ORIGINAL ARTICLE

Cardiovascular disease risk in patients receiving organ transplantation: a national cohort study

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SUMMARY

Although organ transplantation is the definitive treatment for end-stage organ failure, the post-transplant outcomes can be substantially influenced by cardiovascular complications. A national cohort study was performed to estimate risks of cardiovascular diseases in those with heart, lung, kidney, and liver transplantation. This cohort study consisted of 5978 solid organ transplantations identified using the Taiwan National Health Insurance Database. Cardiovascular and mortality risks in transplant recipients were evaluated using standardized incidence ratios, excess absolute risks, and standardized mortality ratios as compared to those in the general population. In heart, kidney, and liver recipients, the standardized incidence ratios of overall cardiovascular diseases were 9.41 (7.75–11.44), 3.32 (2.29–3.77), and 1.4 (1.15–1.7) and the overall standardized mortality ratios were 5.23 (4.54–6.03), 1.48 (1.34–1.63), and 3.95 (3.64–4.28), respectively. Except for heart organ recipients who were at highest risk for coronary artery disease with a standardized incidence ratio of 13.12 (10.57–16.29), kidney and liver organ recipients had a ninefold increased risk in developing deep vein thrombosis post-transplant. In conclusion, solid organ transplant patients are at risk of cardiovascular disease, in particular, deep vein thrombosis, which may warrant early identification of high-risk patients in addition to prompt and adequate thromboprophylaxis perioperatively.

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Key words
cohort study, organ transplantation, population study, vascular disease risk

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Introduction

Solid organ transplantation has become the definitive and life-saving treatment for patients with end organ disease. Although graft complications and infections are still the main causes of mortality, long-term outcomes after transplantation can be substantially influenced by other postoperative complications

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related to thromboembolism and cardiovascular events [1–5].

Cardiovascular disease is a collective term encompassing disorders of the heart and blood vessels, including coronary artery disease (CAD), cerebrovascular disease, peripheral vascular disease, deep vein thrombosis (DVT), and pulmonary embolism (PE). In patients with end-stage renal disease, sudden cardiac death accounted for approximately 25% of all deaths in dialysis patients [6–8]. In renal transplant recipients, although cardiovascular mortality decreases after transplantation, the annual cardiovascular mortality still remained twofold higher than the general population and myocardial infarction is most common in elderly and diabetic patients [9]. Similarly, renal transplant recipients may have reduced risk of cerebrovascular events, and the risk of approximately 1% year incidence is still high compared to the general population [1,10]. The elevated risk is attributed to a set of traditional risk factors such as hypertension, dyslipidemia, diabetes [11], and nontraditional risk factors such as immunosuppression, anemia, inflammation, and proteinuria [12,13]. Not surprisingly, solid organ transplant recipients are also at higher risk of developing venous thromboembolism (VTE) postoperatively, with the reported cumulative incidence of approximately 5% VTE in liver transplant recipient [3,14,15], between 4.6% and 9.1% in kidney transplant recipients [16,17] and between 8.6% and 29% in heart/lung transplant recipients [5,18].

Recent investigations of major cardiovascular events in solid organ transplant recipients have been limited largely by retrospective, single-center data, mostly collected in the Western countries [3,15,19]. However, ethnic disparity may play an important part in the risk of cardiovascular events among Asian organ transplant recipients [20,21]. As Taiwan launched the National Health Insurance (NHI) Program in 1995, with nationwide coverage, the National Health Insurance Research Database (NHIRD) has nationwide representation, large size, and accurate data on diagnosis of cardiovascular events, organ transplant, cohort nature, and long-term follow-up, thus allowing the study of the risk of cardiovascular complications and mortality in Taiwanese organ transplant recipients. This study aimed to estimate the incidence rates of coronary artery disease, cerebrovascular disease, peripheral vascular disease, and deep vein thrombosis in addition to mortality in patients who received heart, kidney, lung, or liver transplantation between 1996 and 2011 and were followed up until 2012.

Methods

This study was approved by the institutional review board of the Chang Gung Memorial Hospital, Taiwan (IRB104-6697B), and the National Health Research Institute, the data holder for the NHI research database. All personal information was fully encrypted; therefore, patient's informed consent was exempted.

Study population

A cohort was established by including all patients who received heart, lung, kidney, or liver transplantation between 1996 and 2011 in Taiwan. The NHIRD included all insurance claims data for the Taiwan NHI program. The NHI coverage rate was over 99.5% in 2010 [22]. The NHIRD was comprised of information about gender, date of birth, place of residence, insurance details (employment categories, sum of insurance amount, enrollment, and discharge date), dates of inpatient and outpatient visits, medical diagnoses, medical expenditures, prescription details, operations, and procedures. We excluded individuals without a valid insurance status, patients who did not undergo their organ transplantation in Taiwan, and patients who had preexisting vascular diseases prior to organ transplantation.

