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Thromboprophylaxis only during hospitalisation in fast-track hip and knee arthroplasty, a prospective cohort study

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ABSTRACT

Objectives: International guidelines recommend thrombosis prophylaxis after total hip arthroplasty (THA) and total knee arthroplasty (TKA) for up to 35 days. However, previous studies often have hospital stays (length of stay; LOS) of 8–12 days and not considering early mobilisation, which may reduce incidence of venous thromboembolic events (VTE). We investigated the incidence of any symptomatic thromboembolic events (TEEs) with only in-hospital prophylaxis if LOS ≤5 days after fast-track THA and TKA.

Design: A prospective descriptive multicentre cohort study in fast-track THA and TKA from February 2010 to December 2011, with complete 90-day follow-up through the Danish National Patient Registry and patient files.

Setting: 6 Danish high-volume centres with a similar standardised fast-track setup, including spinal anaesthesia, opioid-sparing analgesia, early mobilisation, functional discharge criteria and discharge to own home.

Participants: 4924 consecutive unselected unilateral primary THA and TKAs in patients ≥18 years with no preoperative use of continuous 'potent' anticoagulative therapy (vitamin K antagonists).

Exposure: Prophylaxis with low-molecular-weight heparin or factor Xa-inhibitors only during hospitalisation when LOS ≤5 days.

Outcomes: Incidence of symptomatic TEE-related, VTE-related and VTE-related mortality ≤90 days postoperatively.

Results: LOS ≤5 days and thromboprophylaxis only during hospitalisation occurred in 4659 procedures (94.6% of total). Median LOS and prophylaxis duration was 2 days (IQR 2–3) with 0.84% (95% CI 0.62% to 1.15%) TEE and 0.41% (0.26% to 0.64%) VTE during 90-day follow-up. VTE consisted of five pulmonary embolisms (0.11% (0.05% to 0.25%)) and 14 deep venous thrombosis (0.30% (0.18% to 0.50%)). There were four (0.09% (0.04% to 0.23%)) surgery-related deaths, of which 1 (0.02% (0.00% to 0.12%)) was due to pulmonary embolism, and 6 (0.13% (0.06% to 0.28%)) deaths of unknown causes after discharge.

Conclusions: The low incidence of TEE and VTE suggests that in-hospital prophylaxis only, is safe in fast-track THA and TKA patients with LOS of ≤5 days. Guidelines on thromboprophylaxis may need reconsideration in fast-track elective surgery.

Trial Registration: ClinicalTrials.gov: NCT01557725

Strengths and limitations of this study

- A prospective multicentre trial in a large cohort of consecutive unselected patients, with a standardised perioperative fast-track setup.
- Complete 90-day follow-up through the Danish National Patient Registry and patient files.
- Registration of thromboembolic event (TEE) was based on review of patient files, any TEE not mentioned in these would not have been registered.

INTRODUCTION

Venous thromboembolic events (VTE) such as deep venous thrombosis (DVT) and pulmonary embolism (PE) are well-documented risks in hospitalised patients.[1] Surgery presents an independent risk factor for such events, due to both the surgical trauma and postoperative immobilisation. Consequently, guidelines for postoperative thromboprophylaxis have been developed in both general and orthopaedic surgery.[2–4] However, the type and duration of prophylaxis following elective surgery is debatable.[5–7] For example, the American College of Chest Physicians (ACCP) recommends either mechanical prophylaxis using intermittent pneumatic compressive devices (IPCD; grade 1C), or pharmacological prophylaxis (grade 1B), for up to 35 days (grade 2B) after total hip (THA) and knee arthroplasty (TKA),[2] whereas the American Academy of Orthopedic Surgeons find the evidence inconclusive and decide the duration of thromboprophylaxis on an individual basis.[8] Much of the evidence regarding the duration of thromboprophylaxis after orthopaedic surgery has originated from large randomised clinical trials (RCTs) in THA and TKA with prophylaxis of 10–35 days,[9–13] and these studies also contribute to guidelines in general surgery.[3] However, the pathophysiological mechanisms of thrombosis have not been addressed in RCTs, which often have long length of stay (LOS) and lack focus on early

mobilisation, despite the fact that early mobilisation per se may reduce the need for thromboprophylaxis.[14]

Fast-track surgery has been developed to improve recovery by using evidence-based care principles with multimodal opioid-sparing analgesia, reduction of the surgical stress-response, optimised fluid treatment, adjustment of the use of drains and catheters and early mobilisation. These efforts have resulted in improved outcome following various procedures such as colonic surgery and gynaecological procedures[15] and major joint arthroplasty.[16] It has been suggested that reassessment of thromboembolic risk in elective surgery is needed due to a few incidences of VTE[5][17]; preliminary data have supported that fast-track THA and TKA may decrease the risk of VTE and thereby the need for prolonged prophylaxis.[6][18] Consequently, we designed a large prospective cohort study in unselected consecutive patients having fast-track THA or TKA, with thromboprophylaxis only during hospitalisation when the LOS was ≤5 days. We hypothesised that there would be no increase in symptomatic thromboembolic events (TEE) and VTE with prophylaxis only during hospitalisation compared with previous data with prophylaxis of 10–35 days.

