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Late Onset of Thoracic Aortic Disease Events after Abdominal Aortic Aneurysm Repair: Effect on Survival and Possible Associated Factors

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Abstract

We investigated the possible relation between thoracic aortic disease events and long-term survival in patients after open Abdominal Aortic Aneurysm (AAA) repair, as well as factors associated with event occurrence. Pre-AAA-repair demographic, comorbid, and laboratory variables in 48 patients who had an aortic dissection or thoracic aortic aneurysm up to 25 years after AAA repair were compared with the same variables in 522 patients without such an event. Survival rates at 5 and 10 years were 87% and 53%, respectively, in patients with a thoracic aortic event and 74% and 56% in those without an event (*P*=.7). Multivariate analysis showed that the risk of thoracic aortic events was increased by a high hemoglobin level, a high Fibrinogen Degradation Product (FDP) level, and a larger AAA diameter. The only factors significantly associated with thoracic aortic events were an AAA diameter of ≥ 55 mm and a high FDP level.

Keywords: Abdominal aortic aneurysm; Aortic dissection; Thoracic aortic aneurysm; Fibrinogen degradation product

Introduction

The 5-year survival rate after elective open surgical repair of Abdominal Aortic Aneurysm (AAA) is about 70%. Thus, the mortality rate among patients who have undergone repair (30%) is about as high as that among patients with stage II gastric cancer or stage III rectal cancer [1-6]. Possible reasons for the relatively high mortality after AAA repair include the advanced age of the patients and the presence at operation or afterward of various comorbid conditions, especially cardiovascular disease, cerebrovascular disease, and cancer [7-9]. It is also possible that onset of a thoracic aortic disease event such as Thoracic Aortic Aneurysm (TAA) or aortic dissection, the causes of which are similar to those of AAA, may affect the prognosis of a patient in whom AAA repair was performed years earlier [10]. However, the incidence of TAA and aortic dissection after AAA repair, the possible effect of these events on long-term post-repair survival, and factors associated with onset of thoracic aortic events after repair have not been well studied. We therefore assessed the effects on survival after AAA repair of onset of TAA or aortic dissection. We also investigated risk factors for those events by comparing demographic, comorbid, operative, and laboratory variables in patients in whom an event occurred during a follow-up period of up to 25 years with the same variables in patients who did not have an event.

Methods

Study population

The study was an analysis of data obtained from a retrospective review of the medical records of 607 patients who underwent open infrarenal AAA repair consecutively at our institution between 1985 and 2005. Twenty-nine of these patients were subsequently excluded from the analysis because, at the time of their AAA repair, they had TAA or a history of TAA repair or aortic dissection. Eight other patients were excluded because their AAA repair was done with use of a hand-made stent graft. Thus, 570 patients (470 men, 100 women; mean age, 70 years) were included in the study. Aortic reconstruction in these patients consisted of implantation of 15 straight (2.6%) and 555 bifurcated (97.4%) bypass grafts through a transperitoneal or retroperitoneal approach. The graft material was polyethylene in 558 patients (97.9%) and expanded polytetrafluoroethylene (ePTFE) in 12 (2.1%). The proximal diameter of the grafts was 12 (5; 0.9%), 14 (50; 8.8%), 16 (191; 33.5%), 18 (152; 26.7%), 20 (107; 18.8%), 22 (29; 5.1%), 24 (31; 5.4%), or 25 (2; 0.3%) mm. The diameter of three grafts (0.5%) was not recorded. Table 1 shows demographic, comorbid, and operative variables for the patients at the time of AAA repair.

During the follow-up period after AAA repair, 48 of the 570 patients (8%) had an acute aortic dissection (n = 13 [2.3%]) or TAA rupture or first diagnosis of TAA as detected with use of computed tomography (CT) (n = 35 [6.1%]).

