

Long-Term Outcome and Prognostic Factors of Complications in Thromboangiitis Obliterans (Buerger's Disease): A Multicenter Study of 224 Patients

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Background—Data regarding long-term outcome of patients with thromboangiitis obliterans are lacking and most series come from India and Japan. In this study, we assess long-term outcome and prognostic factors in a large cohort of thromboangiitis obliterans.

Methods and Results—Retrospective multicenter study of characteristics and outcomes of 224 thromboangiitis obliterans patients fulfilling Papa's criteria were analyzed. Factors associated with vascular events and amputations were identified. The median age at diagnosis was 38.5 (32–46) years, 51 (23.8%) patients were female, and 81.7% were whites. After a mean follow-up of 5.7 years, vascular events were observed in 58.9%, amputations in 21.4%, and death in 1.4%. The 5-, 10-, and 15-year vascular event-free survival and amputation-free survival were 41% and 85%, 23% and 74%, and 19% and 66%, respectively. Ethnic group (nonwhite) (hazard ratio 2.35 [1.30–4.27] $P=0.005$) and limb infection at diagnosis (hazard ratio 3.29 [1.02–10.6] $P=0.045$) were independent factors of vascular event-free survival. Factor associated with amputation was limb infection (hazard ratio 12.1 [3.5–42.1], $P<0.001$). Patients who stopped their tobacco consumption had lower risk of amputation ($P=0.001$) than those who continued.

Conclusions—This nationwide study shows that 34% of thromboangiitis obliterans patients will experience an amputation within 15 years from diagnosis. We identified high-risk patients for vascular complications and amputations. (*J Am Heart Assoc.* 2018;7:e010677. DOI: 10.1161/JAHA.118.010677)

Key Words: Buerger's disease • outcome • prognosis • thromboangiitis obliterans • vasculitis

Buerger's disease or thromboangiitis obliterans (TAO) is a nonatherosclerotic inflammatory arteritis that involves small-to-medium-size arteries and veins of extremities.^{1,2} Despite its strong association with tobacco exposure, the general pathophysiology of the disease is still unknown. TAO mainly affects young patients who present ischemic ulcers, rest pain, claudication, coldness of extremities, but also

migratory thrombophlebitis and Raynaud phenomenon. Distal arterial occlusions can ultimately lead to limb amputation.^{3,4}

Although it is observed worldwide, TAO seems to be more prevalent in the Middle East and Far East. Prevalence rates among in-hospital-treated patients with peripheral arterial occlusive disease were reported to range from 0.5% to 5.6% in Western Europe, 45% to 63% in India, and 16% to 66% in Korea

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Clinical Perspective

What Is New?

- We report the largest study in Western countries that describes clinical characteristics and prognosis factors of vascular events and amputation.

What Are the Clinical Implications?

- Limb infection at diagnosis is independently associated with the occurrence of vascular events and of amputation; those patients should benefit from a more aggressive and careful therapeutic management.
- Smoking cessation was strongly associated with a lower rate of vascular events and amputation.

and Japan.⁵ Most series of TAO date back to the 1980s. In North America, Olin et al reported 112 patients with TAO from 1970 to 1987 and showed that the clinical spectrum changed over time with an increase in prevalence in women, and that patients who stopped smoking have a lower rate of amputation.⁶ Cooper et al reported 111 patients from 1976 to 1999 at the Mayo Clinic and showed a time-dependent rate of amputation of 48% at 10 years.⁷ In Western Europe, Börner et al showed that the disease resulted in termination of working life by either dismissal or premature retirement.⁸

TAO is considered to be rare in Western countries where clinical descriptions and long-term outcomes are lacking, especially those coming from Europe. Although smoking cessation has shown an overwhelming effect for the prevention of limb amputation,^{3,5,6} data regarding prognostic factors of TAO are scarce.

Our objective was to report the vascular event-free survival, and the amputation-free survival rate in 224 patients with TAO. In this French nationwide study, we analyzed the prognostic factors associated with these 2 outcomes using a multivariate model.

