

Risk of myocardial infarction in Dutch patients following discharge for total hip/knee replacement and matched controls: a population-based cohort study

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Abstract

Introduction

Total joint replacement surgery of the hip and knee has been associated with an increased risk of acute myocardial infarction. However, this risk has not been compared with matched controls without surgery after discharge from the hospital. The aim of this study was to estimate the risk of myocardial infarction in Dutch patients following discharge for total hip/knee replacement and matched controls.

Materials and methods

A population-based retrospective cohort study was conducted with the Dutch PHARMO Record Linkage System. All patients with a primary elective total hip replacement (n = 13,952) or total knee replacement (n = 8239) between 2000 and 2009 were selected, and matched to 47,864 controls (no total hip replacement/total knee replacement) by age, sex and geographical location. Timedependent Cox regression was used to derive disease- and medicationadjusted (adj.) hazard ratios for a

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readmission due to acute myocardial infarction.

Results

The mean age of patients who sustained total hip replacement surgery was 68.5 years (standard deviation: 10.1), which was similar to patients who sustained total knee replacement surgery (68.4 years, standard deviation: 9.9). As compared with controls, the risk of myocardial infarction was not increased within 1 year after discharge for total hip replacement [adj. hazard ratio = 0.83, 95% confidence interval: 0.60-1.16] or total knee replacement [adj. hazard ratio = 0.97, 95% confidence interval: 0.63-1.48]. The corresponding cumulative incidence was 0.4% 1 year after total hip/knee replacement discharge. Furthermore, the hazard ratio of myocardial infarction was not different between patients exposed to total hip/knee replacement and controls, when the surgery was performed more than 1 year ago.

Conclusion

The hazard ratio of acute myocardial infarction was not increased in the year following discharge for total hip/knee replacement surgery or in the subsequent period, as compared with controls without surgery. The incidence of post-discharge acute myocardial infarction was low, which is possibly related to the current treatment regimen, including lowmolecular-weight-heparins for an extended duration of 6 weeks and early revalidation after surgery.

Introduction

Joint replacement surgery provides relief of pain and improvement of function for a large number of

patients with treatment-refractory, end-stage hip or knee osteoarthritis (OA). The number of these procedures will continue to increase in the Netherlands due to demographical changes and increase in overweight¹. Total hip/knee replacements (THR/ TKR) have been associated with periand postoperative acute myocardial infarction (MI). Potential causes include bone marrow embolisation upon surgical invasion of the femoral medullary canal, or haemodynamic stressors such as anaesthesia, blood loss, fluid shifts, arrhythmias and hypoxia^{2,3}. However, antithrombotic drugs are commonly used in these patients and may have the potential to decrease the risk of acute MI⁴. Furthermore, limited exercise during the revalidation period or increased exercise (mobility) as a result of a successful operation may influence the postoperative acute MI risk in the longer term.

Previous studies have shown conflicting postoperative MI rates, ranging from 0.1% to 1.2% within 90 days after surgery⁵⁻¹². This may be explained by differences in baseline characteristics, study design and the operational definition of acute MI. A large population-based cohort study showed an increased risk of MI within 2 weeks after THR (25 times) or TKR (31 times) surgery as compared with matched controls¹³. However, no study determined the risk of acute MI in patients with THR/TKR versus matched controls in the period following discharge. In the past decade, clinical guidelines have encouraged discharging patients with THR/TKR earlier from hospitals to reduce costs. To what

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extent this earlier discharge has influenced post-discharge acute MI events remains unknown. Therefore, we aim to determine the excess risk of acute MI shortly after discharge for THR/TKR surgery as compared with matched controls without surgery for the Dutch setting. In addition, we have examined this risk for a prolonged follow-up period after discharge (<1 year, \geq 1 year).

