Am J Transl Res 2026;18(9):8171-8180
www.ajtr.org /ISSN:1943-8141/AJTR0172266

Original Article

Association between low limb joint replacement with risk of peripheral arterial occlusive disease in osteoarthritis patients

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Received February 25, 2026; Accepted September 2, 2026; Epub September 15, 2026; Published September 30, 2026

Abstract: Objectives: Peripheral arterial occlusive disease (PAOD) is a clinical manifestation of systemic atherosclerosis that is commonly associated with cerebrovascular disease and various complications. This study aimed to investigate the risk of PAOD in patients who had undergone hip or knee joint replacement. Methods: In this study, patients with hip or knee joint replacement were recruited from the Longitudinal Health Insurance Database 2000 (LHID 2000) and their risk of PAOD was studied. Results: A total of 10,346 patients with joint replacement and 99,597 patients without joint replacement were identified. The incidence density of PAOD in joint replacement and non-joint replacement group was 6.71 and 7.08 persons per 1,000 person-years. After adjusting for age, sex, comorbidities, antiplatelet, and anticoagulant, the HR was 0.92 (95% C.I. = 0.81-1.04). Further analysis of knee (HR = 1.23; 95% C.I. = 0.85-1.78) and hip replacement (HR = 2.05; 95% C.I. = 0.87-4.86) compared with non-joint replacement revealed that there was no significant association with peripheral arterial occlusive disease. Conclusions: This cohort study demonstrates that undergoing hip or knee joint replacement does not significantly elevate the likelihood of peripheral arterial occlusive disease, offering reassurance regarding the vascular safety of these procedures in osteoarthritis patients.

Keywords: Joint Replacement, peripheral arterial occlusive diseases, risk, cohort study

Introduction

Low-limb joint replacement is a critical medical intervention for people whose joints are dysfunctional. The main cause of disfunction includes osteoarthritis and osteoarthrosis of the pelvic region and thigh, hip, and knee [1]. Other reasons can be that overuse of the joints which leads to severe arthritis over time, fractures of the hip/knee joints, and autoimmune diseases such as rheumatoid arthritis or psoriatic arthritis [2, 3]. To treat the joints and improve lifestyle, joint replacement is one of the most effective ways. In Taiwan, more than 200,000 patients underwent primary total knee replacement surgery (TKR) between 1996 and 2010 [4].

However, joint replacements can also lead to complications as well as promote better health. While there are risks of complications associated with surgery, such as infection or implant failure, a successful joint replacement can increase a patient's mobility, reduce pain, and enhance overall health. For example, periprosthetic infection or lung complications have been reported in patients receiving joint replacement [5, 6]. Hip and knee joint replacement could also cause venous thromboembolism and other blood vessel injuries [7, 8]. In

https://doi.org/10.62347/EZPY4762

addition to complications, several sequalae have been reported after joint replacement. Some joint replacement cases have been reported to cause cardiovascular outcomes [9]. There is also a study that indicates joint replacement surgery can reduce the risk of mortality and major adverse cardiac events [10].

Peripheral arterial occlusive disease (PAOD) is a clinical manifestation of systemic atherosclerosis, which is always associated with cerebrovascular diseases and various complications [11, 12]. The main causes of PAOD are the formation of thrombosis or embolism in the arteries of the lower extremities which can lead to serious atherosclerotic stenosis, blood vessel occlusion, and even tissue necrosis of the extremities [12, 13]. Although joint replacement surgery led to certain complications and sequelae related to blood vessels, few articles in the literature have mentioned the association of joint replacement with PAOD. In this study, we enrolled patients with hip or knee joint replacement from the Longitudinal Health Insurance Database 2000 (LHID 2000) and analyzed their risk of PAOD.

Materials and methods

Data sources

The longitudinal health insurance database was managed by the Health and Welfare Data Science Center (HWDC) in Taiwan. The database comprised two million beneficiaries who were randomly sampled from the 2000 registry of beneficiaries with the entire Taiwan population. The database contained medical claims, including drug medications, medical operation, procedures, and expenses in outpatients and inpatient care from 2000 to 2018. The diagnosis of disease was based on the International Classification of Diseases, 9th and 10th revision, Clinical Modification (ICD-9-CM; ICD-10-CM). The necessary of written informed consent was discarded by the above organizations. We confirm that all research was performed in accordance with relevant guidelines/regulations.