Statistical analysis

Patients with and without a thoracic aortic disease event after AAA repair were compared to assess the possible effect of such an event on long-term survival and to identify factors associated with event onset. Multivariate logistic analysis was performed by selecting variables found to be significantly associated ($P<.05$) with the presence of a thoracic aortic disease event. This model determined Odds Ratios (ORs) and 95% Confidential Intervals (CIs). The factors analyzed included patients' demographic characteristics, comorbid conditions, and laboratory findings at the time of AAA repair, along with operative data. Categorical variables were compared by using χ^2 tests; continuous variables were compared by using Student's t tests. Kaplan-Meier

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Variable	Value
Mean ± SD age, years (range)	70.5 ± 8.0 (28-89)
Sex: male/female	470 (83)/100 (17)
Current or previous smoker	428 (78)
Hypertensionb	266 (48)
Hyperlipidemia	96 (17)
Diabetes mellitus	53 (10)
Pulmonary insufficiencyc	134 (27)
Coronary artery diseased	79 (14)
Renal insufficiencye	75 (13)
Cerebrovascular disease	19 (3)
Peripheral artery disease	78 (14)
Elective/urgent AAA repair	547 (96)/23 (4)
Mean ± SD AAA diameter (cm)	5.7 ± 1.5
Non ruptured/ruptured AAA	536 (94)/34 (6)
Mean ± SD operating time for AAA repair (min)	280 ± 96

Abbreviation: AAA: Abdominal aortic aneurysm
[a]Values are number (percent) unless otherwise indicated.
[b]Receiving antihypertension therapy, or diastolic blood pressure > 90 mmHg.
[c]Vital capacity < 80% of predicted value.
[d]Current angina pectoris or previous myocardial infarction or coronary revascularization procedure.
[e]Serum creatinine > 1.5 mg/dL.

Table 1: Demographic, Comorbid, and Operative Variables in 570 Patients at the Time of Open AAA Repaira

Variable	OR	95% CI	P
AAA diameter	1.22	1.01-1.48	0.0366
Fibrinogen degradation product level at AAA repair	1.04	1.00-1.08	0.0253
Hemoglobin level at AAA repair	1.76	1.14-2.85	0.0009

Abbreviations: AAA: Abdominal Aortic Aneurysm; CI: Confidence Interval; OR: Odds Ratio

Table 2: Results of a Multivariate Analysis of Variables Significantly Associated with Occurrence of a Thoracic Aortic Event

analysis was employed to calculate survival rate and the incidence rate of any thoracic aortic event, aortic dissection, and TAA in groups of patients; log-rank testing was used to compare rates. A *P* value of <.05 was considered to represent a significant difference between groups of patients or variables.

Results

Nineteen of the 570 patients in the series died within 30 days of AAA repair (perioperative mortality rate, 3.5%). The overall mean ± SD survival rates at 3, 5, and 10 years were 85.3% ± 1.5%, 75.5% ± 2.5%, and 55.3% ± 4.5%, respectively. During the follow-up period (mean time, 6.1 years, with 415 patients followed for 3 years, 328 for 5 years, and 101 for 10 years), aortic dissection occurred in 13 patients (12 men) and TAA in 35 (29 men; *P*=.6561 for the difference between men and women for each event). The mean interval between AAA repair and TAA diagnosis was 5.1 ± 2.4 years, whereas that between AAA repair and aortic dissection was 2.8 ± 2.2 years (P = .005). The survival rates at 5 and 10 years after AAA repair between patients with TAA and those with aortic dissection were not significantly different (5 years: 90.7% ± 5.1% vs 76.9% ± 11.7% [*P*=.1441]; 10 years: 57.8% ± 9.5% vs. 39.9% ± 18.8% [P=.2426]).

Ten of the patients in whom TAA occurred during follow-up had a rupture. Four of the 25 patients with non-ruptured TAA underwent surgical TAA repair. Of the 48 patients who had a thoracic aortic event after AAA repair, 14 died, two because of an acute aortic dissection and six because of TAA rupture. The overall survival rates in patients who did and did not have a thoracic aortic event were 86.9% ± 5.0% and 74.5% ± 2.1%, respectively, at 5 years, and 52.7% ± 8.8% and 55.9% ± 2.8% at 10 years; the differences were not significant (*P*=.7252).

