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

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. 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 ($P = 0.039$).

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.

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

![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.](image)

### 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/m²)                   | 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 (0.8, 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.
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 the post-operative all-cause mortality. A study of the post-operative all-cause mortality. A study of abdominal aortic aneurysms showed that 25 years after the post-operative all-cause mortality. A study of smokers was equal to non-smokers, suggesting that smokers should quit smoking as soon as possible. Studies have shown that one-third of 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. 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/CM9.0000000000006640