Ascertainment of solid organ transplant and cardiovascular diseases

We used the International Classification of Diseases, Ninth Revision (ICD-9) codes for heart (37.5), lung (33.5), kidney (55.69), and liver transplantation (50.5); and the ICD-9 procedure codes for heart (V42.1), lung (V42.6), kidney (V42.0), and liver transplantation (V42.7) to identify patients who received these procedures in Taiwan between 1996 and 2011. Among the solid organ recipients, the ICD-9 diagnosis and procedure codes were used identify those with coronary artery disease (ICD-9 diagnosis codes ranged between 410 and 414 and procedure codes included 36.01, 36.02, 36.05, 36.07, 36.10, 36.11, 36.12) and cerebrovascular disease (ICD-9 diagnosis codes for ranged between 433 and 438 and procedure codes included 00.61, 00.63, 38.1). Also, diagnosis codes for peripheral vascular disease included 250.7, 443, 443.81, 443.9, 785.4, and 442.2 and procedure codes ranged between 84.10 and 84.18. Similarly, diagnosis codes for deep vein thrombosis included 451, 451.1, 451.11, 451.2, 451.81, 451.9, 453.0, 453.1, 453.2, 453.40-453.42, 453.8, and 453.9. The ICD

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coding for cardiovascular diseases has been previously verified [23–26].

Statistical analysis

Crude incidence rates of varied vascular diseases were calculated as the total number of vascular diseases occurred during the follow-up time divided by person-years at risk. Person-years at risk were defined as the sums of patients-time from the date of organ transplantation to vascular disease occurrence, death, deregistration, or December 31, 2012, whichever came first. For age-specific rates, patient age was shifted along with calendar year because these ages contributed data to successive five-year age groups over the follow-up period.

To measure the relative risk of vascular disease in patients receiving transplantation when compared with the general population, we calculated a standardized incidence ratio (SIR) for all types of vascular disease and specific vascular disease type (CAD, cerebrovascular disease, peripheral vascular disease, and DVT). SIRs were computed as the ratios of observed numbers of vascular disease to the expected number of vascular disease on the basis of age-specific incidence rates in five-year age intervals of the general population. Because there was no public data available on the incidence rate of cardiovascular diseases for Taiwan general population, we calculated these rates using the NHIRD. The age-specific incidence rate of cardiovascular diseases for Taiwan general population for each year from 1996 to 2012 was computed as the number of new cardiovascular disease cases in a specific calendar year divided by the population size in the same calendar year. We computed the excess absolute risk (EAR) of cardiovascular disease risk in patients receiving organ transplantation compared with the general population by subtracting the incidence rate of organ recipients from the incidence rate of the general population. We also calculated the standardized mortality ratio (SMR) for all-cause mortality. The SMR was the ratio of the observed number of deaths among organ transplantation recipients to the expected number of deaths in each sex and five-year age group by the corresponding national mortality rates in Taiwan. The mortality of the organ recipients was defined by the permanent deregistration from the NHI. The 95% confidence intervals (CIs) for the SIR, EAR, and SMR were calculated assuming the observed number of events being Poisson-distributed. All tests of statistical hypothesis were based on the two-sided 5% level of significance. All analyses were performed using SAS v. 9.3 (SAS Institute, Cary, NC, USA).

Results

Between 1996 and 2011, 7062 patients underwent organ transplantation, of which 1114 patients were excluded due to pre-existing vascular disease, leaving 5948 patients for statistical analysis (Fig. 1). Approximately 60% of organ recipients were male, and the mean age at transplant was 42.52 years. Of 5948 patients, some