Study group and outcome measurements

This study was conducted by using a retrospective cohort study design. The newly diagnosed osteoarthrosis in the hip and knee (ICD-9-CM = 3715.15, 715.16, 715.25, 715.26, 715.35, 715.36; ICD-10-CM = M16, M17) and greater than or equal to 18 years of age from 2002 to 2017 was defined as the study population criteria. To verify the accuracy of the diagnoses, at least 3 times outpatient visits or one hospitalization was required. The exposure group received hip or knee joint replacement within one year after the diagnosis of osteoarthrosis. The index date was defined as the operation date of hip or knee joint replacement. Criteria excluded the diagnosis of peripheral arterial occlusive disease (PAOD, ICD-9-CM = 443.8, 443.9, 444; ICD-10-CM = I73.81, I73.89, I73.9, I74.01, I74.09, I74.11, I74.2, I74.3, I74.4, I74.5, I74.8, I74.9, I79.1, I79.8) before the index date. Comparison subjects were defined as those without operation of hip or knee joint replacement.

The analytic outcome was defined as the new-onset of peripheral arterial occlusive disease (PAOD, ICD-9-CM = 443.8, 443.9, 444; ICD-10-CM = I73.81, I73.89, I73.9, I74.01, I74.09, I74.11, I74.2, I74.3, I74.4, I74.5, I74.8, I74.9, I79.1, I79.8). To verify the accuracy of the diagnoses, at least 3 times outpatient visits or once hospitalization was required. Both groups were traced until the onset of PAOD, death, or 31 December 2018, whichever occurred first. **Figure 1** presents a detailed flowchart outlining the subject selection process for joint replacement.

Covariates and matching

The baseline characteristics were age, sex, and underlying comorbidities, including hypertension (ICD-9-CM = 401-405; ICD-10-CM = I10-I15), hyperlipidemia (ICD-9-CM = 272; ICD-10-CM = E78), chronic liver disease (ICD-9-CM = 571; ICD-10-CM = K70, K73, K74, K75.4, K75.81, K76.0, K76.89, K76.9), chronic kidney disease (ICD-9-CM = 585; ICD-10-CM = N18.4, N18.5, N18.6, N18.9), diabetes (ICD-9-CM = 250; ICD-10-CM = E10, E11, E13), chronic obstructive pulmonary disease (ICD-9-CM = 491, 492, 496; ICD-10-CM = J41-J44), ischemic heart disease (ICD-9-CM = 410-414; ICD-10-CM = I20-I25), stroke (ICD-9-CM = 433-438; ICD-10-CM = I63, I64), intracranial bleeding (ICD-9-CM = 430-432; ICD-10-CM = I60-I62), deep vein thrombosis (ICD-9-CM = 453.8; ICD-10-CM = I82.21, I82.29, I82.40, I82.41,

