagulants in patients with preoperative vitamin K antagonist (VKA) treatment. We performed 30-day follow-up on in-hospital complications and re-admissions through the Danish National Patient Registry and patient records.

**Results** — Of 13,375 procedures, 649 (4.7%) were in VKA patients with a mean age of 73 (SD 9) years and a median length of stay of 3 days (IQR: 2–4). Preoperative bridging was used in 430 (67%), while 215 (33%) were paused. Of 4 arterial thromboembolic events (ATEs) (0.6%), 2 were in paused patients and 2 were in bridged patients ( $p = 0.6$ ). Of 3 venous thromboembolic events (VTEs) (0.5%), 2 were in paused patients and 1 was in a bridged patient ( $p = 0.3$ ). Of 8 major bleedings (MBs) (1.2%), 1 was in a paused patient and 7 were in bridged patients ( $p = 0.3$ ), 5 of whom received therapeutic bridging. Similar results were found in a propensity-matched cohort.

**Interpretation** — In contrast to recent studies in mixed surgical procedures, no statistically significant differences in ATE, VTE, or MB were found between preoperative bridging and pausation of VKA patients. However, the higher number of thromboembolic

events in paused patients and the higher number of major bleedings in bridged patients warrant more extensive investigation. ■

Perioperative management of patients with preoperative vitamin K antagonists (VKAs) is a challenge in elective surgery. Guidelines have been drawn up to help balance the risk of arterial thromboembolic events (ATEs) such as ischemic stroke, transient ischemic attack (TIA), and peripheral arterial embolism with the risk of procedure-related bleeding, in order to identify which patients may benefit from preoperative heparin bridging (Douketis et al. 2012, Kristensen et al. 2014). Current recommendations for perioperative management of anticoagulants include individual risk assessment by clinicians specializing in periprocedural antithrombotic treatment, the surgeon, and the anesthetist (Douketis et al. 2012, Kristensen et al. 2014). However, the level of evidence is generally low (Douketis et al. 2012) and the benefit of preoperative bridging with low-molecular-weight heparin (LWMH) remains debatable (Douketis 2012, Spyropoulos 2012). The risk of ATE and bleeding depends on the surgical procedure, the indication for anticoagulant treatment, and patient-related risk factors. In patients with atrial fibrillation, patient-related risk factors are incorporated into risk scores such as the CHADS2 (Gage et al. 2001) or more recently the CHA2DS2-VASc (Lip et al. 2010), which may aid clinical decision making (Douketis et al. 2012, Kristensen et al. 2014). Procedure-related risk is more problematic, as defini-

tions of procedures with a high risk of major or critical bleeding differ (Douketis et al. 2012, Daniels 2015).

Furthermore, most published studies, including several recent large randomized and observational trials (Clark et al. 2015, Douketis et al. 2015a, b), have been in selected patients with limited information on perioperative care, and have involved mixed surgical procedures with substantial variation in postoperative complication rates and risk of bleeding (Siegal et al. 2012). For example, 2 studies involving almost 3,700 patients included only about 9% major surgical procedures (Clark et al. 2015, Douketis et al. 2015b). Total hip (THA) and knee arthroplasty (TKA) are often considered to be “high-risk” regarding venous thromboembolic events (VTEs) (Falck-Ytter et al. 2012) and bleeding (Douketis et al. 2012, Douketis et al. 2015b). They are common procedures, with a high number of elderly patients having multiple comorbidities, including conditions requiring VKA treatment. Over the last 2 decades, the development of enhanced recovery protocols or “fast-track” surgery, have reduced postoperative morbidity and hospitalization after THA and TKA (Kehlet 2013). In this context, the incidence of both ATE and VTE may be reduced compared to conventional perioperative care (Husted et al. 2010a, Jorgensen et al. 2013, Khan et al. 2014, Jorgensen and Kehlet 2016). However, the incidence of ATE and major bleeding (MB) in patients with preoperative VKA treatment has not been specifically evaluated in fast-track THA and TKA, and no studies on the potential benefits and harms of preoperative heparin bridging have been performed in a standardized fast-track setting.

