



The incidence, prevalence, and survival rate of thromboangiitis obliterans in Korea: a retrospective population-based study

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Background: Few studies used nationwide data to assess the age-standardized prevalence rate, incidence rate, 10-year survival rate, and death risk of thromboangiitis obliterans (TAO; Buerger's disease).

Methods: Data for 24,392 patients who had newly diagnoses related to TAO (I73.1) from 2006 through 2017 were extracted from the National Health Insurance Service in Korea. The age-standardized prevalence rate, incidence rate, 10-year survival rate, and death risk of TAO were analyzed.

Results: The mean (standard deviation) age of TAO patients overall was 62.0 (15.7) years; 61.3 (15.4) in males and 63.2 (16.1) in females ($P < 0.001$). The proportion of patients older than 50 years old was about 80% overall. The proportion patients who died of TAO was 28.1%. Overall, the age-standardized prevalence rate of TAO decreased from 11.1 persons per 100,000 persons in 2006 to 8.43 persons in 2017, and overall, the incidence rate of TAO decreased from 6.07 persons in 2006 to 3.38 persons in 2017. The age-standardized prevalence rate and incidence rate in males were higher than that in females. The 10-year survival rate of TAO was about 65% (60.7% in males and 72.5% in females). The adjusted hazard ratio increased significantly with older age, male sex, hypertension, diabetes mellitus, myocardial infarction, heart failure, ischemic stroke, hemorrhagic stroke, chronic kidney disease, and malignant neoplasm.

Conclusions: The 10-year survival rate of TAO was about 65%. Even though the age-standardized prevalence rate and incidence rate of TAO is decreased during the study period, the adjusted hazard ratio showed significantly increases with age and with male sex after adjustment for comorbidities.

Keywords: Prevalence; incidence; survival; death risk; thromboangiitis obliterans (TAO)

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Introduction

Thromboangiitis obliterans (TAO; Buerger's disease) is a nonatherosclerotic vascular disease causing recurring, progressive acute and chronic inflammation, and thrombosis in small and medium-sized arteries. TAO showed a distinct

clinical trial in a young man with a history of excessive smoking: claudication of the limbs, Raynaud's phenomenon, and migratory superficial vein thrombophlebitis (1). Arterial angiography is helpful for diagnosing of TAO, which is characterized by a smooth and a gradually diminishing segmental lesion of the distal vessel and collateral vessels,

like a corkscrew. Unlike atherosclerosis of the arteries in the extremities, the proximal large arteries are unaffected, and the internal diameter is smooth (2). The main symptoms of TAO are pain in the affected areas with claudication, cold sensitivity, absence of peripheral pulse, extremities cyanotic blue or reddish blue color changes in the extremities, and thin or shiny skin. Ulceration and gangrene in the extremities are common complications. TAO leads to vasculitis and ischemic changes in the distal parts of limbs that can eventually lead to amputation of the extremities (3). Few studies have reported the prevalence, incidence, survival, and death risk of TAO in Korea. Therefore, we used Korean National Health Insurance Benefit records between 2006 and 2017 to assess the prevalence, incidence, survival, and death risk for TAO in Korea. We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/cdt-20-582>).

Methods

Study population

Data were collected from the Korean National Health Insurance benefit records from 2006 through 2017 (n=24,392; ratio of male to female = 2:1). A main diagnosis was extracted from the records of the Korean National Health Insurance benefit system when the data contained a primary diagnosis based on complaints and symptoms without confirmation during the period of treatment. The data consisted of primary diagnoses related to TAO (I73.1) according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), irrespective of Olin's criteria (2). We excluded atherosclerosis (ICD-10: I70). In this study, we also used the death data for Korean people from 2006 through 2018.

Definition of variables

Age was categorized as 0–9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and 80 years or older.

Comorbidities

We defined comorbidities from primary and secondary diagnoses: hypertension (ICD-10: I10, I11, I12, I13, I15); diabetes mellitus (ICD-10: E10, E11, E12, E13, E14);

myocardial infarction (ICD-10: I21, I22, I25.2); heart failure (ICD-10: I11.1, I50, I97.1); ischemic stroke (ICD-10: I63, I64); hemorrhagic stroke (ICD-10: I60, I61, I62); chronic kidney disease (ICD-10: N18, N19); and malignant neoplasm (ICD-10: C00–C97).

Statistical analysis

The differences in characteristics were analyzed using the Student's *t*-test for continuous variables and the χ^2 test for categorical variables. The age-standardized prevalence and incidence of TAO were calculated with the direct method using the beneficiaries of health insurance from the Korean National Health Insurance Statistical Yearbook from 2006 through 2017 and the estimated Korean population in 2015 as a reference (4). The Kaplan-Meier method was also used with log-rank tests to compare survival among patients with TAO by age group and sex. Simple and multiple Cox proportional hazards analyses were carried out using the variables of age, sex, and comorbidities (hypertension, diabetes mellitus, myocardial infarction, heart failure, ischemic stroke, hemorrhagic stroke, chronic kidney disease, and malignant neoplasm).

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Review Board (IRB) of Samsung Medical Center (No. 2018-03-023). And informed consent was exempted. Because this study does not exceed the minimum risk for the subject. The exemption of consent does not adversely affect the rights or well-being of the study subject. It is practically impossible to obtain the consent from the subjects during the timeframe of research process. There is no reason to presume the subject's refusal to consent. Even if we do not give consent, the risk level for the subjects is extremely low.

Results

The mean age (standard deviation) of TAO patients overall was 62.0 (15.7) years, 61.3 (15.4) years in males and 63.2 (16.1) years in females ($P<0.001$). The proportion of TAO patients overall who were ≥ 50 years old was about 80%. The proportion of comorbidities with TAO was 8.87% with hypertension, 8.20% with diabetes mellitus, 0.31% with myocardial infarction, 0.50% with heart failure, 1.12% with ischemic stroke, 0.04% with hemorrhagic stroke, 0.38% with chronic kidney disease, and 0.27% with malignant neoplasm. The proportion of patients who died in TAO

Table 1 Distribution of general characteristics and comorbidities by sex and death risk from thromboangiitis obliterans (TAO) (n=24,392)