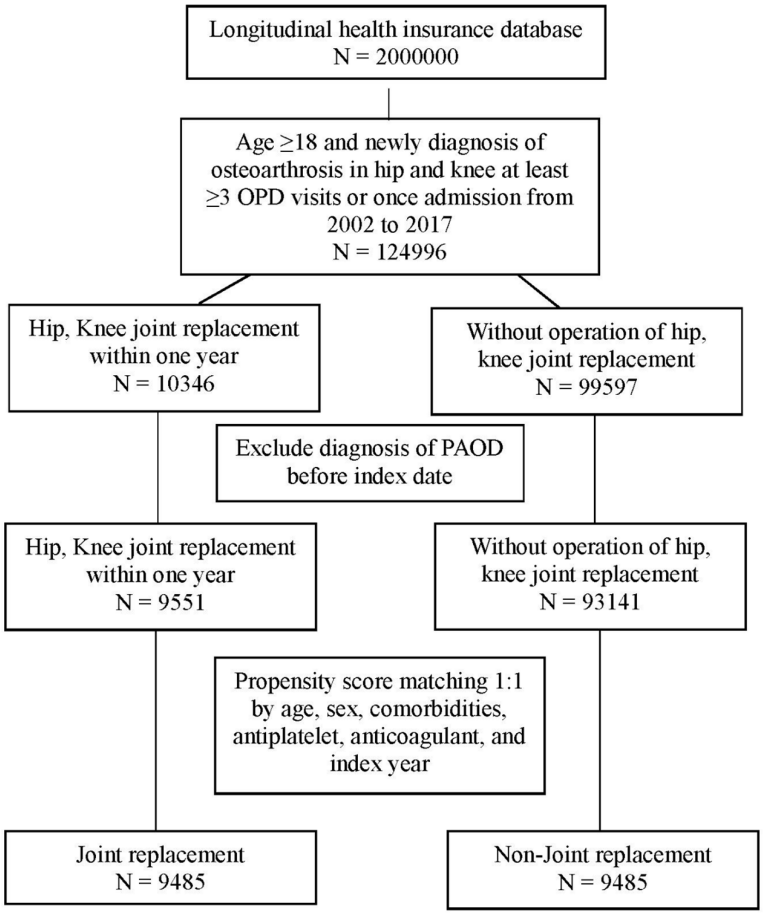


Figure 1. Study flowchart of selection participants.

I82.42, I82.43, I82.44, I82.49, I82.4Y, I82.4Z, I82.50, I82.51, I82.52, I82.53, I82.54, I82.59, I82.5Y, I82.5Z, I82.60, I82.61, I82.62, I82.70, I82.71, I82.72, I82.81, I82.89, I82.9, I82.A, I82.B, I82.C), varicose veins of lower extremities (ICD-9-CM = 454; ICD-10-CM = I83), psoriasis (ICD-9-CM = 696; ICD-10-CM = L40, L41, L42, L44, L45, L30.5, L94.5). Those comorbidities were defined before the index date within one year and at least three outpatient visits or once hospitalization. In addition, use of antiplatelets (ATC code: B01AC04, B01AC06, B01AC22, B01AC23, B01AC24, B01AC30, N02BA01) and anticoagulant (ATC codes: B01AA03, B01AB05, B01AE07, B01AF01, B01AF02, B01AF03) was included and limited as at least greater than or equal to 3 prescriptions during the study period.

Then, propensity score matching was performed by age, sex, comorbidities, antiplatelet, anticoagulant, and index year. The propensity score was a probability from zero to one that was estimated through logistic regression. The joint replacement and the non-joint replacement group was the binary variable. By matching the propensity score, the heterogeneity of both groups was harmonious.

Statistical analysis

The comparison of the joint replacement group and non-joint replacement group were performed by the absolute standardized differences (ASD). When the absolute standardized differences less than 0.1, the divergence of both groups were small [14]. Poisson regression model was used to calculate the relative risk (RR) between the joint replacement group and non-joint replacement group. Kaplan-Meier analysis was used to calculate the cumulative incidence of PAOD among the two groups and the significance was tested by the log-rank test. The multivariate Cox proportional hazard model was used to estimate the hazard ratios between both groups. To validate the robustness of the results, we conducted sensitivity analysis on a group of individuals diagnosed with osteoarthritis who underwent physical therapy within one year. Furthermore, we categorized the individuals into knee and hip group to perform their risk of peripheral arterial occlusive disease (PAOD). The SAS version 9.4 (SAS Institute Inc, Cary, NC, USA) was used for statistical analysis, with the significance level set at 0.05.