Materials and methods

Data source

Utilising the Dutch PHARMO Record Linkage System (PHARMO RLS), we conducted a population-based retrospective cohort study. The PHARMO RLS (Institute for Drug Outcome Research) is a database that contains the pharmacy dispensing data of approximately three million community-dwelling inhabitants in the Netherlands. These pharmacy dispensing records are linked to the Dutch national hospitalisation registry. Diagnoses are coded according to the International Classification of Disease, 9th revision codes (ICD-9). PHARMO RLS has been used before for the exposure to THR/TKR surgery¹⁴ and the outcome of acute MI^{15,16}.

Study population

We have included all patients aged \geq 40 years with an elective primary THR or TKR (ICD-9 procedure code; THR 81.51, TKR 81.54) between 1 January 2000 and 31 December 2009. Each patient who underwent primary THR or TKR surgery was matched by age, gender and geographical location to a maximum of three patients who did not undergo this surgery using the incidence density sampling technique. The index date was defined as the discharge date for THR/TKR and was the same for the matched unexposed patients. To derive a study population with an elective THR/ TKR due to OA, we have excluded patients with a history or a record within 3 months after the index date for fracture of the hip or knee, rheumatoid arthritis (including exposure to disease-modifying antirheumatic drugs or biologics specific for rheumatoid arthritis) and osteoporosis drugs. Finally, we have excluded patients with a previous MI within 6 weeks before the index date, to minimise the possibility of a recurrent MI. This was done for both patients exposed to THR/TKR and controls.

Study outcomes

All patients were followed up from the index date until the occurrence of acute MI (classified using ICD-9 code: 410), death, hip or knee replacement revision, migration or end of the study period (31 December 2009), whichever came first. Acute MIs that occur during hospitalisation for THR/TKR surgery are not properly registered in the Dutch national hospitalisation registry. Therefore, occurrence of an acute MI was defined as 'a hospital admission after the index date (discharge for THR/ TKR surgery in the exposed cohort or matched dummy index date for the unexposed cohort)'.

Definition of covariates

We considered age, male gender, a history of cardiovascular disease [ischaemic heart disease (IHD) including an acute MI ≥6 weeks before the index date or ≥ 2 prescriptions of nitrates in the past, congestive heart failure, vascular disease], chronic kidney disease, cerebrovascular disease and malignancies as potential determinants of acute MI or confounders for the association between THR/TKR and the occurrence of an acute MI. Furthermore, a prescription for thiazide diuretics, loop diuretics, β blockers, calcium-channel blockers, antiarrhythmic drugs, rennin-angiotensinaldosterone inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs), statins, vitamin K antagonists, antiplatelet drugs, other antithrombotic drugs including heparins, direct thrombin inhibitors and thrombolytic agents, oestrogen-containing drugs, inhaled β -2-agonists^{17,18} and anti-diabetic drugs within 6 months were also considered as determinants and potential confounders for the association.

Research Study

Statistical analysis

To study the association between the THR/TKR and the occurrence of an acute MI, the total followup time was divided into three periods-<6 weeks, 6 weeks to <1 year and ≥ 1 year. Using the PHREG procedure from SAS 9.1.3, we calculated the hazard ratios (HRs) for risk of acute MI among patients with THR/TKR versus the matched unexposed patients for each previously mentioned time period separately. The presence of potential determinants or confounders was evaluated before and during follow-up, and confounders were added to the final model if they independently changed the β coefficient for THR/TKR by at least 5%. Additionally, Kaplan-Meier plots were used to present the cumulative incidence rates of acute MI over time (follow-up of 1 year) for patients and controls.

Potential effect modifiers were evaluated for each time period. We evaluated potential effect modifiers by including an interaction term into the model (THR or TKR × covariate).

To identify the potential determinants of acute MI in the previously mentioned time intervals in patients with THR or TKR, we included only the patients with THR/TKR. Potential determinants of acute MI among patients with THR/TKR were identified when they were significantly (p < 0.05) associated with the outcome in a full regression model (including all covariates into the model).

Results

We have identified 22,191 patients who underwent primary elective total joint replacement surgery that was most likely to be the result of OA (THR: 13,952 patients,

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Figure 1: Kaplan–Meier plot of the cumulative incidence rates of acute MI for patients exposed to THR and matched controls.



