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Tuberculosis and increased risk of cardio-cerebrovascular disease: A nationwide cohort study

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ABSTRACT

Objectives: To determine the association between tuberculosis (TB) and cardio-cerebrovascular diseases (CVDs).
Methods: This population-based retrospective study used National Health Insurance database to compare CVD incidence, including myocardial infarction (MI), arrhythmia, heart failure, and cerebrovascular accident (CVA), between TB survivors and 1:1 age-, sex-, income-, region-, and registration date-matched controls in Republic of Korea. Cox proportional hazard models were used to analyze associations between CVDs and TB.
Results: We assessed 70,458 individuals with TB and 70,458 matched controls. During a mean 70.2-month follow-up, CVD occurred in 4127 (5.9%) TB survivors and 3408 (4.8%) controls. The overall CVD incidence was 1035.24 and 801.46 per 100,000 person-years in the TB and control groups, respectively. Multivariable Cox proportional hazard analysis showed that TB was associated with a higher risk of overall CVD (adjusted hazard ratio [aHR] 1.305, 95% confidence interval [CI] 1.244-1.370), MI (aHR 1.245, 95% CI: 1.134-1.367), arrhythmia (aHR 1.417, 95% CI: 1.294-1.551), heart failure (aHR 1.666, 95% CI: 1.451-1.914), and CVA (aHR 1.133, 95% CI: 1.040-1.234) than matched controls.
Conclusion: We observed a higher CVD risk in TB survivors than in matched controls. Our findings indicate that preventive measures against CVDs should be considered for this population.

Introduction

Tuberculosis (TB) is one of the leading causes of illness and death worldwide [1]. Before the coronavirus disease 2019 (COVID-19) pandemic, TB was known to be the single infectious agent that caused the majority of deaths [1]. Accordingly, TB is recognized as a global public health emergency, and multiple efforts have been made to end the epidemic worldwide [2,3]. Consequently, improvements in the TB burden have been made through various efforts despite recent disruptions during the COVID-19 pandemic [4]. However, even after TB treatment, patients show higher long-term all-cause mortality and post-TB morbidity than the general population [5]. This might be because comorbidities are more common in TB survivors than in the general population, and several chronic diseases are associated with TB [5]. These chronic diseases are thought to contribute to high mortality rates. In addition, Romanowski et al. [5] suggested that patients might not engage in medical care after TB treatment completion, and this phenomenon might be attributable to the delay in the detection of recurrence or chronic diseases.

Cardio-cerebrovascular disease (CVD) is the most common chronic disease and one of the leading causes of death [6]. Furthermore, CVD is known to be the leading cause of death in TB

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survivors; several studies have suggested an association between TB and CVD, such as ischemic heart disease and stroke, and several mechanisms have been proposed [5–9]. However, the association between overall CVDs and TB has not yet been studied. As CVDs remain a leading cause of chronic disability and death worldwide, understanding the association between overall CVDs and TB is crucial to comprehensively understand the burden of TB [10]. Furthermore, given that developing countries such as China, India, and Indonesia are major contributors to the prevalence of TB and that the focus on CVDs is expected to grow in these regions as healthcare services improve, early diagnosing CVDs as well as any post-TB-related comorbidities is crucial for reducing the global disease burden of TB.

Therefore, we conducted this study to determine the association between TB and CVDs, including ischemic heart disease, cerebrovascular accident (CVA), heart failure, and arrhythmia, using a nationwide database in Republic of Korea.

Methods

Study design and data sources

This retrospective study compared the incidence of CVDs between TB survivors and matched controls in Republic of Korea using nationwide population data from the National Health Insurance Service (NHIS)-National Health Information Database (NHID). In Republic of Korea, the NHIS is a mandatory universal insurance system, and majority of the Korean population (97.1% in 2022) will subscribe to the NHIS [11]. The NHIS-NHID contains participants' identifiers, sex, birth date, income levels, residence, comorbidities, and claims data, such as prescription drugs and records of diagnoses indicated by the International Classification of Diseases 10th revision (ICD-10) codes. In addition, we merged the NHIS-NHID and National Health Insurance Service-Health Screening (NHIS-HEALS) databases, which contain information about height, weight, body mass index (BMI), blood pressure, questionnaires about alcohol consumption and smoking, and laboratory tests (fasting glucose, creatinine, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglyceride) obtained through a biennial health check-up mandatory for all insured citizens aged ≥40 years. In addition, physicians identifying newly diagnosed patients with TB must report new TB cases, and all patients with TB are given a rare intractable disease (RID) code that guarantees coverage of 90% of the medical costs in Republic of Korea. New TB cases are reported based on valid radiological and clinical findings, bacteriological diagnosis, or histological diagnosis.