Results

Characteristics of the study subjects

In our study, 10,346 patients with joint replacement and 99,597 patients without joint replacement were identified. After the patients who were diagnosed with PAOD before the index date were excluded, and there remained

Table 1. Demographic characteristics of joint replacement and non-joint replacement

	Before PSM matching				After PSM matching			
	Non-Joint replacement (N = 93141)	Joint replacement (N = 9551)	*p* value	ASD	Non-Joint replacement (N = 9485)	Joint replacement (N = 9485)	*p* value	ASD
Age			< 0.001	-0.47			0.867	0.0024
< 65	53817 (57.78)	3328 (34.84)			3295 (34.74)	3306 (34.86)		
≥ 65	39324 (42.22)	6223 (65.16)			6190 (65.26)	6179 (65.14)		
Mean ± SD	61.58 ± 12.89	67.03 ± 11.19	< 0.001	0.45	67.12 ± 11.55	67.03 ± 11.19	0.556	0.009
Sex			< 0.001	0.05			0.534	0.009
Female	57922 (62.19)	6155 (64.44)			6079 (64.09)	6120 (64.52)		
Male	35219 (37.81)	3396 (35.56)			3406 (35.91)	3365 (35.48)		
Hypertension	32157 (34.53)	4529 (47.42)	< 0.001	0.264	4492 (47.36)	4501 (47.45)	0.896	0.002
Hyperlipidemia	14960 (16.06)	1707 (17.87)	< 0.001	0.048	1657 (17.47)	1688 (17.80)	0.555	0.009
Chronic liver disease	4752 (5.10)	544 (5.70)	0.0125	0.026	450 (4.74)	538 (5.67)	0.004	0.042
Chronic kidney disease	1330 (1.43)	246 (2.58)	< 0.001	0.082	186 (1.96)	244 (2.57)	0.005	0.041
Diabetes	13596 (14.60)	1771 (18.54)	< 0.001	0.106	1674 (17.65)	1751 (18.46)	0.146	0.021
Chronic obstructive pulmonary disease	3771 (4.05)	407 (4.26)	0.3165	0.011	308 (3.25)	401 (4.23)	0.000	0.052
Ischemic heart disease	8909 (9.57)	1118 (11.71)	< 0.001	0.069	994 (10.48)	1112 (11.72)	0.006	0.040
Stroke	4733 (5.08)	509 (5.33)	0.2948	0.011	399 (4.21)	508 (5.36)	0.000	0.054
Intracranial bleeding	376 (0.40)	36 (0.38)	0.6935	0.004	28 (0.30)	35 (0.37)	0.377	0.013
Deep vein thrombosis	65 (0.07)	28 (0.29)	< 0.001	0.053	23 (0.24)	24 (0.25)	0.884	0.002
Varicose veins of lower extremities	170 (0.18)	47 (0.49)	< 0.001	0.053	34 (0.36)	45 (0.47)	0.215	0.018
Psoriasis	247 (0.27)	24 (0.25)	0.8008	0.003	18 (0.19)	24 (0.25)	0.354	0.013
Antiplatelet	32523 (34.92)	4061 (42.52)	< 0.001	0.157	4033 (42.52)	4053 (42.73)	0.769	0.004
Anticoagulant	3564 (3.83)	607 (6.36)	< 0.001	0.115	515 (5.43)	603 (6.36)	0.007	0.039

Table 2. Poisson regression of relative risk of joint replacement and non-joint replacement

	Non-Joint replacement	Joint replacement
N	9485	9485
Person-years	72473	70501
No. of PAOD	513	473
ID (95% C.I.)	7.08 (6.49-7.72)	6.71 (6.13-7.34)
Relative risk (95% C.I.)	Reference	0.95 (0.84-1.07)

ID: incidence density (per 1000 person-years).

9,551 patients on joint replacement cohorts. To analyze the risk of PAOD, both cohorts were conducted with 1:1 propensity sore matching. Finally, 9,485 patients in the joint replacement cohort and 9,485 patients without joint replacement in matched cohorts were analyzed for their risk of PAOD (**Figure 1**). Demographic characteristics of both study cohorts are shown in **Table 1**. The mean age of joint replacement and non-joint replacement were 67.03 and 67.12 respectively. The majority was female (64%). After propensity score matching, all absolute standardized differences were less than 0.1. It appeared that the divergence of age, sex, comorbidities, and medications between both groups were minor. The mean follow-up duration of joint replacement and non-joint replacement was 7.4 years (SD: 4.4 years) and 7.6 years (SD: 4.5 years). The average time to PAOD onset of joint replacement and non-joint replacement was 5.0 years (SD: 3.7 years) and 5.1 years (SD: 3.8 years).