Variables	TAO total (n=24,392)	Male (n=16,044)	Female (n=8,348)	P value [†]	Crude hazard ratio (HR) and 95% CI	Adjusted HR and 95% CI [‡]
Age (years)						
Mean ± SD	62.0±15.7	61.3±15.4	63.2±16.1	<0.001	–	–
Median [IQR]	64 [51, 74]	63 [51, 73]	66 [52.5, 76]	<0.001	–	–
0–9	5 (0.02)	4 (0.02)	1 (0.01)	<0.001	0.00	0.00
10–19	188 (0.77)	109 (0.68)	79 (0.95)		0.00	0.00
20–29	630 (2.60)	423 (2.64)	207 (2.48)		1.0	1.0
30–39	1,361 (5.61)	942 (5.87)	419 (5.02)		1.42 (0.81–2.49)	1.47 (0.84–2.58)
40–49	3,027 (12.5)	2,102 (13.1)	925 (11.1)		3.70 (2.26–6.06)*	3.69 (2.25–6.04)*
50–59	4,816 (19.6)	3,207 (20.0)	1,609 (19.3)		5.87 (3.62–9.51)*	5.89 (3.63–9.54)*
60–69	5,393 (22.2)	3,689 (23.0)	1,707 (20.4)		12.6 (7.83–20.4)*	12.6 (7.81–20.3)*
70–79	5,998 (24.5)	3,906 (24.3)	2,092 (25.1)		30.3 (18.8–48.9)*	32.3 (20.0–52.1)*
80+	2,971 (12.2)	1,662 (10.4)	1,309 (15.7)		70.5 (43.7–113.7)*	77.4 (47.9–124.8)*
Sex, male	16,044 (65.7)	16,044 (100)	0 (0.00)	–	1.54 (1.46–1.63)*	1.93 (1.83–2.05)*
Comorbidities						
Hypertension	2,166 (8.87)	1,377 (8.58)	789 (9.45)	0.023	1.62 (1.51–1.74)*	1.09 (1.01–1.18)**
Diabetes mellitus	2,001 (8.20)	1,388 (8.65)	613 (7.34)	<0.001	2.03 (1.89–2.18)*	1.63 (1.52–1.76)*
Myocardial infarction	76 (0.31)	59 (0.36)	17 (0.20)	0.029	2.72 (2.02–3.65)*	1.93 (1.43–2.60)*
Heart failure	124 (0.50)	79 (0.49)	45 (0.53)	0.626	3.94 (3.19–4.87)*	1.94 (1.57–2.41)*
Ischemic stroke	275 (1.12)	187 (1.16)	88 (1.05)	0.434	1.98 (1.66–2.37)*	1.45 (1.21–1.73)*
Hemorrhagic stroke	11 (0.04)	8 (0.04)	3 (0.03)	0.626	2.55 (1.14–5.69)**	2.63 (1.18–5.89)**
Chronic kidney disease	94 (0.38)	71 (0.44)	23 (0.27)	0.045	5.27 (4.18–6.65)*	3.14 (2.48–3.97)*
Malignant neoplasm	68 (0.27)	55 (0.34)	13 (0.15)	0.008	3.08 (2.23–4.26)*	2.06 (1.49–2.86)*
Death	6,580 (27.0)	4,961 (30.9)	1,619 (19.3)	0.011	–	–

Data are shown as mean ± SD, median [IQR], or number (percentage). [†], Student's *t*-test or χ^2 test; [‡], estimated by Cox proportional Hazard model analysis using the variables indicated in the table; *, P<0.001; **, P<0.0001. SD, standard deviation; IQR, interquartile range.

was 27.0%. The adjusted hazard ratio (HR) of death from TAO by age group was 3.69 [95% confidence interval (CI): 2.25–6.04] among 40–49 years old, 5.89 (95% CI: 3.63–9.54) among 50–59 years old, 12.6 (95% CI: 7.81–20.3) among 60–69 years old, 32.3 (95% CI: 20.0–52.1) among 70–79 years old, and 77.4 (95% CI: 47.9–124.8) among people 80 years or older. The adjusted HR of death from male TAO was 1.93 (95% CI: 1.83–2.05). The adjusted HR of death from TAO in the presence of underlying diseases was 1.09 (95% CI: 1.01–1.18) with hypertension, 1.63 (95% CI: 1.52–1.76) with diabetes mellitus, 1.93 (95% CI: 1.43–2.60) with myocardial infarction, 1.94 (95% CI: 1.57–2.41) with

heart failure, 1.45 (95% CI: 1.21–1.73) with ischemic stroke, 2.63 (95% CI: 1.18–5.89) with hemorrhagic stroke, 3.14 (95% CI: 2.48–3.97) with chronic kidney disease, and 2.06 (95% CI: 1.49–2.86) in malignant neoplasm (Table 1).

Overall, the age-standardized prevalence of TAO decreased from 11.1 persons per 100,000 persons in 2006 to 8.43 persons per 100,000 persons in 2017. The age-standardized prevalence of TAO in males also decreased from 18.1 persons per 100,000 in 2006 to 11.8 persons per 100,000 in 2017. However, the age-standardized prevalence of TAO in females increased from 4.17 persons per 100,000 persons in 2006 to 4.78 persons per 100,000 in 2017