Figure 2: Kaplan–Meier plot of the cumulative incidence rates of acute MI for patients exposed to TKR and matched controls.

TKR: 8239 patients), and a total of 47,864 matched control subjects. The proportion of males and mean age (standard deviation; SD) among exposed patients (THR: 36.6% male, mean age 68.5 (10.1) years, TKR: 34.9% male, mean age 68.4 (9.9) years) were similar to that of control subjects due to matching. Patients who underwent THR or

TKR surgery were more likely to be exposed to NSAIDs, other analgesic drugs and antithrombotic drugs in the 6 months before the index date than their matched population. In addition, patients exposed to TKR were significantly more often diagnosed with ischemic heart disease (IHD) than their matched controls (Table 1).

Research Study

Page 3 of 8

Due to a small number of events in the first 6 weeks after discharge for THR/TKR surgery, we have merged the <6 week and 6 weeks to <1 year periods into a 1-year period. As compared with the matched control subjects, the 1-year HR of acute MI was not increased after exposure to THR [adjusted (adj.) HR 0.83, 95% confidence interval (CI): 0.60-1.16] or TKR surgery (adj. HR 0.97, 95% CI: 0.63-1.48). Similar HRs were seen when these procedures were performed more than 1 year ago (Table 2). Among patients who have undergone elective THR, 0.36% showed to have an acute MI within 1 year post-THR discharge. The corresponding cumulative incidence of the population-based matched controls was 0.44% (Figure 1). Similarly, among patients who have undergone elective TKR, 0.38% showed to have an acute MI within 1 year post-TKR discharge while 0.40% of the matched controls developed an acute MI in this period (Figure 2). In addition, we did not find any effect modifiers for the relationship between THR/TKR surgery and the risk of acute MI for both follow-up periods (Table 2).

Among patients exposed to THR, the 1-year HR of acute MI was almost three-fold higher for patients with a history of IHD or having at least two prescriptions for organic nitrates in the past (full model HR 2.98, 95% CI: 1.41-6.31) (Table 3). Among patients exposed to TKR, we did not identify any significant determinant for the 1-year risk of acute MI (Table 3). When we sought for potential determinants of acute MI among patients with THR after 1 year of follow-up (THR surgery was performed more than 1 year ago), a history of IHD lost significance. However, for this follow-up period, age older than 60 years and male gender appeared to be significant determinants of acute MI. Among patients exposed to TKR, significant determinants included male gender and use of anti-diabetic drugs within 6 months.