Influence of joint replacement and other related factors on PAOD risk

Next, Poisson regression was employed to compare the relative risk of joint replacement and non-joint replacement. The incidence density of PAOD in joint replacement and non-joint replacement group was 6.71 and 7.08 persons per 1,000 person-years. The relative risk was 0.95 (95% C.I. = 0.84-1.07) (**Table 2**). The cumulative incidence of PAOD risk revealed that it was not significant in either group (log-rank test, P = 0.400) (**Figure 2**).

Stratified analysis based on patients with different age, sex and comorbidities

When analyzing the risk of PAOD by Cox proportional hazard model, results indicated that

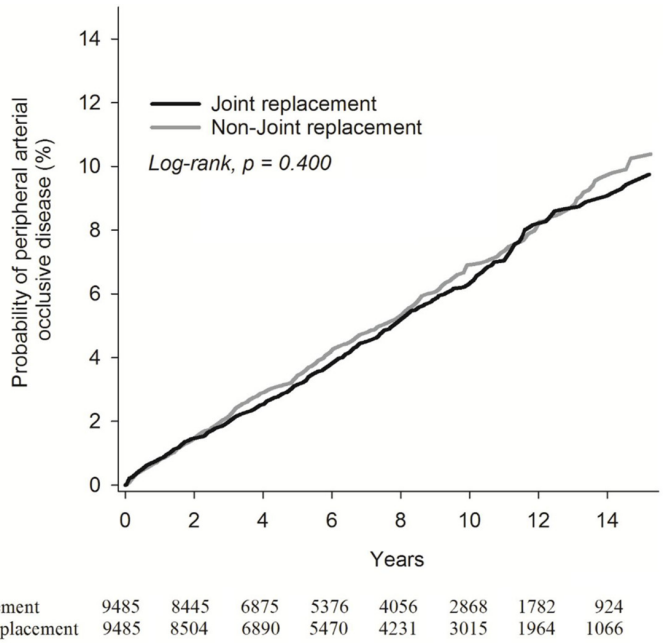


Figure 2. Kaplan-Meier curves of the cumulative proportions of PAOD in joint replacement and non-joint replacement patients.

the joint replacement group did not have a higher risk of PAOD risk (HR = 0.92; 95% C.I. = 0.81-1.04). The risk of PAOD was higher among patients aged equal or greater than 65 years (HR = 2.01; 95% C.I. = 1.72-2.35) compared with aged less than 65 years. Males (HR = 1.17; 95% C.I. = 1.02-1.33) had a higher risk of PAOD than females. In addition, comorbidities such as hypertension, chronic kidney disease, diabetes, ischemic heart disease, and stroke were higher risk factors of PAOD. Comparatively, the use of antiplatelets and anticoagulants had lower risk of PAOD (**Table 3**). A sensitivity analysis was performed on a population of osteoarthritis patients who had undergone physical therapy. After adjusting for age, sex, comorbidities, antiplatelets, and anticoagulants, the result revealed no difference in PAOD risk (HR = 1.27; 95% C.I. = 0.89-1.83) between the joint replacement group and the non-joint replacement group (**Table 4**). Further analysis of knee (HR = 1.23; 95% C.I. = 0.85-1.78) and hip replacement (HR = 2.05; 95% C.I. = 0.87-4.86) compared with non-joint replacement revealed that there was not significant association with peripheral arterial occlusive disease (**Table 5**). Furthermore, in subgroup analysis, the joint replacement group did not reveal significant risk of PAOD in different stratifications (**Figure 3**).

Discussion

In this study, a total of 9,485 patients who received joint replacement and same number of patients who have not received joint replacement were enrolled. The result of the Kaplan-Meier curve of the cumulative probability of PAOD did not show a positive relationship between the joint replacement group and the non-joint replacement group. The risk of PAOD events did not differ in either group in the Cox proportional hazard model. To date, few studies have reported either knee or hip joint replacement as a risk factor for the development of PAOD. A cohort study showed that hip replacement could increase the risk of peripheral arterial disease [15]. In contrast to earlier findings of Chou's study, our results indicated that there was no association between the risk of PAOD and hip replacement.