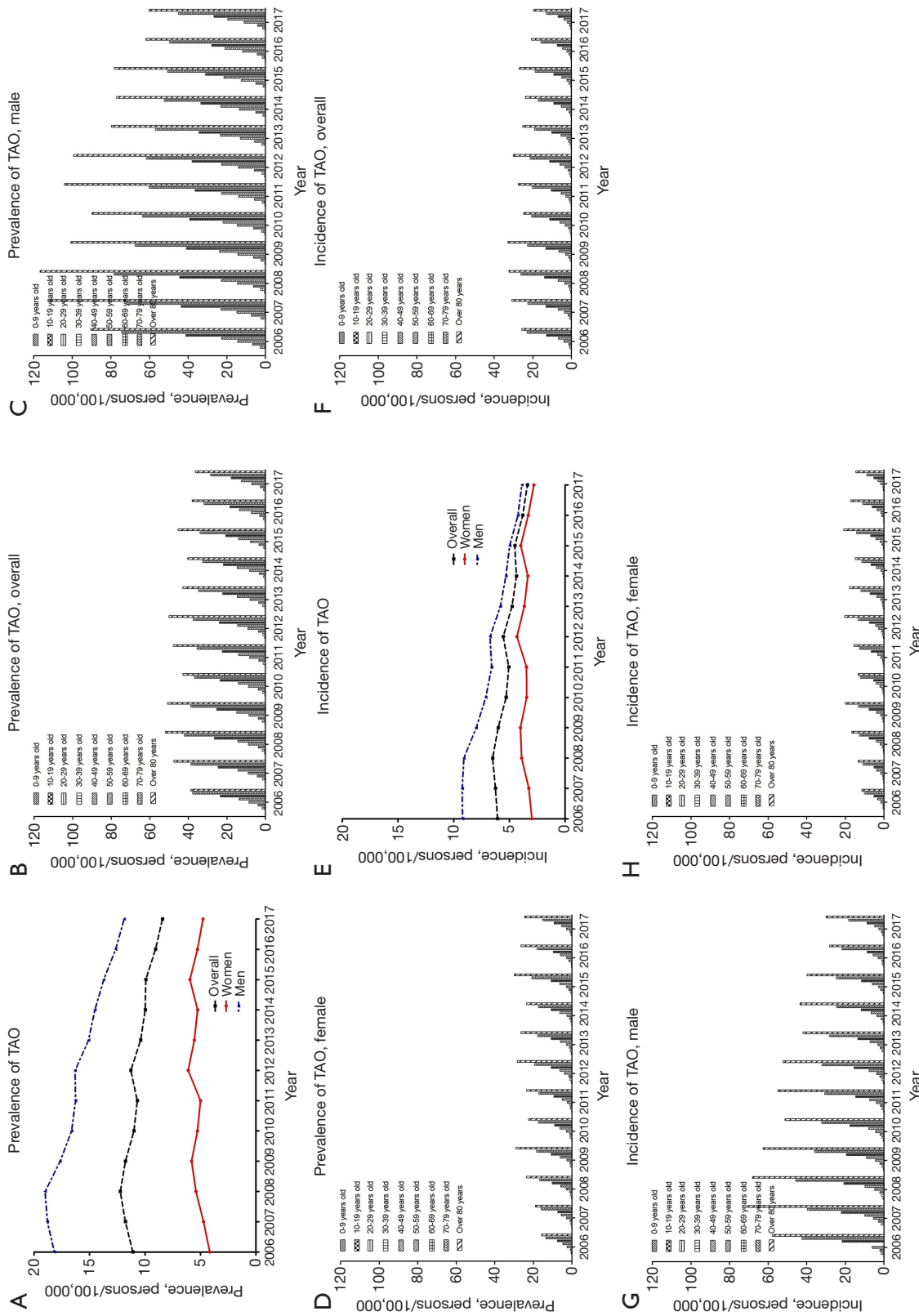


Figure 1 Age-standardized prevalence and incidence of TAO overall, by age group, by sex, and by year per 100,000 persons between 2006 and 2017. (A) Age-standardized prevalence of TAO overall (middle), by sex (male: upper; female: lower), and by year per 100,000 persons between 2006 and 2017; (B) age-standardized prevalence of TAO overall by age group and by year per 100,000 persons between 2006 and 2017; (C) age-standardized prevalence of TAO in males by age group and by year per 100,000 persons between 2006 and 2017; (D) age-standardized incidence of TAO overall (middle), by sex (male: upper; female: lower), and by year per 100,000 persons between 2006 and 2017; (E) age-standardized incidence of TAO overall by age group and by year per 100,000 persons between 2006 and 2017; (F) age-standardized incidence of TAO in males by age group and by year per 100,000 persons between 2006 and 2017; (G) age-standardized incidence of TAO in females by age group and by year per 100,000 persons between 2006 and 2017; (H) age-standardized incidence of TAO in females by age group and by year per 100,000 persons between 2006 and 2017.

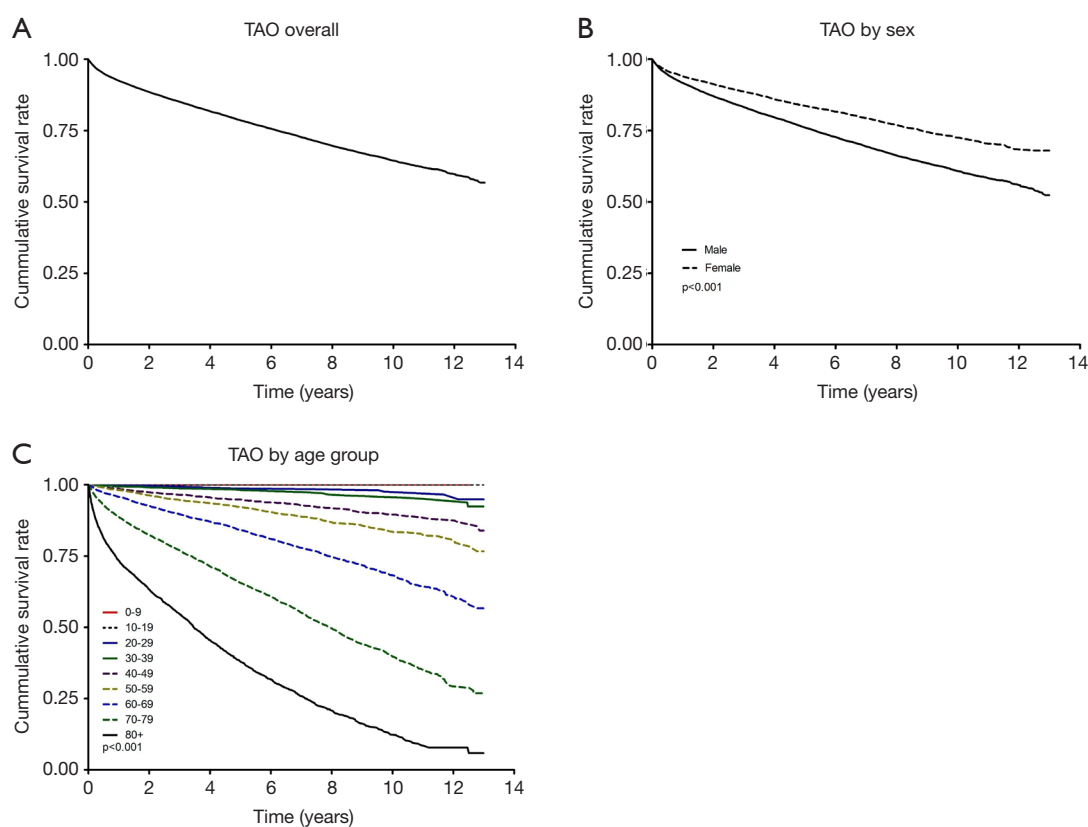


Figure 2 Survival curve of TAO overall (A), by sex (B, $P < 0.001$), and by age group (C, $P < 0.001$) from 2006 through 2018.

(Figure 1A,B,C,D and Table S1). Overall, the age-standardized incidence of TAO decreased from 6.07 persons per 100,000 in 2006 to 3.38 persons per 100,000 in 2017. The age-standardized incidence of TAO in males decreased from 9.21 persons per 100,000 in 2006 to 3.89 persons per 100,000 in 2017, and the age-standardized incidence of TAO in females was 2.98 persons per 100,000 in 2006 and 2.81 persons per 100,000 in 2017 (Figure 1E,F,G,H and Table S2).

