Smoking history increases the risk of long-term mortality after thoracic endovascular aortic repair in patients with an uncomplicated type B dissection

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Abstract

Background: The preferred treatment for uncomplicated type B dissection (thoracic endovascular aortic repair [TEVAR] or medical) is still under debate. Since 2001, our center has performed TEVAR for uncomplicated type B dissection. Based on our data, 5- and 10-year survival rates among patients with uncomplicated type B dissection after TEVAR were 96.5% and 83.0%, respectively. We, therefore, believe that TEVAR is preferable for uncomplicated type B dissections. This study analyzed the impact of a pre-operative smoking history on long-term survival after TEVAR in patients with uncomplicated type B dissections.

Methods: From May 2001 to December 2013, data from 751 patients with type B dissections were collected and analyzed. Patients were divided into two groups (337 smoking patients and 414 non-smoking patients). The Kaplan-Meier method and log-rank test were used to compare survival curves of the two groups. Multivariable analyses using the Cox proportional hazards model were used to estimate the effects of smoking on survival rates.

Results: The 5- and 10-year survival rates of non-smokers were 97.6% (95% confidence interval [CI], 96.0%–99.2%) and 87.0% (95% CI, 81.6%–92.7%), respectively, and 94.9% (95% CI, 92.2%–97.7%) and 73.8% (95% CI, 62.3%–87.5%) for smokers, respectively (Log-rank test, $P = 0.006$). Multivariable analyses showed that smoking increased the risk of death during follow-up, 2.1-fold when compared to non-smokers ($P = 0.039$).

Conclusion: A pre-operative smoking history increases long-term mortality rates after TEVAR in patients with uncomplicated type B dissections.

Keywords: Smoking; TEVAR; Uncomplicated type B dissection; Survival rate

Introduction

The optimal treatment for uncomplicated type B dissection is still under debate. Traditionally, patients with uncomplicated type B dissections will undergo optimal medical treatment,[1-3] but more and more evidence supports thoracic endovascular aortic repair (TEVAR) as the preferred treatment method.[4-6] Few studies have focused on the long-term efficacy of TEVAR in patients with uncomplicated type B dissections, and it is unclear which factors affect the long-term outcomes of patients with uncomplicated type B dissections, treated with TEVAR. Smoking is an independent risk factor for a number of cardiovascular diseases, such as coronary artery disease and aneurysm,[7-9] and it is also a risk factor for adverse outcomes after surgery.[10-13] This study aimed to determine the relationship between a pre-operative smoking history and long-term mortality rates in patients with uncomplicated type B dissections treated with TEVAR.

Methods

Ethics approval

The study was approved by the Anzhen Hospital Ethics Committee (No. 2015027X) and informed consent was obtained from each patient.

Patients

The data of patients with uncomplicated type B dissection who underwent TEVAR at the Anzhen Hospital from May 2001 to December 2013 were retrospectively collected for analysis. This was a cohort study [Figure 1]. Patient

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000000640

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Chinese Medical Journal 2020;133(4)

Received: 28-06-2019 **Edited by:** Ning-Ning Wang

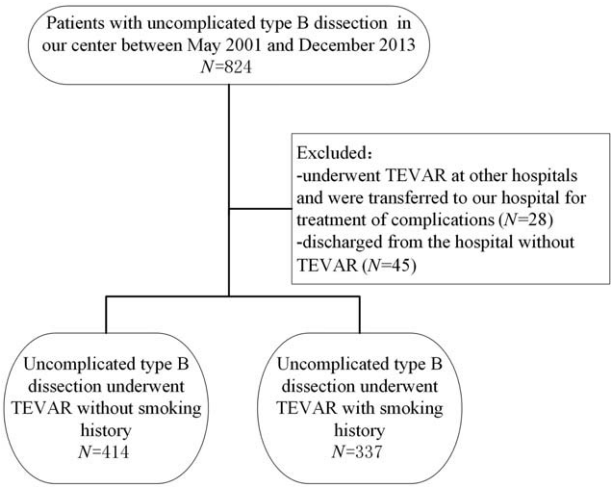

Figure 1: Flow chart of patients with an uncomplicated type B dissection after thoracic endovascular aortic repair.