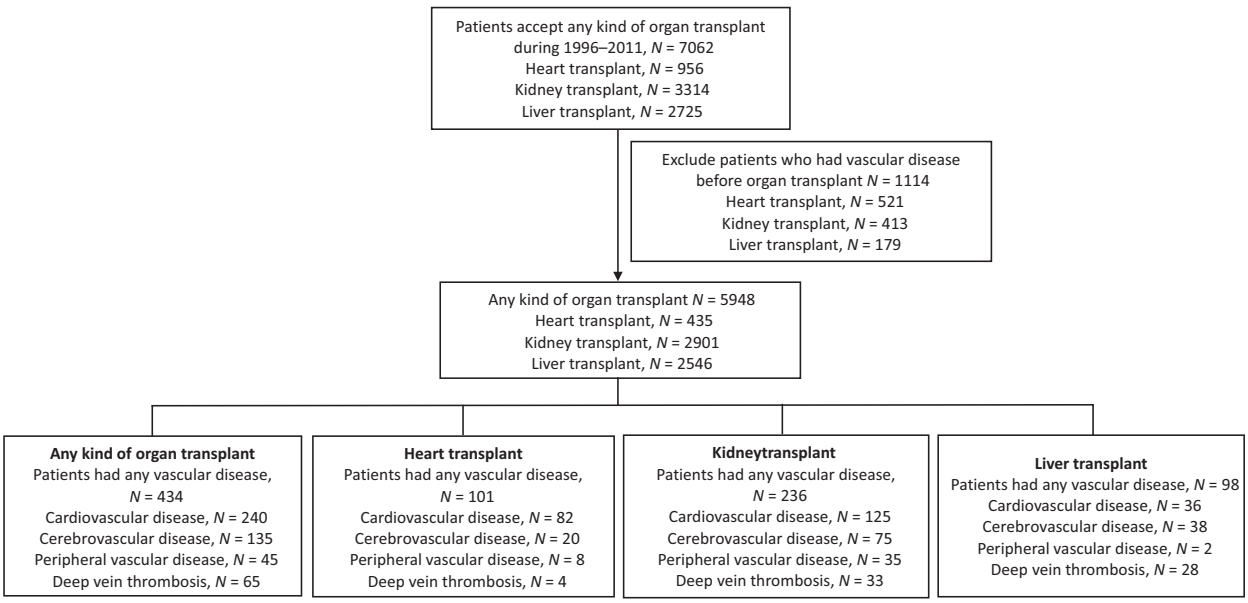

Figure 1 Flowchart of including organ transplant patients during 1996–2011.

received more than one solid organ transplantations, giving a total of 5978 transplantations. The most commonly transplanted organ was the kidney (48.52%), followed by the liver (42.59%), the heart (7.28%), and the lung (1.61%). Overall, more males received organ transplantation, in which male transplant recipients predominated in heart and liver transplantation while female recipients slightly predominated in kidney and lung transplantation (Table 1). Recipients of kidney and liver transplantation appeared to have a higher socioeconomic status than heart and lung recipients.

The mortality rate (per 1000 person-years) was highest for lung recipients (274.9), followed by heart (81.57), liver (55.25), and kidney (20.88). The mortality was significantly higher in patients receiving organ transplantation than the general population, with a SMR of 2.68 (95% CI, 2.53–2.83). Again, patients receiving lung transplantation had the highest SMR (16.05, 95% CI, 12.67–20.32), followed by heart recipients (SMR = 5.23, 95% CI, 4.54–6.03), liver recipients (SMR = 3.95, 95% CI, 3.64–4.28), and kidney recipients (SMR = 1.48, 95% CI, 1.34–1.63). Figure 2 showed the

Table 1. Demographic characteristics and mortality of solid organ transplant recipients from 1996 through 2011 in Taiwan.

Variables	All types of transplant	Heart	Kidney	Lung	Liver
No.	5978	435	2901	96	2546
Age (years) (mean ± standard deviation)	42.51 ± 15.67	39.64 ± 16.10	40.76 ± 12.30	42.51 ± 11.61	44.98 ± 18.55
Sex					
Male	3561 (59.57)	319 (73.33)	1435 (49.47)	44 (45.83)	1763 (69.25)
Female	2417 (40.43)	116 (26.67)	1466 (50.53)	52 (54.17)	783 (30.75)
Place of residence, no. (%)					
Urban	1957 (32.74)	145 (33.33)	1078 (37.16)	31 (32.29)	703 (27.61)
Suburban	1730 (28.94)	119 (27.36)	861 (29.68)	27 (28.13)	723 (28.40)
Rural	2120 (35.46)	156 (35.86)	886 (30.54)	36 (37.50)	1042 (40.93)
Unknown	171 (2.86)	15 (3.45)	76 (2.62)	2 (2.08)	78 (3.06)
Income levels, no. (%)					
Quintile 1	990 (16.56)	86 (19.77)	487 (16.79)	24 (25.00)	393 (15.44)
Quintile 2	643 (10.76)	66 (15.17)	357 (12.31)	11 (11.46)	209 (8.21)
Quintile 3	1636 (27.37)	102 (23.45)	794 (27.37)	30 (31.25)	710 (27.89)
Quintile 4	1264 (21.14)	87 (20.00)	567 (19.54)	16 (16.67)	594 (23.33)
Quintile 5	1380 (23.08)	85 (19.54)	674 (23.23)	14 (14.58)	607 (23.84)
Unknown	65 (1.09)	9 (2.07)	22 (0.76)	1 (1.04)	33 (1.30)
Occupation, no. (%)					
Dependents of the insured individuals	1501 (25.11)	113 (25.98)	565 (19.48)	21 (21.88)	802 (31.50)
Civil servants, teachers, military personnel and veterans	298 (4.98)	17 (3.91)	156 (5.38)	3 (3.13)	122 (4.79)
Nonmanual workers and professionals	1511 (25.28)	124 (28.51)	860 (29.64)	19 (19.79)	508 (19.95)
Manual workers	2120 (35.46)	123 (28.28)	1049 (36.16)	38 (39.58)	910 (35.74)
Other	548 (9.17)	58 (13.33)	271 (9.34)	15 (15.63)	204 (8.01)
Person-years of follow-up (years)	33 264	2329	19 969	251	10 715
Died (per 1000 person-years)	1268 (38.12)	190 (81.58)	417 (20.88)	69 (274.90)	592 (55.25)
SMR (95% CI)	2.68 (2.53–2.83)	5.23 (4.54–6.03)	1.48 (1.34–1.63)	16.05 (12.67–20.32)	3.95 (3.64–4.28)