We therefore wanted to investigate the occurrence of ATE, VTE, and MB in patients with preoperative VKA treatment with and without preoperative bridging.

## Patients and methods

We initially included all primary unilateral elective THAs and TKAs performed in 8 participating departments between January 1, 2010 and November 1, 2013. Information on preoperative patient characteristics (including use of any type of anticoagulant therapy, use of walking aids, and pharmacologically treated heart disease) was obtained through a patient-reported questionnaire, which has been described in detail elsewhere (Jorgensen and Kehlet 2013). Data on the specific type of anticoagulant therapy was acquired from the Danish National Database on Reimbursed Prescriptions (DNDRP). The DNDRP registers all prescriptions qualifying for reimbursement dispensed at Danish pharmacies, including medications distributed through nursing homes (Johannesdottir et al. 2012). During the study period, dabigatran, rivaroxaban, and apixaban qualified for reimbursement in > 99.5% of all dispensed prescriptions while adenosine diphosphate (ADP) receptor inhibitors qualified in 97.4% of cases and dipyridamole in 99.9% of cases (Danish statistics: [www.medstat.dk](http://www.medstat.dk)).

Acetylsalicylic acid (ASA) qualified for reimbursement in only 87.5% of dispensed prescriptions, and consequently 536 patents (3.9%) who had no prescriptions on anticoagulants but who reported using anticoagulants in the preoperative questionnaire were considered to have used ASA.

In patients with confirmed VKA, we registered the following data using the medical records: indication for VKA, date and value of INR (international normalized ratio), and preoperative management (preoperative bridging/pause). The CHA2DS2-VASc was used for thromboembolic risk stratification of patients with atrial fibrillation, and was calculated using the patients’ preoperative questionnaires and medical records for information on diabetes, hypertension, previous stroke/TIA, heart failure, and vascular disease.

Information on index admission and 30-day follow-up was acquired through the DNPR. DNPR records all admissions to Danish hospitals, allowing a follow-up of > 99% (Andersen et al. 1999). Re-admissions were defined as requiring at least 1 night in hospital and being (potentially) related to surgery, as previously described (Jorgensen and Kehlet 2013). Any procedure requiring > 4 nights in hospital and all admissions after surgery were evaluated regarding morbidity using discharge papers and any case of suspected ATE (ischemic stroke, TIA, and peripheral embolism but excluding myocardial infarction), VTE (deep venous thrombosis (DVT) or pulmonary embolism (PE)), or major bleeding (MB) was followed by review of the entire medical records and other available material (autopsy reports, computed tomography scans, ultrasound, etc.). ATE, VTE, and MB were defined according to ISTH criteria (Schulman et al. 2010), and follow-up was done 30 days postoperatively as recommended internationally (Spyropoulos et al. 2012).

All the participating departments used similar fast-track protocols, including spinal anesthesia, multimodal opioid sparing analgesia, early mobilization, and discharge to own home (Husted et al. 2010b). In 6 of the participating departments, preoperative bridging of high-risk VKA patients was initiated 3–4 days before surgery with therapeutic doses of LMWH. Doses were reduced on the day before surgery, with the last dose being given 12–24 hours preoperatively. VKA was resumed in the evening of surgery or on the day after, depending on adequate hemostasis, and with postoperative bridging using prophylactic doses on the first postoperative day followed by therapeutic doses until INR > 2.0. Patients who did not receive preoperative bridging were bridged postoperatively with prophylactic doses until INR > 2.0.

2 departments followed the same routines but used only prophylactic doses in all patients. (For details of the perioperative regimens, see Supplementary data). Any patient with ASA or ADP antagonist treatment was paused 5–7 days preoperatively.