Participants

We retrieved the data of patients newly diagnosed and treated for TB between January 2010 and December 2017. Among patients with an ICD-10 diagnosis code for TB, those who were assigned an RID code for TB were defined as patients with TB [12]. Additionally, patients aged <40 years were excluded to merge with the NHIS-HEALS database. Detailed information on the ICD-10 codes, RID codes, and definitions of TB is provided in Table S1.

The study population consisted of the following processes: In the NHIS database, we identified 518,396 patients with TB from 2010 to 2017, of which 270,753 cases were diagnosed with a first episode of TB after 2010. Among them, 187,766 patients with RID codes for TB were identified, and 158,550 patients remained after excluding those aged <40 years. To compare the CVD incidence, we extracted a control group of 792,750 patients without TB, matched at a 1:5 ratio according to sex, age, income level, region of residence, and registration date from the NHIS database.

Among the 158,550 patients in the TB group, 79,072 who underwent health check-ups within 2 years of the index date were included. After excluding those with a medical history of CVD during the 2-year washout period, a final case group of 70,458 patients was analyzed. Among the 792,750 patients in the control group, 420,775 who underwent health check-ups within 2 years were included. After excluding patients with a medical history of CVD during the 2-year washout period, 390,067 patients were identified. Among them, a matched control group of 70,458 individuals was composed of 1:1 propensity score matching (PSM) with the TB group based on sex, age, income, region, and index year.

Patient and public involvement

This research was conducted without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop outcome measures or interpret the results. Patients were not invited to choose the methods for dissemination of the study results.

Definition of study variables

In this study, CVDs included myocardial infarction (MI), arrhythmia, heart failure, and CVA. Furthermore, CVDs were identified using the ICD-10 diagnosis code, number of diagnoses in the NHIS, and claims for diagnostic tests or treatment. Detailed information on the definitions of CVD outcomes is provided in Table S2. To analyze baseline comorbidities, diabetes mellitus, hypertension, dyslipidemia, chronic kidney disease, end-stage renal disease, chronic liver disease, chronic obstructive pulmonary disease (COPD), and inflammatory diseases (rheumatoid arthritis, Crohn's disease, ulcerative colitis, ankylosing spondylitis, and psoriasis) were identified using ICD-10 diagnosis codes. Baseline comorbidities were defined as those confirmed up to 2 years prior to the index date. Detailed information on the ICD-10 codes and definitions of the comorbidities is provided in Table S1.

Statistical analysis

Categorical variables are presented as frequencies and percentages and were compared using the chi-squared test. Continuous variables are presented as mean and standard deviation and were compared using Student's *t*-test. The incidence rates of CVD were estimated by dividing the total number of CVD occurrences during the follow-up period by the total person-years at risk, and presented per 100,000 person-years. The cumulative incidences of specific CVDs according to the presence or absence of TB were plotted, and the differences in the cumulative incidences were analyzed using Gray's test. The association between CVDs and TB was analyzed using the Cox proportional hazards model. Covariates were incorporated into the multivariate analysis to calculate adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs), including age and sex (Model 1); Model 1 + hypertension, diabetes mellitus, and dyslipidemia (Model 2); and Model 2 + socioeconomic status, area of residence, BMI, alcohol consumption, smoking, regular exercise, fasting glucose, creatinine, and total cholesterol (Model 3).

Results

Baseline characteristics

During the study period, 70,458 individuals with TB were identified from the NHIS database and included in the study (Figure 1).