METHODS

We investigated consecutive unselected primary elective unilateral THA and TKA between 1 February 2010 and 1 December 2011 in patients ≥18 years with a Danish social security number and no prescriptions on 'potent' anticoagulant therapy (ie, vitamin K antagonists, dabigatran, rivaroxaban) ≤6 months preoperatively. Procedures in patients with more than one THA or TKA during the study period were excluded if <45 days between operations.

Five departments participated throughout the study period, with a sixth department pausing between March 2010 and April 2011. All departments had a known mean LOS of about 3–4 days, with a similar fast-track setup including mobilisation on the day of surgery, identical functional discharge criteria and discharge to own home.[19] Patients with the preoperative use of platelet inhibitors (acetylsalicylic acid, clopidogrel, dipyridamole, etc) ceased treatment 3–5 days prior to admission and resumed treatment the day after surgery. All patients completed a preoperative questionnaire on characteristics and comorbidity which was then entered into the Lundbeck Foundation Centre Database (LCDB[20]; see online supplementary appendix 1). Thromboprophylaxis was only given during hospitalisation in patients with LOS of ≤5 days. If the LOS was >5 days, prophylaxis was prescribed by the attending surgeon according to local guidelines. The first dose of prophylaxis was given 6–8 h after surgery and consisted of either rivaroxaban (Xarelto, Bayer Pharma, Berlin, Germany) 10 mg/day, enoxaparin (Klexane, Sanofi-Aventis, Paris, France) 4000 IU/day, dalteparin (Fragmin, Pfizer Health Care, New York, USA) 5000 IU/day or fondaparinux (Arixtra, GlaxoSmithKline, London, UK) 2.5 mg/day. No departments used IPCD. An interim analysis and a random-sample audit on treatment and

data completion were conducted and approved by the steering committee in 2011 (see online supplementary appendix 2).

Preoperative data were cross-referenced with the Danish National Patient Registry (DNPR) regarding LOS and 90-day readmissions (including emergency room contacts, but excluding outpatient visits as clinical practice on treatment of TEE in Denmark includes an initial admission to hospital[21]). LOS was defined as the number of postoperative nights in the hospital (including transferal to other departments) till discharge to the patients' own home. The DNPR registers all hospitalisations (including transferals, diagnoses and surgical procedures) at Danish hospitals, allowing information on the LOS and readmissions regardless of localisation. Reporting is mandatory for receiving reimbursement ensuring completeness of data of about 99.4%.[22][23] To detect TEE during primary admission the complete medical records of patients with diagnosis codes related to TEE according to the International Classification of Diseases 10th revision, all transfers to other wards and the discharge summary of any patients with LOS ≥5 days were investigated. In case of readmission ≤90 days, discharge files and/or patient files were investigated with regard to relation to surgery.[20] The criteria for TEE were predefined as: DVT confirmed by ultrasound; PE confirmed by spiral CT; ventilation-perfusion scintigraphy or pathological removal of embolus and myocardial infarction (MI) with rise in biomarkers and ischaemic symptoms; diagnostic ECG changes; and primary coronary intervention or a coronary bypass graft. An ischaemic stroke was defined as a neurological symptom >24 h and a positive CT scan, and a transient ischaemic attack was defined as a neurological symptom lasting less than 24 h and no new changes on CT scan. Mortality was obtained through the Central Office of Civil Registration using unique Danish social security numbers. The cause of death was obtained from the patient files/autopsies. In case of death outside the hospital with no autopsy, the patient's general practitioner was contacted regarding the cause of death. Adjudication of discharge summaries and patient files, apart from reasons for LOS ≥5 days and death during admission, was blinded with regard to the duration of thrombosis prophylaxis. Adjudication was carried out by the first author (CCJ), and in case of possible TEE, the first author (CCJ) and senior author (HK) adjudicated cases together.