selection was based on the medical history, symptoms, signs, and auxiliary examination results. The inclusion criteria were: (1) typical dissection patients with primary tears and blood flowing in the false lumen; and (2) uncomplicated type B dissection patients treated with TEVAR. The exclusion criteria were: (1) atypical diseases, such as aortic intramural hematoma and penetrating aortic ulcer; (2) complicated type B dissection patients with symptoms of poor perfusion, refractory hypertension, impending rupture, or rapid aortic expansion (>1 cm per year); (3) patients with complications resulting from TEVAR performed in other hospitals; and (4) patients who did not undergo TEVAR for anatomic reasons or patients who declined TEVAR. All patient data were from inpatient medical records, which were entered, sorted, and cross-checked by three trained participants. All data were saved in the Mdruby Clinical Research System (Mdruby Clinical Research System 2.3.3, Beijing Mdruby Technology Co., Ltd., Beijing, China). We defined patients with a history of pre-operative smoking as patients who had a sustained smoking behavior before surgery and had a total smoking count >100 cigarettes. This study only investigated if patients had a smoking behavior before surgery and did not distinguish between mild or severe smoking. In this study we focused on the effect of a pre-operative smoking history on the long-term survival rate of patients with uncomplicated type B dissections. Patient death was considered an endpoint event without a distinction between the specific causes of death. The deaths used in this study were all-cause mortality during follow-up.

TEVAR procedure

The TEVAR procedure used was the same as the procedure reported in the existing literature.[14,15] The patient underwent CT angiography (CTA) before surgery to determine the location of the primary tear and whether or not the surgical approach was unobstructed. A total aortic angiography was performed from a pigtail catheter to confirm the anatomy of the lesion. The diameter of the anchoring zone was determined in conjunction with CTA and the aortic angiography results, and the stent diameter was selected with an oversize of 5% to 10%. After positioning, the stent was released and the angiography was repeated. If the stent was in a suitable position, the primary rupture was well-sealed with no endoleak and the procedure was terminated. If the distal aorta of the stent had a large re-rupture or if the true lumen distal to the stent was not fully expanded, then a second stent was implanted.[16] A tapered stent without a longitude bar was typically used or a straight stent was used, followed by a tapered stent to better attach the tapered aorta, thus avoiding excessive distal diameters and stent-induced new entry. Upon completion of the procedure, the need for cerebrospinal fluid drainage was determined based on whether or not the patient had a lower limb sensory dyskinesia so as to avoid paraplegia.

Follow-up

After the patient was discharged from the hospital, he/she was asked to return to the hospital every year to review the aortic CTA, ultrasound, and other examination findings to evaluate aortic remodeling, determine whether or not the aortic diameter had progressively expanded, and whether or not intervention was needed. If international patients could not return to our hospital for review, the patients communicated with our hospital physicians after local review and relevant information was recorded. Patients who did not have a review record were followed by telephone or surface mail. Patient survival status was recorded and the patient was advised to return to the hospital for an in-person review. Patients who could not be contacted were recorded as lost to follow-up. The follow-up evaluations ended in November 2016.

Statistical analysis

Continuous variables are expressed as the mean ± standard deviation or median (with associated range or interquartile range). Categorical variables are expressed as frequencies and percentages. Comparisons between groups were analyzed with a Student's t test, Chi-square test, or Kruskal-Wallis test where appropriate. All variables associated with mortality during follow-up with a $P < 0.1$ on univariate analysis were adjusted for multivariate analysis using a multiple regression combined with Cox proportional hazards model. $P < 0.05$ was considered statistically significant. The survival curve was drawn by the Kaplan-Meier method and GraphPad Prism 7 (GraphPad Software, Inc., La Jolla, CA, USA), and a log-rank test was used to compare the differences between the two groups. All analyses were performed with R (http://www.R-project.org) and Empower Stats software (www.empowerstats.com, X&Y Solutions, Inc., Boston, MA, USA).

Results

Between May 2001 and December 2013, a total of 751 patients with uncomplicated type B dissections met the inclusion criteria and were treated with TEVAR; 73 patients with uncomplicated type B dissections and 168 complicated type B dissections were excluded. The demographic, peri-operative, and follow-up data of the 751 patients who met the inclusion criteria are shown in

Table 1: The demographic data, perioperative data, and follow-up data of the 751 patients.