Figure 2A shows the survival rates of TAO from 2006 through 2018. The 10-year survival rate with TAO was 64.4% (95% CI: 63.6–65.2%). The 10-year survival rate by sex was 60.7% (95% CI: 59.8–61.7) in males and 72.5% (95% CI: 71.2–73.9%) in females (Figure 2B). The 10-year survival rate for the 0–9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and 80 years or older groups was 100%, 100%, 97.6% (95% CI: 95.3–98.7%), 95.8% (95% CI: 94.1–96.9%), 89.6% (95% CI: 88.1–90.8%), 83.5% (95% CI: 82.1–85.0%), 68.2% (95% CI: 66.5–69.9%), 39.7% (95% CI: 37.8–41.6%), and 12.4% (95% CI: 10.4–14.6%), respectively (Figure 2C).

Discussion

The adjusted HR for TAO increased with older age, male sex, and comorbidities (hypertension, diabetes mellitus, myocardial infarction, heart failure, ischemic stroke, hemorrhagic stroke, chronic kidney disease, and malignant neoplasm). Few studies have found HRs for TAO. However, a study by Le Joncour *et al.* of 224 patients in a French TAO network from 1970 to 2016 demonstrated a different HR results from ours: a non-significantly lower HR with male sex, hypertension, and dyslipidemia (5). This difference could be due to ethnic differences or their study design, which used Papa's criteria (6). Our study includes only Asian patients and a diagnosis of I73.1 in ICD-10 in a national collection of big data, irrespective of Buerger's disease diagnosis criteria, whereas the Le Joncour *et al.* study population contained mostly white patients with TAO diagnosed by the Papa's criteria than non-white.

Our results demonstrate that the male age-standardized prevalence and incidence of TAO decreased from 2006 through 2017. Although research into the prevalence and

incidence of TAO research using a national collection of big data is extremely rare, the results from 78 TAO patients in northern Thailand from 1988 to 2002 (7) and 158 patients in Taiwan from 2002 to 2011 (8) correspond well with our results; the prevalence and incidence of TAO also decreased over time in those studies. Few studies have reported the age-standardized prevalence and incidence of TAO by sex. Therefore, the results in this study cannot be compared with those from other geographic or ethnic groups. Considering that the incidence of TAO could be correlated with smoking (9-11), it is relevant that the daily smoking rate in Korea decreased from about 23% in 2007 to about 17% in 2017, according to Organization for Economic Cooperation and Development indicators (12). In the same period, the smoking rate in males decreased from 25.3% to 22.3%, and the smoking rate in females increased from 5.3% to 6.0%, according to the 2017 Korea National Health and Nutrition Examination Survey (13).

TAO was diagnosed more commonly in males than females. In our results, males had about a two times higher incidence of TAO than females, which is consistent with the higher male distribution of TAO found in Taiwan (80.5%) (8).

In this study, the 10-year survival rate of TAO was about 65%. This is similar to the amputation-free 10-year survival rate in a French nationwide study, which was around 70% (5). We cannot directly compare our 10-year survival rate because no other studies have reported the 10-year survival rate by sex and age group using a nationwide collected of big data. In this study, the 10-year survival rate was lower in older age groups, but this result was similar to the overall death rate pattern in Korea found in Statistics Korea data from 2014 (14). The 10-year survival rate with TAO was lower in males than in females because Korean males overall have a higher 10-year mortality rate and lower life expectancy than Korean females (14,15). For males, the HR for TAO was also significantly higher than for females.

Our study has several limitations. First, the National Health Insurance benefit records might have missed TAO patients who did not use medical services or paid for their own medical expenses. For this reason, the prevalence or incidence of TAO in this study might be under- or overestimated. Second, we could not evaluate the severity of TAO, the risk factors such as smoking habits (16,17) or clinical data such as laboratory findings from blood tests, the Allen's test, angiograms, medical/surgical treatments, medical history taking (5), or amputation information (1) because of data limitations.

Conclusions

Overall, the age-standardized prevalence and incidence of TAO in 2017 were about 9 and about 4 persons per 100,000 persons, respectively. Although the male age-standardized prevalence and incidence decreased during the study period, they were still higher proportion in males than in females. The 10-year survival rate with TAO was about 65%. Adjusted HRs increased significantly with age, male sex, and comorbidities.

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Footnote

Reporting Checklist: The authors present the study in accordance with the STROBE reporting checklist. Available at <http://dx.doi.org/10.21037/cdt-20-582>

Data Sharing Statement: Available at <http://dx.doi.org/10.21037/cdt-20-582>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/cdt-20-582>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Review Board (IRB) of Samsung Medical Center (No. 2018-03-023). And informed consent was exempted. Because this study does not exceed the minimum risk for the subject. The exemption of consent does not adversely affect the rights or well-being of the study subject. It is practically impossible to obtain the consent from the subjects during the timeframe of research process. There is no reason to presume the subject's refusal to consent. Even if we do not give consent, the risk level for

the subjects is extremely low.

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Supplementary

Table S1 Age-standardized prevalence^a and 95% confidence interval (CI) of thromboangiitis obliterans (TAO) overall and by sex (per 100,000)

