ORIGINAL RESEARCH

Risk of Heart Disease in Patients With Amputation: A Nationwide Cohort Study in South Korea

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BACKGROUND: Amputation confers disabilities upon patients and is linked to substantial morbidity and death attributed to heart disease. While some studies have focused on traumatic amputees in veterans, few studies have focused on traumatic amputees within the general population. Therefore, the present study aimed to assess the risk of heart disease in patients with traumatic amputation with disability within the general population using a large-scale nationwide population-based cohort.

METHODS AND RESULTS: We used data from the Korean National Health Insurance System. A total of 22 950 participants with amputation were selected with 1:3 age, sex-matched controls between 2010 and 2018. We used Cox proportional hazard models to calculate the risk of myocardial infarction, heart failure, and atrial fibrillation among amputees. Participants with amputation had a higher risk of myocardial infarction (adjusted hazard ratio [aHR], 1.30 [95% Cl, 1.14–1.47]), heart failure (aHR, 1.27 [95% Cl, 1.17–1.38]), and atrial fibrillation (aHR, 1.17 [95% Cl, 1.03–1.33]). The risks of myocardial infarction and heart failure were further increased by the presence of disability (aHR, 1.43 [95% Cl, 1.04–1.95]; and aHR, 1.38 [95% Cl, 1.13–1.67], respectively).

CONCLUSIONS: We demonstrate an increased risk of myocardial infarction, heart failure, and atrial fibrillation among individuals with amputation, and the risk further increased in those with disabilities. Clinicians should pay attention to the increased risk for heart disease in patients with amputation.

Key Words: amputation
cohort studies
heart diseases

mputation is the surgical removal of a limb or extremity that is performed under various medical conditions to sustain life. Amputation can leave patients with disabilities and is associated with significant death and morbidity.^{1,2} One of the major causes of increased mortality risk among patients with amputation is heart disease.^{3,4} Growing evidence has revealed

the association between amputation and various heart diseases.

Increased cardiac-related death in amputation has been investigated in previous cohort studies conducted in the United States. A cohort study of American Indians with diabetes demonstrated that 134 patients with lower extremity amputation showed

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Patients With Amputation and Heart Disease

CLINICAL PERSPECTIVE

What Is New?

- The population of patients with traumatic amputation is at increased risk of myocardial infarction, heart failure, and atrial fibrillation.
- Disability after amputation further increases the risk of heart disease.
- Amputation itself, rather than vascular causes, can contribute to developing heart disease.

What Are the Clinical Implications?

- This study highlights the importance of preventing heart disease in the population of patients with traumatic amputation.
- Clinicians should closely monitor patients after amputation and provide timely intervention.
- Implementing rehabilitation programs for patients with amputation with disabilities is essential to reduce their risk of developing heart disease.

Nonstandard Abbreviations and Acronyms

NDR National Disability RegistryNHIS National Health Insurance System

90% increased cardiovascular disease mortality risk compared with 1974 patients without amputation.⁵ A retrospective study on combat veterans with lower extremity amputation demonstrated an association between amputation and cardiovascular disease risk factors, including mean arterial pressure, triglycerides, and high-density lipoprotein cholesterol.⁶ The study further showed that individuals with bilateral lower limb amputation had a 2.25-fold higher risk of metabolic syndrome compared with those without amputation. In addition, a small cohort study with 162 participants with amputation reported a 3.78-fold risk for major cardiovascular events in people with transfemoral amputation compared with 1:10 age, sex, and residency duration matched controls.⁷ These studies assert that amputation is attributable to not only increasing mortality rates, but also to increasing the incidence of heart disease.