Variables	Overall ($N=751$)	Smoking		$t/Z/\chi^2$	P
		No ($n=414$)	Yes ($n=337$)		
Age (years)	52.8 ± 10.9	53.4 ± 11.1	52.1 ± 10.7	1.579*	0.115
BMI (kg/m^2)	26.0 ± 3.8	25.6 ± 3.6	26.5 ± 4.0	−1.916†	0.055
Gender (male)	619 (82.4)	293 (70.8)	326 (96.7)	86.440	<0.001
Hypertension	552 (73.5)	299 (72.2)	253 (75.1)	0.776	0.378
CAD	51 (6.8)	33 (8.0)	18 (5.3)	2.030	0.154
Diabetes	38 (5.1)	23 (5.6)	15 (4.5)	0.472	0.492
Drinking	165 (22.0)	36 (8.7)	129 (38.3)	94.838	<0.001
Disease staging				18.060	<0.001
Acute phase	408 (54.3)	201 (48.6)	207 (61.4)		
Sub-acute phase	240 (32.0)	139 (33.6)	101 (30.0)		
Chronic phase	103 (13.7)	74 (17.9)	29 (8.6)		
Number of stents used				0.693	0.707
1	638 (87.5)	348 (88.3)	290 (86.6)		
2	84 (11.5)	43 (10.9)	41 (12.2)		
3	7 (1.0)	3 (0.8)	4 (1.2)		
Brand of the stent				20.442	0.002
Talent	20 (2.7)	11 (2.7)	9 (2.7)		
Valiant	173 (23.0)	81 (19.6)	92 (27.3)		
GRIMED	234 (31.2)	148 (35.7)	86 (25.5)		
Hercules	125 (16.6)	77 (18.6)	48 (14.2)		
Zenith TX2	86 (11.5)	47 (11.4)	39 (11.6)		
Relay	76 (10.1)	37 (8.9)	39 (11.6)		
E-vita	37 (4.9)	13 (3.1)	24 (7.1)		
Peri-operative death	5 (0.7)	3 (0.7)	2 (0.6)	0.048	0.826
Reintervention	42 (5.6)	21 (5.1)	21 (6.2)	0.487	0.486
RTAD	7 (0.9)	3 (0.7)	4 (1.2)	0.435	0.509
SINE	10 (1.3)	3 (0.7)	7 (2.1)	2.603	0.107
Endoleak	10 (1.3)	6 (1.4)	4 (1.2)	0.094	0.759
Follow-up death	57 (7.6)	29 (7.1)	28 (8.4)	0.444	0.505

Data were presented with mean ± standard deviation or n (%). *t-test; †Kruskal-Wallis test; the others are Chi-square test. BMI: Body mass index; CAD: Coronary artery disease; RTAD: Retrograde type A dissection; SINE: Stent-induced new entry.

Table 1. According to the staging method proposed by European experts,[17] there were 408 patients in the acute phase, 240 in the sub-acute phase, and 103 in the chronic phase.

The median follow-up time was 70 months (range, 1–170 months). One hundred seventy-two patients (22.9%) were lost to follow-up. According to the patient's follow-up all-cause mortality curve, the 5- and 10-year survival rates of non-smokers were 97.6% (95% confidence interval [CI], 96.0%–99.2%) and 87.0% (95% CI, 81.6%–92.7%), respectively, and 94.9% (95% CI, 92.2%–97.7%) and 73.8% (95% CI, 62.3%–87.5%) for smokers, respectively. The survival rate of smokers was significantly lower than patients without a smoking history ($P=0.0059$) [Figure 2].

The results of univariate analysis and multivariable analyses using the Cox proportional hazards model are shown in Tables 2 and 3. When adjusting for age, gender, body mass index, alcohol consumption history, diabetes, and number of stents used, the risk of death in pre-operative smokers during follow-up was 2.1-fold higher than non-smokers ($P=0.039$).

During the follow-up period, 21 (6.2%) and 21 (5.1%) patients in the pre-operative smoking and no smoking groups underwent intervention, respectively; univariate ($P=0.486$) and multivariate analyses (hazard ratio = 1.3, 95% CI: 0.6- 2.7, $P=0.523$) showed that the difference was not significant.