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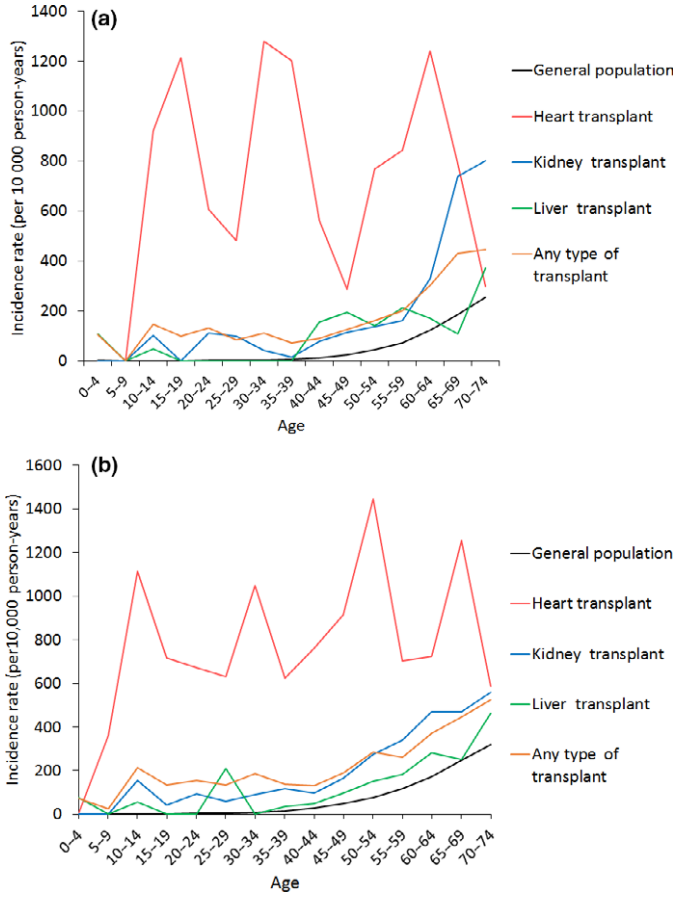

Figure 2 Age—and sex-specific vascular disease incidence rate by sex. Female (a) and male (b).

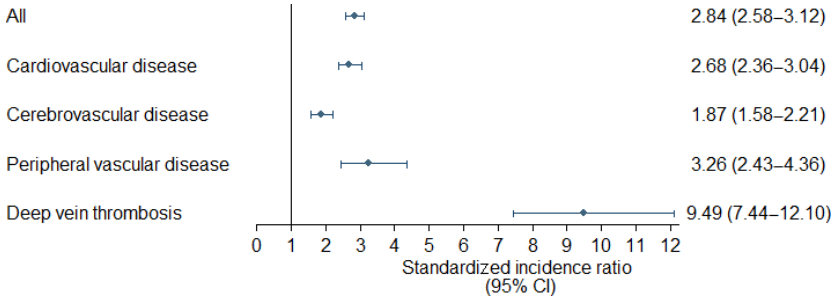

Figure 3 Risk of vascular disease in heart, kidney, liver, lung transplant recipients.

age- and sex-specific vascular disease incidence rate by sex.