## Statistics

No pre-study power calculation was conducted, as all primary elective unilateral procedures available in the LCDB

were included. Distribution of data was analyzed using visual inspection of histograms and q-q plots. Mean and standard deviation (SD) are reported for parametric data and median with interquartile range (IQR) is given for non-parametric data. Comparisons of means for continuous parametric data and medians for non-parametric data were done using Student's t-test for independent samples and the Mann-Whitney U-test, respectively. Proportions were compared using Fisher's exact test. Proportions are reported as percentage with 95% confidence interval (CI). Propensity score (PS) was calculated using a logistic regression model including characteristics previously related to postoperative outcomes or thromboembolic/bleeding risk: age; gender; joint of surgery; use of walking aids; BMI; smoking; alcohol use > 24 g/day; living with other/alone/in institution; anemia; diabetes; treatment for cardiac, pulmonary or psychiatric disease; previous cerebral stroke; previous VTE; hypertension; and hypercholesterolemia. PS matching was done using a greedy matching algorithm with a caliper of 0.2 and discarding patients with a PS outside the area of common support. Covariance balance was assessed using standardized differences (STDs) (Austin 2009) with an STD of > 0.2 chosen to indicate major imbalance. A weighted analysis was done using the Mantel-Haenszel statistic, and common odds ratio (OR) estimate was used for the PS-matched analysis. Statistical analysis was performed using SPSS version 22 with a PS-matching add-on (Thoemmes 2012; <http://www.vassarstats.net/propl.html>).

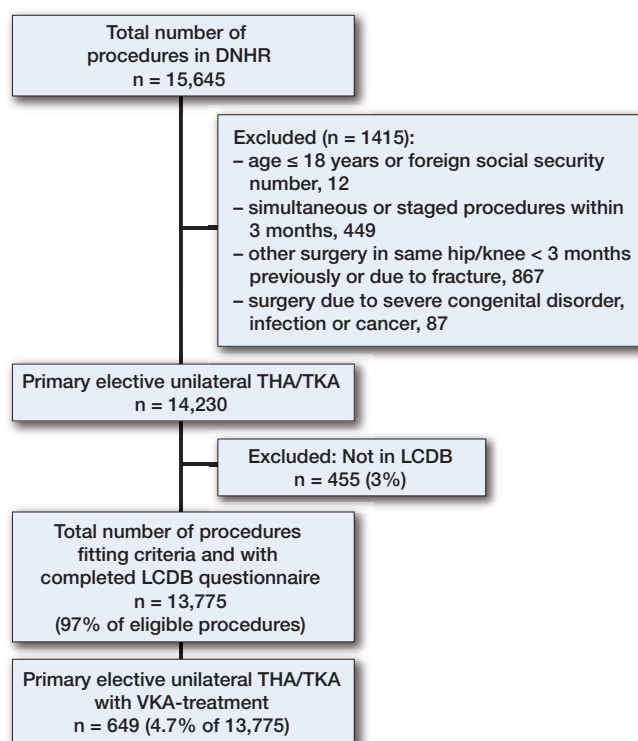
### Ethics and registration

No approval from the regional ethics committee was required, as this was a non-interventional study. Permission to review and store patient records without obtaining informed consent was acquired from the Danish Data Protection Agency (entry no. 30-0623) and the Danish National Board of Health (entry no. 3-3013-56/1/HKR).

The study was based on the Lundbeck Foundation Center database (LCDB), which is a prospective database of preoperative patient characteristics in patients undergoing elective THA or TKA in Danish orthopedic departments that participate in the Lundbeck Foundation Center for Fast-track Hip and Knee Replacement Collaboration. It is registered at ClinicalTrials.gov as an ongoing study registry (identifier NCT01515670).

### Results

The initial cohort consisted of 13,775 procedures (7,222 THAs and 6,553 TKAs) with a median length of stay (LOS) of 2 days (IQR: 2–3). The mean age of patients was 68 (SD 11) years and 58% were women. After evaluation of discharge records followed by evaluation of the complete medical records, 27 ATEs (0.2%, CI: 0.1–0.3), 61 VTEs (0.5%, CI: 0.4–0.6), and 87 MBs (0.6%, CI: 0.5–0.8) were found within 30 days after surgery.