All prescriptions on 'potent' anticoagulant therapy and platelet inhibitors 6 months before and 3 months after surgery were investigated using The Danish National Database of Reimbursed Prescriptions (DNDRP). During the study period all prescriptions on 'potent' anticoagulant treatment received government reimbursements securing 100% completeness of data.[24] Patients without prescriptions on anticoagulative therapy but answering 'yes' in the questionnaire were assumed to use platelet inhibitors. In 21 procedures in patients with LOS ≤5 days we found only postoperative prescriptions on 'potent' anticoagulative therapy. All hospital contacts of these

patients were reviewed and, if insufficient for determining the cause of the prescription, we contacted their general practitioner. In two cases the prescription was due to DVT found during outpatient visits without regular hospital admission, while seven cases were due to perioperative atrial-flutter with treatment initiated ≥22 days after discharge. These were all retained in the study cohort. The remaining 12 cases were due to specific surgical considerations, discharge from other wards or readmission with treatment despite unverified VTE. These were considered protocol violations and included in the unsuccessful early discharge cohort.

Outcomes

The primary outcome was the occurrence of symptomatic TEE (DVT, PE, arterial embolism, MI, ischaemic stroke or TCA) and VTE (DVT or PE) 90 days after THA/TKA in patients with prophylaxis only during admission.

The secondary outcome was the occurrence of the primary outcome in patients with thromboprophylaxis after discharge. Bleeding events were protocolled as a safety endpoint, but were hindered by incomplete registration. A separate analysis on patients not in the LCDB was carried out to identify potential bias.

Statistics and power calculation

A prestudy power analysis using a two-tailed one sample difference from constant test, found that 2838 patients were needed to detect a 1% increase in TEE when assuming a TEE rate of 3%, β: 82 and α: 0.05. Correspondingly, 2076 patients were needed to detect a 1% increase in symptomatic VTE assuming a 90-day baseline risk of 2%.[2]

Data were tested for normality using q–q plots and histograms. Comparisons of continuous data were made using Mann-Whitney U test and t test and for categorical data with χ^2 test or Fisher's exact test, as appropriate. Events (incident cases) are reported as actual numbers and percentages with 95% CI using http://www.vassarstats.net/prop1.html. All other analysis was carried out in SPSS V.20 (IBM Corporation, Armonk, New York, USA).

RESULTS
Total cohort

A total of 4924 procedures in 4718 patients were included. The median LOS was 2 days (IQR 2–3), and readmissions occurred after 400 (8.1%) of all procedures. We found 50 (1.12%) TEE, of which 30 (0.58%) were VTE. Symptomatic in-hospital TEE occurred after 7 (0.14% (0.07% to 0.29%)) procedures, of which 4 (0.08% (0.03% to 0.21%)) were VTE. All-cause mortality was 0.42%, including one fatal PE (0.04%) and six deaths of unknown causes (0.1%; table 2).

Successful early discharge cohort

Early discharge with LOS ≤5 days occurred in 4659 (94.6%) procedures in 4455 patients (figure 1). These patients had a mean age of 66.8 years (SD 10.7) with a

median LOS and prophylaxis duration of 2 days (IQR 2–3; table 1). There were 353 (7.6%) surgery-related readmissions of which 2.9% were due to 'surgical' morbidity (hip displacements, prosthesis infections, knee manipulation, etc) and 4.7% were due to 'medical' morbidity, such as anaemia, cardiac arrhythmia, pneumonia, unverified prosthesis infection and pain.

A total of 39 (0.84%) TEE were found within 90 days, of which 24 (0.52%, 95% CI 0.35% to 0.77%) occurred during the first postoperative month. One patient was readmitted twice due to ischaemic strokes on postoperative days 8 and 46. According to the medical records, the second stroke was cardiac in origin as the patient was known to have an atrial flutter, but treated only with acetylsalicylic acid due to gastrointestinal bleeding. There were 19 (0.41%) symptomatic VTE (figures 2 and 3A), consisting of 5 (0.11%) PEs and 14 (0.30%) DVTs of which 9 were proximal (table 2). Median time to VTE was 21 days (IQR 8–39), with 12 VTE ≤30 days postoperatively (30-day VTE rate 0.26%, 95% CI 0.15% to 0.45%).

There were 13 (0.28%) deaths during follow-up. Of these three (0.06%) were unrelated to surgery (cancer and gastric morbidity >45 days after surgery) and six (0.13%) were of unknown causes outside hospital (postoperative day: 19, 27, 36, 44, 48 and 85). Thus, four (0.09%) deaths were confirmed surgically related (table 2), one due to an autopsy confirmed PE on postoperative day 41 and one due to intracerebral bleeding on day 26. The remaining two deaths were due to paralytic ileus on postoperative day 36 and sepsis on postoperative day 24.