Vascular risks relative to general population: all transplant recipients

After a total of 33 264 person-years of follow-up for the transplant recipients, 434 patients had overall vascular diseases, corresponding to an incidence rate of 130 per 1000 person-years. The risk of vascular diseases for the transplant recipients was significantly higher than that of the general population with a SIR of 2.84 (95% CI, 2.58–3.12). Among overall vascular diseases, deep vein thrombosis was the vascular disease with the highest SIR (9.49, 95% CI, 7.44–12.10), followed by peripheral vascular disease with a SIR of 3.26 (95% CI, 2.43–4.36), coronary artery disease with a SIR of 2.68 (95% CI, 2.36–3.04), and cerebrovascular disease with a SIR of 1.87 (95% CI, 1.58–2.21), when compared with the general population (Fig. 3). Figure 4 showed cumulative

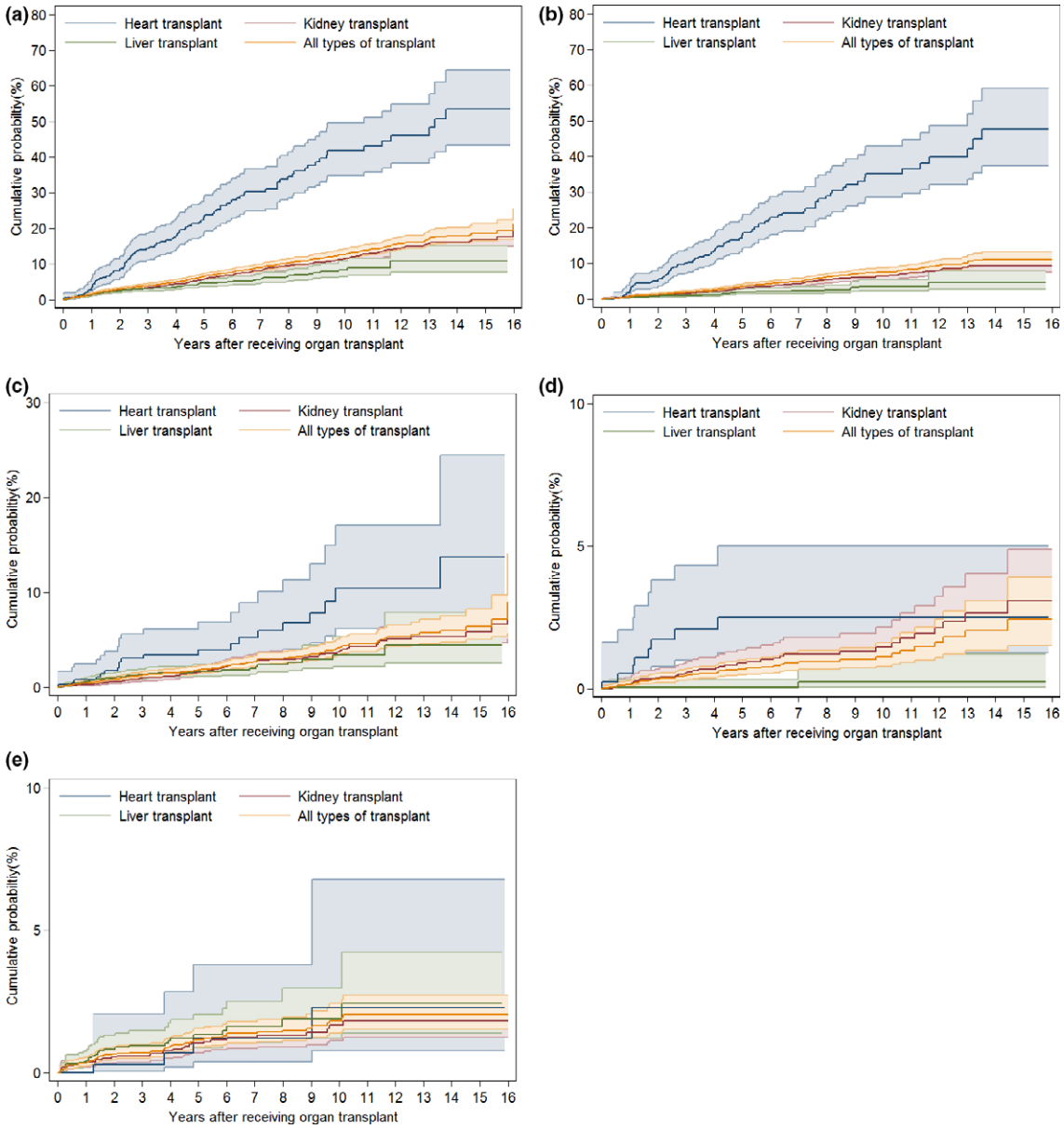

Figure 4 Cumulative probability of vascular disease from years after organ transplant. Any kind of vascular disease (a), cardiovascular disease (b), cerebrovascular disease (c), peripheral vascular disease (d), and deep vein thrombosis (e).

Table 2. Risk of vascular disease in heart transplant recipients.