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Research Study

Page 4 of 8

Table 1. Baseline characteristics of patients with THR/TKR and matched unexposed patients.						
	Total hip replacement			Total knee replacement		
Characteristic	Exposed	Unexposed		Exposed Unexposed		
	n = 13,952	n = 30,795	p value*	n = 8,239	n = 17,069	<i>p</i> value*
Mean follow-up time (years, SD)	4.3 (2.7)	4.0 (2.7)	0.784	3.8 (2.6)	3.6 (2.6)	0.273
Males (%)	36.6	36.1	-	34.9	34.6	-
Mean age (years, SD)	68.5 (10.1)	68.8 (10.3)	-	68.4 (9.9)	68.3 (10.0)	-
Mean THR/TKR hospital stay (days, SD)	8.4 (6.5)		-	8.2 (6.4)		-
Disease history (%)						
IHD or ≥2 prescriptions of organic nitrates	9.1	9.6	0.066	11.4	9.9	< 0.001
Congestive heart failure	0.6	1.0	< 0.001	0.6	0.8	0.069
Vascular disease	0.9	1.0	0.347	1.0	1.2	0.161
Cerebrovascular disease	1.5	1.7	0.104	1.5	1.9	0.030
Chronic kidney disease	0.1	0.2	0.158	0.1	0.2	0.700
Malignancy	4.3	4.0	0.103	4.3	4.1	0.501
Drug use 6 months before index date (%)						
Paracetamol	10.4	4.3	< 0.001	9.5	3.7	< 0.001
NSAIDs	51.5	17.3	< 0.001	49.1	17.5	< 0.001
Opioids (tramadol or stronger)	13.4	3.8	< 0.001	12.7	4.0	<0.001
Antiplatelet drugs	19.2	19.7	0.219	19.7	20.9	0.018
Vitamin K antagonists	9.6	5.3	<0.001	9.6	5.5	<0.001
Other antithrombotic agents	14.2	0.3	< 0.001	16.2	0.5	< 0.001
RAAS inhibitors	24.0	22.4	< 0.001	28.4	23.5	< 0.001
Thiazide diuretics	20.1	17.1	< 0.001	24.1	17.8	< 0.001
Loop diuretics	7.3	7.8	0.06	9.3	8.0	< 0.001
β Blockers	20.6	19.4	<0.05	23.5	20.2	< 0.001
Calcium channel antagonists	12.2	11.1	< 0.001	14.6	11.5	< 0.001
Antiarrhythmic drugs	2.0	1.8	0.163	2.2	2.0	0.299
Statins	19.2	19.1	0.934	22.5	21.1	< 0.05
Bronchodilators	9.6	10.4	< 0.05	10.6	10.9	0.352
Anti-diabetics	8.5	10.4	< 0.001	11.7	10.8	< 0.05
Estrogen-containing drugs	3.8	3.5	0.07	4.0	3.8	0.538

IHD, ischaemic heart disease; NSAIDs, non-steroidal anti-inflammatory drugs; RAAS, renin–angiotensin–aldosterone system; SD, standard deviation; THR, total hip replacement; TKR, total knee replacement.

**p* values for differences between exposed/non-exposed groups have been obtained using Chi-square tests for proportions and independent samples *t*-tests for means.

Discussion

This study shows that the HR of acute MI is not increased in the year following discharge after THR or TKR surgery or in the subsequent period, as compared with population-based matched controls. A significant determinant of the 1-year acute MI risk included a history of IHD (or \geq 2 prescriptions of organic nitrates) among patients exposed to THR, while there were no significant determinants identified among patients exposed to TKR. When surgery was performed more than 1 year ago, significant determinants of acute MI included older age (>60 years) and male gender among patients exposed to THR, while use of anti-diabetics within 6 months and male gender were determinants among patients

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Research	Study
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Page 5 of 8