Unsuccessful early discharge cohort: This cohort of 265 (5.4%) procedures in 263 patients (figure 1), was older and had more comorbidity than the early discharge cohort (table 1). The median LOS was 7 days (IQR 6–9) with 47 (17.7%) surgically related readmissions (5.7% 'surgical' and 12% 'medical' morbidity). Of 11 (4.97%) TEE with 7 (2.65%) VTE (table 2), 7 and 4, respectively, occurred during index hospitalisation consequently resulting in LOS >5 days. Of the four (1.51% (95% CI 0.59% to 3.82%)) TEE after discharge, one (0.38% (0.07% to 2.11%)) was an ischaemic stroke and three were VTE (1.13% (0.38% to 3.27%)), with two PEs (0.75% (0.21% to 2.70%)) and one DVT (0.38% (0.07% to 2.11%)). Median time to VTE was 3 days (IQR 2–53; figure 3B). We found three (1.13%) surgically related deaths, one death unrelated to surgery (paralytic ileus on day 70 in a patient refusing treatment) and no VTE-related deaths or deaths of unknown causes (0.00% (0.00% to 1.43%)).

Patients not in LCDB (3.6%)

In these 194 (108 THA/86 TKA) procedures in 191 patients, the mean age was 68.5 years (SD 11.0) and 178 (91.8%) had LOS ≤5 days. In these 178 procedures there was one (0.56% (0.10% to 3.11%)) readmission due to an MI, no VTE and no deaths. No further

Figure 1 Flow chart of the study population. THA, total hip arthroplasty; TKA, total knee arthroplasty.
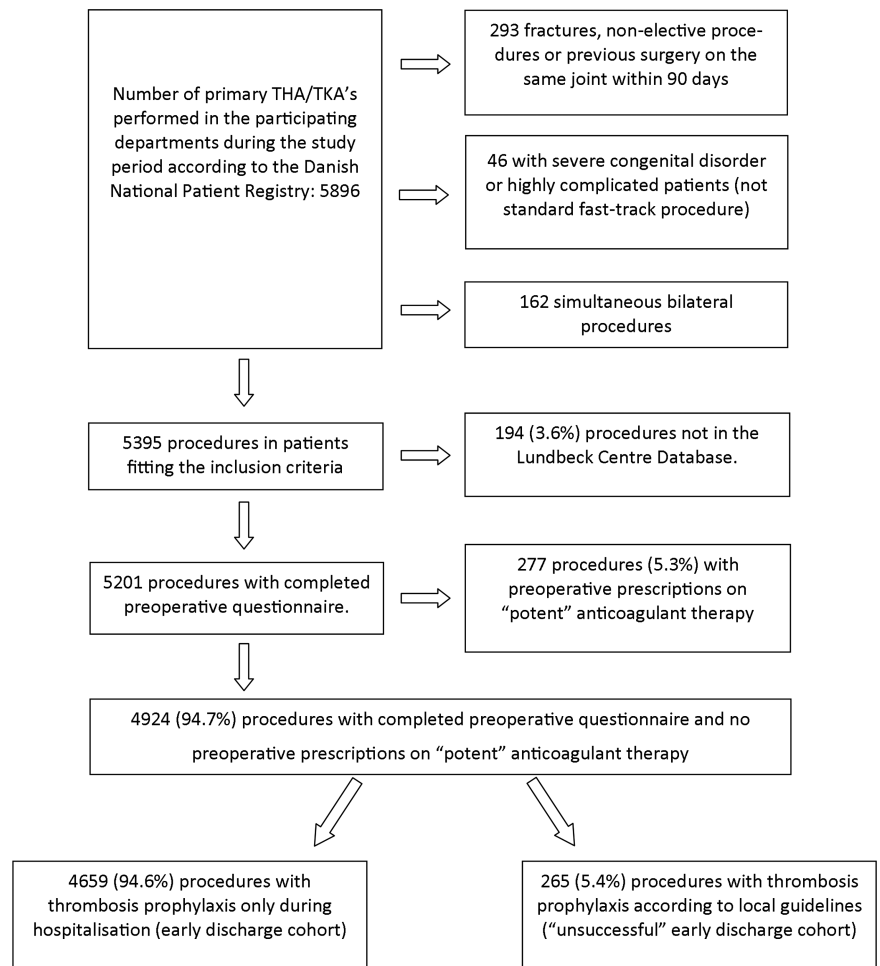
analysis was carried out as no bias was apparent compared to the study population.

DISCUSSION

In this prospective study in fast-track primary THAs and TKAs, we found 90-day postoperative rates of symptomatic TEE and VTE of 0.84% and 0.41%, respectively, in patients with LOS ≤5 days and in-hospital thromboprophylaxis only. The patients receiving prophylaxis only during index hospitalisation (median 2 days) contributed 94.6% of the total number of performed procedures, as 5.4% had LOS >5 days and consequently received longer prophylaxis. The study has several strengths, such as a consecutive unselected population including high-risk patients with various types of comorbidity, a standardised perioperative fast-track setup and complete detailed 90-day follow-up.