	Heart			Incidence/10 000*		EAR/10 000
	Observed no.	Expected no.	SIR (95% CI)	Observed	Expected	Person-years (95% CI)
All	101	10.7	9.41 (7.75–11.44)	512.8	54.5	458.3 (362.5–551.2)
Coronary artery disease	82	6.3	13.12 (10.57–16.29)	416.3	31.7	384.6 (299.1–472.5)
Cerebrovascular disease	20	5.3	3.78 (2.44–5.86)	101.5	26.9	74.7 (37.6–114.7)
Peripheral vascular disease	8	1.0	7.77 (3.88–15.53)	40.6	5.2	35.4 (14.3–73.2)
Deep vein thrombosis	4	0.4	9.30 (3.49–24.79)	20.3	2.2	18.1 (5.5–52)

*During 1969.51 person-years.

probability of different types of vascular disease from years after organ transplant.

Vascular risks relative to general population: by transplanted organ

The incidence of vascular disease was highest in patients receiving heart transplantation (512.8 cases per 100 000 person-years) followed by those receiving kidney (123.4 per 100 000 person-years) and liver (93.7 cases per 100 000 person-years) (Fig. 3).

Among heart transplant recipients, the risks of all types of vascular diseases were elevated with an overall SIR of 9.41 (95% CI, 7.75–11.44) and EAR of 458.3 per 10 000 person-years (95% CI, 362.5–551.2). Heart recipients also appeared to be at high risk of developing coronary artery disease, in association with the highest SIR of 13.12 (95% CI, 10.57–16.29), followed by deep vein thrombosis with a SIR of 9.30 (95% CI, 3.49–24.79) and peripheral vascular disease with a SIR of 7.77 (95% CI, 3.88–15.53) (Table 2).

Among kidney recipients, deep vein thrombosis occurred more frequently than other types of vascular with an SIR of 9.46 (95% CI, 6.72–13.3) and EAR of 15.4 (95% CI, 10.1–21.3) followed by peripheral vascular disease with a SIR of 5.24 (95% CI, 3.76–7.3) and EAR of 14.8 (95% CI 9.2–20.1). These patients also had higher risk of developing coronary artery disease and cerebrovascular disease with SIR of 3.07 (95% CI, 2.57–3.66) and 2.29 (95% CI, 1.83–2.87), respectively (Table 3). Similar to kidney transplant recipients, liver transplant recipients were at high risk of developing deep vein thrombosis with a SIR of 9.69 (95% CI, 6.69–14.03) and EAR of 24 (95% CI, 14.5–33.3) (Table 4). We observed that kidney and heart transplant recipients were at higher risks of developing various types of vascular disease and all transplant recipients, regardless of the organ transplanted, were at least ninefold more likely to develop deep vein thrombosis during post-transplant years as compared to the general population.

As previously stated, in this cohort study, patients with existing vascular disease were initially excluded to give a picture of newly developed cardiovascular disease after organ transplantation. However, whether existing cardiovascular disease had any effects on the development of new cardiovascular events after organ transplantation was further evaluated and demonstrated as Table 5, in which SIRs were calculated in patients with previous cardiovascular disease for each organ transplantation group. As shown in the Table 5, for heart transplant recipients with previous cardiovascular disease, they have demonstrated an overall SIR of 5.13 (95% CI 4.20–6.26) as compared to a SIR of 9.41 in those without previous cardiovascular disease. Interestingly, such

Table 3. Risk of vascular disease in kidney transplant recipients.

	Kidney			Incidence/10 000*		EAR/10 000
	Observed no.	Expected no.	SIR (95% CI)	Observed	Expected	Person-years (95% CI)
All	236	71.2	3.32 (2.92–3.77)	123.4	37.2	86.2 (73.1–99.4)
Coronary artery disease	125	40.7	3.07 (2.57–3.66)	65.3	21.3	44.0 (34.5–53.3)
Cerebrovascular disease	75	32.8	2.29 (1.83–2.87)	39.2	17.1	22.1 (15.3–28.6)
Peripheral vascular disease	35	6.7	5.24 (3.76–7.3)	18.3	3.5	14.8 (9.2–20.1)
Deep vein thrombosis	33	3.5	9.46 (6.72–13.3)	17.3	1.8	15.4 (10.1–21.3)

*During 19129.5 person-years.

Table 4. Risk of vascular disease in liver transplant recipients.

	Liver			Incidence/10 000*		EAR/10 000
	Observe d no.	Expected no.	SIR (95% CI)	Observed	Expected	Person-years (95% CI)
All	98	70.2	1.40 (1.15–1.7)	93.7	67.1	26.6 (16.8–36.7)
Coronary artery disease	36	42.1	0.85 (0.62–1.18)	34.4	40.3	−5.9 (−12.5 to −2.1)
Cerebrovascular disease	38	33.9	1.12 (0.82–1.54)	36.3	32.4	3.9 (1–9.8)
Peripheral vascular disease	2	6.0	0.33 (0.08–1.33)	1.9	5.8	−3.8 (−9.8 to −1)
Deep vein thrombosis	28	2.9	9.69 (6.69–14.03)	26.8	2.8	24.0 (14.5–33.3)

*During 10463.58 person-years.