Joint replacement can affect the vascular system. Both arteries and vein injuries have been described in hip and knee arthroplasty. In a nationwide study, there was an average incidence of 13.74 per 100,000 person-years of cases of vascular injury in patients with total knee arthroplasty in Taiwan [16]. The complications involved both the vein and the artery. In vein injury, venous thromboembolism (VTE) is one of the leading causes of perioperative morbidity and mortality after TKA, but has never resulted in death [17]. In contrast to vein injury, artery injury is always acute and serious. In total hip arthroplasty, the incidence of vascular injury is 0.04% to 0.1%. Direct injury to the external iliac or common femoral artery is the most common cause of injury [18]. In total knee arthroplasty, the incidence of vascular injuries during arthroplasty ranges from 0.057% to 0.19%. The vessels most injured are the geniculate, popliteal, superficial, and anterior tibial arteries [19]. Indirect damage to the popliteal artery is more common, causing internal ruptures, thrombosis, and ischemia, but direct damage to the vascular system can occur [20].

Table 3. Cox proportional hazard model analysis for risk of PAOD

	Univariable		Multivariable†	
	HR (95% C.I.)	*p* value	HR (95% C.I.)	*p* value
Group				
Non-Joint replacement	Reference		Reference	
Joint replacement	0.95 (0.84-1.07)	0.400	0.92 (0.81-1.04)	0.194
Age				
< 65	Reference		Reference	
≥ 65	2.12 (1.83-2.47)	< 0.001	2.01 (1.72-2.35)	< 0.001
Sex				
Female	Reference		Reference	
Male	1.08 (0.95-1.23)	0.250	1.17 (1.02-1.33)	0.024
Hypertension	1.66 (1.46-1.88)	< 0.001	1.36 (1.19-1.57)	< 0.001
Hyperlipidemia	1.13 (0.96-1.34)	0.148	0.88 (0.74-1.05)	0.163
Chronic liver disease	1.31 (1.02-1.70)	0.037	1.22 (0.94-1.58)	0.131
Chronic kidney disease	3.68 (2.78-4.89)	< 0.001	2.87 (2.15-3.82)	< 0.001
Diabetes	1.79 (1.55-2.07)	< 0.001	1.60 (1.37-1.87)	< 0.001
Chronic obstructive pulmonary disease	1.43 (1.07-1.91)	0.016	1.16 (0.87-1.56)	0.317
Ischemic heart disease	1.60 (1.34-1.90)	< 0.001	1.37 (1.14-1.64)	< 0.001
Stroke	1.58 (1.23-2.03)	< 0.001	1.31 (1.02-1.70)	0.037
Intracranial bleeding	1.09 (0.35-3.38)	0.881	0.97 (0.31-3.03)	0.957
Deep vein thrombosis	2.20 (0.92-5.30)	0.078	1.89 (0.78-4.56)	0.160
Varicose veins of lower extremities	1.79 (0.89-3.58)	0.102	1.67 (0.83-3.36)	0.148
Antiplatelet	0.93 (0.82-1.06)	0.289	0.68 (0.52-0.90)	0.007
Anticoagulant	0.79 (0.60-1.04)	0.093	0.72 (0.63-0.82)	< 0.001

†Adjusted for age, sex, comorbidities, antiplatelet, and anticoagulant.

Various situations of postoperative arterial complications involving arteries after TKA such as hemorrhage and arterial transections, ischemia and thrombosis, pseudoaneurysm, were mentioned in a systemic review [21]. Although there is a lot of evidence to show that THA or TKA can contribute to both artery and vein injury, although it has not yet be proven that joint replacement increases the risk of PAOD.

Several risk factors for PAOD have been identified. Underlying diseases, such as hypertension, diabetes, ageing, and sex, are also risk factors for PAOD that have been reported for decades [22, 23]. Furthermore, systemic lupus erythematosus, cataract, hemorrhoids, migraine, were recently shown as risk factors in Taiwan's studies [24-27]. In our study, 65-year-old patients, men, and patients with diabetes were shown to have a higher risk of developing PAOD.

