SAS Journal of Medicine ISSN 2454-5112
SAS J. Med., Volume-3; Issue-5 (May, 2017); p-87-92
Available online at http://sassociety.com/sasjm/

Original Research Article

An analysis of the factors associated with the outcomes of acute non traumatic aortic disease in patients transported to the emergency department

Toshihiko Yoshizawa[1], Youichi Yanagawa[1]*, Kouhei Ishikawa[1], Hiromichi Ohsaka[1], Kei Jitsuiki[1], Kazuhiko Omori[1], Hiroshi Ito[2], Manabu Sugita[3]

[1]Department of Acute Critical Care Medicine, Shizuoka Hospital, Juntendo University, Izunokuni city, Shizuoka, Japan
[2]Numazu City Hospital, Shizuoka, Japan
[3]Department of Emergency and Critical Care Medicine, Juntendo University Nerima Hospital, Japan

***Corresponding author**
Youchi Yanagawa
Email: yyanaga@juntendo.ac.jp

Abstract: We retrospectively investigated the outcomes of patients with acute non-traumatic aortic disease (ANAD) who were transported to the emergency department (ED). From April 2012 to March 2016, we performed a retrospective medical chart review of patients who had been diagnosed with ANAD based on computed tomography (CT) and blood examination findings in the ED of Numazu City Hospital. The subjects were divided into two groups: the Survival group, which included patients who survived after treatments; and the Fatal group, which included patients who died. The Survival and Fatal groups included 29 patients and 41 patients, respectively. An altered level of consciousness was the most frequent initial complaint, followed by back pain. The age, percentage of female patients, and the incidence of consciousness disturbance, cardiac arrest, and cardiac tamponade in the Survival group were significantly lower in comparison to the Fatal group. In contrast the incidence of back pain in the Survival group was significantly higher than that in the Fatal group. There rate at which cases were misdiagnosed did not differ between the two groups to a statistically significant extent (Survival, 58.6 %; Fatal, 58.5 %). The present study demonstrated that among patients who were diagnosed with ANAD at the ED, advanced age, female gender, unconsciousness, the absence of back pain, cardiac tamponade and cardiac arrest were risk factors for a fatal outcome. However, the outcome was not affected by a delayed diagnosis.

Keywords: non-traumatic aortic disease; risk factor; outcome.

INTRODUCTION

Acute non-traumatic aortic disease (ANAD), such as dissection or aneurysm rupture is associated with high rates of mortality and morbidity, and requires an immediate diagnosis [1-4]. A rapid diagnostic evaluation followed by immediate and appropriate treatment for ANAD is thought to be associated with favorable outcomes [5,6]**.** The typical chief complaint in patients with ANAD is back, chest or abdomen pain at the site of the ANAD [5]. However, many cases present non-typical symptoms; thus, approximately 40% of ANAD cases were reported to have been initially misdiagnosed [6-8]. Although there have been many reports concerning the outcomes of surgery or stenting procedures in patients with ANAD, there have been few reports concerning the outcome of ANAD patients who were transported to the emergency department (ED) [2,5]. In addition, Japan is a front-runner among the world's super-aged societies. In Japan, elderly individuals (≥65 years of age) accounted for 25% of the population in 2013 and 27% in 2016 [9]. The male to female ratio in the Japanese elderly population was 1.3:1 (Statistic Japan, http://www.stat.go.jp/english/index.htm). No studies have been performed to investigate the outcomes of ANAD among patients who are transported to the ED in this unique population. Hence, we retrospectively investigated the outcomes of patients who were transported to the ED in Numazu City Hospital and who were then diagnosed with ANAD.

METHODS

The protocol of this retrospective study was approved by the review board of Numazu City Hospital and Juntendo Shizuoka Hospital. Numazu City Hospital, which is a 500 bed hospital in Numazu city (located near Tokyo), has a medical emergency center and serves a population of approximately 200,000. Although this hospital has an ED, the number of emergency physicians is insufficient; thus, staff members of Shizuoka Hospital, Juntendo University support their activities.