Patients and Methods

We conducted a retrospective multicenter study in referral centers from the French TAO network between 1970 and 2016. We identified 224 patients fulfilling Papa's criteria⁹ for TAO. This study was approved by the local ethics committee, and informed consent was waived.

Exclusion criteria were evidence of proximal emboli or atherosclerotic disease, thrombophilia, connective-tissue disease (ie, scleroderma, systemic lupus erythematosus, rheumatoid arthritis, mixed connective-tissue disease), and diabetes mellitus.

Baseline clinical characteristics included age at onset and diagnosis, sex, ethnicity, clinical history, tobacco use (pack-year),

other addictions and drugs exposure, cardiovascular risk factors, associated diseases, main clinical (claudication, limb ischemia defined as rest pain and skin color change, ischemic ulcers or necrosis defined as tissue loss, limb infection, phlebitis, arthralgia, Raynaud phenomenon), biological features (complete blood count, serum creatinine, C-reactive protein levels), and treatments.

Ethnicity was defined as the country of origin of the patient's parents and grandparents, and subjects were classified into 1 of the following defined ethnic groups: white and nonwhite (ie, North African, sub-Saharan African, and Middle or Far East. Three patients who originated from Turkey were classified as nonwhite).

Definitions of Study End Points

A vascular event was defined as an acute worsening of the disease course requiring treatment modification (ie, occurrence of a claudication worsening, a limb ischemia, ulcers, necrosis, a superficial vein thrombosis, and/or a limb infection related to ischemia or death).

An amputation was defined as major if it involved the tibiotarsal articulation for lower limbs and if it involved the metacarpo-phalangeal articulation for upper limbs.

At each visit, criteria for disease activity were assessed based on symptoms assessment, physical examination, laboratory studies, and imaging. Clinical evaluation, duplex-ultrasound, angio-computed tomography, and/or angiography were performed every 6 months or sooner if there was suspicion of disease flare or disease progression.

Smoking Cessation

Smoking patients at diagnosis who stopped their consumption at 1 year were considered as ex-smokers. Their smoking status was checked at each visit based on self-declaration. If they declared that they had resumed their consumption during follow-up or at the amputation, they were considered as smokers.

Statistical Analysis

Continuous variables are presented as median (interquartile range); categorical variables are presented as count (percent). Fifteen-year vascular event-free survival was defined as the time from the date of TAO diagnosis and the date of the first vascular event, amputation, death, or last follow-up. Fifteen-year amputation-free survival was defined as the time from the date of TAO diagnosis and the date of the first amputation. Patients with amputation or vascular event before the diagnosis of TAO were excluded for survival analysis only.