Flow chart of the study population. DNHR: the Danish National Health Registry; THA: total hip arthroplasty; TKA: total knee arthroplasty; LCDB: the Lundbeck Foundation Center for Fast-track Hip and Knee Replacement database; VKA: vitamin K antagonist.

649 patients (4.7%) had preoperative VKA treatment with a median LOS of 3 days (IQR: 2–4) (Figure). The most common indication for VKA was atrial fibrillation (76%), followed by previous VTE (12%) (Table 1), and the mean INR prior to surgery was 1.2 (SD 0.2). Of the VKA patients, 430 (67%) received preoperative bridging and 215 (33%) were paused, while information was unavailable for 4 patients (0.6%). 4 TEs (0.6%, CI: 0.2–1.6), 2 in bridged patients (0.5% CI: 0.1–1.7) and 2 in paused patients (0.9%, CI: 0.3–3.3;  $p = 0.6$ , Fisher's exact test) occurred within 30 days of surgery. Of the ATEs in bridged patients, 1 was in a patient receiving therapeutic doses of LMWH (0.4%, CI: 0.06–2.1) and 1 was in a patient receiving prophylactic doses of LMWH (0.6%, CI: 0.1–3.4;  $p = 1.0$ ). Of 3 VTEs (0.5%, CI: 0.2–1.4), 2 (0.9%, CI: 0.3–3.3) were in paused patients and 1 (0.2%, CI: 0.04–1.3) was in a bridged patient ( $p = 0.3$ ) (Table 2). The rates of VTEs were similar regardless of whether there were therapeutic doses of LMWH (0.4%, CI: 0.06–2.1) or prophylactic doses of LMWH (0.0%, CI: 0.0–2.3;  $p = 1.0$ ). Finally, we found 8 MBs (1.2%, CI: 0.6–2.4), of which 1 (0.5%, CI: 0.08–2.6) was in a paused patient and 7 (1.6%, CI: 0.8–3.3;  $p = 0.3$ ) were in bridged patients. 6 of the 7 MBs in bridged patients occurred in those receiving therapeutic doses of LMWH (2.2%, CI: 1.0–4.8) and 1 was in a patient receiving prophylactic doses of LMWH (0.6%, CI: 0.1–3.4;  $p = 0.3$ ) (Table 2).