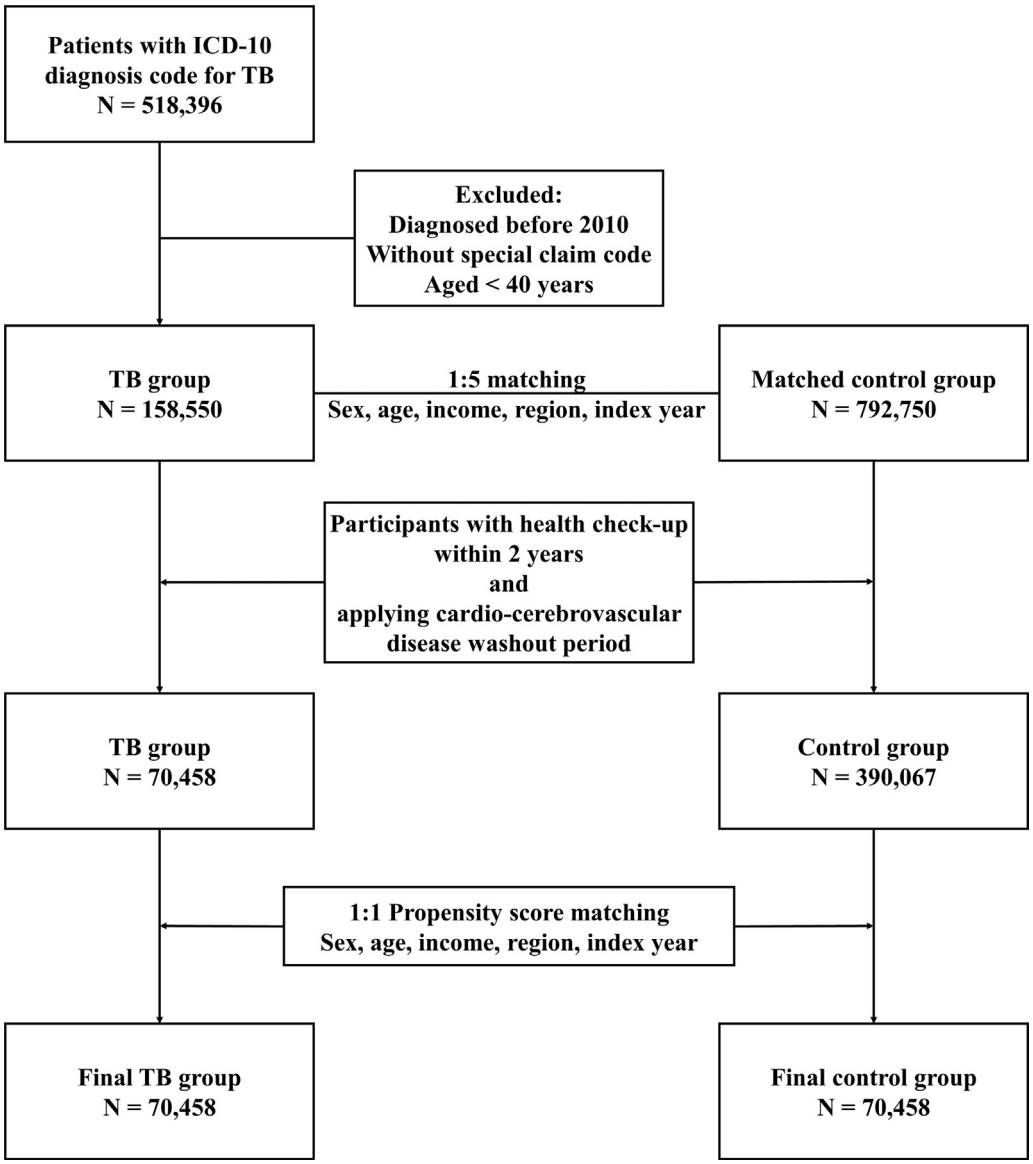

Figure 1. Flow chart of study participants.

After 1:1 PSM among the 390,067 control individuals, a final control group of 70,458 participants was established. The characteristics of both groups before and after PSM are presented in Table 1. After PSM, the median follow-up duration for the TB and control groups was 67.90 ± 30.78 and 72.42 ± 28.22 months, respectively. The mean age was 61.30 ± 12.58 years in the TB group and 61.13 ± 12.37 years in the control group. In both groups, 57.1% of the patients were men. After PSM, the standardized differences showed that both groups were balanced in terms of age, sex, income level, and residential area.