Table 2 shows the results of the multivariate analysis of the possible relation between occurrence of a thoracic aortic disease event and individual demographic, comorbid, operative, and laboratory variables at the time of AAA repair. The analysis showed that the risk of thoracic aortic event occurrence was increased in patients with a high level of hemoglobin (OR, 1.76; 95% CI, 1.14-2.85; *P*=.0009), a high level of Fibrinogen Degradation Product ([FDP]; OR, 1.04; 95% CI, 1.00-1.08; *P*=.0253), and a larger AAA diameter (OR, 1.22; 95% CI 95%, 1.01-1.48; *P*=.0366). None of the other variables, including the size, configuration, or material composing the graft (polyethylene vs. ePTFE), studied showed such an association.

However, as shown in Table 3, an analysis of the relation between demographic, comorbid, and laboratory variables at the time of AAA repair and the incidence of thoracic aortic events for 10 years found that only a larger AAA diameter (>55 mm) and a high level (> 15 μg/dL) of FDP were significantly associated with a greater event incidence, at both follow-up times (*P*=.0034 for AAA diameter and *P*=.0401 for FDP level). None of the other variables studied showed such an association. Figures 1 and 2 are Kaplan-Meier curves demonstrating the relation between the cumulative (up to 10 years) incidence of thoracic aortic events and pre-AAA-repair FDP level and AAA diameter, respectively.

Discussion

Many patients with AAA have a comorbid condition that can affect their prognosis after AAA repair [7-9]. TAA rupture has a mortality rate as high as 97% to 100% [11]. The mortality rate associated with acute aortic dissection (23.9%) is lower but remains discouraging [12]. In our series of 570 patients who underwent AAA repair, the incidence of thoracic aortic disease events was 6.7% at 5 years and 15.5% at 10 years. These results indicate that thoracic aortic disease may occur in patients who have undergone AAA repair, and they underscore the need for careful, long-term monitoring of such patients, even though, as Cambria et al. [13] observed, only 5% of acute dissections occur in the aorta of patients with coexistent or previously treated degenerative aneurysmal disease.

In our study, the occurrence of thoracic aortic disease events

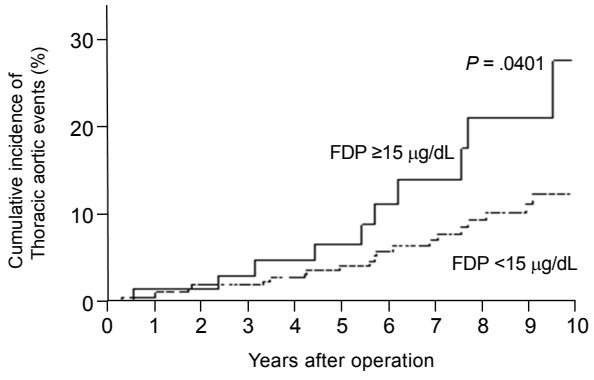

Figure 1: Cumulative incidence of thoracic aortic disease events up to 10 years after abdominal aortic aneurysm repair, according to whether patients had a fibrinogen degradation product level of ≥ 15 (solid line) or < 15 (broken line) μg/dL at the time of repair.
Abbreviation: FDP: Fibrinogen Degradation Product