Table 1. Preoperative characteristics of VKA patients

Characteristic (%)	All VKA patients n = 649	PS-matched bridged VKA patients n = 288	PS-matched paused VKA patients n = 182	STD
Age, mean (SD)	73 (8.6)	73.9 (8.2)	73.9 (7.7)	0
Sex				
Male	357 (55.0)	158 (54.9)	105 (57.7)	0.056
Female	292 (45.0)	130 (45.1)	77 (42.3)	
Joint surgery				
THA	338 (52.1)	149 (51.6)	98 (53.8)	0.044
TKA	311 (47.9)	139 (48.4)	84 (46.2)	
Living				
with spouse/relatives	406 (62.6)	179 (62.1)	115 (63.2)	0.023
alone	239 (36.8)	109 (37.9)	67 (36.8)	0.023
at institution	3 (0.5)	0 (0.0)	0 (0.0)	0
missing	1 (0.2)	–	–	–
Use of walking aids	231 (35.6)	105 (36.5)	68 (37.4)	0.019
missing	18 (2.8)	–	–	–
BMI, mean (SD)	28.7 (5.1)	28.6 (5.2)	26.8 (5.2)	0.019
missing	2 (0.3)	–	–	–
Smoker	64 (9.9)	26 (9.1)	18 (9.9)	0.027
missing	7 (1.1)	–	–	–
Alcohol use > 24 g/day	61 (9.4)	29 (10.2)	22 (12.1)	0.060
missing	6 (0.9)	–	–	–
Antihypertensive treatment	533 (82.1)	247 (85.7)	157 (86.3)	0.017
missing	1 (0.2)	–	–	–
Anticholesterol treatment	416 (64.1)	186 (64.6)	115 (63.2)	0.029
missing	10 (1.5)	–	–	–
Diabetes mellitus				
insulin-dependent	26 (4.0)	6 (1.9)	3 (1.6)	0.023
non-insulin-dependent	81 (12.5)	36 (12.6)	24 (13.2)	0.018
missing	1 (0.2)	–	–	–
Preop. anemia <sup>a</sup>	119 (18.3)	48 (16.8)	33 (18.1)	0.034
missing	7 (1.1)	–	–	–
Pharmacologically treated:				
Cardiac disease	559 (86.1)	260 (90.1)	167 (91.8)	0.059
missing	0 (0.0)	–	–	–
Pulmonary disease	58 (8.9)	25 (8.8)	18 (9.9)	0.038
missing	8 (1.2)	–	–	–
Psychiatric disease	108 (16.6)	40 (13.7)	25 (13.7)	0
missing	4 (0.6)	–	–	–
Previous stroke/TIA	111 (17.1)	40 (13.7)	26 (14.3)	0.017
missing	0 (0.0)	–	–	–
Previous VTE	161 (24.8)	57 (19.8)	38 (20.9)	0.027
missing	0 (0.0)	–	–	–
ADP2 inhibitors	6 (0.9)	4 (1.4)	0 (0.0)	–
Dipyridimole	3 (0.5)	1 (0.3)	0 (0.0)	–
Acetylsalicylic acid	114 (17.6)	40 (13.7)	22 (12.1)	–
Bridging				
therapeutic	268 (41.3)	172 (59.9)	–	–
prophylactic	162 (25.0)	116 (40.1)	–	–
pausation	215 (33.1)	–	182 (100.0)	–
missing	4 (0.6)	–	–	–
Indication for VKA treatment				
atrial fibrillation	495 (76.3)	254 (88.2)	163 (89.6)	–
previous VTE	84 (12.9)	24 (8.2)	13 (7.1)	–
heart valve	44 (6.8)	3 (1.1)	2 (1.1)	–
genetic disposition	19 (2.9)	6 (2.2)	3 (1.6)	–
other causes	7 (1.1)	0 (0.0)	0 (0.0)	–
CHA2DS2-VASc, mean (SD) <sup>b</sup>	3.7 (1.6)	3.7 (1.5)	3.6 (1.7)	–

PS: propensity score; a standardized difference (STD) of > 0.2 was chosen as being indicative of imbalance; THA: total hip arthroplasty; TKA: total knee arthroplasty; BMI: body mass index; TIA: transient ischemic attack.

<sup>a</sup> women : 12 g/dL; men: 13 g/dL.

<sup>b</sup> Patients with atrial fibrillation only.

PS matching was possible in 288 bridged and in 182 paused VKA patients. There were 2 ATEs in both bridged (0.7%, CI: 0.2–2.5) and paused patients (1.0%, CI: 0.3–3.6; OR = 0.8, CI: 0.1–4.6; p = 0.8), and only 1 VTE in a bridged patient (0.4%, CI: 0.06–1.9; OR not available). Finally, there were 3 MBs (1.0%, CI: 0.4–3.0) in the 288 bridged patients and 1 (0.5%, CI: 0.09–2.8; OR = 0.4, CI: 0.1–3.1; p = 0.4) in the 198 patients who were paused.

## Discussion

This procedure-specific study of VKA-treated patients undergoing fast-track THA or TKA raises several questions regarding the benefits and consequences of preoperative bridging compared to pausation. Thus, although there were no statistically significant differences in ATEs, VTEs, and MBs between the 2 groups, the incidence of MBs was 3 times higher in bridged patients than in paused patients, and even higher when the comparison was done with therapeutically bridged patients. On the other hand, although the occurrence of ATEs and VTEs was rare, 2 of 4 ATEs and 1 of 3 VTEs were fatal, which highlights the importance of preventing these critical events.