Table 1. Main Characteristics of Patients With TAO According to Ethnicity

	All Patients (N=224) n (%); Med. [IQR 25, IQR 75]	White* (N=183) n (%); Med. [IQR 25, IQR 75]	Nonwhite* (N=41) n (%); Med. [IQR 25, IQR 75]
Epidemiological features			
Sex, female	51 (22.8)	43 (23.5)	8 (19.51)
Age at onset of symptoms (y)	36 [29–44]	36 [28–43]	36 [30–45]
Age at diagnosis (y)	38.5 [32–46]	39 [32–46]	38 [32–46]
Cardiovascular risk factors			
BMI (kg m ⁻²) (n=98)	23.4 [21.2–26.5]	23.5 [21.2–26.1]	23 [21.2–26.67]
Familial history	15 (6.7)	13 (7.1)	2 (4.9)
Hypertension	20 (8.9)	15 (8.2)	5 (12.2)
Dyslipidemia	20 (8.9)	16 (8.7)	4 (9.8)
Addiction			
Tobacco	221 (98.7)	181 (98.9)	40 (97.6)
Pack-y (n=199)	22 [12–30]	23.5 [12–30]	20 [10–30]
Age at onset (y) (n=144)	18 [15–20]	18 [15–20]	18 [16–23]
Cannabis (n=222)	51 (22.8)	42 (23.2)	9 (22)
Joints per wk (n=34)	7 [3–19]	7 [3–21]	5 [3–9]
Alcohol (n=168)	3 (1.8)	3 (2.29)	0 (0)
Cocaine (n=168)	3 (1.8)	2 (1.5)	1 (2.7)
Heroin (n=168)	2 (1.2)	2 (1.5)	0 (0)
Symptoms at diagnosis			
Upper limb only	63 (28.5)	56 (31.1)	7 (17.1)
Claudication	4 (6.3)	3 (5.4)	1 (14.3)
Limb ischemia	59 (93.7)	53 (94.6)	6 (85.71)
Ischemic ulcers/necrosis	19 (30.2)	17 (30.4)	2 (28.6)
Limb infection	4 (6.4)	4 (7.1)	0 (0)
Lower limb only	119 (53.1)	92 (51.1)	27 (65.8)
Claudication	93 (81.6)	69 (79.3)	24 (88.9)
WD <100 m	44/77 (57.9)	32/56 (57.1)	12/20 (60)
100 m <WD <500 m	25/77 (32.9)	18/56 (32.1)	7/20 (35)
WD >500 m	7/77 (9.2)	6/56 (10.71)	1/20 (5)
Limb ischemia	84 (70.6)	67 (73.6)	17 (62.96)
Ischemic ulcers/necrosis	43 (36.1)	34 (37.4)	9 (33.3)
Limb infection	14 (11.8)	12 (13.33)	2 (8)
Both upper and lower limb	21 (9.33)	16 (8.9)	5 (12.2)
Claudication	16 (76.2)	11 (68.75)	5 (100)
Limb ischemia	16 (76.2)	13 (81.25)	3 (60)
Ischemic ulcers/necrosis	7 (33.3)	5 (31.25)	2 (40)
Limb infection	1 (4.7)	1 (6.25)	0 (0)
Superficial thrombophlebitis	41 (18.3)	36 (19.7)	5 (12.2)
Raynaud phenomenon	93 (41.7)	78 (42.9)	15 (36.6)
Arthralgia	17 (7.6)	11 (6.0)	6 (14.6)

Continued

Table 1. Continued

	All Patients (N=224) n (%); Med. [IQR 25, IQR 75]	White* (N=183) n (%); Med. [IQR 25, IQR 75]	Nonwhite* (N=41) n (%); Med. [IQR 25, IQR 75]
Laboratory findings at diagnosis			
White blood cell count, $\times 10^3 \text{ mm}^{-3}$	8.2 [6.6–10.6]	8.6 [6.9–10.9]	7.4 [6–8.9]
Hemoglobin, g dL ⁻¹	14.2 [13.2–15]	14.3 [13.3–15.1]	14 [13–15]
Platelets count, $\times 10^3 \text{ mm}^{-3}$	264 [226–330]	264 [226–325]	255 [229–340]
C-reactive protein, mg L ⁻¹	4 [0–8.3]	4 [0–8]	4 [0–8]
Serum creatinine, $\mu\text{mol L}^{-1}$	57 [8.6–76]	54 [8.4–76]	64 [9–76]

BMI indicates body mass index; Med. [interquartile range (IQR) 25, IQR 75], median [25th percentile, 75th percentile]; TAO, thromboangiitis obliterans; WD, walking distance (m).
*Characteristics were not different between white and nonwhite, $P>0.05$ for all items.

Survival curves were estimated using Kaplan-Meier product-limit estimator. Factors associated with overall survival were analyzed using Cox proportional hazards models. The proportional hazards assumption was checked by examination of Schoenfeld residuals. For the different end points, univariate analyses were first carried out, then a multivariate analysis was used where all factors with $P<0.20$ in the univariate analysis were considered. If needed, factors were then sequentially removed from the adjusted model based on the Akaike information criterion (AIC) criteria. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Results

Characteristics of the Study Population and Treatment

Main demography, clinical characteristics, and laboratory findings of the 224 patients with TAO are presented in Table 1. The median [lower quartile, upper quartile] age at symptom onset and diagnosis was 36 [29–44] and 38.5 [32–46] years, respectively. Fifty-one patients (22.8%) were women. One hundred eighty-three patients (81.7%) were classified as white, the other 41 patients (18.3%), classified as nonwhite, originated from North Africa (31 [13.8%]), Sub-Saharan Africa (6 [2.7%]), and Far East (4 [1.7%]). All but 3 patients declared they were current smokers with a median consumption of 22 [12–30] pack-year. Fifty-one (23%) patients were also cannabis users. Demographic characteristics were not different between men and women or between whites and nonwhites.