Sex is a risk factor for PAOD, but data is inconsistent to whether men or women are more likely to have this risk. In our results, we observed that men had a higher risk of PAOD than women. Jacobi et al. and Yeh et al. obtained similar results and showed that men had a higher risk of PAOD in periodontitis patients [28, 29]. In contrast, two studies showed that women had a higher risk of PAOD. However, the impact of different comorbidities can affect the gender variation on the risk of PAOD [30]. For example, the risk of PAOD in women could involve a lack of sex hormone in postmenopausal women and an average of higher levels of C-reactive protein than in men [31, 32]. Furthermore, in type-2 diabetic patients, atherosclerotic lesions of the superficial femoral artery, deep femoral artery, and peroneal artery in the hip joint were significantly higher in women than in men. On the contrary, the atherosclerotic lesion of the common iliac artery was significantly higher in men than in women [33].

Our result showed that patients using antiplatelets and anticoagulants had a lower risk of

Table 4. Sensitivity analysis for risk of PAOD among joint replacement compared with non-joint replacement

	Univariable		Multivariable†	
	HR (95% C.I.)	*p* value	HR (95% C.I.)	*p* value
Group				
Non-Joint replacement	Reference		Reference	
Joint replacement	1.31 (0.91-1.88)	0.146	1.27 (0.89-1.83)	0.193
Age				
< 65	Reference		Reference	
≥ 65	1.97 (1.29-3.01)	0.002	1.86 (1.19-2.89)	0.006
Sex				
Female	Reference		Reference	
Male	1.20 (0.82-1.75)	0.353	1.16 (0.79-1.70)	0.463
Hypertension	1.55 (1.08-2.22)	0.018	1.27 (0.85-1.90)	0.243
Hyperlipidemia	1.01 (0.62-1.63)	0.972	0.78 (0.47-1.30)	0.345
Chronic liver disease	1.02 (0.47-2.18)	0.966	1.03 (0.47-2.23)	0.944
Chronic kidney disease	4.13 (1.92-8.91)	< 0.001	3.45 (1.57-7.58)	0.002
Diabetes	1.81 (1.21-2.71)	0.004	1.63 (1.05-2.53)	0.029
Chronic obstructive pulmonary disease	1.19 (0.49-2.91)	0.704	0.95 (0.38-2.34)	0.903
Ischemic heart disease	1.11 (0.64-1.90)	0.713	0.93 (0.53-1.64)	0.794
Stroke/TIA	2.32 (1.35-3.99)	0.002	1.86 (1.05-3.30)	0.033
Deep vein thrombosis	2.85 (0.40-20.37)	0.298	3.69 (0.50-27.16)	0.201
Antiplatelet	1.11 (0.78-1.60)	0.561	0.84 (0.57-1.25)	0.390
Anticoagulant	0.78 (0.34-1.78)	0.556	0.56 (0.24-1.30)	0.178

†Adjusted for age, sex, comorbidities, antiplatelet, and anticoagulant.

Table 5. Sensitivity analysis for risk of PAOD between knee and hip replacement compared with non-joint replacement

	Univariable		Multivariable†	
	HR (95% C.I.)	*p* value	HR (95% C.I.)	*p* value
Group				
Non-Joint replacement	Reference		Reference	
Knee replacement	1.25 (0.87-1.81)	0.234	1.23 (0.85-1.78)	0.273
Hip replacement	2.52 (1.08-5.89)	0.032	2.05 (0.87-4.86)	0.103

†Adjusted for age, sex, comorbidities, antiplatelet, and anticoagulant.