Table 2. Effect modification of the hazard ratio of acute MI following discharge for joint replacement surgery versus matched unexposed controls.						
	Total hip repla	cement surgery	Total knee replacement surgery			
	<1 year	≥1 year	<1 year	≥1 year		
	Adj. HR (95% Cl)*	Adj. HR (95% Cl)*	Adj. HR (95% Cl)*	Adj. HR (95% Cl)*		
Overall (all patients)	0.83 (0.60–1.16)	1.04 (0.86–1.26)	0.97 (0.63–1.48)	0.86 (0.64–1.15)		
By gender						
Males	0.92 (0.64–1.33)	1.15 (0.89–1.48)	1.06 (0.65–1.73)	0.94 (0.64–1.39)		
Females	0.75 (0.51–1.09)	0.94 (0.72–1.22)	0.88 (0.54–1.45)	0.79 (0.54–1.15)		
By age						
<60 years	0.83 (0.51–1.33)	0.94 (0.60–1.50)	1.02 (0.55–1.88)	0.95 (0.52–1.74)		
>60 years	0.92 (0.72–1.18)	1.05 (0.86–1.29)	0.90 (0.65–1.25)	0.84 (0.62–1.15)		
By disease history						
No IHD or ≥2 organic nitrate prescriptions	0.91 (0.65–1.29)	1.13 (0.91–1.40)	1.10 (0.70–1.72)	0.98 (0.70–1.35)		
IHD or ≥2 organic nitrate prescriptions	0.65 (0.41–1.04)	0.81 (0.55–1.17)	0.68 (0.36–1.28)	0.61 (0.36–1.03)		
By drug use in the 6 months before						
No NSAIDs	0.83 (0.59–1.16)	1.04 (0.85–1.27)	1.01 (0.66–1.56)	0.89 (0.66–1.20)		
NSAIDs	0.83 (0.36–1.94)	1.04 (0.46–2.37)	0.19 (0.02–1.54)	0.17 (0.02–1.33)		
No β blockers	0.85 (0.60–1.20)	1.06 (0.84–1.33)	0.97 (0.61–1.53)	0.86 (0.61–1.20)		
β Blockers	0.81 (0.53–1.23)	1.01 (0.74–1.38)	0.98 (0.56–1.71)	0.87 (0.55–1.37)		
No anti-diabetics	0.88 (0.62–1.23)	1.10 (0.90–1.36)	0.89 (0.57–1.38)	0.78 (0.56–1.08)		
Anti-diabetics	0.61 (0.36–1.04)	0.77 (0.48–1.21)	1.39 (0.73–2.70)	1.22 (0.71–2.11)		
By antithrombotic agents in the 6 months before (ref = no use 6 months before)						
No anticoagulant use	1.12 (0.84–1.49)	1.17 (0.92–1.48)	1.06 (0.72–1.57)	0.85 (0.60–1.22)		
Vitamin K antagonist only	0.70 (0.41-1.21)	0.74 (0.43–1.26)	0.35 (0.13–0.94)	0.28 (0.10–0.76)		
Anti-platelet drugs only	0.92 (0.66–1.29)	0.96 (0.71–1.29)	1.35 (0.87–2.08)	1.08 (0.72–1.63)		
Others/mixed use	0 72 (0 34–1 53)	0 75 (0 35-1 64)	0 85 (0 27-2 62)	0.68(0.21-2.20)		

*Adjusted for IHD, cardiovascular drugs (RAAS inhibitors, thiazide diuretics, loop diuretics, β blockers and calciumchannel blockers), anticoagulants, statins and anti-diabetics.

IHD, ischemic heart disease; MI, myocardial infarction; NSAIDs, non-steroidal anti-inflammatory drugs.

exposed to TKR. However, no modification of the relationship between THR or TKR surgery and acute MI could be identified for both follow-up periods. This indicates that patients with a higher risk of acute MI do not have a surgery-induced excess risk after discharge for elective THR or TKR surgery.

To our knowledge, this is the first Dutch study that compared the risk of acute MI following THR or TKR surgery with population-based matched controls directly after discharge from the hospital and for a long-term follow-up period. The other large study that has evaluated the excess risk of acute MI in a Danish cohort of patients, found an elevated risk of acute MI for patients exposed to THR (25 times higher) and TKR (31 times higher) when compared with matched controls within 2 weeks after surgery¹³. Our study could detect very few events within 2 weeks after discharge for THR and TKR surgery (Figures 1 and 2). However, the first study also included acute MIs that occurred during hospitalisation for THR/TKR surgery. A US observational study within 10,244 THR and TKR patients reported an incidence rate for acute MI of 0.4% within 30 days from surgery¹¹. This study reported a median time to acute MI of 1 day and 83% of all recorded MIs occurred within 3 days after surgery. Since the mean duration of hospital stay was, respectively, 8.4 days and 8.2 days for THR and TKR surgery in the present study, this may explain the lower cumulative incidence rate for acute MI and no increased risk as compared with controls without surgery. Studies