At diagnosis, 114 (52.8%) patients had a claudication, 162 (73.3%) a limb ischemia, 69 (31.5%) ischemic ulcers or necrosis, and 19 (8.8%) a limb infection. Exclusive lower-limb involvement was more frequent with 119 patients (53.9%), and involvement of both upper and lower limb was present in 21 patients (9.5%). Superficial thrombophlebitis, Raynaud

phenomenon, and arthralgia were present in 41 (18.3%), 93 (41.5%), and 17 (7.6%) patients, respectively. Raynaud phenomenon was more frequent in women than in men, 29 (56.9%) versus 64 (37.2%), respectively, $P=0.019$. Clinical presentation was not different between white and nonwhite (Table 1), and between patients who consumed cannabis or not.

Laboratory findings were not different between whites and nonwhites. Hemoglobin and serum creatinine levels were higher in men compared with women, 14.6 g/dL versus 12.6 g/dL, $P<0.001$ and 65 $\mu\text{mol/L}$ versus 49 $\mu\text{mol/L}$, $P=0.024$, respectively.

One hundred seventy-six patients (78.9%) received aspirin, 75 (33.8%) clopidogrel, 114 (51.1%) statins, 88 (39.5%) a calcium channel blocker, and 14 (6%) colchicine. A sympathectomy, an arterial bypass, and a percutaneous intervention were performed in 18 (8%), 25 (11.1%), and 24 (10.7%) patients, respectively. Treatments were not different between men and women or between white and nonwhite.

Vascular Event

The mean follow-up was 5.7 years, and there were 3 deaths of unknown origin. One hundred thirty-two patients had at least 1 event other than amputation with a mean of 1.3 events per patient (including events before diagnosis). Thirty of the patients had a claudication worsening, 66 a limb ischemia, and 58 an ischemic ulcer or necrosis. The remaining 21 had a limb infection or superficial thrombosis. Vascular event-free survival rates at 5 and 10 years were 41% and 23%, respectively (Figure 1). In the univariate analysis, nonwhite origin was associated with higher vascular event rate (hazard ratio [HR], 2.03; 95% confidence interval [CI], 1.23–3.36; $P=0.006$). In multivariable analysis, nonwhite origin (HR, 2.35; 95% CI, 1.30–4.27; $P=0.005$) and limb infection (HR, 3.29; 95% CI, 1.02–10.6; $P=0.045$) were associated with a higher vascular event rate (Table 2).

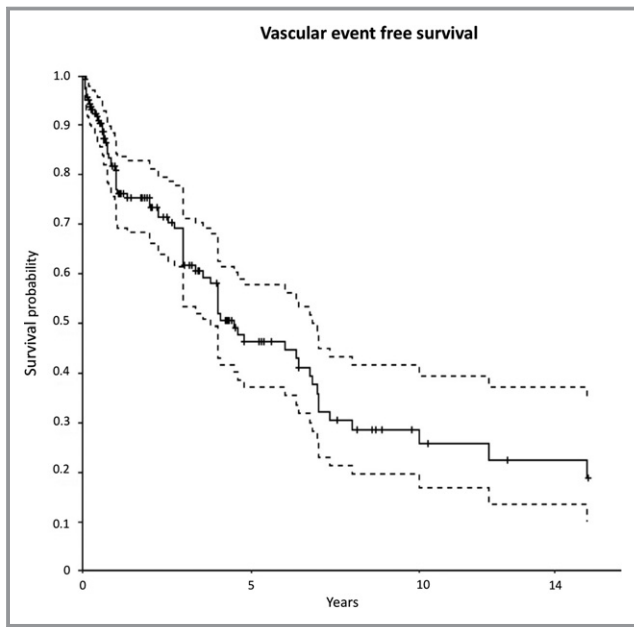


Figure 1. Vascular event-free survival in patients with thromboangiitis obliterans (n=164). (Dotted line: 95% confidence interval).