Variables	2006		2007		2008		2009		2010		2011		2012		2013		2014		2015		2016		2017	
	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)	n	Prevalence (95% CI)
All	3,671	11.1 (10.7–11.5)	4,031	11.7 (11.3–12.1)	4,332	12.2 (11.8–12.6)	4,385	11.7 (11.3–12.1)	4,325	10.9 (10.6–11.3)	4,343	10.6 (10.3–11.0)	4,807	11.2 (10.9–11.6)	4,633	10.3 (10.0–10.7)	4,630	9.98 (9.69–10.2)	4,714	9.93 (9.64–10.2)	4,498	9.05 (8.79–9.32)	4,309	8.43 (8.17–8.68)
0–9 years old	1	0.00 (0.00–0.04)	1	0.00 (0.00–0.03)	0	0.00 (0.00–0.00)	1	0.00 (0.00–0.04)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	1	0.00 (0.00–0.04)	0	0.00 (0.00–0.00)	1	0.02 (0.00–0.06)
10–19 years old	12	0.18 (0.07–0.29)	15	0.23 (0.11–0.35)	32	0.48 (0.31–0.65)	19	0.28 (0.15–0.41)	21	0.32 (0.18–0.46)	20	0.30 (0.16–0.44)	26	0.41 (0.24–0.57)	19	0.30 (0.16–0.44)	15	0.25 (0.11–0.38)	11	0.19 (0.07–0.31)	16	0.28 (0.14–0.42)	9	0.16 (0.04–0.27)
20–29 years old	125	1.65 (1.36–1.94)	115	1.55 (1.27–1.84)	124	1.69 (1.39–1.99)	118	1.65 (1.35–1.95)	107	1.54 (1.24–1.83)	87	1.27 (1.00–1.54)	101	1.49 (1.20–1.79)	95	1.41 (1.13–1.70)	67	0.98 (0.74–1.22)	65	0.95 (0.71–1.18)	75	1.09 (0.84–1.33)	70	1.01 (0.77–1.25)
30–39 years old	335	3.84 (3.43–4.25)	368	4.23 (3.79–4.66)	317	3.73 (3.32–4.14)	315	3.73 (3.31–4.14)	312	3.73 (3.34–4.14)	286	3.44 (3.04–3.84)	301	3.66 (3.24–4.07)	284	3.51 (3.10–3.92)	251	3.16 (2.77–3.55)	262	3.35 (2.94–3.76)	228	2.96 (2.57–3.34)	197	2.61 (2.24–2.97)
40–49 years old	706	8.57 (7.94–9.20)	747	8.95 (8.31–9.60)	751	8.85 (8.21–9.48)	734	8.57 (7.94–9.19)	762	8.90 (8.26–9.53)	720	8.35 (7.74–8.96)	789	9.12 (8.48–9.76)	706	8.06 (7.46–8.65)	722	8.20 (7.60–8.80)	684	7.82 (7.24–8.41)	640	7.35 (6.78–7.92)	608	7.03 (6.47–7.59)
50–59 years old	739	13.7 (12.7–14.7)	817	14.3 (13.3–15.3)	859	14.3 (13.3–15.2)	954	14.9 (14.0–15.9)	961	14.1 (13.2–15.0)	1012	13.9 (13.0–14.7)	1,099	14.5 (13.6–15.3)	1,149	14.7 (13.8–15.5)	1,184	14.7 (13.9–15.5)	1,136	13.9 (13.1–14.7)	1,117	13.5 (6.78–7.92)	1,036	12.4 (11.6–13.1)
60–69 years old	827	23.5 (21.9–25.1)	901	24.6 (23.0–26.2)	1004	26.5 (24.9–28.1)	982	25.2 (23.7–26.8)	938	23.5 (22.0–25.0)	903	22.4 (21.0–23.9)	993	23.9 (22.4–25.4)	956	22.2 (20.8–23.6)	990	21.8 (20.4–23.1)	1,010	20.6 (19.4–21.9)	961	18.5 (17.3–19.6)	975	17.8 (16.7–18.9)
70–79 years old	693	37.8 (34.9–40.6)	759	38.6 (35.8–41.3)	882	42.0 (39.3–44.8)	875	38.7 (36.2–41.3)	875	36.8 (34.4–39.3)	897	35.4 (33.1–37.8)	1,025	37.5 (35.2–39.8)	985	34.7 (32.5–36.9)	950	32.6 (30.5–34.7)	993	33.9 (31.8–36.0)	958	31.9 (29.9–34.0)	893	28.4 (26.6–30.3)
80 years or older	233	38.7 (33.7–43.6)	308	47.5 (42.2–52.8)	363	52.0 (46.6–57.3)	387	50.8 (45.7–55.9)	349	42.9 (38.4–47.4)	418	47.9 (43.3–52.5)	473	50.0 (45.5–54.5)	439	42.9 (38.8–46.9)	451	40.3 (36.5–44.0)	552	45.3 (41.5–49.1)	503	38.0 (34.6–41.3)	520	36.3 (33.2–39.4)
Females	641	4.17 (3.83–4.52)	759	4.73 (4.37–5.09)	899	5.40 (5.03–5.78)	993	5.80 (5.42–6.18)	973	5.28 (4.93–5.62)	949	5.00 (4.67–5.33)	1,234	6.11 (5.75–6.46)	1,162	5.56 (5.23–5.89)	1,153	5.26 (4.95–5.57)	1,332	5.95 (5.63–6.28)	1,236	5.27 (4.98–5.57)	1,158	4.78 (4.50–5.06)
0–9 years old	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	1	0.00 (0.00–0.08)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)
10–19 years old	4	0.11 (0.00–0.24)	9	0.26 (0.06–0.45)	11	0.33 (0.12–0.55)	5	0.14 (0.01–0.29)	7	0.22 (0.05–0.39)	7	0.22 (0.05–0.39)	12	0.37 (0.14–0.60)	13	0.44 (0.20–0.69)	8	0.26 (0.06–0.46)	7	0.26 (0.06–0.45)	8	0.29 (0.08–0.51)	3	0.11 (0.00–0.25)
20–29 years old	18	0.46 (0.23–0.69)	23	0.62 (0.36–0.89)	24	0.66 (0.38–0.93)	28	0.79 (0.48–1.09)	34	1.02 (0.67–1.37)	25	0.76 (0.45–1.06)	36	1.12 (0.75–1.49)	29	0.89 (0.55–1.22)	18	0.56 (0.30–0.82)	19	0.59 (0.32–0.86)	13	0.39 (0.17–0.61)	16	0.46 (0.22–0.70)
30–39 years old	37	0.85 (0.57–1.13)	40	0.94 (0.64–1.23)	44	1.05 (0.73–1.36)	44	1.05 (0.73–1.37)	46	1.10 (0.77–1.43)	41	0.99 (0.68–1.30)	62	1.55 (1.16–1.93)	51	1.27 (0.91–1.62)	46	1.19 (0.84–1.53)	60	1.57 (1.17–1.98)	59	1.57 (1.17–1.98)	38	1.02 (0.69–1.35)