Most studies of patients with amputation have been conducted in the West and have focused on patients with amputations due to nontraumatic causes (Table S1). This is because in the United States, vascular diseases such as peripheral artery disease or as a result of diabetic comorbidity account for up to 81.9% of major causes of amputation.^{8,9} Therefore, interpretation of the association between amputation due to vascular cause and heart disease is based on patients who are already at risk for cardiovascular disease, so caution should be exercised in interpreting whether amputation itself increases the risk of heart disease. Traumatic amputation is the next most common cause, accounting for about 16.4% of patients with amputation,⁹ but most studies that focused on subjects with traumatic amputation were conducted with small sample sizes and were limited to lower extremity amputation because the participants were mainly veterans.^{6,10} In contrast, according to the fact sheet of amputees in Korea, upper limb amputation is more prevalent than lower limb amputation. As reported in 2020, traumatic injury due to accident is the most common cause of amputation, accounting for 92.9% of 122 240 patients with upper limb amputation and 76.3% of 49516 patients with lower limb amputation.¹¹ Therefore, it is possible to conduct research on patients with amputation due to traumatic causes in Korea using subjects from the general population instead of being limited to a specific group of veterans or patients with lower limb amputation, which will be helpful to better understand the cardiovascular effects of amputation itself. With this strength, we conducted the present study to investigate the risk of various heart diseases, including myocardial infarction (MI), heart failure (HF), and atrial fibrillation (AF), among patients with traumatic amputation using a nationwide, large, population-based cohort with consideration of the disability status of patients with amputation.

METHODS

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Data Source and Study Setting

This study was based on data provided by the National Health Insurance System (NHIS) in Korea. The NHIS provides mandatory universal health insurance to \approx 97% of the Korean population, and the Medical Aid program provides insurance to the remaining 3% of the population with the lowest income. The NHIS recommends general health screening for all insured individuals conducted at least biennially for the prevention and early detection of diseases, including cardiovascular disease.¹² The NHIS contains information on medical and social history, anthropometric measurements, and laboratory tests. In addition, the NHIS retains a medical treatment database that is based on medical expense claims from medical service providers. Therefore, the

NHIS incorporates an extensive health information data set of the entire Korean population.

Study Population

We identified 59392 participants with amputation that occurred between 2010 and 2018. The definition of amputation was based on the International Classification of Diseases, Tenth Revision (ICD-10) codes as follows: Z89 (acquired absence of limb), S48 (traumatic amputation of shoulder joint), S58 (traumatic amputation of forearm), S68 (traumatic amputation of wrist, finger), S78 (traumatic amputation of hip), S88 (traumatic amputation of knee), and S98 (traumatic amputation of ankle, toe). We included participants who underwent health screening within 2 years before the index date (n=27832). We then excluded participants who were aged <20 years (n=22), and those with a history of the following medical conditions: (1) diabetes with complications including ulcer of lower limb (ICD-10 codes E10.6, E11.6, E12.6, E13.6, E14.6, L97, or E11.621), (2) thromboangiitis obliterans (ICD-10 173.1), (3) arterial embolism and thrombosis (ICD-10 174), (3) MI (ICD-10 I21 or I22 with \geq 1 hospitalizations), (4) HF (ICD-10 I50 with \geq 1 hospitalizations), or (5) AF (ICD-10 I48 with ≥1 hospitalizations or at least 2 outpatient visits). Participants with missing information were excluded (n=1038), which resulted in a total of 22950 participants with amputation.

To select the control group, we conducted 1:3 age and sex matching serially year by year, ensuring that participants with amputation diagnosed in a specific year were matched to control participants who were alive during the same year. Each control participant was assigned an index date corresponding to the date of amputation for their matched participant with amputation. After applying the same exclusion criteria, a total of 76645 matched controls were included in the analysis. The selection process for the study population is illustrated in Figure 1.

This study was approved by the Institutional Review Board of Samsung Medical Center (Institutional Review Board File No. 2020-12-068). The review board waived written informed consent because the data are public and anonymized under confidentiality guidelines.

Severity of Disability Due to Amputation

To consider the effect of disability, we used disability grade registered in the NDR (National Disability Registry) of the Ministry of Health and Welfare.¹³ In Korea, people with a disability are registered to obtain social benefit from the government. Specialist physicians document the disability diagnosis with physical examination and radiographs, and submission of validated documents is required. The degree of disability ranges from grade 1, the most severe, to grade 6, the mildest (Tables S2 and S3). In general, the severity of disability varies depending on the site of proximal amputation. For example, grade 1 disability from upper extremity amputation is defined by amputation above the wrist joint of both arms, whereas grade 6 disability is defined by amputation of one thumb above the interphalangeal joint. In this study, those who were registered in the NDR within 1 year from the index date were classified as the disability group, and they were further divided into mild to moderate (grade 4–6) and severe (grade 1–3) disability groups.