Because the study spanned 50 years, we assessed whether the year of diagnosis modified the vascular event-free survival rate. Year of diagnosis (disease diagnosed before versus in/after 2007, being the median year of diagnosis) has no significant effect on vascular event-free survival (HR=1.18 [0.72–1.95], $P=0.51$). Nevertheless, we conducted a sensitivity analysis stratified on year of diagnosis (variable coded as described above) with no major change in results.

Amputations

Forty-eight patients had at least 1 amputation (including amputation before the diagnosis) and among them 24 had more than 1 (Table 3). Amputations were more frequent in the lower limb, as 38 of the 48 patients (79%) had an amputation in lower limbs. Amputation remained exclusively minor in 33 of the 48 patients (66%). Amputation-free survival rates at 5, 10, and 15 years were 85%, 74%, and 66%, respectively. Major amputation-free survival rates at 5, 10, and 15 years were 94%, 91%, and 91%, respectively (Figure 2A). In the univariate analysis, limb infection at diagnosis was associated with 15-year amputation-free survival (HR, 9.46; 95% CI, 2.81–31.8; $P<0.001$). Cannabis consumption was not associated with a poor prognosis. In the multivariate analysis, limb infection at diagnosis (HR, 12.1; 95% CI, 3.5–42.1; $P<0.001$) was associated with a higher amputation rate (limb ischemia, ischemic ulcers/necrosis, limb infection, and arthralgia were the variables used in the multivariable model). Kaplan-Meier curve of amputation-free

survival in patients with TAO according to symptoms at diagnosis is shown in Figure 2B.

Because the study spanned 50 years, we assessed whether the year of diagnosis modified the amputation-free survival rate. Year of diagnosis (disease diagnosed before versus in/after 2007, being the median year of diagnosis) has no significant effect on amputation-free survival (HR=0.62 [0.29–1.31], $P=0.21$). Nevertheless, we conducted a sensitivity analysis stratified on year of diagnosis (variable coded as described above) with no major changes on results.

Effect of Smoking Cessation

In order to assess the effect of smoking cessation on the occurrence of amputation, patients who stopped their tobacco consumption at 1 year of follow-up were considered as ex-smokers, and patients who did not stop their consumption or who declared resuming smoking during follow-up or at the amputation were considered as smokers. The next 4-year amputation-free survival rate was analyzed. Patients who stopped their tobacco consumption had a lower risk of amputation than those who continued ($P=0.001$) (Figure 3A). At the first amputation, among 48 patients, 5 (10.4%) were ex-smokers and 43 (89.6%) were current smokers. At next amputation, among 34 patients, 8 (23.5%) were ex-smokers and 26 (76%) were current smokers (Figure 3B). Smoking age at onset and amount of tobacco exposure at diagnosis were not associated with amputation rate.

Discussion

This study is the largest reported to date that assessed long-term outcome of TAO in a Western country. This French nationwide multicenter study provides important data regarding the prognostic factors associated with vascular events and amputations. The most striking conclusions drawn by this study are that (1) nonwhite patients had a 2-fold higher risk of vascular events than white patients; (2) the 10- and 15-year amputation rates were 26% and 34%, respectively; (3) limb infection at diagnosis was independently associated with the occurrence of vascular events and of amputation; and (4) smoking cessation was strongly associated with a lower incidence of amputation.

Compared with other cohorts, our French TAO cohort was broadly similar in its demographic features with a predominance of males.^{4,8,10–12} Lower limb involvement and claudication were the most prevalent symptoms. Ischemic ulcers or necrosis were present in 30% of cases, whereas they are reported in 76% in the United States⁶ and in more than 45% of patients in the Far East and Middle East.^{10,13,14} Limb infection at diagnosis was evidenced in 8.5% of patients. Clinical