40–49 years old	100	2.48 (1.99–2.97)	115	2.81 (2.30–3.33)	123	2.95 (2.43–3.48)	107	2.53 (2.04–3.01)	120	2.86 (2.35–3.37)	103	2.43 (1.96–2.90)	167	3.93 (3.33–4.53)	124	2.88 (2.37–3.39)	113	2.60 (2.11–3.08)	126	2.93 (2.42–3.44)	116	2.69 (2.20–3.19)	120	2.81 (2.30–3.32)
50–59 years old	127	4.70 (3.88–5.52)	158	5.56 (4.69–6.42)	173	5.78 (4.92–6.64)	193	6.06 (5.20–6.91)	212	6.21 (5.37–7.05)	184	5.03 (4.30–5.76)	238	6.28 (5.48–7.08)	232	5.93 (5.17–6.70)	250	6.23 (5.46–7.01)	256	6.28 (5.51–7.06)	245	5.96 (5.21–6.70)	220	5.28 (4.58–5.98)
60–69 years old	140	7.52 (6.27–8.77)	141	7.32 (6.10–8.53)	202	10.2 (8.81–11.6)	219	10.8 (9.38–12.2)	186	8.99 (7.69–10.2)	195	9.35 (8.03–10.6)	230	10.7 (9.35–12.1)	238	10.7 (9.37–12.1)	250	10.7 (9.41–12.0)	272	10.8 (9.53–12.1)	257	9.62 (8.44–10.8)	261	9.27 (8.14–10.4)
70–79 years old	149	13.4 (11.2–15.6)	188	16.0 (13.7–18.3)	207	16.7 (14.4–19.0)	242	18.3 (16.0–20.6)	240	17.4 (15.2–19.6)	250	17.1 (15.0–19.2)	302	19.3 (17.1–21.5)	288	17.8 (15.7–19.9)	287	17.3 (15.3–19.4)	344	20.8 (18.6–23.0)	302	18.0 (15.9–20.0)	265	15.1 (13.3–17.0)
80 years or older	66	15.7 (11.9–19.5)	85	18.8 (14.8–22.9)	115	23.6 (19.3–28.0)	154	29.0 (24.4–33.6)	128	22.5 (18.6–26.4)	144	23.6 (19.7–27.4)	187	28.3 (24.3–32.4)	187	26.4 (22.6–30.1)	181	23.6 (20.1–27.0)	248	29.8 (26.1–33.6)	236	26.4 (23.0–29.7)	235	24.5 (21.3–27.6)
Males	3,030	18.1 (17.4–18.8)	3,272	18.7 (18.1–19.4)	3,433	19.0 (18.3–19.6)	3,392	17.6 (17.0–18.2)	3,352	16.6 (16.0–17.2)	3,394	16.2 (15.6–16.8)	3,573	16.3 (15.7–16.8)	3,471	15.0 (14.5–15.5)	3,477	14.5 (14.0–15.0)	3,382	13.7 (13.2–14.1)	3,262	12.6 (12.2–13.0)	3,151	11.8 (11.4–12.2)
0–9 years old	1	0.00 (0.00–0.07)	1	0.00 (0.00–0.07)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	1	0.00 (0.00–0.08)	0	0.00 (0.00–0.00)	1	0.04 (0.00–0.13)
10–19 years old	8	0.20 (0.04–0.37)	6	0.17 (0.03–0.31)	21	0.58 (0.32–0.84)	14	0.37 (0.16–0.59)	14	0.37 (0.16–0.59)	13	0.37 (0.16–0.58)	14	0.41 (0.18–0.63)	6	0.17 (0.01–0.32)	7	0.20 (0.03–0.37)	4	0.13 (0.01–0.27)	8	0.27 (0.07–0.46)	6	0.20 (0.02–0.38)
20–29 years old	107	2.74 (2.21–3.26)	92	2.41 (1.92–2.91)	100	2.65 (2.13–3.17)	90	2.44 (1.94–2.95)	73	2.03 (1.56–2.50)	62	1.74 (1.30–2.17)	65	1.82 (1.37–2.28)	66	1.85 (1.40–2.31)	49	1.35 (0.97–1.74)	46	1.26 (0.89–1.63)	62	1.68 (1.25–2.10)	54	1.47 (1.08–1.86)
30–39 years old	298	6.66 (5.90–7.42)	328	7.37 (6.57–8.17)	273	6.24 (5.49–6.98)	271	6.26 (5.51–7.01)	266	6.18 (5.44–6.93)	245	5.76 (5.04–6.48)	239	5.68 (4.96–6.40)	233	5.60 (4.88–6.32)	205	5.02 (4.33–5.71)	202	5.02 (4.32–5.71)	169	4.25 (3.61–4.90)	159	4.07 (3.43–4.70)
40–49 years old	606	14.3 (13.2–15.5)	632	14.8 (13.6–15.9)	628	14.5 (13.3–15.6)	627	14.3 (13.2–15.4)	642	14.6 (13.5–15.7)	617	13.9 (12.8–15.0)	622	14.0 (12.9–15.1)	582	13.0 (11.9–14.0)	609	13.5 (12.4–14.6)	558	12.5 (11.4–13.5)	524	11.8 (10.8–12.8)	488	11.0 (10.1–12.0)
50–59 years old	612	22.7 (20.9–24.5)	659	23.1 (21.3–24.8)	686	22.8 (21.1–24.5)	761	23.8 (22.1–25.5)	749	22.0 (20.4–23.5)	828	22.7 (21.2–24.3)	861	22.7 (21.2–24.2)	917	23.4 (21.9–24.9)	934	23.2 (21.7–24.7)	880	21.5 (20.1–23.0)	872	21.0 (19.6–22.4)	816	19.5 (18.2–20.8)
60–69 years old	687	41.2 (38.2–44.3)	760	43.7 (40.5–46.8)	802	44.4 (41.3–47.4)	763	40.9 (38.0–43.9)	752	39.2 (36.4–42.0)	708	36.5 (33.8–39.2)	763	38.0 (35.3–40.7)	718	34.4 (31.9–36.9)	740	33.5 (31.0–35.9)	738	31.0 (28.8–33.2)	704	27.8 (25.8–29.9)	714	26.7 (24.7–28.7)
70–79 years old	544	74.5 (68.2–80.8)	571	71.7 (65.8–77.5)	675	78.4 (72.4–84.3)	633	67.5 (62.3–72.8)	635	63.6 (58.6–68.5)	647	60.2 (55.6–64.9)	723	61.7 (57.2–66.2)	697	57.0 (52.7–61.2)	663	52.4 (48.4–56.4)	649	50.6 (46.7–54.5)	656	49.6 (45.8–53.4)	628	45.0 (41.5–48.5)
80 years or older	167	90.3 (76.6–104.1)	223	112.6 (97.8–127.4)	248	116.7 (102.1–131.2)	233	100.7 (87.8–113.7)	221	89.8 (77.9–101.7)	274	104.1 (91.7–116.4)	286	99.4 (87.9–111.0)	252	79.8 (69.9–89.7)	270	77.0 (67.8–86.2)	304	78.1 (69.3–86.9)	267	62.0 (54.5–69.5)	285	60.3 (53.3–67.4)