Discussion

Smoking is an independent risk factor for cardiovascular disease, especially in the development of coronary heart disease and aneurysms.[7-9,18-20] Studies have shown that smoking can change systolic and diastolic functions of the aorta, increasing expansion of the aneurysm wall, and accelerating aneurysm progression.[18,21] Smoking is also a risk factor for poor prognosis after cardiovascular surgery. Smoking can weaken vasodilation functions and strengthen the contractility of the saphenous vein bridge after bypass surgery,[22] promoting the accumulation of lipids in plaques of the saphenous vein bridge,[13] thereby increasing the risk of occlusion of the saphenous vein bridge after bypass surgery. Smoking also accelerates the structural deterioration of bioprosthetic valves after heart valve replacement.[12] Smoking has been widely recognized as a

risk factor for cardiovascular disease, but the impact of smoking on post-operative survival in patients with uncomplicated type B dissections treated with TEVAR is still lacking. In this study, post-operative survival data of 751 patients with uncomplicated type B dissections, who underwent TEVAR for 13 consecutive years at our center, were collected. The dataset showed that the 5- and 10-year survival rates of patients, with uncomplicated type B dissections, were 96.5% and 83.0%, respectively. The results of the multivariable analyses using the Cox proportional hazards model showed that the risk of death for smokers during follow-up was 2.1-fold higher than non-smokers.

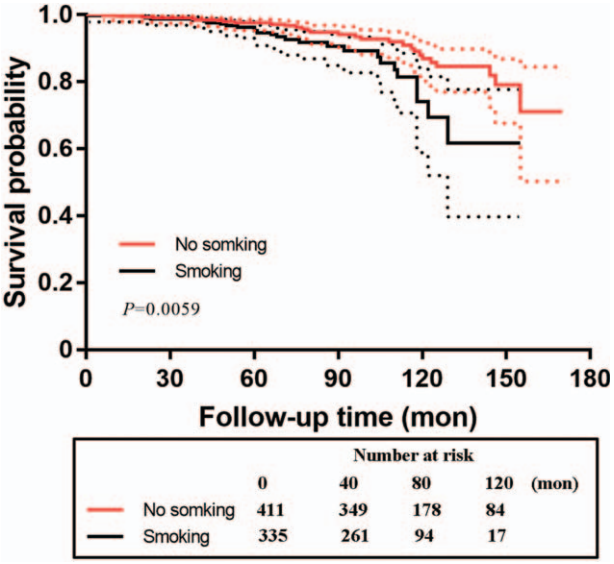

Figure 2: The 5- and 10-year survival rates of non-smokers ($n = 414$) were 97.6% (95% CI, 96.0%–99.2%) and 87.0% (95% CI, 81.6%–92.7%), respectively, and 94.9% (95% CI, 92.2%–97.7%) and 73.8% (95% CI, 62.3%–87.5%) for smokers ($n = 337$), respectively. The log-rank test shows $P = 0.0059$. CI: Confidence interval.

There are no targeted studies to indicate the mechanism whereby smoking increases the long-term mortality of uncomplicated type B dissection patients, treated with TEVAR. Given the current mechanisms where smoking affects the prognosis of other cardiovascular diseases, we suggest the following mechanism whereby a smoking history increases the risk of long-term mortality in patients with uncomplicated type B dissections. First, smoking may increase the risk of residual dissection distal to the stent expansion in patients with uncomplicated type B dissections,[18,21] leading to an increased risk of aortic rupture. Second, smokers often have more severe aortic atherosclerosis and calcifications in the aorta wall, which reduces aortic diastolic functions, decreases compliance in the aorta in the presence of a pulsating blood pressure,[21] and increases the probability of residual dissection rupture. Smoking is an independent risk factor for a variety of cardiovascular diseases, especially coronary heart disease,[20] which increases the risk of death from other cardiovascular diseases, such as

Table 2: Univariate analysis for follow-up death rate of the 751 uncomplicated type B dissection patients underwent TEVAR.