Table 2. Predictive Factors of Vascular Event in Patients With TAO

	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P Value
Demographic				
Sex, male	0.96 (0.54–1.69)	0.88		
Age at diagnosis				
<39 y	1			
≥39 y	1.33 (0.84–2.13)	0.23		
Diagnosis delay				
<24 mo	1			
≥24 mo	1.29 (0.78–2.14)	0.32		
Ethnicity				
White	1		1	
Nonwhite	2.03 (1.23–3.36)	0.006	2.35 (1.30–4.27)	0.005
BMI				
25<BMI<30	1			
BMI<25	1.54 (0.72–3.3)	0.26		
BMI>30	0.70 (0.19–2.6)	0.60		
Cardiovascular risk factors				
Familial history	0.89 (0.38–2.05)	0.78		
Hypertension	0.71 (0.29–1.77)	0.46		
Dyslipidemia	0.81 (0.39–1.7)	0.58		
Addiction				
Tobacco (PY)				
<22	1			
≥22	1.00 (0.61–1.63)	0.99		
Cannabis	1.42 (0.81–2.49)	0.22		
Symptoms at diagnosis				
General				
Superficial phlebitis	1.02 (0.54–1.95)	0.94		
Raynaud phenomenon	0.81 (0.5–1.31)	0.39		
Arthralgia	1.29 (0.56–2.99)	0.55		
Vascular				
Claudication	1	...	1	...
Limb ischemia	1.27 (0.66–2.44)	0.47	1.59 (0.80–3.14)	0.18
Ischemic ulcers/necrosis	1.45 (0.72–2.93)	0.29	1.29 (0.64–2.62)	0.47
Limb infection	2.42 (0.78–7.52)	0.13	3.29 (1.02–10.6)	0.045

BMI indicates body mass index; CI, confidence interval; HR, hazard ratio; PY, pack-y; TAO, thromboangiitis obliterans.

characteristics of TAO did not differ between white and nonwhite as well as between cannabis users and nonusers, as previously described.¹⁵

We observed a vascular event-free survival at 10 years of 23%. Limb ischemia and ulcers were the most frequent events. Ohta et al also described that ulcers/gangrene were

the most frequent symptoms during the clinical course of the disease.¹⁶ Prognostic factors have not been well studied in TAO. Although the harmful role of tobacco has been widely demonstrated,⁴ the impact of ethnicity, other toxics, and/or sex have never been studied. Herein, we demonstrated that limb infection and nonwhite origin were independently

Table 3. Main Characteristics of Amputations in Patients With TAO

	All Patients (N=224) n (%); Med. [IQR 25, IQR 75]
Time from onset of symptoms to amputation, y	4 [1–12]
Age at the first amputation, y	38.8 [32.8–47]
No. of patients with at least 1 amputation	48 (21.4)
No. of patients with	
1 amputation	24/48 (50)
2 amputations	15/48 (31.3)
3 amputations	9/48 (18.8)
No. of patients with	
Lower limb amputation	34/48 (71)
Upper limb amputation	10/48 (21)
Both lower/upper limb amputation	4/48 (8)
No. of patients with	
Unilateral amputation	37/48 (77)
Bilateral amputation	11/48 (23)
No. of patients with	
Only minor amputation	32/48 (66.6)
At least 1 major amputation	15/48 (31.3)

Med. [interquartile range (IQR) 25, IQR 75]: median [25th percentile, 75th percentile]. TAO, thromboangiitis obliterans.

associated with vascular events. Ethnic origin had never yet been reported as a prognostic factor in TAO. White and nonwhite did not differ in terms of clinical features, treatments, or smoking status. Thus, the increase in vascular-event rates might be explained by genetics, socioeconomic, or immunologic factors.¹⁷

We observed only 3 deaths. TAO is not a life-threatening disease. Previous series have reported a 6% death rate.^{6,16}

However, the functional prognosis is seriously impaired. The 10- and 15-year amputation rate was 26% and 34%, respectively, in our study. In other series with a time-dependent evaluation of amputations, the amputation rate ranged between 20% and 50% at 10 years.^{7,14,18} The lower rate of amputation in our cohort compared with previous published reports could be explained by the difference of severity of patients across reports. Thirty percent of our TAO patients