Table 5. Patients with existing cardiovascular disease prior to organ transplantation.

Type of transplant/outcome	Observed no.	Expected no.	SIR (95% CI)
Heart transplant recipients			
All	97	18.91	5.13 (4.20–6.26)
Coronary artery disease	77	11.20	6.88 (5.50–8.60)
Cerebrovascular disease	15	9.72	1.54 (0.93–2.56)
Peripheral vascular disease	12	1.75	6.86 (3.89–12.1)
Deep vein thrombosis	3	0.68	4.41 (1.42–13.7)
Kidney transplant recipients			
All	47	10.28	4.57 (3.44–6.09)
Coronary artery disease	29	6.06	4.79 (3.33–6.89)
Cerebrovascular disease	7	5.04	1.39 (0.66–2.91)
Peripheral vascular disease	14	0.94	14. 9 (8.82–25.2)
Deep vein thrombosis	9	0.45	20.0 (10.4–38.4)
Liver transplant recipients			
All	8	4.53	1.77 (0.88–3.53)
Coronary artery disease	3	2.73	1.10 (0.35–3.41)
Cerebrovascular disease	4	2.33	1.72 (0.64–4.57)
Peripheral vascular disease	1	0.41	2.44 (0.34–17.3)
Deep vein thrombosis	0	0.19	–

pattern is not observed for kidney and liver transplant recipients. Among other organ transplant recipients with previous cardiovascular disease, kidney transplant recipients had a SIR of 4.57 (95% CI 3.44–6.09) and liver transplant recipients had a SIR 1.77 (95% CI 0.88–3.53) as compared to SIR of 3.32 (95% CI 2.92–3.77) and 1.40 (95% CI 1.15–1.7) without previous cardiovascular disease, respectively.

Additionally, comorbidities such as diabetes mellitus (DM) have also gained our interest during cohort analysis. As shown in Table 6, recipients without DM appeared to have higher risks for cardiovascular disease after organ transplantation than those with DM. Patients with DM had highest risk for deep vein thrombosis than coronary artery disease, cerebrovascular disease, or peripheral vascular disease, with a SIR of 6.25 (95% CI 2.02–19.4), 6.02 (95% CI 3.24–11.2), and 3.02 (95% CI 1.44–6.33) after heart, kidney, and liver transplantation, respectively. In the non-DM group, kidney and liver transplant recipients were similarly at highest risk for DVT with SIR of 10.3 (95% CI 6.85–15.5) and 14.6 (95% CI 9.51–22.4), respectively. However, heart transplant recipients were at highest risk for coronary artery disease with SIR 13.9 (95% CI 10.6–18.4).

Discussion

In this cohort study, we demonstrated that organ transplant recipients were at a roughly threefold risk of developing any type of vascular disease, which is a major cause of morbidity and mortality after organ transplantation. Besides the high risk of CAD among heart transplant recipients, DVT accounted for the majority of cardiovascular complications in heart, kidney, and liver transplant recipients.

Few recent studies have demonstrated a roughly 5% incidence of DVT and/or PE after liver transplantation [3,14,27]. As the majority of coagulation factors and inhibitors as well as components of fibrinolytic systems are synthesized by liver, liver transplant recipients demonstrated transient liver dysfunction, such as prolonged prothrombin time, activated partial thromboplastin time (aPTT), and low platelet count, which had led to the belief that such dysfunction could lead to higher bleeding tendency, which in turn might exert a protective effect against DVT. However, a growing body of evidence has established that patients with cirrhosis and those after liver transplantation may actually demonstrate a hypercoagulative state during and after the transplant procedure [28]. As complex and unpredictable in onset and severity, a few risk factors for venous thromboembolism after liver transplantation were identified, for example, prolonged immobilization, administration of excessive procoagulant factors, and peripherally inserted central catheter lines [14,15]. Other factors involved defects in the proteins that normally regulated anticoagulation, such as protein C, protein S, and antithrombin deficiency, transmitted from donors to recipients [29–32], and this can be missed

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Table 6. Effect of diabetes mellitus on cardiovascular disease after organ transplantation.