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Research Study

Page 6 of 8

Table 3. Determinants of acute MI after discharge within THR/TKR patients.						
	Total hip replace	cement surgery	Total knee replacement surgery			
	<1 year ≥1 year		<1 year	≥1 year		
	HR (95% CI)*	HR (95% CI)*	HR (95% CI)*	HR (95% CI)*		
Males (ref = females)	1.53 (0.86–2.71)	2.48 (1.77–3.47)	1.15 (0.55–2.40)	2.54 (1.51–4.28)		
Age (ref ≤60 years)						
>60 years	1.07 (0.51–2.26)	2.30 (1.33–3.98)	3.79 (0.90–16.1)	1.52 (0.74–3.13)		
Disease history (ref = no history)						
IHD or ≥2 organic nitrate prescriptions	2.98 (1.41–6.31)	1.01 (0.62–1.64)	1.33 (0.50–3.54)	1.06 (0.54–2.10)		
Drug use 6 months before (ref = no use 6 months before)						
NSAIDs	1.01 (0.42–2.39)	1.75 (0.94–3.28)	1.60 (0.64–3.99)	0.30 (0.04–2.18)		
β Blockers	1.25 (0.64–2.44)	1.37 (0.93–2.01)	1.51 (0.68–3.39)	1.10 (0.60–2.01)		
Anti-diabetics	0.72 (0.25–2.07)	1.22 (0.75–1.97)	1.45 (0.57–3.64)	2.16 (1.20-3.90)		
Antithrombotic agents in the 6 months before (ref = no use 6 months before)						
Vitamin K antagonists only	1.11 (0.46–2.67)	0.56 (0.26–1.20)	0.36 (0.08–1.67)	0.29 (0.06–1.31)		
Anti-platelet drugs only	1.46 (0.59–3.59)	1.14 (0.76–1.71)	1.61 (0.61–4.30)	1.46 (0.79–2.70)		
Others/mixed use	1.12 (0.55–2.28)	0.63 (0.20–2.01)	0.75 (0.31–1.81)	0.43 (0.06–3.24)		

*Full model included: gender, age (<60 years; \geq 60 years); history of IHD, IHD or \geq 1 prescription(s) for organic nitrates, IHD or \geq 2 prescriptions for organic nitrates, heart failure, vascular disease, malignancy, cerebrovascular disease; a prescription of NSAIDs, anti-arrhythmic drugs, thiazide diuretics, loop diuretics, β blockers, RAAS inhibitors, calcium channel blockers, anti-diabetics, vitamin K antagonists, anti-platelet drugs (others/mixed use of antithrombotic drugs) in the 6 months before.

IHD, ischaemic heart disease; MI, myocardial infarction; NSAIDs, non-steroidal anti-inflammatory drugs; THR, total hip replacement; TKR, total knee replacement.

that have determined the readmission rates for acute MI following TKR or THR surgery showed incidence rates between $0.1\%^5$ and $1.0\%^{10}$ within 90 days after surgery. Our findings are in line with the lower rate of 0.1% that was reported for 15,943 American TKR patients with a very similar age and sex distribution (mean age 68 years, 38% was male) as compared with TKR patients in the present study⁵.

The biological mechanism for an elevated acute MI risk shortly after THR or TKR surgery may be explained by bone marrow embolisation upon the surgical invasion of the femoral medullary canal or by haemodynamic stressors (such as anaesthesia, blood loss, fluid shifts, arrhythmias and hypoxia)^{2,3}. In addition, the amount of exercise (time to initiation of the revalidation period or increased mobility after a

successful operation) and pharmacological treatment may influence this risk for prolonged periods after THR or TKR surgery. In the Netherlands, 87% of all patients who undergo THR or TKR surgery are treated with low-molecular-weight heparins (LMWHs) and 13% are treated with fondaparinux. This treatment is administered for a prolonged out-ofhospital period of 6 weeks or longer in a substantial number of THR/ TKR patients (91%)¹⁹. Similarly, Danish guidelines and the American College of Chest Physicians recommend thromboprophylaxis (predominantly with LMWHs) to be extended beyond 10 days and up to 35 days after THR/TKR surgery^{13,20}. A metaanalysis of randomised clinical trials has shown that extended, out-ofhospital, administration of LMWHs for 6 weeks resulted in a significantly reduced risk of thromboembolic events²¹. In addition, these agents were able to significantly reduce the risk of MI during the first month of therapy in patients (n = 1049) with unstable coronary artery disease⁴. Another trial showed that the 2-year incidence of recurrent acute MI was significantly reduced with LMWHs as compared with placebo in elderly patients²².