^a, age-standardized prevalence rates of TAO were calculated according to the direct method using the estimated Korean population in 2015 as a reference.

Table S2 Age-standardized incidence^a and 95% confidence interval (CI) of thromboangiitis obliterans (TAO) overall and by sex (per 100,000)

Variables	2006		2007		2008		2009		2010		2011		2012		2013		2014		2015		2016		2017	
	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)	n	Incidence (95% CI)
All	3,151	6.07 (5.78–6.35)	2,062	6.25 (5.96–6.53)	2,224	32.4 (28.1–36.6)	2,151	6.01 (5.74–6.28)	2,030	5.30 (5.06–5.54)	1,994	5.05 (4.82–5.28)	2,314	5.55 (5.32–5.78)	2,067	4.76 (4.55–4.97)	1,971	4.37 (4.17–4.56)	2,091	4.51 (4.31–4.71)	1,858	3.80 (3.63–3.98)	1,705	3.38 (3.22–3.55)
0–9 years old	1	0.00 (0.00–0.03)	1	0.00 (0.00–0.03)	0	0.00 (0.00–0.00)	1	0.00 (0.00–0.04)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	1	0.00 (0.00–0.04)	0	0.00 (0.00–0.00)	1	0.02 (0.00–0.06)
10–19 years old	6	0.14 (0.04–0.24)	14	0.21 (0.10–0.32)	28	0.42 (0.26–0.59)	14	0.21 (0.10–0.32)	21	0.32 (0.18–0.46)	18	0.26 (0.13–0.39)	26	0.41 (0.24–0.57)	16	0.25 (0.11–0.38)	13	0.21 (0.09–0.33)	9	0.16 (0.05–0.26)	13	0.23 (0.10–0.36)	6	0.10 (0.01–0.20)
20–29 years old	54	0.95 (0.72–1.17)	69	0.93 (0.71–1.15)	64	0.87 (0.65–1.08)	56	0.77 (0.57–0.98)	58	0.82 (0.60–1.04)	55	0.81 (0.59–1.02)	66	0.98 (0.74–1.22)	57	0.84 (0.61–1.06)	32	0.46 (0.30–0.63)	29	0.42 (0.26–0.57)	38	0.54 (0.36–0.72)	34	0.48 (0.31–0.64)
30–39 years old	159	1.35 (1.10–1.59)	153	1.75 (1.47–2.03)	125	1.46 (1.20–1.71)	123	1.46 (1.20–1.71)	124	1.47 (1.21–1.73)	109	1.31 (1.06–1.55)	137	1.66 (1.38–1.94)	116	1.43 (1.17–1.69)	90	1.13 (0.90–1.37)	103	1.31 (1.05–1.56)	88	1.13 (0.89–1.37)	74	0.97 (0.74–1.19)
40–49 years old	488	3.90 (3.47–4.32)	304	3.64 (3.23–4.05)	289	3.40 (3.01–3.79)	261	3.04 (2.67–3.41)	277	3.23 (2.84–3.61)	247	2.86 (2.50–3.22)	291	3.35 (2.97–3.74)	210	2.39 (2.06–2.71)	227	2.56 (2.23–2.90)	206	2.35 (2.03–2.67)	205	2.34 (2.02–2.66)	188	2.16 (1.85–2.48)
50–59 years old	816	6.79 (6.09–7.48)	393	6.90 (6.22–7.58)	414	6.90 (6.23–7.57)	415	6.51 (5.89–7.14)	408	5.99 (5.41–6.57)	389	5.34 (4.81–5.87)	453	5.98 (5.42–6.53)	428	5.46 (4.94–5.98)	424	5.28 (4.77–5.78)	415	5.09 (4.60–5.58)	381	4.60 (4.14–5.07)	330	3.95 (3.53–4.38)
60–69 years old	714	12.9 (11.7–14.1)	484	13.2 (12.0–14.4)	527	13.9 (12.7–15.1)	517	13.3 (12.1–14.4)	449	11.2 (10.2–12.3)	421	10.4 (9.47–11.4)	471	11.3 (10.3–12.3)	440	10.2 (9.27–11.1)	417	9.18 (8.30–10.0)	449	9.18 (8.33–10.0)	383	7.38 (6.64–8.12)	381	6.95 (6.25–7.65)
70–79 years old	628	23.0 (20.8–25.2)	444	22.5 (20.4–24.6)	551	26.3 (24.1–28.5)	513	22.7 (20.7–24.7)	491	20.6 (18.8–22.5)	515	20.3 (18.6–22.1)	585	21.4 (19.6–23.1)	541	19.0 (17.4–20.6)	500	17.1 (15.6–18.6)	551	18.8 (17.2–20.3)	475	15.8 (14.4–17.2)	409	13.0 (11.7–14.2)
80 years or older	285	25.7 (21.6–29.7)	200	30.8 (26.5–35.1)	226	32.4 (28.1–36.6)	251	32.9 (28.9–37.0)	202	24.8 (21.3–28.2)	240	27.5 (24.0–30.9)	285	30.1 (26.6–33.6)	259	25.3 (22.2–28.3)	268	23.9 (21.0–26.8)	328	26.9 (24.0–29.8)	275	20.7 (18.3–23.2)	282	19.7 (17.3–22.0)
Females	457	2.98 (2.69–3.28)	523	3.26 (2.96–3.56)	652	3.91 (3.59–4.23)	688	4.02 (3.70–4.34)	648	3.45 (3.18–3.73)	663	3.46 (3.19–3.74)	875	4.32 (4.03–4.62)	764	3.67 (3.40–3.93)	732	3.34 (3.09–3.59)	889	3.99 (3.72–4.26)	776	3.32 (3.08–3.56)	681	2.81 (2.59–3.02)
0–9 years old	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	1	0.00 (0.00–0.08)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)
10–19 years old	3	0.07 (0.00–0.18)	9	0.26 (0.06–0.45)	9	0.26 (0.06–0.45)	2	0.03 (0.00–0.12)	7	0.22 (0.05–0.39)	7	0.22 (0.05–0.39)	12	0.37 (0.14–0.60)	10	0.33 (0.11–0.55)	6	0.18 (0.01–0.36)	6	0.22 (0.04–0.40)	6	0.22 (0.04–0.40)	2	0.07 (0.00–0.18)
20–29 years old	17	0.46 (0.24–0.68)	18	0.49 (0.26–0.72)	16	0.43 (0.20–0.65)	19	0.52 (0.27–0.77)	21	0.62 (0.35–0.90)	18	0.52 (0.27–0.78)	29	0.89 (0.56–1.22)	22	0.69 (0.40–0.98)	13	0.39 (0.17–0.61)	13	0.39 (0.17–0.61)	8	0.23 (0.05–0.40)	13	0.39 (0.17–0.61)
30–39 years old	25	0.58 (0.35–0.81)	29	0.66 (0.41–0.91)	36	0.85 (0.57–1.14)	33	0.80 (0.52–1.07)	38	0.91 (0.61–1.21)	32	0.77 (0.49–1.05)	51	1.27 (0.92–1.62)	38	0.94 (0.63–1.24)	31	0.80 (0.51–1.08)	38	0.99 (0.67–1.31)	45	1.19 (0.83–1.54)	23	0.60 (0.35–0.86)