Association between TB and the incidence of CVDs

During the follow-up period, 7535 participants were diagnosed with CVDs (4127 in the TB group and 3408 in the control group). The incidence rate of CVD in the TB group was 1035.24 per 100,000 person-years and 801.46 per 100,000 person-years in the control group (Table 2). Multivariable Cox proportional hazard analysis showed that TB was associated with a higher risk of overall CVDs (Model 3: aHR: 1.305, 95% CI: 1.244-1.370, $P < 0.0001$) than the controls. When the risk of CVDs was analyzed in specific diseases, such as MI (aHR: 1.245, 95% CI: 1.134-1.367, $P < 0.0001$), arrhythmia (aHR: 1.417, 95% CI: 1.294-1.551, $P < 0.0001$), heart failure (aHR: 1.666, 95% CI: 1.451-1.914, $P < 0.0001$), and CVA (aHR: 1.133, 95% CI: 1.040-1.234, $P = 0.0043$), TB still showed significant associations in multivariable analyzes (Model 3, Figure 2). Cumulative incidence curves also showed a significantly higher incidence of CVDs in the TB group (overall CVD, $P < 0.0001$; MI, $P < 0.0001$; arrhythmia, $P < 0.0001$; heart failure, $P < 0.0001$; CVA, $P = 0.0011$, Gray's test) (Figure 3). The results of comparing variables, including TB, by dividing the study population according to the presence or absence of CVDs are shown in Table S3. The CVD group was older and had higher BMI, fasting blood glucose, serum creatinine, and total cholesterol levels than those without CVDs.

Subgroup analyzes

Subgroup analyzes stratified by age (40-49, 50-59, 60-69, and ≥70 years) and sex are shown in Table S4. In each sex and age group, patients with TB showed a higher risk of CVD in the ad-

Table 1
Baseline characteristics before and after propensity score matching in study population.

	Before PSM		After PSM			
	Tuberculosis (*N* = 70,458)	Control (*N* = 390,067)	Tuberculosis (*N* = 70,458)	Control (*N* = 70,458)	*P*	*Standardized difference*
Follow-up (month), mean (SD)	**67.90 (±30.78)**	**71.66 (±28.16)**	**67.90 (±30.78)**	**72.42 (±28.22)**	**<0.0001**	
Age (years)						
Mean ± SD	61.30 (±12.58)	61.17 (±12.29)	61.30 (±12.58)	61.13 (±12.37)		
40-49	14,893 (21.1)	81,056 (20.8)	14,893 (21.1)	14,932 (21.2)		
50-59	18,599 (26.4)	103,962 (26.7)	18,599 (26.4)	18,642 (26.5)		0.00138
60-69	15,752 (22.4)	88,595 (22.7)	15,752 (22.4)	15,752 (22.4)		0.00001
≥70	21,214 (30.1)	116,454 (29.9)	21,214 (30.1)	21,132 (30.0)		−0.00254
Sex						
Male	40,210 (57.1)	234,180 (60.0)	40,210 (57.1)	40,210 (57.1)		
Female	30,248 (42.9)	155,887 (40.0)	30,248 (42.9)	30,248 (42.9)		0.00001
Income level						
1st quintile	13,666 (19.4)	80,631 (20.7)	13,666 (19.4)	13,610 (19.3)		
2nd quintile	10,248 (14.5)	56,815 (14.6)	10,248 (14.5)	10,256 (14.6)		0.00032
3rd quintile	11,928 (16.9)	65,898 (16.9)	11,928 (16.9)	11,945 (17.0)		0.00064
4th quintile	14,987 (21.3)	80,168 (20.6)	14,987 (21.3)	14,987 (21.3)		0.00001
5th quintile	19,629 (27.9)	106,555 (27.3)	19,629 (27.9)	19,660 (27.9)		0.00098
Region						
Seoul	12,293 (17.4)	69,613 (17.8)	12,293 (17.4)	12,293 (17.4)		
Gyeonggi	13,680 (19.4)	76,740 (19.7)	13,680 (19.4)	13,663 (19.4)		−0.00061
Metropolitan	17,581 (25.0)	96,505 (24.7)	17,581 (25.0)	17,599 (25.0)		0.00059
Rural	26,904 (38.2)	147,209 (37.7)	26,904 (38.2)	26,903 (38.2)		−0.00003
Smoking history						
Never	40,629 (57.7)	228,585 (58.6)	40,629 (57.7)	42,792 (60.7)	<0.0001	
Former	11,787 (16.7)	80,039 (20.5)	11,787 (16.7)	13,631 (19.3)		
Current	18,042 (25.6)	81,443 (20.9)	18,042 (25.6)	14,035 (19.9)		
Alcohol consumption						
≤1 time/week	51,521 (73.1)	286,119 (73.4)	51,521 (73.1)	52,329 (74.3)	<0.0001	
2-4 times/week	13,360 (19.0)	80,497 (20.6)	13,360 (19.0)	13,943 (19.8)		
≥5 times/week	5577 (7.9)	23,451 (6.0)	5577 (7.9)	4186 (5.9)		
Regular exercise						
No	39,995 (56.8)	196,657 (50.4)	39,995 (56.8)	35,836 (50.9)	<0.0001	
Yes	30,463 (43.2)	193,410 (49.6)	30,463 (43.2)	34,622 (49.1)		
BMI, mean (SD)	22.35 (±3.09)	24.02 (±3.10)	22.35 (±3.09)	24.00 (±3.11)	<0.0001	
Baseline comorbidity						
Diabetes mellitus	11,991 (17.0)	49,390 (12.7)	11,991 (17.0)	8736 (12.4)	<0.0001	
Hypertension	23,933 (34.0)	143,959 (36.9	23,933 (34.0)	25,895 (36.8)	<0.0001	
Dyslipidemia	13,922 (19.8)	90,044 (23.1)	13,922 (19.8)	16,098 (22.8)	<0.0001	
CKD + ESRD	1068 (1.5)	2726 (0.7)	1068 (1.5)	451 (0.6)	<0.0001	
Chronic liver disease	4093 (5.8)	14,531 (3.7)	4093 (5.8)	2634 (3.7)	0.0188	
COPD	14,091 (20.0)	29,435 (7.5)	14,091 (20.0)	5384 (7.6)	<0.0001	
Inflammatory disease[a]	1843 (2.6)	6401 (1.6)	1843 (2.6)	1128 (1.6)	0.4514	
Laboratory results, mean (SD)						
Fasting blood sugar	107.1 (±40.69)	102.7 (±26.73)	107.1 (±40.69)	102.4 (±26.31)	<0.0001	
Creatinine	0.95 (±0.93)	0.94 (±0.74)	0.95 (±0.93)	0.94 (±0.82)	0.0039	
Total cholesterol	188.7 (±39.76)	196.7 (±40.20)	188.7 (±39.76)	196.8 (±40.49)	<0.0001	