	Incidence of Thoracic Aortic Events (%)		
Variable	At 5 Years	At 10 Years	P[b]
Age: > 70/≤ 70 years	5.8 ± 1.7/7.7 ± 1.8	15.8 ± 3.8/15.8 ± 2.9	0.6320
Hypertension: Yes/No	7.2 ± 1.9/6.5 ± 1.7	14.4 ± 2.9/16.9 ± 3.5	0.7110
Hyperlipidemia: Yes/No	8.3 ± 3.3/6.5 ± 1.4	16.4 ± 4.9/15.7 ± 2.6	0.5103
Diabetes mellitus: Yes/No	10.9 ± 5.2/6.4 ± 1.3	21.3 ± 8.6/15.2 ± 2.4	0.4222
Cardiovascular disease: Yes/No	11.6 ± 4.6/6.1 ± 1.3	19.1 ± 6.6/15.3 ± 2.5	0.3558
WBC count: > 6000/≤ 6000 mm3	7.2 ± 1.9/6.1 ± 1.7	15.1 ± 3.4/16.3 ± 3.4	0.7708
Hemoglobin: > 12.5/≤ 12.5 g/dL	5.5 ± 1.6/7.9 ± 2.0	16.3 ± 3.3/14.7 ± 3.2	0.9339
Platelet count: > 25/≤ 25 x 104/mm3	11.6 ± 3.5/5.5 ±1.3	17.2 ± 4.5/15.6 ± 2.7	0.2037
C-reactive protein: > 1.1/≤ 1.1 mg/dL	8.6 ± 4.3/6.6 ± 1.5	18.4 ± 7.7/17.1 ± 3.1	0.4912
Fibrinogen: > 300/≤ 300 mg/dL	6.2 ± 1.8/4.3 ± 1.6	17.5 ± 3.9/13.2 ± 3.3	0.3838
FDP: > 15/≤ 15 μg/dL	6.5 ± 3.2/4 ± 1.3	27.8 ± 8.8/12.3 ± 2.7	0.0401
AAA diameter: > 5.5/≤ 5. cm	9.8 ± 2.4/4.6 ± 1.4	23.9 ± 4.6/8.9 ± 2.2	0.0034

Abbreviations: AAA: Abdominal aortic aneurysm; WBC: White blood cell; FDP: Fibrinogen degradation product
[a]Values at 5 and 10 years are means ± SD.
[b]For the difference between categorical variables for 10 years.

Table 3: Demographic, Comorbid, and Laboratory Variables in 570 Patients at the Time of Open AAA Repair in Relation to the Incidence of Thoracic Aortic Events for 10 Years after Repaira

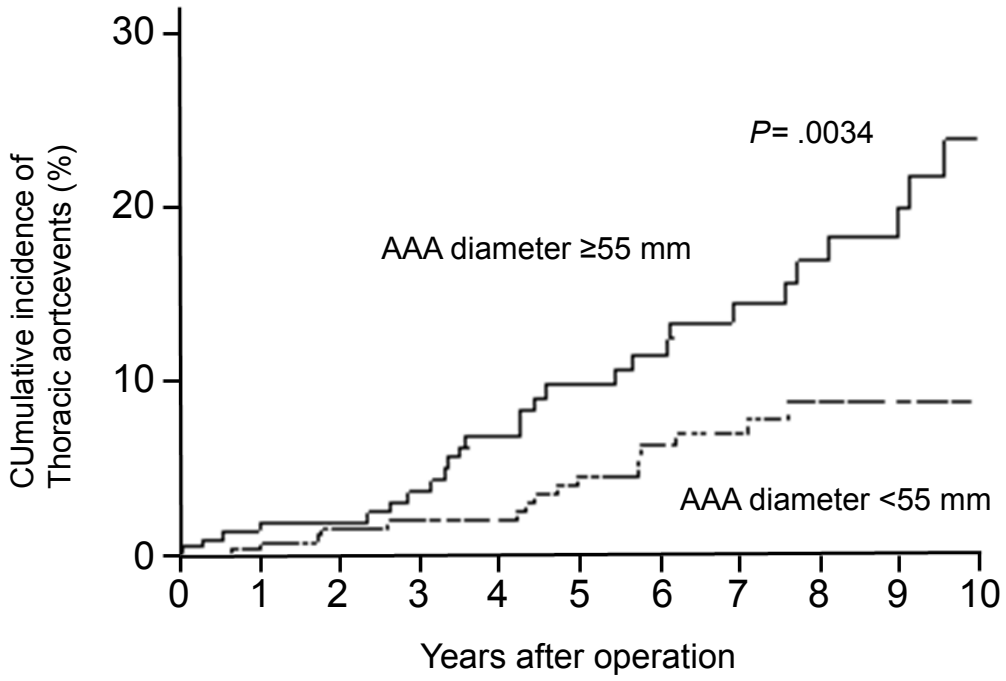

Figure 2: Cumulative incidence of thoracic aortic disease events up to 10 years after abdominal aortic aneurysm repair, according to whether patients had an aneurysm diameter of ≥ 55 (solid line) or < 55 (broken line) mm at the time of repair.
Abbreviation: AAA: Abdominal Aortic Aneurysm