We used any TEE as primary endpoint in order not to overlook a potential worsened outcome. Stroke and MI have been included as safety endpoints in most RCTs,[10–12] but are often neglected in reviews and database studies.[25–27] We found no increase in the occurrence of ischaemic stroke as compared with previous studies of in-hospital stroke in THA[28] and strokes ≤30 days in both TKA and THA,[29] despite our follow-up being 90 days and not relying

on diagnostic codes. Neither was there any apparent increase in the occurrence of MI compared with a recent study which found MI in 0.51% of THA and 0.21% of TKA after 6 weeks.[30] The numbers of symptomatic VTE were lower or comparable to the RCTs with prophylaxis of 10–35 days.[10–13] However, LOS in these RCTs was 8–12 days with unspecified discharge locations, whereas LOS after 94.6% of procedures in our study was ≤5 days until discharge to own home. The long LOS in these studies may include partial immobilisation, thereby increasing the risk of VTE and consequently the need for thromboprophylaxis. Correspondingly, a previous small-scale study in 247 TKA found a decreased risk of DVT following mobilisation within 24 h of surgery,[14] and an earlier fast-track single-centre study with prophylaxis only during admission in 1977 THA and TKAs with a mean LOS of about 3.5 days found 0.86% symptomatic VTE within 90 days.[18]

Another main difference between our study and the RCTs is that there was no preoperative selection of patients, as the duration of prophylaxis depended only on discharge within 5 days, regardless of comorbidity. Thus, our results reflect 'everyday patients', whereas the exclusion criteria in the RCTs may have reduced occurrences of TEE.[8 31] The only excluded patients in our study were those using preoperative 'potent' anticoagulant therapy, since they obviously needed continuation

Table 1 Preoperative patient characteristics and prophylaxis duration

Characteristic	Early discharge N: 4659	'Unsuccessful' early discharge N: 265	p Value	Characteristic	Early discharge N: 4659	'Unsuccessful' early discharge N: 265	p Value
Age (SD) (years)	66.8 (10.7)	73.0 (12.1)	<0.001	BMI (SD)	28.4 (5.1)	27.9 (5.7)	0.110
<50	313 (6.7)	11 (4.2)		<18.5	35 (0.8)	5 (1.9)	
50–60	855 (18.4)	28 (10.6)		18.5–24.9	1186 (25.6)	79 (30.4)	
61–65	779 (16.7)	19 (7.2)		25.0–29.9	1865 (40.2)	102 (39.2)	
66–70	916 (19.7)	34 (12.8)		30.0–39.9	1426 (30.7)	63 (26.0)	
71–75	807 (17.3)	47 (17.7)		≥40	126 (2.7)	11 (3.7)	
76–80	585 (12.6)	50 (18.9)		Missing	21 (0.5)	5 (1.9)	
81–86	302 (6.5)	45 (17.0)					
>86	102 (2.2)	31 (11.7)					
Gender			0.002	Joint			0.961
Females	2654 (57.0)	177 (66.8)		THA	2451 (52.6)	139 (52.5)	
Males	2005 (43.0)	88 (33.2)		TKA	2208 (47.4)	126 (47.5)	
Use of compressive stockings			<0.001	Diabetes			0.426
				T1D	14 (0.3)	2 (0.7)	
Yes	250 (5.5)	35 (13.7)		T2D	505 (10.9)	30 (11.5)	
No	4267 (94.5)	220 (86.3)		None	4112 (88.8)	230 (87.8)	
Missing	142 (3.0)	10 (3.8)		Missing	28 (0.6)	3 (1.1)	
Social situation			<0.001	Hypertension			<0.001
Living with others	3117 (66.9)	117 (44.2)		Yes	2291 (49.5)	161 (61.2)	
Living alone	1502 (32.2)	139 (52.5)		No	2335 (50.5)	102 (38.8)	
Nursing home, etc	40 (0.9)	9 (3.4)		Missing	33 (0.7)	2 (0.8)	
Use of walking aid	1078 (23.7)	142 (55.0)	<0.001	Pharmacologically treated PsD			<0.001
Yes	3469 (76.3)	116 (45.0)		Yes	311 (6.7)	33 (12.6)	
No	112 (2.4)	7 (2.6)		No	4308 (93.3)	228 (87.4)	
Missing				Missing	40 (0.9)	4 (1.5)	
Hypercholesterolaemia			0.044	Prior cerebral stroke			<0.001
Yes	1289 (28.0)	89 (33.7)					
No	3321 (72.0)	175 (66.3)		Yes	250 (5.5)	29 (11.2)	
Missing	49 (1.1)	1 (0.4)		No	4336 (94.5)	229 (88.8)	
				Missing	73 (1.6)	7 (2.6)	
Smoking			0.058	Prior VTE			<0.001
Yes	703 (15.2)	51 (19.2)		Yes	179 (3.9)	22 (8.5)	
No	3908 (84.8)	209 (80.4)		No	4401 (96.1.0)	261 (91.5)	
Missing	48 (1.0)	5 (1.9)		Missing	79 (1.7)	6 (2.3)	
Alcohol >2 units daily			0.015	Relative with VTE			0.023
Yes	345 (7.5)	9 (3.4)		Yes	507 (12.2)	16 (7.1)	
No	4263 (91.5)	252 (96.6)		No	3643 (87.8)	208 (92.9)	
Missing	51 (1.1)	4 (1.5)		Missing	509 (10.9)	41 (15.5)	
Pharmacologically treated PD			0.094	Anticoagulative treatment			<0.001
Yes	333 (7.2)	26 (10.0)		Platelet inhibitors	1284 (26.2)	120 (39.7)	
No	4286 (92.8)	264 (90.0)		None	3375 (68.9)	145 (48.0)	
Missing	44 (0.9)	5 (1.9)		Missing	0 (0)	0 (0)	
Pharmacologically treated CD			0.005	Duration of prophylaxis			
Yes	418 (9.1)	37 (14.4)		Mean (SD)	2.5 (0.91)	N/A	
No	4175 (90.9)	220 (85.6)		Median (IQR)	2 (2–3)	N/A	
Missing	66 (1.4)	8 (3.0)					