Study Outcomes and Follow-Up

The study outcomes were newly diagnosed MI, HF, or AF on the basis of *ICD-10* codes during follow-up. MI was defined as a claim with *ICD-10* I21 or I22 codes with \geq 1 hospitalizations.^{14–16} HF was defined as a claim with an I50 code with \geq 1 hospitalizations.¹⁷ AF was defined as a claim with an I48 code with \geq 1 hospitalizations or at least 2 visits to an outpatient clinic.¹⁸ The cohort was followed from the index date to the first occurrence of MI, HF, AF, death, or until the last follow-up date (December 31, 2019), whichever came first.

Covariates

Sociodemographic information including age, sex, income level, and residential area were provided by the NHIS database. Alcohol consumption was divided into none, mild to moderate (<30 g of alcohol/day), and heavy (≥30 g/day) drinker. Smoking status was divided into never, former smoker, and current smoker. Regular physical activity was defined as either moderate physical activity for >30 minutes per session ≥5 days per week or vigorous physical activity for >20 minutes per session ≥3 days per week. Comorbidities were identified on the basis of claims data before the screening date and health screening results. Hypertension was defined as a claim with I10, I11, I12, I13, or I15 codes and antihypertensive medication, or systolic/diastolic blood pressure≥140/90 mmHg. Type 2 diabetes was defined as a claim with E11, E12, E13, or E14 codes and antidiabetic medication prescription or fasting glucose level≥126 mg/dL. Dyslipidemia was defined as a claim with an E78 code and lipid-lowering medications, or total cholesterol level≥240 mg/dL. To assess overall comorbidity load, we used the primary care equivalent of the Charlson comorbidity index based on the ICD-10 code.19

Statistical Analysis

Descriptive analysis of study subjects was performed to compare the basic characteristics of survivors with amputation and their matched controls. Cox proportional hazards regression analysis was performed to calculate hazard ratio (HR) and 95% CI for study



Figure 1. Study population flowchart.

outcomes among participants with amputation. Each study outcome event was followed, and analysis was performed independently. Model 1 was adjusted for age, sex, and Charlson comorbidity index. Model 2 was further adjusted for socioeconomic status (income level and place of residence), health behaviors (alcohol consumption, smoking, and regular physical activity), and comorbidities (hypertension, type 2 diabetes, and dyslipidemia). In addition, we used a 1-year lag sensitivity analysis to mitigate surveillance bias, where individuals with amputation are more likely to undergo medical examinations compared with those without amputation. This analysis excluded participants with end point occurrences within 1 year of follow-up, and the lag was calculated using a time-series analysis technique.²⁰ The operational definition of sensitivity analysis is illustrated in Figure S1.

Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC), and a *P* value <0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

Baseline characteristics of the study population are presented in Table 1. In participants with amputation, the mean age was 53.5 (SD, 12) years, and 76.5% were men. Compared with controls, participants with amputation had lower income and were more likely to live in a rural area, be heavy drinkers, be current smokers, and were less likely to engage in physical activity. They had more comorbidities, including hypertension and type 2 diabetes, and higher Charlson comorbidity index scores.

Variables	Matched controls (N=76645)	Individuals with amputation (N=22950)	P value			
Age, y	52.8±11.8	53.5±12.0	<0.001			
Sex, male	60046 (78.3)	17 551 (76.5)	<0.001			
Income (Medicaid+lowest 20%)	13219 (17.3)	4313 (18.8)	<0.001			
Place of residence (urban)	35088 (45.8)	7810 (34.0)	<0.001			
Alcohol consumption			<0.001			
None	32940 (43.0)	10 152 (44.6)				
Mild to moderate	35620 (46.5)	9717 (42.4)				
Heavy	8085 (10.6)	4027 (17.6)				
Smoking status			<0.001			
Never	33833 (44.1)	10 183 (44.4)				
Former	19 125 (25.0)	4859 (21.2)				
Current	23687 (30.7)	7908 (34.5)				
Regular physical activity	16852 (22.0)	4027 (17.6)	<0.001			
Body mass index, kg/m ²	24.2±3.1	24.1±3.1	<0.001			
Systolic blood pressure, mmHg	124.1±14.3	124.1±14.6	0.674			
Diastolic blood pressure, mmHg	77.5±9.8	77.4±10.0	0.168			
Fasting glucose, mg/dL	101.0±24.5	101.6±26.9	<0.001			
Total cholesterol, mg/dL	197.4±37.1	196.0±37.4	<0.001			
Comorbidities						
Hypertension	24298 (31.7)	7414 (32.3)	0.085			
Type 2 diabetes	8944 (11.7)	2825 (12.3)	0.008			
Dyslipidemia	19383 (25.3)	5631 (24.5)	0.021			
Charlson comorbidity index	1.1±1.5	1.4±1.6	<0.001			

Table 1. Baseline Characteristics of the Study Population

Data are presented as number (%) or mean±SD.