The lack of any difference in ATEs between bridged and paused VKA patients has been found in previous studies on mixed surgical procedures, with few major orthopedic procedures and limited information on perioperative care (Clark et al. 2015, Douketis et al. 2015a). It has been argued that preoperative bridging reduces the risk of ATE to the same levels as in those patients who only need pausation (Siegal et al. 2012, Spyropoulos 2012), but a recent randomized study and a metaanalysis found no benefit of preoperative bridging in patients with atrial fibrillation (Douketis et al. 2015b, Ayoub et al. 2016). We found more ATEs in the paused patients, although this was not statistically significant. That there were numerically more ATEs in the paused patients could possibly be due to a large fraction of paused patients having similar risk profiles to those who were bridged. However, it must be kept in mind that international guidelines on perioperative risk evaluation are conflicting. Thus, if we had adhered to the ESC/ESA (Kristensen et al. 2014) instead of the American College of Chest Physicians (ACCP) recommendations

Table 2. Types and timing of ATE, VTE, and major bleeding

Events	Preoperative pause n = 215	Any bridging n = 430	Prophylactic bridging n = 162	Therapeutic bridging n = 268
Arterial thromboembolic event	2 (0.9%)	2 (0.5%)	1 (0.6%)	1 (0.4%)
Arterial embolism	1 (day 15, fatal)			
Stroke	1 (day 1, fatal)	2 (day 2, 2)	1 (day 2)	1 (day 2)
Venous thromboembolic event	2 (0.9%)	1 (0.2%)	0 (0.0%)	1 (0.4%)
Deep venous thrombosis;	2 (days 11,23)			
Pulmonary embolism		1 (day 7, fatal)		1 (day 7, fatal)
Major bleeding	1 (0.5%)	7 (1.6%)	1 (0.6%)	6 (2.2%)
Cerebral hemorrhage		1 (day 3, fatal)	1 (day 3, fatal)	
Retroperitoneal bleeding		1 (day 10)		1 (day 10)
Hematoma with transfusion/ surgical intervention	1 (day 22)	5 (days 1, 7, 9, 10, 20)		5 (days 1, 7, 9, 10, 20)

(Douketis et al. 2012), 1 of the paused patients who suffered from an ATE should have received preoperative bridging. Furthermore, the ESC/ESA recommendations use CHA<sub>2</sub>DS<sub>2</sub>-VASc and the ACCP recommendations use CHA<sub>2</sub>DS for patients with atrial fibrillation, potentially increasing the number of patients who qualify for bridging when adhering to ESC/ESA recommendations. This reflects the increased complexity of perioperative VKA treatment, as opposed to the new direct oral anticoagulants (DOACs), where the main issue is prolonged half-life in patients with reduced renal function (Douketis et al. 2012). However, although the use of DOACs is on the increase, it seems likely that perioperative VKA treatment will remain a clinical problem for a considerable time.

We found similar VTE rates in bridged and paused VKA patients. This is in accordance with the results of a previous retrospective study of 1,178 patients who mainly received VKA because of recurrent VTE (Clark et al. 2015). However, the study included a wide range of mainly minor procedures, only about 14% of which were orthopedic, and with major differences in baseline risk of VTE between paused and bridged patients.

Increased bleeding risk in bridged VKA patients is well documented (Siegal et al. 2012, Douketis et al. 2015a, b, Clark et al. 2015, Ayoub et al. 2016, Breen et al. 2016), and it has been argued that the risk of postoperative bleeding associated with bridging may be understated (Douketis 2012). Furthermore, the increased bleeding risk may be related to the use of therapeutic doses of LMWH rather than prophylactic doses (Pengo et al. 2009). In THA and TKA, even “less” severe MBs may lead to serious complications due to a subsequent increased risk of reoperation, immobilization, and prosthetic infection (McDougall et al. 2013, Leijtens et al. 2014). In the present study, MBs occurred in less than 2% of bridged patients, despite the fact that THA and TKA may be considered to be high-risk procedures (Douketis et al. 2012). This contrasts with 2 other small cohort studies in THA and TKA, which had major bleeding rates of 92% and 33% (Leijtens et al. 2014, Haighton et al.