From April 2012 to March 2016, a medical chart review was retrospectively performed for all patients who were diagnosed with ANAD in the ED of Numazu City Hospital based on computed tomography (CT) and blood examination findings. The diagnosis of ANAD was made based on the interpretation of radiology reports in Numazu City Hospital. The level of fibrinogen/fibrin degradation product (FDP) is also an indicator of enhanced fibrinolysis and is a useful marker in patients with aortic disease [10, 11]. An FDP level of >2.00 μg/mL is used to diagnose ANAD and to identify cases of acute myocardial infarction [10]. The patients who survived and those who died were classified into the Survival group and the Fatal group, respectively. The characteristics of the patients in the two groups, including their age, sex, initial complaint, the time from the onset of symptoms to arrival, the presence/absence of cardiogenic cardiac arrest before and after arrival, the classification of the ANAD, and the presence/absence of cardiac tamponade were recorded. The cases in which the diagnosis was delayed (cases in which transportation to Numazu City Hospital was initiated at >30 minutes after the manifestation of symptoms) were identified and the reasons for the delayed diagnosis were classified into two categories: "physician", and "self". In the case of "physician" misdiagnosis, the patient with ANAD was first misdiagnosed by a physician, and the misdiagnosis delayed their transportation to Numazu City Hospital. As a result, it took more than 30 minutes from the onset of symptoms to arrival at the hospital. In the case of "self", the time from the onset of symptoms to arrival at the hospital was more than 30 minutes, even though the subject was transported directly to Numazu City Hospital.

The chi-squared test, a contingency table analysis, and a non-paired Student's *t*-test were used for the statistical analyses. P values of <0.05 were considered to indicate statistical significance. In addition, the factors that were found to be significant according to a univariate analysis and a multivariate analysis with logistic regression, which was performed to determine the factors that were independently associated with a fatal outcome.

RESULTS

During the investigation period, a total of 19,343 patients were treated in the ED of Numazu City Hospital. Among these patients, 70 patients were diagnosed with ANAD. The classifications were as follows: Stanford A (n=45), Stanford B acute aortic dissection (n=14), rupture of thoracic aortic aneurysm (n=2) and rupture of abdominal aortic aneurysm (n=9). The FDP levels of all 70 cases were >2.0 μg/mL. Twenty-nine patients survived, and were classified into the Survival group; 41 died and were classified into the Fatal group. Table 1 lists the initial complaints of the patients. An altered level of consciousness was the most frequent initial complaint, followed by back pain. Back pain was the most frequent initial complaint of patients at the scene. These initial complaints did not include comments that surviving patients made in their interviews.

Table-1: The number of patients with each initial complaint

Unconsciousness	33
Back pain	19
Chest pain	9
Dyspnea	6
Left shoulder pain	2
Vomiting	2
Nausea	1
Headache	1
Toothache	1
Convulsion	1
Left hemiparesis	1
Hemoptysis	1
General pain	1
Difficulty of standing	1
Appetite loss	1

The results of the analyses of two groups are summarized in Table 2. The age, percentage of female patients, and the rates of consciousness disturbance, cardiac arrest, cardiac tamponade were significantly lower in the Survival group than in the Fatal group. In contrast the rate of back pain in the Survival group was significantly higher than that in the Fatal group. There were no significant differences between the two groups with regard to the ANAD classifications or in the percentage of cases in which the diagnosis was delayed (Survival, 58.6%; Fatal, 58.5%). After excluding subjects with thoracic and abdominal aortic aneurysm

rupture, the incidence of Stanford A was significantly lower in the Survival group. Among the 35 subjects who experienced cardiac arrest, the initial rhythm at scene was asystole (n=20), pulseless activity (n=12), sinus (n=2) and ventricular fibrillation (n=1). The diagnosis was delayed for 14 of 35 (40.0 %) subjects with cardiac arrest due to self-misjudgment (n=10) or a misdiagnosis by a medical facility (n=4). Eight cases (22.8%) were found in an unconscious state. The rest of the cases called an ambulance immediately after the manifestation of symptoms but eventually experienced cardiac arrest.

The multivariate analysis (with a logistic regression analysis) revealed that cardiac arrest was the only factor that was independently associated with the outcome.

Table-2: The background characteristics of the subjects and the results of the analysis

	Survival (n=29)	Fatal (n=41)	p value
Age	68.3 ± 2.6	78.4 ± 1.8	
< 0.01			
Sex (Male/Female)	6/23	20/21	< 0.05
Initial sign			
Unconsciousness	5 (17.2%)	28 (68.2%)	<0.0001
Back pain	14 (48.2%)	5 (12.1%)	<0.01
Complication			
Cardiac tamponade	4 (5.7%)	26 (37.1%)	<0.0001
Cardiac arrest	0	34 (82.9%)	<0.0001
Time from onset to arrival (min)			
n.s.			
Delayed diagnosis	17 (58.6%)	24 (58.5%)	n.s.
Self	11	20	
Physician	6	4	
Classification of aortic disease			n.s.
Aortic dissection (AD)	27 (93.1 %)	32 (78.0%)	
Thoracic aneurysmal rupture	0	2 (5.0%)	
Abdominal aneurysmal rupture	2 (6.9 %)	7 (17.0%)	
Type of AD	n=27	n=32	<0.0001
Type A	14 (48.2%)	31 (75.6%)	
Type B	13 (44.8%)		1 (2.4%)