Data reported as n (%) for counts and mean for continuous variables unless otherwise specified.
BMI, body mass index; CD, cardiac disease; LOS, length of hospital stay; N, procedures; N/A, not available; PD, pulmonary disease; PsD, psychiatric disease; T1D, type 1 diabetes; T2D, type 2 diabetes; THA, total hip arthroplasty; TKA, total knee arthroplasty; VTE, venous thromboembolic event.

after discharge. Two Danish nationwide studies found symptomatic VTE in >1% of THA and TKA despite prolonged prophylaxis, and that the incidence was increasing across the study periods (1995–2007).[26] [32] The difference between these data and ours may be due to the fast-track set-up including early mobilisation in
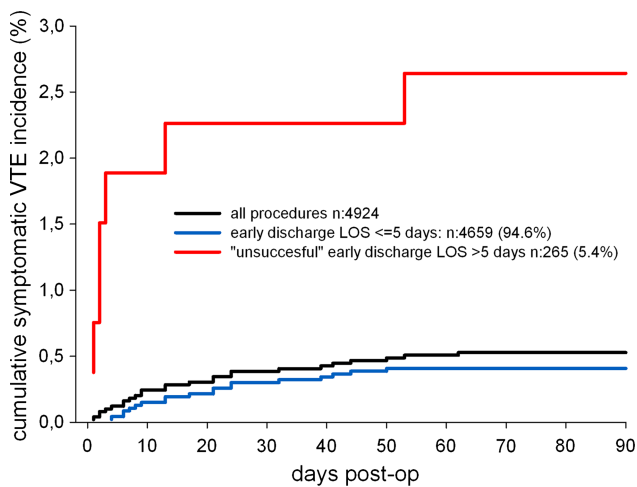
Figure 2 Cumulated incidence of symptomatic venous thromboembolic events.

VTE, with the majority occurring within the first month is consistent with previous studies,[2 34] we believe that the low incidence questions the benefits of prolonged prophylaxis in all patients after fast-track THA and TKA. Further studies are needed to identify whether certain patient subgroups may benefit from more extensive or intensive prophylaxis, and how to avoid in-hospital TEE while patients are receiving recommended treatment. However, due to the few events the numbers of patients needed for such studies pose major challenges.

Finally, we report both confirmed VTE-related death and a 'worst case' scenario, with death of unknown causes being considered VTE-related, despite that cause of death after THA/TKA often is found unrelated to VTE.[35] Thus, we found only one verified fatal PE, and a 90-day all-cause mortality comparable to or lower than previous studies.[27 36–38]

The 'unsuccessful' early discharge cohort was older with more comorbidity and readmissions. This is not surprising, as we have previously found an association with LOS and readmissions after fast-track THA and TKA in such patients.[20] There were about 2% PEs in these patients, but this is in accordance with comorbidities such as cardiac disease or previous TEE, being associated with cardiac and thromboembolic complications after arthroplasty.[27] Furthermore, complications per se

our study, and since LOS in Denmark was about 11 days in year 2000.[33]

The occurrence of in-hospital TEE in the total 4924 procedures in the LCDB was low (0.14%), and particularly the incidence of symptomatic in-hospital VTE (<0.10%) was lower than the 0.5% in THA and 1% in TKA found in a recent review.[25] Although the timing of