Risk of MI, HF, and AF Among Participants With Amputation

During a mean follow-up period of 5.2 (SD, 2.5) years, there were 335 incident MI cases (2.8 per 1000 person-years), 781 incident HF cases (6.5 per 1000 person-years), and 338 incident AF cases (2.8 per 1000 person-years) observed among participants with amputation (Table 2). Kaplan-Meier curves show that the incidence probabilities of MI, HF, and AF in participants with amputation was higher than controls (log-rank P<0.001; Figure 2). Compared with controls, participants with amputation had a higher risk of MI (adjusted HR [aHR], 1.30 [95% CI, 1.14-1.47]), HF (aHR, 1.27 [95% CI, 1.17-1.38]), and AF (aHR, 1.17 [95% CI, 1.03-1.33]). The risks were further increased by the presence of disability; MI (aHR, 1.43 [95% CI, 1.04-1.95]) and HF (aHR, 1.38 [95% Cl, 1.13-1.67]). In particular, those with severe disability had the highest risk of HF (aHR, 2.34 [95% CI, 1.62-3.38]). The consistent results were noted with a 1-year lag period (Table 3).

DISCUSSION

This nationwide, large, population-based cohort study to assess the risk of heart disease among patients with traumatic amputation with disabilities found that individuals with amputation are at higher risk of heart disease than patients without amputation, and the risk further increased with an increase in amputation severity, especially for HF.

Amputation and MI

Our study showed an increased risk for developing MI in patients with amputation. This result is concurrent with prior studies in which patients with amputation had greater risk for developing MI compared with patients without amputation.7,21,22 A possible explanation for the increased incidence of MI after amputation is due to the increased prevalence of traditional cardiovascular disease risk factors such as obesity, physical inactivity,²³ hypertension,²⁴ dyslipidemia,²⁵ and insulin resistance²⁶ among amputees. Amputation is also known to alter the structure of endothelial cells within coronary arteries, rendering them more susceptible to ischemia due to hemodynamic changes and arterial remodeling.²⁷ In terms of hemodynamic consequences, amputation increases both shear stress and circumferential arterial wall stress, thereby promoting a thrombotic and inflammatory environment in the vascular system.²⁸

		Myocardial infarction			Heart failure			Atrial fibrillation		
	N	Cases/IR	Model 1	Model 2	Cases/IR	Model 1	Model 2	Cases/IR	Model 1	Model 2
Matched controls	76645	844/2.0	1 (Ref.)	1 (Ref.)	1939/4.7	1 (Ref.)	1 (Ref.)	949/2.3	1 (Ref.)	1 (Ref.)
Individuals with amputation	22950	335/2.8	1.29 (1.14–1.47)*	1.30 (1.14–1.47)*	781/6.5	1.30 (1.20–1.42)*	1.27 (1.17–1.38)*	338/2.8	1.17 (1.03–1.32)*	1.17 (1.03–1.33)*
By presence o	By presence of disability									
No disability	21 135	293/2.6	1.3 (1.14–1.48)*	1.28 (1.12–1.46)*	677/6.1	1.29 (1.18–1.40)*	1.25 (1.15–1.37)*	293/2.6	1.15 (1.01–1.31)*	1.15 (1.01–1.31)*
Disability	1815	42/4.2	2.03 (1.49–2.77)*	1.43 (1.04–1.95)*	104/10.4	1.43 (1.17–1.74)*	1.38 (1.13–1.69)*	45/4.5	1.29 (0.95–1.73)	1.30 (0.97–1.76)
By severity of	disability									
Mild to moderate	1477	33/4.0	1.36 (0.96–1.92)	1.35 (0.95–1.92)	75/9.2	1.23 (0.98–1.55)	1.20 (0.95–1.51)	36/4.4	1.24 (0.89–1.73)	1.26 (0.90–1.76)
Severe	338	9/5.0	1.76 (0.91–3.40)	1.81 (0.94–3.49)	29/16.3	2.40 (1.66–3.46)*	2.34 (1.62–3.38)*	9/5.0	1.50 (0.78–2.89)	1.52 (0.79–2.94)

Table 2.	Hazard Ratios and 95% CIs for the Incidence of Heart Diseases Among Individuals With Amputation Compared
With the	Matched Controls

Model 1: adjusted for age, sex, and Charlson comorbidity index. Model 2: model 1+adjusted for socioeconomic position (income level and place of residence), smoking, alcohol consumption, physical activity, and comorbidities (hypertension, type 2 diabetes, and dyslipidemia). IR indicates incidence rate (numbers of cases per 1000 person-years).