DISCUSSION

This is the first report to demonstrate that advanced age, female gender, unconsciousness, the absence of back pain, cardiac tamponade and cardiac arrest (in the prehospital setting or in hospital), were associated with the risk of a fatal outcome in among patients who were diagnosed with ANAD at the ED. Conversely, the presence of back pain without unconsciousness and cardiac arrest, were key factors associated with a favorable outcome. Among these risk factors, cardiac arrest was the only factor to be independently associated with the outcome. Moreover, the diagnosis was delayed until the patient was transported to the ER in 58% of all patients and 40% of the patients with cardiac arrest. However, the delay itself did not affect the outcome.

With regard to advanced age, elderly individuals tend to have various underlying diseases [12-14]. These complications may result in a fatal outcome [14]. In contrast, Caus et al. reported that operative mortality was not significantly affected by age in patients of >70 years of age, if patients did not present any of the following complications at admission: tamponade, shock, endotracheal intubation upon arrival or evidence of brain, myocardial, mesenteric, renal or limb malperfusion [15]. Our study included many patients with these conditions; thus our results differed from the results of Caus *et al*.

With regard to sex differences, Divchev *et al*. reported that aortic disease traditionally affected men more frequently than women, but with a varying gender ratio [16]. Nevertheless, in the setting of acute aortic dissection, the International Registry of Acute Aortic Dissections suggests that women are at an increased risk of both dying from aortic dissection and having aorta-related complications than men [16]. In addition, Grubb et al. reported that female patients with thoracic aortic disease had worse outcomes and a higher rate of mortality than men [17]. Accordingly, they hypothesized that a hormonal or molecular mechanism

may underlie the sex differences in aortic disease and suggested that the difference was partly explained by a failure of the medical community to recognize atypical clinical presentations in women, which led to a delay in management. In Japan, which is a front-runner among the world's super-aged societies, women tend to survive longer than men [9]. This tendency may have affected the results of the present study.

Previous reports have shown that a patient's preoperative condition did not predict a fatal outcome. The important predictors of mortality were consciousness disturbance, tamponade, heart failure or visceral malperfusion, similar to our results [12, 18-20]. Among these factors, cardiac arrest had the greatest impact. Meron *et al*. reported that among 46 patients with cardiac arrest due to aortic dissection or rupture, return of spontaneous circulation occurred in 12 (26%) patients, emergency surgery was performed in 8 of these patients; 2 (4%) survived to discharge in a good neurological condition [21]. As a result, they concluded that the mortality of patients with cardiac arrest caused by aortic dissection or rupture remained very high, even when circulation could initially be restored. We also reported that the rate of mortality was high in ANAD patients who experienced cardiac arrest [8].

A rapid diagnostic evaluation followed by immediate and appropriate treatment for ANAD is thought to be associated with a favorable outcome [3, 4]. However, this study failed to show that a delayed diagnosis led to a fatal outcome. Interestingly, von Bierbrauer *et al*. reported that the actual mortality rate of these patients, even those who received a prompt correct diagnosis and appropriate treatment, was still currently higher than 40% [22]. This high mortality rate was one of the reasons for our results. ANAD is associated with a wide range of clinical symptoms [22, 23]. These are often initially unspecific and frequently lead to delays in establishing the correct diagnosis; thus, ANAD may be first recognized at autopsy [24]. Similarly to us, Kurabayashi *et al*. and Asouhidou *et al*. reported that a misdiagnosis or a delayed diagnosis did not themselves affect the final outcome [24, 25].

The ultrasound assessment of patients in shock is becoming the standard of care in emergency and critical care settings worldwide [26, 27]. Based on the present results, the medical first responder should use bedside ultrasound to investigate the possibility of cardiac tamponade or dissection, especially in patients who were found unconscious or in cardiac arrest. Gaspari *et al.* reported that patients with cardiac arrest in whom pericardial effusion was detected by ultrasound and who underwent pericardiocentesis demonstrated higher survival rates in comparison to all other cardiac patients [28]. A more rapid diagnostic evaluation using ultrasound followed by immediate and appropriate treatment for ANAD may improve the outcomes in the future.

The present study is associated with some limitations, including its retrospective design, the small number of cases, and the impact of the super-aged society. This would raise the possibility that risk factors for fatal outcomes in the present study may not be applicable to other institutions or other patient populations. Thus, future prospective studies in larger study populations should be performed to further examine this issue.