Strengths of this study include its population-based design, large sample size and completeness of follow-up (approximately 4 years for both patients exposed to THR/ TKR and matched controls). We also had access to reliable data on outpatient prescription drugs, which made adjustment for medication use possible (e.g. NSAIDs, which may have the potential to increase the risk of acute MI²³). Finally, we were able to interpret the magnitude of acute MI incidence as compared with

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the general population with the inclusion of a matched populationbased control cohort. A drawback of this study includes the incomplete capture of acute MIs that have occurred during the hospital admission period for THR or TKR surgery (mean duration of 8 days). This is due to an unreliable registration because hospitals are not obliged to register these events during the admission period for the major indication/procedure (THR/TKR surgery). However, there is also a good rationale for determining the excess risk of acute MI following discharge for THR/TKR. In the past decade, clinical guidelines have encouraged discharging THR/TKR patients earlier from hospitals to reduce costs. To what extent this earlier discharge has influenced post-surgical (in particular postdischarge) acute MI events was previously unknown. Moreover, we had no data on un-hospitalised fatal acute MIs. Those events are not registered in the Dutch national hospitalisation registry and accounts for 40% of all acute MI cases in the Netherlands²⁴. This may have led to an underestimation of the true acute MI incidence in our study population. However, we do not expect that the number of fatal, out-of-hospital, acute MIs would vary differentially between patients exposed to THR/TKR and controls. In addition, healthy user bias cannot be ruled out since Dutch physicians and orthopaedics may predominantly select patients who are healthy enough to undergo this type of surgery. Last, we had no information about some general risk factors of acute MI such as body mass index (BMI), smoking, blood pressure and in-hospital use of antithrombotic therapy. Some of these factors may be somewhat higher in patients who are exposed to THR/TKR due to OA (e.g. BMI). This could have masked an actual increased risk of acute MI among patients with THR/ TKR patients as compared with

controls. However, selection for surgery might decrease this effect. Also, as explained earlier, a very high percentage of patients who undergo THR or TKR surgery are treated with LMWHs, which is initiated within 6 h post-operatively and used (out-of-hospital) for an extended duration of 6 weeks¹⁹.

Conclusion

This study shows a very low readmission rate for acute MI within 6 weeks after discharge for THR or TKR surgery. In addition, the risk of acute MI was not increased in the year after discharge or in the subsequent period, as compared with patients who have not undergone this surgery. The low risk of acute MI after discharge for THR or TKR surgery in the Netherlands is possibly related to the current treatment regimen including LMWHs for an extended out-of-hospital period and early revalidation after surgery.

Conflict of interest

The Division of Pharmacoepidemiology & Clinical Pharmacology (employing C.K., F.V., A.L.) has received unrestricted funding from the Netherlands Organisation for Health Research and Development (ZonMW), the Dutch Health Care Insurance Board (CVZ), the Royal Dutch Pharmacists Association (KNMP), the private-public funded Top Institute Pharma (www.tipharma. nl), (includes co-funding from universities, government, and industry), the EU Innovative Medicines Initiative (IMI), the EU 7th Framework Program (FP7) and the Dutch Ministry of Health and industry (including GlaxoSmithKline, Pfizer and others).

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Research Study

for example IMI, TI Pharma (www. tipharma.nl) is accepted under the condition that no companyspecific product or company-related study is conducted. The Centre has received unrestricted research funding from public sources, for example Netherlands Organisation for Health Research and Development (ZonMW), the Dutch Health Care Insurance Board (CVZ), EU 7th Framework Program (FP7), Dutch Medicines Evaluation Board (MEB) and the Dutch Ministry of Health.

Abbreviations list

BMI, body mass index; CI, confidence interval; HR, hazard ratio; IHD, ischemic heart disease; LMWH, low-molecular-weight heparin; MI, myocardial infarction; NSAID, nonsteroidal anti-inflammatory drug; OA, osteoarthritis; THR/TKR, total hip/knee replacement.

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