40–49 years old	67	1.64 (1.24–2.04)	72	1.74 (1.33–2.15)	81	1.93 (1.50–2.35)	71	1.67 (1.27–2.06)	88	2.10 (1.66–2.54)	71	1.67 (1.27–2.06)	121	2.86 (2.35–3.37)	69	1.59 (1.21–1.97)	65	1.50 (1.13–1.87)	81	1.88 (1.47–2.29)	67	1.55 (1.17–1.92)	72	1.69 (1.30–2.08)
50–59 years old	89	3.28 (2.59–3.96)	109	3.83 (3.11–4.55)	120	4.00 (3.28–4.72)	125	3.90 (3.21–4.59)	139	4.08 (3.40–4.76)	118	3.23 (2.64–3.81)	160	4.23 (3.57–4.89)	146	3.73 (3.12–4.34)	156	3.88 (3.27–4.49)	170	4.18 (3.55–4.81)	147	3.58 (3.00–4.16)	130	3.10 (2.56–3.64)
60–69 years old	96	5.17 (4.13–6.20)	99	5.13 (4.11–6.14)	152	7.67 (6.45–8.90)	156	7.71 (6.50–8.93)	110	5.33 (4.33–6.32)	137	6.56 (5.46–7.67)	160	7.48 (6.32–8.64)	158	7.12 (6.00–8.23)	156	6.68 (5.63–7.73)	173	6.88 (5.85–7.91)	163	6.08 (5.14–7.02)	147	5.21 (4.36–6.06)
70–79 years old	112	10.1 (8.25–12.0)	127	10.8 (8.97–12.7)	157	12.7 (10.7–14.7)	175	13.2 (11.2–15.1)	169	12.2 (10.4–14.1)	185	12.7 (10.8–14.5)	208	13.3 (11.5–15.1)	194	11.9 (10.2–13.6)	190	11.4 (9.84–13.1)	235	14.2 (12.4–16.0)	186	11.0 (9.49–12.6)	154	8.83 (7.44–10.2)
80 years or older	48	11.4 (8.20–14.7)	60	13.2 (9.90–16.6)	81	16.6 (13.0–20.3)	106	20.0 (16.2–23.8)	76	13.3 (10.3–16.3)	95	15.5 (12.4–18.6)	134	20.3 (16.8–23.7)	127	17.9 (14.7–21.0)	115	14.9 (12.2–17.6)	173	20.8 (17.7–23.9)	154	17.2 (14.5–19.9)	140	14.5 (12.1–16.9)
Males	1,468	9.21 (8.71–9.71)	1,539	9.24 (8.75–9.72)	1,572	9.09 (8.62–9.56)	1,463	7.98 (7.55–8.40)	1,382	7.11 (6.72–7.50)	1,331	6.60 (6.23–6.97)	1,439	6.73 (6.38–7.09)	1,303	5.81 (5.49–6.13)	1,239	5.32 (5.02–5.62)	1,202	4.97 (4.69–5.26)	1,082	4.24 (3.98–4.49)	1,024	3.89 (3.65–4.13)
0–9 years old	1	0.00 (0.00–0.07)	1	0.00 (0.00–0.07)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	0	0.00 (0.00–0.00)	1	0.00 (0.00–0.08)	0	0.00 (0.00–0.00)	1	0.04 (0.00–0.13)
10–19 years old	7	0.20 (0.05–0.35)	5	0.13 (0.01–0.26)	19	0.54 (0.29–0.79)	12	0.34 (0.14–0.54)	14	0.37 (0.16–0.59)	11	0.30 (0.11–0.50)	14	0.41 (0.18–0.63)	6	0.17 (0.01–0.32)	7	0.20 (0.03–0.37)	3	0.10 (0.00–0.22)	7	0.24 (0.05–0.42)	4	0.13 (0.00–0.28)
20–29 years old	55	1.41 (1.04–1.79)	51	1.32 (0.95–1.69)	48	1.26 (0.90–1.62)	37	1.00 (0.67–1.32)	37	1.00 (0.67–1.33)	37	1.03 (0.69–1.36)	37	1.03 (0.69–1.37)	35	0.97 (0.64–1.30)	19	0.53 (0.29–0.77)	16	0.44 (0.22–0.66)	30	0.82 (0.52–1.12)	21	0.56 (0.31–0.80)
30–39 years old	94	2.08 (1.66–2.51)	124	2.77 (2.28–3.26)	89	2.03 (1.61–2.45)	90	2.06 (1.63–2.49)	86	1.98 (1.55–2.40)	77	1.79 (1.39–2.20)	86	2.03 (1.60–2.46)	78	1.87 (1.45–2.29)	59	1.42 (1.05–1.79)	65	1.61 (1.21–2.00)	43	1.08 (0.75–1.40)	51	1.29 (0.93–1.65)
40–49 years old	255	6.03 (5.28–6.77)	232	5.45 (4.74–6.15)	208	4.79 (4.14–5.45)	190	4.33 (3.71–4.95)	189	4.30 (3.69–4.92)	176	3.98 (3.39–4.57)	170	3.84 (3.26–4.42)	141	3.14 (2.62–3.66)	162	3.61 (3.05–4.16)	125	2.79 (2.30–3.28)	138	3.09 (2.57–3.61)	116	2.63 (2.15–3.11)
50–59 years old	277	10.2 (9.06–11.4)	284	9.95 (8.79–11.1)	294	9.78 (8.66–10.9)	290	9.08 (8.03–10.1)	269	7.89 (6.94–8.83)	271	7.44 (6.55–8.33)	293	7.74 (6.85–8.62)	282	7.19 (6.35–8.03)	268	6.64 (5.84–7.44)	245	5.99 (5.24–6.75)	234	5.62 (4.90–6.34)	200	4.77 (4.11–5.44)
60–69 years old	361	21.6 (19.4–23.8)	385	22.1 (19.9–24.3)	375	20.7 (18.6–22.8)	361	19.3 (17.3–21.3)	339	17.6 (15.7–19.5)	284	14.6 (12.9–16.3)	311	15.4 (13.7–17.2)	282	13.4 (11.9–15.0)	261	11.8 (10.3–13.2)	276	11.5 (10.2–12.9)	220	8.71 (7.56–9.86)	234	8.75 (7.63–9.88)
70–79 years old	311	42.6 (37.8–47.3)	317	39.7 (35.3–44.1)	394	45.7 (41.2–50.2)	338	36.0 (32.1–39.8)	322	32.2 (28.7–35.7)	330	30.7 (27.4–34.0)	377	32.1 (28.9–35.4)	347	28.3 (25.3–31.3)	310	24.5 (21.8–27.2)	316	24.6 (21.9–27.4)	289	21.8 (19.3–24.3)	255	18.2 (16.0–20.5)
80 years or older	107	57.7 (46.8–68.7)	140	70.5 (58.8–82.2)	145	68.1 (57.0–79.2)	145	62.6 (52.3–72.8)	126	51.3 (42.3–60.2)	145	55.0 (46.0–63.9)	151	52.4 (44.0–60.8)	132	41.8 (34.7–49.0)	153	43.5 (36.6–50.4)	155	39.8 (33.5–46.1)	121	28.1 (23.1–33.1)	142	30.0 (25.0–34.9)

^a, age-standardized incidence rates of TAO were calculated according to the direct method using the estimated Korean population in 2015 as a reference.