Continuous variables were described as mean ± standard deviation, and categorical variables were described as numbers (percentages).
BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; PSM, propensity score matching.
[a] Inflammatory disease consisted of rheumatoid arthritis, Crohn's disease, ulcerative colitis, ankylosing spondylitis, and psoriasis.

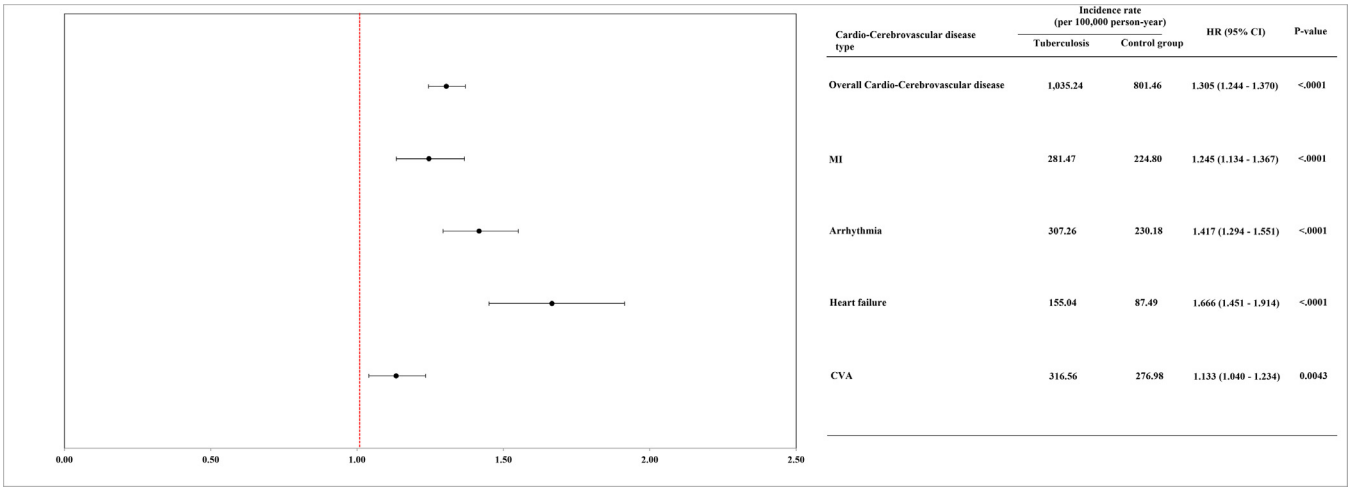

Figure 2. Forest plot for Cox proportional hazard model by specific cardio-cerebrovascular disease CVA, cerebrovascular accident; MI, myocardial infarction.