	DM			Non-DM		
Type of transplant/outcome	Observed no.	Expected no.	SIR (95% CI)	Observed no.	Expected no.	SIR (95% CI)
Heart transplant recipients						
All	38	17.11	2.22 (1.62–3.05)	63	6.22	10.1 (7.91–13.0)
Coronary artery disease	32	9.54	3.35 (2.37–4.74)	50	3.59	13.9 (10.6–18.4)
Cerebrovascular disease	4	8.82	0.45 (0.17–1.21)	16	2.88	5.56 (3.40–9.07)
Peripheral vascular disease	5	3.22	1.55 (0.65–3.73)	3	0.36	8.33 (2.69–25.84)
Deep vein thrombosis	3	0.48	6.25 (2.02–19.4)	1	0.28	3.57 (0.50–25.35)
Kidney transplant recipients						
All	91	46.88	1.94 (1.58–2.38)	145	40.34	3.59 (3.05–4.23)
Coronary artery disease	47	26.88	1.75 (1.31–2.33)	78	22.60	3.45 (2.76–4.31)
Cerebrovascular disease	26	23.20	1.12 (0.76–1.65)	49	17.49	2.80 (2.12–3.71)
Peripheral vascular disease	24	8.43	2.85 (1.91–4.25)	11	2.55	4.31 (2.39–7.79)
Deep vein thrombosis	10	1.66	6.02 (3.24–11.2)	23	2.23	10.3 (6.85–15.5)
Liver transplant recipients						
All	49	72.10	0.68 (0.51–0.90)	49	31.95	1.53 (1.16–2.03)
Coronary artery disease	24	42.89	0.56 (0.38–0.83)	12	18.89	0.64 (0.36–1.12)
Cerebrovascular disease	19	36.81	0.52 (0.33–0.81)	19	14.46	1.31 (0.84–2.06)
Peripheral vascular disease	1	12.05	0.08 (0.01–0.59)	1	1.48	0.68 (0.10–4.80)
Deep vein thrombosis	7	2.32	3.02 (1.44–6.33)	21	1.44	(9.51–22.4)

preoperatively if donors were not screened for thrombophilic abnormalities.

Similarly, kidney and heart transplant recipients have been reported to be at risk of venous thromboembolism as mentioned previously [16,18,33–35]. In heart transplant recipients, Elboudwarej *et al.* [19] even demonstrated that lower extremity DVT posed a high risk of pulmonary embolism and death despite use of thromboprophylactic regimens. In kidney transplant recipients, evidence has shown platelet hypercoagulability plays an important role in increasing the risk of venous thromboembolism, leading to graft loss as a consequence [36,37]. Thus far, no guideline is available to start chemical DVT prophylaxis postoperatively.

As this is a retrospective cohort study, limitations apply. First, we could be biased by selection and information inherent to this type of study. However, as our cohort study included large size and the representative sampling of all Taiwanese transplant recipients, this may adequately allow an overview and comparison of vascular risk across transplanted organs in the Asian population. Our choice to stratify patients based on gender, age, socioeconomic status, and transplanted organ provided major demographic and clinical characteristics related to vascular risk. Other limitations included the lack of relevant laboratory data such as coagulation profile and possible asymptomatic VTE that was not recorded and the use of medications such as immunosuppressants and anticoagulants. In addition, cardiovascular disease-related mortality may provide further information on vascular risk, but only the all-cause mortality rate was determined in the current study. Meanwhile, large, randomized, prospective studies will be needed to guide the clinicians in improving outcomes in the post-transplant period.

In clinical practice, it can be difficult for clinicians to determine the state of coagulation postoperatively, especially when the recipients are usually started on immunosuppressive drugs such as cyclosporine, tacrolimus, and dexamethasone, which may also play a role in increasing platelet aggregation and thrombogenicity [38]. There is still limited evidence regarding venous thromboembolism in organ transplant recipients in the immediate postoperative phase. Our studies showed that solid organ transplant patients were at risk of deep vein thrombosis. The use of thromboprophylaxis such as low dose unfractionated heparin or low molecular weight heparin in patients after solid organ transplantation might reduce the risk without elevating the risk of bleeding [15,39].

In conclusion, solid organ transplant patients are at risk of cardiovascular disease, in particular, deep vein thrombosis. The decision to start DVT prophylaxis postoperatively should be made on a case-by-case basis in an effort to reduce the incidence of venous thrombosis.

Authorship

HIT: contributed to the concept of the work, drafted initial manuscript, edited the manuscript and approved the final manuscript. FCL: collected data, drafted initial manuscript, edited the manuscript and approved the final manuscript. CWL: collected data, drafted initial manuscript and approved the final manuscript. CFK and LCS: contributed to the concept of the work and interpretation of results, edited and approved manuscript. TTC: performed statistical analysis and approved manuscript. HPY: contributed to the concept of the work, drafted manuscript, revised and approved final manuscript.

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Conflicts of interest

The authors report no conflicts of interest.

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