PAOD. Our findings confirm those of earlier studies showing that administration of antiplatelet and anticoagulant drugs could improve revascularisation or recanalisation in the obstructive arterial segment in PAOD patients and could also prevent cardiovascular diseases [34]. Another study indicated that Cilostazol, an anticoagulant, was shown to improve the severity of PAOD in diabetic patients [35]. Furthermore, our results also show that the joint replacement group did not reveal significant risk of PAOD in different stratifications including age, sex, comorbidities, antiplatelet, and anticoagulant. By undergoing surgery, patients can potentially experience significant improvements in their lower extremity function, overall mobility, and quality of life. We recommended that patients who consider lower extremity replacement surgery can alleviate their concerns due to possible complications of PAOD.

Limitations

This study has several limitations. First, the information recorded in NHIRD did not include patients' activity ability or personal behaviors,

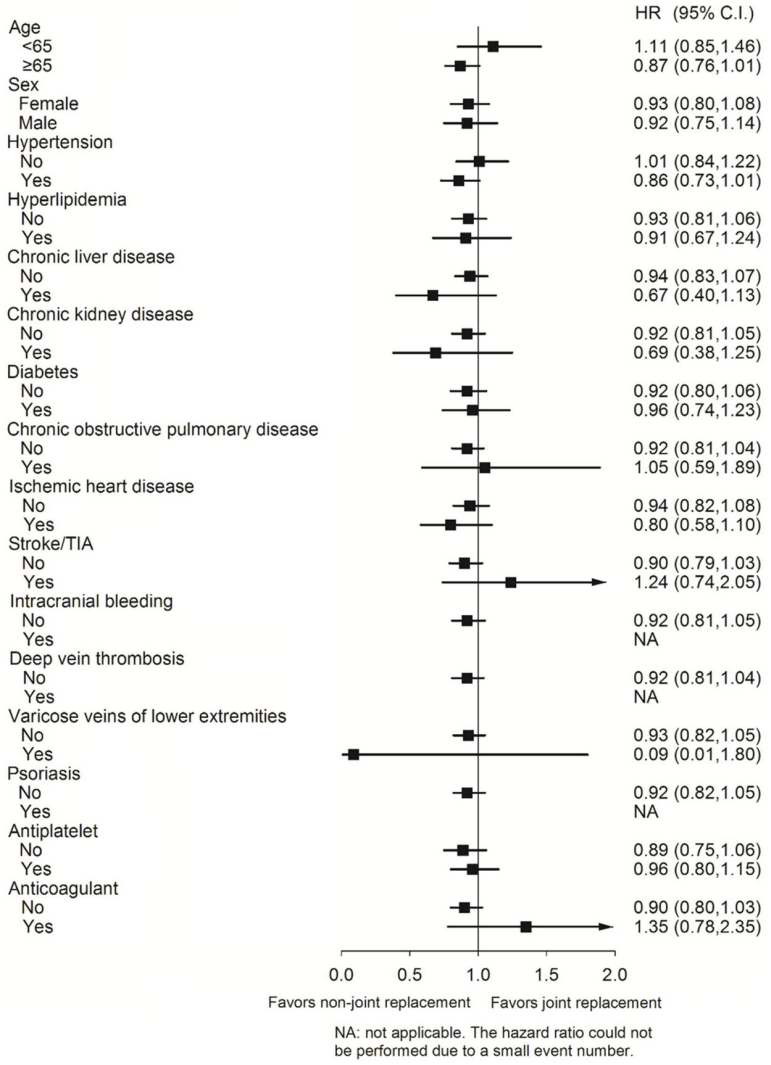


Figure 3. Forest plot of subgroup analysis for risk of PAOD in joint replacement and non-joint replacement patients.

such as smoking, obesity, or Activities of Daily Living (ADL). These factors also influence the risk of PAOD. Second, our results cannot be generalized to patients in other countries, primarily due to potential variations in the risk factors of PAOD based on race and the differing prevalence of joint replacements compared to other countries. Finally, further investigation is needed to explore the association between joint replacements and the risk of PAOD occurrence.

Conclusions

In summary, the findings of this cohort study showed that joint replacement is not associated with an increased risk of PAOD. Furthermore, the results remained robust in subgroups based on age, sex, and duration of follow-up. Due to the risk of PAOD, other unwarranted major risk factors should be considered in addition to joint replacement operation. Further research is needed to validate these findings.

Disclosure of conflict of interest

None

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