Figure 3 (A and B) Timing of type of TEE in the early discharge cohort (A) and the 'unsuccessful' early discharge cohort (B). TEE, thromboembolic event; VTE, venous thromboembolic event. Dotted line marks postoperative day 30.
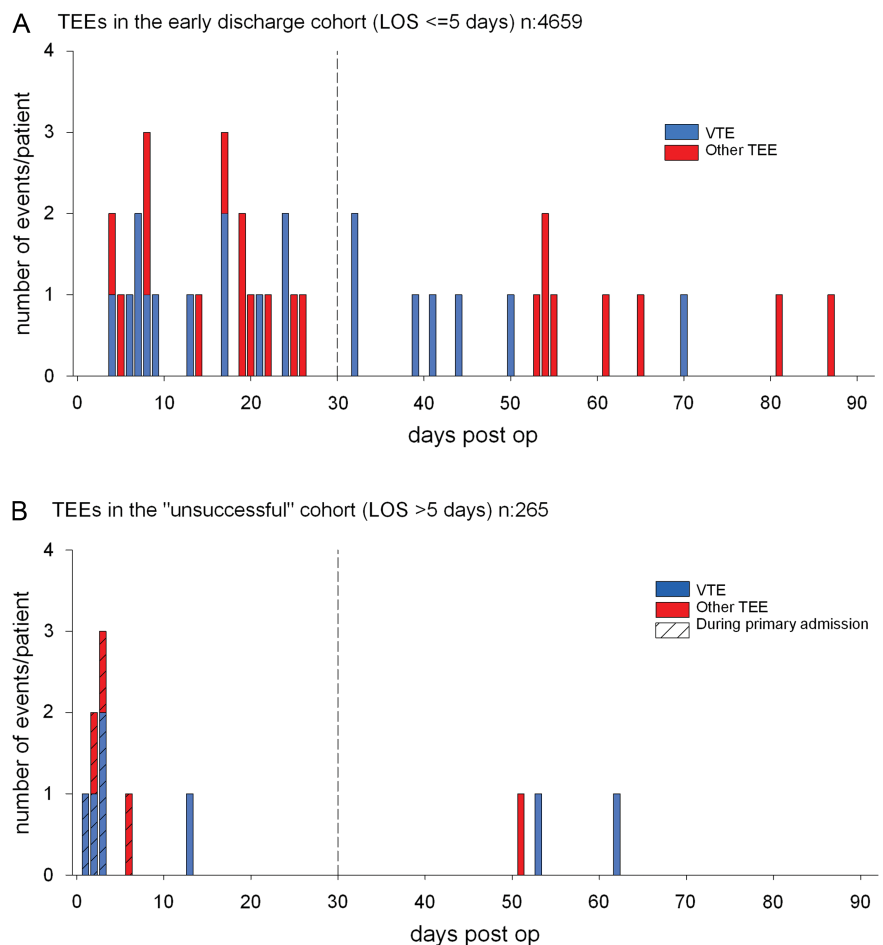
Table 2 VTEs, all TEEs and mortality

Outcomes	All procedures (n: 4924)	Early discharge (n: 4659)	'Unsuccessful' early discharge (n: 265)
PE	10 (0.21; (0.12 to 0.38))	5 (0.11; (0.05 to 0.25))	5 (1.99; (0.92 to 4.27))
Any DVT	16 (0.37; (0.24 to 0.58))	14 (0.30; (0.18 to 0.50))	2 (0.67; (0.18 to 2.38))
Proximal DVT	11 (0.23; (0.13 to 0.41))	9 (0.19; (0.10 to 0.36))	2 (0.67; (0.18 to 2.38))
Any VTE	30 (0.58; (0.41 to 0.83))	19 (0.41; (0.26 to 0.64))	7 (2.65; (1.35 to 5.14))
Any VTE (THA/TKA)	17/13 (0.62; (0.39 to 0.99))/ (0.53; (0.31 to 0.90))	15/4 (0.61; (0.37 to 1.00))/ (0.18; (0.07 to 0.46))	1/6 (0.65; (0.11 to 3.60))/ (4.70; (2.31 to 9.38))
Myocardial infarction	8 (0.17; (0.09 to 0.32))	7 (0.15; (0.07 to 0.31))	1 (0.33; (0.06 to 1.85))
Ischaemic stroke	8 (0.19; (0.10 to 0.35))	6 (0.13; (0.06 to 0.28))	2 (0.99; (0.34 to 2.87))
Transient ischaemic attack	7 (0.15; (0.08 to 0.30))	7 (0.15; (0.07 to 0.31))	0 (0.33; (0.06 to 1.85))
Arterial embolus	1 (0.04; (0.01 to 0.14))	0 (0.00; (0.00 to 0.08))	1 (0.66; (0.18 to 2.38))
Any TEE	50 (1.12; (0.87 to 1.44))	39 (0.84; (0.62 to 1.15))	11 (4.97; (3.04 to 8.04))
Any TEE (THA/TKA)	29/21 (1.17; (0.83 to 1.65))/ (1.05; (0.72 to 1.53))	27/12 (1.10; (0.76 to 1.60))/ (0.54; (0.31 to 0.94))	2/9 (1.96; (0.67 to 5.60))/ (8.05; (4.66 to 13.54))
All-cause mortality	17 (0.42; (0.28 to 0.64))	13 (0.28; (0.16 to 0.49))	4 (1.99; (0.92 to 4.27))
Unrelated to surgery	4 (0.10; (0.04 to 0.23))	3 (0.06; (0.01 to 0.20))	1 (0.33; (0.06 to 1.85))
Surgically related mortality	7 (0.19; (0.10 to 0.35))	4 (0.09; (0.04 to 0.23))	3 (1.66; (0.71 to 3.82))
Death of unknown cause	6 (0.13; (0.06 to 0.27))	6 (0.13; (0.06 to 0.28))	0 (0.00; (0.00 to 1.26))
Fatal PE	1 (0.04; (0.01 to 0.14))	1 (0.02; (0.00 to 0.12))	0 (0.33; (0.06 to 1.85))
Fatal PE/death of unknown cause	7 (0.17; (0.09 to 0.32))	7 (0.15; (0.07 to 0.31))	0 (0.33; (0.06 to 1.85))
Any VTE or death of unknown cause	32 (0.71; (0.52 to 0.98))	25 (0.54; (0.37 to 0.80))	7 (2.65; (1.35 to 5.14))
Any TEE or death of unknown cause	56 (1.25; (0.98 to 1.59))	45 (0.97; (0.73 to 1.29))	11 (4.97; (3.04 to 8.04))