*Significant at p<0.05.

Furthermore, shear stress has been demonstrated to affect the production of prostacyclin and plasminogen activators, which can be factors contributing to atherosclerosis.^{29–31} Atherosclerotic change was observed in an in vitro study with mice that underwent ligation of the right carotid artery,³² suggesting that vessel ligation due to amputation can result in arterial remodeling that leads to atherosclerosis. In addition, amputees exhibit increased levels of blood coagulating factors such as fibrinopeptide A and factor VII, and their higher coagulability may contribute to increased atherosclerosis and ischemic vascular injury.²⁵ Overall, altered hemodynamic changes, hyperinsulinemia, and increased sympathetic and

coagulation activity act as complex factors to explain increased risk for MI among individuals with amputation.

Amputation and HF

Our findings demonstrated that patients with amputation are at a greater risk of developing HF when compared with matched controls. A retrospective cohort study conducted in Scotland reported that the risk of HF was 1.95fold (95% CI, 1.14–3.33) higher in patients with incident lower extremity amputation,³³ which is consistent with the degree of risk in our study. Considering that the most common cause of HF is ischemic heart disease and





A, Myocardial infarction; (B) heart failure; (C) atrial fibrillation.

		Myocardial infarction			Heart failure			Atrial fibrillation		
	N	Cases/IR	Model 1	Model 2	Cases/IR	Model 1	Model 2	Cases/IR	Model 1	Model 2
Matched controls	76236	724/2.15	1 (Ref.)	1 (Ref.)	1753/5.2	1 (Ref.)	1 (Ref.)	810/2.4	1 (Ref.)	1 (Ref.)
Individuals with amputation	22701	272/2.8	1.24 (1.08–1.43)*	1.23 (1.07–1.42)*	685/7.0	1.28 (1.17–1.40)*	1.25 (1.14–1.37)*	283/2.9	1.16 (1.01–1.33)*	1.17 (1.02–1.34)*
By presence of	By presence of disability									
No disability	20920	241/2.7	1.24 (1.07–1.43)*	1.23 (1.06–1.43)*	598/6.7	1.27 (1.16–1.39)*	1.24 (1.13–1.36)*	244/2.7	1.14 (0.99–1.31)	1.15 (0.99–1.32)
Disability	1781	31/3.8	1.24 (0.07–2.02)*	1.24 (0.86–1.78)*	87/10.7	1.33 (1.07–1.65)*	1.30 (1.04–1.61)*	39/4.8	1.32 (0.96–1.82)	1.36 (0.98–1.87)
By severity of disability										
Mild to moderate	1457	26/3.9	1.25 (0.84–1.85)	1.24 (0.84–1.84)	67/10.0	1.23 (0.96–1.57)	1.19 (0.93–1.53)	31/4.6	1.25 (0.88–1.80)	1.29 (0.90–1.85)
Severe	324	5/3.4	1.19 (0.49–2.86)	1.21 (0.50–2.92)	20/14.0	1.88 (1.21–2.92)*	1.83 (1.18–2.84)*	8/5.6	1.65 (0.82–3.31)	1.71 (0.85–3.43)

Table 3.	Hazard Ratios and 95% CIs for the Incidence of Heart Diseases Among Individuals With Amputation Compared
With the	Matched Controls

The sensitivity analysis excluded participants with the occurrence of end points within 1 y of follow-up. Model 1: adjusted for age, sex, and Charlson comorbidity index. Model 2: model 1+adjusted for socioeconomic position (income level and place of residence), smoking, alcohol consumption, physical activity, and comorbidities (hypertension, type 2 diabetes, and dyslipidemia). IR indicates incidence rate (numbers of cases per 1000 person-years). *Significant at p<0.05.