Table 2
Incidence and hazard ratios for cardio-cerebrovascular disease in TB group compared to the control group.

	Tuberculosis		Control group		Model 1[a]		Model 2[b]		Model 3[c]	
	Events	IR (per 100,000 person-year)	Events	IR (per 100,000 person-year)	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Overall cardio-cerebrovascular disease	4127	1035.24	3408	801.46	1.345 (1.285-1.407)	<0.0001	1.315 (1.255-1.378)	<0.0001	1.305 (1.244-1.370)	<0.0001
MI (myocardial infarction, coronary revascularization)	1096	281.47	935	224.80	1.305 (1.196-1.424)	<0.0001	1.247 (1.139-1.364)	<0.0001	1.245 (1.134-1.367)	<0.0001
Arrhythmia (atrial fibrillation, sick sinus syndrome, atrioventricular block, pacemaker implantation)	1196	307.26	957	230.18	1.380 (1.267-1.502)	<0.0001	1.380 (1.264-1.506)	<0.0001	1.417 (1.294-1.551)	<0.0001
Heart failure	601	155.04	362	87.49	1.853 (1.626-2.111)	<0.0001	1.727 (1.509-1.976)	<0.0001	1.666 (1.451-1.914)	<0.0001
CVA (ischemic stroke, intracranial hemorrhage)	1234	316.56	1154	276.98	1.191 (1.099-1.291)	<0.0001	1.184 (1.090-1.285)	<0.0001	1.133 (1.040-1.234)	0.0043

CI, confidential interval; HR, hazard ratio; IR, incident rate.
[a] Model 1, Adjusted for age and sex.
[b] Model 2, Adjusted for Model 1 + hypertension, diabetes mellitus, and dyslipidemia.
[c] Model 3, Adjusted for Model 2 + socioeconomic status, area of residence, BMI, alcohol consumption, smoking, regular exercise, fasting glucose, creatinine, and total cholesterol.

justed models, except for those in the 40-49 years age group. Additionally, the risk of CVD showed significant differences between sexes and age groups (*P*-for interaction <0.0001).

Discussion

This study comprehensively investigated the association between CVDs and TB using a nationwide database. Our study demonstrated that patients with TB had a higher overall incidence of CVDs than those without TB. Furthermore, TB survivors had a higher incidence of MI, arrhythmia, heart failure, and CVA than those without TB, after adjusting for age, sex, lifestyle, and comorbidities.

The suggested mechanisms responsible for the association between TB and CVDs include direct effects on the myocardium and coronary arteries, increased expression of pro-inflammatory cytokines, monocyte/macrophage immune activation, CD4+ TH1 and TH17 cell immune activation, and autoimmunity mediated by antibodies against mycobacterial HSP65 [6]. Additionally, some studies suggest an association between antibiotic use and CVDs [13,14]. Proposed mechanisms for this association include antibiotic-induced macrophage activation leading to lipid accumulation and atherosclerosis, as well as alterations in the gut microbiota caused by antibiotics, which may also contribute to atherosclerosis [14]. Notably, TB is presumed to cause chronic inflammation even after treatment, which may be attributed to the progression of arteriosclerosis, an essential mechanism in the development of CVDs [15,16]. In addition, lung damage caused by TB often persists and results in chronic lung diseases (such as COPD), which may also affect the occurrence of CVD [17]. Post-TB sequelae have usually focused on the respiratory complications and the psychosocial morbidities [18,19]. However, because CVD is the leading cause of death, its association with CVD after TB deserves attention. In the case of CVD, early detection is vital to prevent progression. Consequently, our study suggests that patients with TB require continued attention for CVD, even if their TB is successfully treated [20]. Usually, patient care ends with treatment completion, and the successful completion of TB treatment might discourage patients from using medical services [5,21]. Therefore, periodic screening tests for chronic diseases in patients should be considered even after treatment for TB. In this study, the association between CVD and TB was significant in patients >50 years of age; therefore, paying attention to early detection of CVD in patients of this age would be helpful for their long-term prognosis.