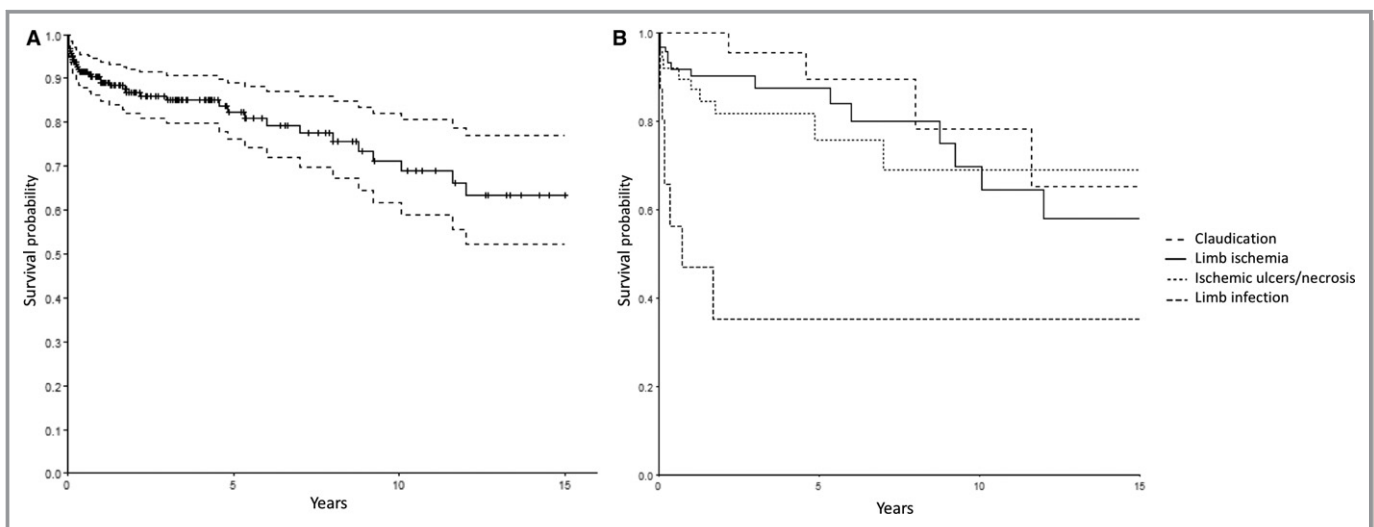


Figure 2. Amputation-free survival in patients with thromboangiitis obliterans (TAO) (n=214). (Dotted line, 95% confidence interval) (A). Amputation-free survival in patients with TAO according to symptoms at diagnosis (B).