Data reported as counts n (%; (95% CI)).
DVT, deep venous thrombosis; PE, pulmonary embolism; TEE, thromboembolic events; THA, total hip arthroplasty; TKA, total knee arthroplasty; VTE, venous thromboembolic events.

may lead to prolonged LOS and thereby longer prophylaxis. Thus, about 60% of TEE and VTE in this cohort occurred during primary admission. However, it does not argue against our conclusion that prophylaxis only during admission is safe when LOS ≤5 days.

Our study has limitations, foremost regarding the follow-up which was based on hospital contacts. However, although the reliability of diagnostic codes for VTE in DNPR may be low,[39] the completion of data regarding somatic admissions is close to 100%.[22 39] Consequently, we investigated all admissions through discharge summaries and patient files instead of relying only on diagnostic codes, as often carried out in large-scale cohort studies.[26 32 40] Although TEE may have been left out of the discharge summary, this seems unlikely, as they require treatment after discharge. We also used the DNDRP to detect procedures followed by a postoperative prescription of potent anticoagulant therapy, thereby ensuring that any TEE diagnosed in outpatient clinics would be registered. The DNDRP is ideally suited for this, as all prescriptions on oral anticoagulants in Denmark receive reimbursement and are therefore recorded. Regarding TEE during primary admission, ideally we should have investigated the discharge summaries of every procedure with LOS ≤5 days. However, as TEEs are serious complications they would require prolonged hospitalisation. Thus, LOS in all seven patients with TEE during primary admission was >5 days (figure 3B).

The local guidelines for thrombosis prophylaxis in the participating departments were 6–10 days after discharge when LOS >5 days, and therefore it may be problematic that

we do not have exact data on the duration of prophylaxis for the secondary cohort. However, this does not change the conclusion—that prophylaxis only during admission is safe in THA and TKA with LOS ≤5 days. It could also be argued that our study should have been carried out as an RCT. However we did not attempt to compare two types of treatment. Instead, for complex medical situations detailed cohort studies have been proposed as a viable, and sometimes preferable, alternative.[41 42] In this context, a post hoc analysis assuming a 2% baseline risk of symptomatic VTE with extended LMWH prophylaxis of about 35 days[2] found the actual power of our study to be 99% due to the large number of patients. Whether our cut-off of 5 days LOS is an optimal way of deciding on duration of prophylaxis is uncertain, but it seems unlikely that patients with a satisfactory fast-track procedure would have a longer LOS.[33 37] However, it is worth noticing that >75% of procedures were followed by LOS, and consequently thromboprophylaxis, for ≤3 days and that about 95% of all procedures had LOS ≤5 days.

In conclusion, we found low rates of TEE and VTE after primary elective fast-track THA and TKA with thromboprophylaxis only during hospitalisation in patients with LOS ≤5 days. These results support previous findings from other types of surgery, suggesting that guidelines on postoperative thromboprophylaxis need reconsideration in modern elective surgical procedures.

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