after AAA repair did not affect long-term survival: the survival rate in patients with such an event was not significantly different from that in patients without an event. However, if all our patients who had a thoracic aortic event had died (the 30-day mortality rate for thoracic events was 15.4%), the survival rate in that group would have been significantly lower than that in patients without a thoracic event. Moreover, the overall incidence of thoracic aortic events in our series was low, and this may have contributed to the observed lack of effect of such events on long-term survival.

The ratio of type A to type B dissections has been reported to be about 2:1 and acute type A dissections have been found to have a higher mortality rate than type B dissections [12,14]. Compared with type A dissections, type B dissections occur more commonly after AAA repair, although the reasons for this remain unknown [15]. In our series, the ratio of type A to type B dissections after AAA repair was approximately 1:2, but only two patients with dissection died. Although the coexistence of aortic dissection and previous atherosclerotic aneurysm increases the risk of rupture our results support the use of AAA repair with an abdominal aortic graft [11].

It was previously observed that 12.6% of patients with AAA

subsequently had development of a metachronous thoracic aneurysm [16,17]. In our study, a metachronous aneurysm occurred in 6.6% of patients after AAA repair, and 26.3% developed a TAA after rupture of the repaired AAA. Therefore, careful post-AAA repair monitoring of patients for new lesions is crucial.

FDP, which is produced by the degradation of fibrinogen and fibrin, is a marker for enhanced primary and secondary fibrinolysis. In our study, thoracic aortic events were significantly more likely to occur in patients with a relatively high FDP level at the time of AAA repair than in those with a lower level. Similarly, Kitada et al. [18] reported that an FDP level of 20 μg/dL or higher at hospital admission because of acute type B aortic dissection was an independent predictor of aortic events at 1 year. We speculate that the reason why FDP is an important marker whereas fibrinogen itself is not is that FDP is composed largely of fibrin rather than fibrinogen. The fibrinogen in FDP has not been lysed by plasmin, so FDP and fibrinogen levels do not change in parallel. Our findings suggest that patients with a high FDP level at the time of AAA repair should undergo more frequent clinical, laboratory, and imaging assessments of the thoracic aorta postoperatively.

In our series, the risk of thoracic aortic events after AAA repair was significantly higher in patients with a larger AAA diameter at the time of repair. This is consistent with the results of Chaer et al. [16] who conducted a logistic regression analysis which found that predictors of a diagnosis of TAA included a family history of TAA, hypertension, obesity, and an AAA diameter of greater than 50 mm on presentation. Larger aneurysm size has also been found to markedly increase the risk of rupture, dissection, and death [19].

Our multivariate analysis showed that the risk of thoracic aortic event occurrence was increased by a high preoperative hemoglobin level. However, hemoglobin level was not significantly associated with a greater event incidence for 10 years after AAA repair. These results may have been related to the relatively low number of patients in our study who had an event and represent a limitation of our study.

Cambria et al. [15] reported that the longest interval between AAA repair and spontaneous aortic dissection in 18 patients was 7 years but was shorter than 3 years in most patients. Similarly, in our study, the mean interval between AAA repair and spontaneous dissection was 2.8 years. However, the mean interval between AAA repair and TAA diagnosis was 5.1 years, indicating that follow-up clinical examinations and CT to detect thoracic aortic events should be performed on a long-term basis after AAA repair.

Conclusions

In a series of 570 patients who underwent AAA repair, there was no significant difference in the overall survival rate at 5 and 10 years between the 48 patients (8%) with and the 522 patients (92%) without a thoracic aortic event after repair. Significant risk factors for a thoracic aortic event during follow-up that were present at AAA repair were an AAA diameter of 55 mm or larger and an FDP level of 15 μg/dL or higher. Because of the relatively high incidence of thoracic aortic events after AAA repair, long-term post-repair monitoring of patients for such events is mandatory.

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