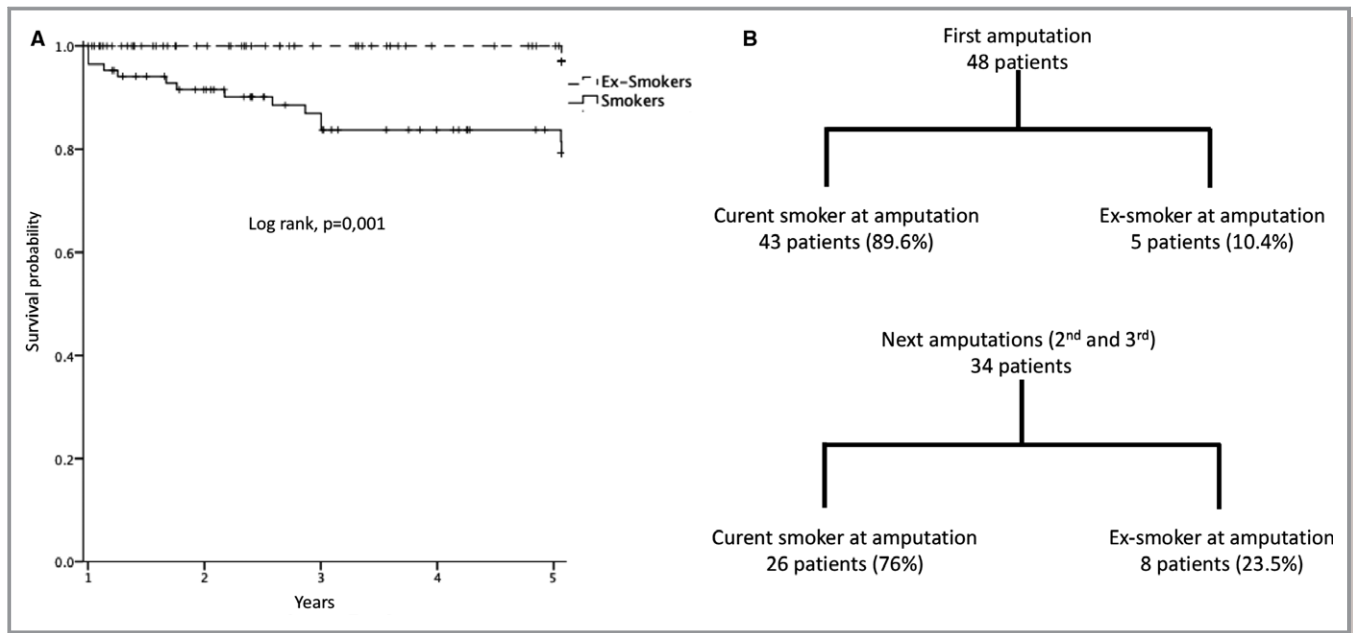


Figure 3. Effect of smoking cessation on patients with thromboangiitis obliterans (TAO). Amputation-free survival in patients with TAO according to smoking withdrawal. (Dotted line: patients who stopped their tobacco consumption; solid line: patients who continued their tobacco consumption) (A). Smoking status at amputation (B).

had ischemic ulcers or necrosis at baseline, whereas it was observed in 45% to 80% of patients in other cohorts.^{6–8,10,13,14,18,19} The study by Fazeli et al, who reported a similar amputation rate (ie, 30%) as in our cohort, had a similar percentage of ischemic ulcers and gangrene (ie, 20%–23%) at baseline.²⁰

In the present study, limb infection at diagnosis was associated with a 4-fold higher risk of amputation. Fazeli et al reported that smoking duration was the only independent factor associated with major amputations.²⁰ Interestingly, gangrene or ulcers were not associated with a worse prognosis. Limb infection has not been studied in TAO but it has been proposed as an important prognostic factor in atherosclerotic critical leg ischemia, more specifically in diabetic patients.²¹ In diabetics, limb infection increased the odds of amputation by 3-fold.²² Therefore, TAO patients with a limb infection may be those who should benefit from a more aggressive and careful therapeutic management.

We found that ex-smokers did not experience an amputation within 4 years of tobacco cessation. In addition, at the time of the first amputation, 90% of patients were still smokers. These data confirm previous observations that tobacco cessation is the cornerstone of TAO management. In Olin's series of 120 patients with TAO, 94% of ex-smokers avoided amputation, while 43% of smokers required amputation. Ohta et al reported that all 41 ex-smokers were free from limb amputation, while 13 of 69 smokers underwent amputation.^{3,5,6} Fazeli et al confirmed that smoking cessation was highly protective for major amputation events.²⁰

However, Sugimoto et al did not observe a significant difference in the long-term limb salvage rate between ex-smokers and smokers at 20 years.¹⁸ In our study, we did not find a negative association between amputation and the duration of smoking exposure nor with the amount of tobacco consumption. Cannabis consumption was not independently associated with a worse prognosis as previously described in a study of 38 patients with TAO.¹⁵ In a review of the literature, the amputation rate in cannabis-related limb arteritis was 58%, but no comparison could be done.²³

We acknowledge some limitations in our study. Our analysis was performed as a retrospective review. We were unable to collect complete longitudinal data on patients who were seen only on an intermittent consultation basis. Because of the retrospective design of this study, smoking status was made by self-declaration and patients may have been misclassified. For further prospective studies, tests for carboxyhemoglobin level and urine nicotine level should be obtained. Prospective enrollment and data collection from the time of diagnosis would have been ideal but are difficult to achieve with such rare diseases.

In conclusion, this French nationwide study shows that 34% of TAO patients are likely to experience an amputation within 15 years of initial diagnosis. Nonwhite patients and limb infection at diagnosis were independently associated with the occurrence of vascular events. Limb infection at diagnosis was associated with a 4-fold higher risk of amputation. We further confirmed that smoking cessation was strongly associated with a lower rate of vascular events and amputation.

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Disclosures

None.

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