Variables	Values	HR (95% CI)	*P*
Age (years)	52.8 ± 10.9	1.0 (1.0, 1.1)	<0.001
Gender (female)	132 (17.7)	0.7 (0.3, 1.6)	0.403
BMI (kg/m^2)	26.0 ± 3.8	1.0 (0.9, 1.1)	0.925
Hypertension	549 (73.6)	1.2 (0.6, 2.1)	0.637
CAD	51 (6.8)	1.4 (0.6, 3.5)	0.480
Diabetes	38 (5.1)	2.6 (1.1, 6.2)	0.025
Smoking	335 (44.9)	2.1 (1.2, 3.6)	0.007
Drinking	165 (22.1)	1.8 (1.0, 3.4)	0.058
Onset-to-TEVAR time (days)	13 (8–32)	1.0 (1.0, 1.0)	0.285
Disease staging			
Chronic phase	102 (13.7)	1.0	1.000
Sub-acute phase	240 (32.2)	0.7 (0.4, 1.4)	0.349
Acute phase	404 (54.2)	0.7 (0.4, 1.4)	0.338
Number of stents used			
1	634 (87.6)	1.0	1.000
2	83 (11.5)	2.0 (1.0, 4.3)	0.064
3	7 (1.0)	0.0 (0.0, Inf)	0.996
Brand of the stent			
Talent	20 (2.7)	1.0	1.000
Valiant	172 (23.1)	0.9 (0.2, 3.8)	0.907
GRIMED	230 (30.8)	1.2 (0.3, 3.8)	0.814
Hercules	125 (16.8)	1.7 (0.5, 5.8)	0.432
Zenith TX2	86 (11.5)	1.7 (0.4, 8.1)	0.500
Relay	76 (10.2)	1.3 (0.3, 6.0)	0.762
E-vita	37 (5.0)	2.3 (0.4, 14.7)	0.374

Data were presented as mean ± SD or *n* (%) or median (interquartile range). HR: Hazard ratio; CI: Confidence interval; BMI: Body mass index; CAD: Coronary artery disease; TEVAR: Thoracic endovascular aortic repair; SD: Standard deviation.

Table 3: Multivariable analyses between smoking history and follow-up death rate.

	Non-adjusted		Adjust I		Adjust II	
Smoking history	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
No	1 (1.0, 1.0)	1.000	1 (1.0, 1.0)	1.000	1 (1.0, 1.0)	1.000
Yes	2.1 (1.2, 3.6)	0.007	2.4 (1.3, 4.5)	0.008	2.1 (1.0, 4.1)	0.039

Non-adjusted model adjust for: None; Adjust I model adjust for: age, gender, BMI; Adjust II model adjust for: age, gender, BMI, diabetes, drinking history, number of stents used. HR: Hazard ratio; CI: Confidence interval; BMI: Body mass index.

acute myocardial infarction. Finally, smoking is a risk factor for lung cancer and stroke. Smoking may increase the post-operative all-cause mortality. A study of abdominal aortic aneurysms showed that 25 years after smoking cessation, the risk of abdominal aortic aneurysm formation in smokers was equal to non-smokers,[23] suggesting that smokers should quit smoking as soon as possible. Studies have shown that one-third of cardiovascular disease patients who smoke, will continue to smoke after surgery,[24] which reinforces the need for rehabilitation programs after surgery.

This was a retrospective study that determined the effects of a pre-operative smoking history on long-term survival, but did not classify the degree of smoking in patients. Thus, whether or not there was a difference between patients with mild and severe smoking is not clear. At the same time, we did not analyze the different effects of smoking cessation or continued smoking on long-term survival in patients with a smoking history, and did not analyze patients who started smoking after TEVAR. This is unfortunate and further research is needed.

As an independent risk factor for several cardiovascular diseases, pre-operative smoking also affects the prognosis of uncomplicated type B dissection patients treated with TEVAR, increasing the risk of follow-up mortality rates by 2.1-fold. We recommend that smokers quit smoking as soon as possible, and we also recommend a strict smoking cessation program for patients who continue to smoke after TEVAR.

Funding

This work was supported by a grant from the National Natural Science Foundation of China (No.11972215).

Conflicts of interest

None.

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How to cite this article: Gao HQ, Ren CW, Yang S, Huang LJ, Sun LZ, Xu SD. Smoking history increases the risk of long-term mortality after thoracic endovascular aortic repair in patients with an uncomplicated type B dissection. Chin Med J 2020;133:402–407. doi: 10.1097/CM9.0000000000000640