the risk of MI increases in patients with amputation as mentioned above, the risk of developing HF of ischemic origin may be increased. In addition, changes in cardiac function that occur after amputation can increase the incidence of HF.^{26,34} For example, an increase in resting heart rate and blood pressure due to a decrease in functional capacity and an inability to increase stroke volume in work or stress may contribute to the development of HF.^{35–38} An additional explanation for the increased incidence of HF after amputation is an increased prevalence of traditional cardiovascular disease risk factors, including increased insulin resistance,^{24,25} arterial stiffness,^{35,39} and endothelial dysfunction.⁴⁰

Amputation and AF

In this study, amputation increased the incidence of AF, albeit to a lesser extent compared with MI and HF. As we show in the baseline characteristics, patients with amputation are prone to have more AF risk factors such as old age, alcohol consumption, and hypertension than the general population without amputation. In addition, physical or psychological stress may contribute to AF development.^{41–44} Previous studies reported that cardiovascular remolding after amputation such as increased arterial stiffness, thickened intima media, and higher pulse wave velocity, could result in AF development.⁴⁵

Patients With Amputation With Disabilities and Heart Disease

In our study, the risk of MI and HF was found to be even higher in patients with amputation with disabilities, and the risk of HF further increased by 2.34-fold in those with severe disabilities. Prior research has suggested that higher levels of amputations lead to greater hemodynamic changes and cardiovascular responses,^{46,47} supporting our result showing an increased risk of heart disease as the site of amputation becomes more proximal (Table S4). In a study involving patients with traumatic lower limb amputation,⁴⁷ patients with transfemoral amputation exhibited higher energy expenditure and more significant changes in the cardiovascular system compared with patients with transtibial amputation. In particular, patients with transfemoral amputation demonstrated an increase in oxygen consumption, which may indicate a reduction in cardiorespiratory fitness and could be a potential explanation for the increased risk of heart disease48 in patients with amputation with severe disabilities. Although there are not many comparative studies on heart disease risk specifically in patients with disabilities and amputation, psychological factors related to disability could be involved. Previous studies^{25,41-44,49} reported that psychological stress may increase sympathetic tone, blood coagulability, and shear stress force, which are changes contributing to an increased risk of heart disease. In addition, as the degree of disability becomes more severe in patients with amputation, they may become socially isolated and encounter environmental barriers that lead to a decrease in physical activity, an increase in obesity, and changes in lifestyle such as smoking and drinking alcohol, which are the factors that also contribute to an increased risk of heart disease.^{50,51} However, before and after comparison of health behaviors between the patients with amputation and matched controls revealed minimal differences in changes of smoking, drinking, and physical activity level between the 2 groups (Table S5). This suggests that, rather than traditional risk factors, hemodynamic changes resulting from amputation play a major role in the increased risk observed in patients with amputation.

Clinical Implications

Overall, our results highlighted the importance of preventing heart disease in patients with amputation, especially those with severe disabilities. It is notable that many cardiovascular disease risk factors can be modified through treatment.⁶ Therefore, clinicians should closely monitor patients after amputation and provide them with timely interventions such as relevant medications. It is also important to consider promptly implementing rehabilitation programs for patients with amputation with disabilities to improve their physical and mental well-being and reduce their risk of developing heart disease.

Limitations

Despite the strengths and the clinical implications, our study has some limitations. Since we used claims data, determining the precise cause of amputation beyond the information provided by ICD-10 codes poses a challenge. Nevertheless, we meticulously eliminated potential vascular causes of amputation through the use of ICD-10 codes. Moreover, our results show that patients with amputation with severe disabilities were at higher risk for only HF with statistical significance, despite the fact that MI and AF also showed increased risk in comparison with those with mild disabilities. This could be due to the smaller number of cases for MI and AF that were claimed as ICD-10 codes. Due to limited access to medical care for individuals with amputations, there is a possibility that the risk of heart disease may have been underestimated. Finally, generalization of our results requires caution due to the fact that the data primarily consisted of Korean participants.

CONCLUSIONS

Individuals with acquired amputation are at higher risk of developing heart disease than those without amputation, and the risk increases as the severity of disability increases. Our study suggests that timely preventive measures against cardiovascular disease should be taken for individuals who have undergone amputation.

ARTICLE INFORMATION

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None.

Supplemental Material

Tables S1–S5 Figure S1 References 5,52–54

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