In this study, the TB group showed a significantly higher risk (aHR: 1.245, 95% CI: 1.134-1.367) of MI. This finding is consistent with results from previous studies, which have also reported an elevated risk of MI among TB survivors [7,22]. The magnitude of the effect size in our study differed from that reported by Huaman et al. [7], but the study was performed in a population with a higher prevalence of chronic diseases, such as hypertension and chronic kidney disease, which results in a different risk profile for developing acute MI. Additionally, similar to our study, Lee et al. [22] used the NHIS database and suggested that TB survivors had a higher risk of developing ischemic heart disease. However, their study only excluded patients previously diagnosed with ischemic heart disease. Therefore, unlike the present study population, patients with a history of heart failure or CVA may have been included. Additionally, unlike the study by Lee et al., we matched income quintiles when composing the matched controls for the TB survivor group. Since low socioeconomic status is associated with a higher incidence of TB but also a higher incidence of CVD, our study could independently identify the impact of TB on CVD incidence by matching income quintiles [23,24].

Among the CVDs, the aHR for heart failure tended to be higher than those for other CVDs in our study. Pericardial involvement in TB is relatively common, and cardiac involvement in TB can lead to heart failure [25]. Nevertheless, the high aHR for heart failure is unlikely to be explained solely by cardiac involvement in TB. Furthermore, ischemic heart disease is a major causative factor for heart failure [26]. Given the potential role of TB in atherosclerosis and previous studies showing an association between atherosclerosis-mediated disease and TB, ischemic heart failure may contribute to a higher aHR for heart failure [6,7]. Although our study cannot demonstrate the mechanism of association between TB and CVDs, to the best of our knowledge, this is the first population-based study to suggest previously unemphasized adverse effects of TB associated with heart failure.

Our study has several strengths. First, by merging and analyzing the NHIS-NHID and NHIS-HEALS data, we were able to com-