2015). The difference may be due to different definitions of bleeding and methods of data collection, and allowances must be made for subjectivity, even within the ISTH recommendations. Although MBs were rare in our study, we did find a considerable numerical increase in MBs in the bridged patients compared to the paused patients, especially when the comparison was done with bridged patients who received therapeutic doses. Consequently, the lack of statistical significance may have been due to the limited sample size. Finally, the MBs in our study were highly clinically relevant, as they all resulted in death, surgical interventions, or repeated blood transfusions. In this context, almost one-third of the registered thromboembolic or bleeding events were fatal. This contrasts with most of the recent trials in mixed patients, where ATE-, VTE-, and MB-related mortality has been extremely rare (Dunn et al. 2007, Douketis et al. 2015a, b). Consequently, whether the results of studies in selected mixed patient populations can be uncritically extrapolated to specific major surgical procedures in everyday patients seems questionable.

The most important limitation of the present study was the rarity of events, combined with less than 5% of the initial cohort using VKA. Thus, despite the fact that we initially included almost 14,000 patients, our study remained at risk of being subject to type-II error. This is a common problem in bridging studies, including RCTs (Dunn et al. 2007, Douketis et al. 2015b), and highlights the need for international collaboration to achieve the necessary number of events, especially in procedure-specific studies. Another limitation, potentially influencing the relatively low incidence of MB, may be that we only evaluated the medical records of patients who were noted as having a clinically relevant bleeding episode in their discharge papers. This, as well as a lack of transfusion data, may lead to an underestimation of bleeding episodes, but on the other hand it ensured that the bleedings were considered of clinical importance. With regard to whether the bridged patients received therapeutic or prophylactic doses, we assumed that all patients were treated according to the depart-

mental guidelines, as no-patient level data were available. Furthermore, it may be questioned whether some of the MB episodes were related to other drugs, e.g. NSAIDs, which are common in this population. Finally, as our study was observational, there was a risk of confounding by indication, which is why we performed a secondary analysis on a PS-matched dataset—which showed similar results.

The study had several strengths, including a large well-described consecutive unselected cohort of specific major surgical procedures with similar fast-track protocols, prospective recording of preoperative characteristics supplemented with nationwide data on reimbursed prescriptions (Johannesdotir et al. 2012), and complete 30-day follow-up through the DNPR. Also, all participating departments were large regional or university hospitals that contributed about one-third of all primary THA and TKA procedures in 2012 (The Danish Hip Arthroplasty Registry 2013, The Danish Knee Registry 2015), with the fast-track protocol being considered the standard of care and no selection bias when reporting to the LCDB (Jørgensen and Kehlet 2013). Furthermore, our cohort included patients who received VKA treatment on a wide range of indications, such as heart valves and genetic predisposition for VTE, in contrast to other recent studies—which have focused on patients with atrial fibrillation (Douketis et al. 2015a, b). Thus, our results reflect modern clinical practice in unselected THA and TKA patients. Finally, instead of using diagnostic codes, we reviewed the discharge papers of all patients with a length of stay of > 4 days or 30-day re-admissions, followed by review of the complete medical record in case of recorded thromboembolic or bleeding episodes. This approach may be superior to relying on administrative data or diagnostic codes (Severinsen et al. 2010, van Walraven et al. 2011).

In conclusion, no statistically significant differences in TE, VTE, or MB were found in preoperatively bridged and paused VKA patients after fast-track THA and TKA. However, the higher number of thromboembolic events in paused patients and of MBs in bridged patients warrants further large-scale investigation of indications for and optimal dosing of preoperative bridging with LMWH.

### Supplementary data

Appendices are available on the website of Acta Orthopaedica ([www.actaorthop.org](http://www.actaorthop.org)), identification number 10437.

CJ collected and analyzed data, wrote the initial draft, revised it appropriately, and approved the final submission. HK analyzed data, revised the initial draft, and approved the final submission. All collaborators revised the manuscript critically and approved the final submission.

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