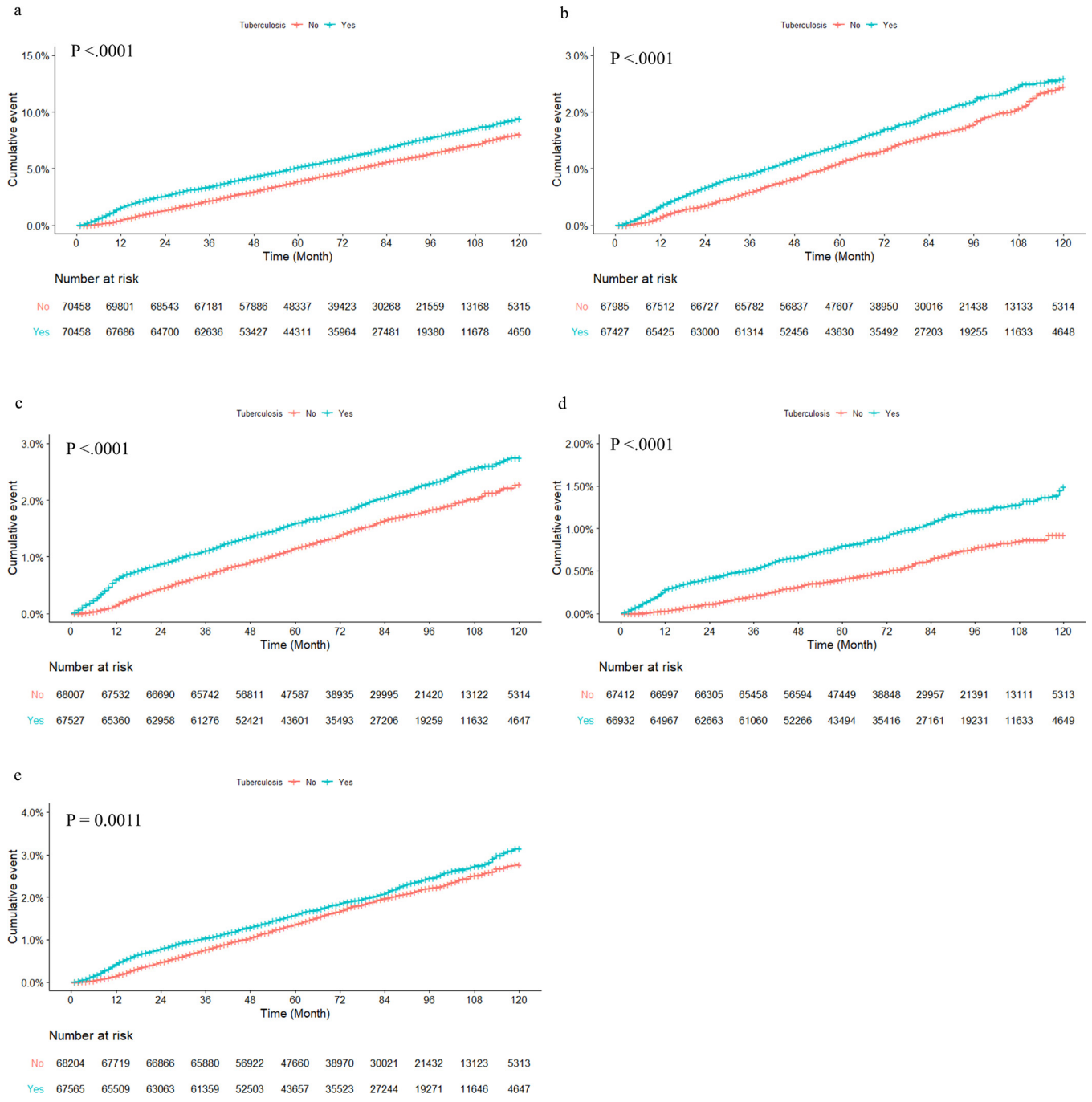

Figure 3. Cumulative incidence of cardio-cerebrovascular disease according to TB. (a) Overall cardio-cerebrovascular disease; (b) myocardial infarction; (c) arrhythmia; (d) heart failure; (e) cerebrovascular accident.

pose a matched study population for income level and region of residence and adjust for variables such as smoking and drinking. Because socioeconomic status is associated with the incidence of TB and CVD, and smoking and drinking are relatively common in patients with TB and are risk factors for CVDs, our study was able to analyze the independent effect of TB on CVD through an adjustment process [23,24, 27–29]. Second, by conducting research targeting overall CVDs rather than the risk for specific CVDs, such as MI, including arrhythmia and heart failure, not addressed by existing population-based studies, we were able to gain a deeper understanding of the impact of TB and calculate the risk for overall CVDs in TB survivors. This study is the first population-based study to suggest an association between TB, arrhythmia, and heart failure. Third, as patients with TB are given the RID code in Republic of Korea, more accurate identification of patients with TB is possible than in other population-based studies with an operational definition of TB, allowing this study to conduct a reliable and detailed analysis. Fourth, using a nationwide database, we compared the incidence rates of CVDs between the TB and control groups in a large population. Fifth, through subgroup analysis of sex and age groups, the contribution of TB to CVD occurrence could be compared by group, serving as background data for healthcare policy.

However, this study has several limitations. First, to accurately analyze the occurrence of CVD, long-term follow-up is necessary; however, our study period might be insufficient to identify the occurrence of CVD. However, since the cumulative incidence curve

showed a relatively constant upward trend in cumulative CVD over time, similar results would be expected in studies with extended follow-up periods. Second, we adjusted for lifestyle habits such as smoking, drinking, and regular exercise by merging the health check-up data; however, we could not reflect changes in the lifestyle habits of the participants during the study period. Third, as this study was conducted using a nationwide database in Republic of Korea, additional research is needed to determine whether similar results will be shown for patients with different lifestyles, ethnicities, and environments. Fourth, drug-resistant TB may cause a more severe inflammatory response than drug-susceptible TB, which could affect the risk of CVD [30]. Additionally, the duration of antibiotic use may also influence CVD risk [14]. However, our study could not include these factors in the analysis.

Conclusion

In a nationwide population-based cohort study, we observed a higher risk of CVDs in TB survivors than in age-, sex-, income-, region-, and index-year-matched controls. Efforts for the prevention and early detection of CVDs should be considered in TB survivors. Further studies are needed on this association and to provide detailed recommendations for preventive measures against CVD in TB survivors.

Funding

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Ethical approval

This study was approved by the Institutional Review Board of the National Health Insurance Service Ilsan Hospital (Institutional Review Board No: NHIMC 2022-08-023), and permission to analyze the NHIS databases was granted. De-identified and anonymized data were used for the analyzes, and the requirement for informed consent was waived. This study was conducted in accordance with the ethical standards outlined in the 1964 Declaration of Helsinki and its subsequent amendments.

Author contributions

J.W.K., S.H.P., and J.H.K. conceptualized and designed the study. J.W.K., H.P., and W-R.L. performed data curation and statistical analysis. S.J.L, J.Y.A, S.J.J., N.S.K., J.Y.C., J-S.Y., S.H.P., and J.H.K interpreted data. S.J.L., S.H.P., and J.H.K. wrote the manuscript. All authors performed critical revision of the manuscript, and read and approved the final version of the manuscript.

Data availability

The claims data analyzed in this study are available from the Korean National Health Insurance Sharing Service, which is open to researchers on request with approval by the institutional review board.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2025.108337.

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