CONCLUSION

The present study demonstrated that advanced age, female gender, unconsciousness, the absence of back pain, cardiac tamponade and cardiac arrest were risk factors for a fatal outcome in patients who were diagnosed with ANAD at the ED. The diagnosis of 58% of all subjects and 40% of the subjects with cardiac arrest was delayed; however, the delay itself did not affect the outcome.

Conflict of interest statement

The authors declare no conflicts of interest in association with the present study.

Support

This study received financial support from Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT)-Supported Program for the Strategic Research Foundation at Private Universities, 2015-2019, Pfizer and Shionogi, Inc.

REFERENCES

1. Kurabayashi M, Miwa N, Ueshima D, Sugiyama K, Yoshimura K, Shimura T, Aoyagi H, Azegami K, Okishige K, Isobe M. Factors leading to failure to diagnose acute aortic dissection in the emergency room. Journal of cardiology. 2011 Nov 30; 58(3):287-93.
2. Chua M, Ibrahim I, Neo X, Sorokin V, Shen L, Ooi SB. Acute aortic dissection in the ED: risk factors and predictors for missed diagnosis. The American journal of emergency medicine. 2012 Oct 31; 30(8):1622-6.
3. Butler J, Ormerod OJ, Giannopoulos N, Pillai R, Westaby S. Diagnostic delay and outcome in surgery for type A aortic dissection. QJM. 1991 May 1; 79(2):391-6.
4. Tolenaar JL, Hutchison SJ, Montgomery D, O'Gara P, Fattori R, Pyeritz RE, Pape L, Suzuki T, Evangelista A, Moll FL, Rampoldi V. Painless Type B Aortic Dissection: Insights From the International Registry of Acute Aortic Dissection. Aorta. 2013 Jul;1(2):96.
5. Nienaber CA, Clough RE. Management of acute aortic dissection. The Lancet. 2015 Mar 6;385(9970):800-11.

6. Jelinek GA, Bugeja LC, Spanos PA, Neate SL, Bergman RL, Ranson DL. Collaboration between the coroner and emergency physicians: efforts to improve outcomes from aortic dissection. Med J Aust. 2014 Nov 17;201(10):607-9.
7. Ayrik C, Cece H, Aslan O, Karcioglu O, Yilmaz E. Seeing the invisible: painless aortic dissection in the emergency setting. Emergency Medicine Journal. 2006 Mar 1; 23(3):e24-.
8. Yanagawa Y, Sakamoto T. Characteristics of patients that experience cardiopulmonary arrest following aortic dissection and aneurysm. Journal of emergencies, trauma, and shock. 2013 Jul; 6(3):159.
9. Arai H, Ouchi Y, Yokode M, Ito H, Uematsu H, Eto F, Oshima S, Ota K, Saito Y, Sasaki H, Tsubota K. Toward the realization of a better aged society: messages from gerontology and geriatrics. Geriatrics & gerontology international. 2012 Jan 1; 12(1):16-22.
10. Nagaoka K, Sadamatsu K, Yamawaki T, Shikada T, Sagara S, Ohe K, Morishige K, Tanaka E, Tashiro H. Fibrinogen/fibrin degradation products in acute aortic dissection. Internal Medicine. 2010; 49(18):1943-7.
11. Yamazumi K, Ojiro M, Okumura H, Aikou T. An activated state of blood coagulation and fibrinolysis in patients with abdominal aortic aneurysm. The American journal of surgery. 1998 Apr 30; 175(4):297-301.
12. Caus T, Frapier JM, Giorgi R, Aymard T, Riberi A, Albat B, Chaptal PA, Mesana T. Clinical outcome after repair of acute type A dissection in patients over 70 years-old. European journal of cardio-thoracic surgery. 2002 Aug 1;22(2):211-7.
13. Rylski B, Hoffmann I, Beyersdorf F, Suedkamp M, Siepe M, Nitsch B, Blettner M, Borger MA, Weigang E. Acute aortic dissection type A: age-related management and outcomes reported in the German Registry for Acute Aortic Dissection Type A (GERAADA) of over 2000 patients. Annals of surgery. 2014 Mar 1; 259(3):598-604.
14. Neri E, Toscano T, Massetti M, Capannini G, Carone E, Tucci E, Diciolla F, Scolletta S, Morello R, Sassi C. Operation for acute type A aortic dissection in octogenarians: is it justified?. The Journal of thoracic and cardiovascular surgery. 2001 Feb 28;121(2):259-67.
15. Caus T, Frapier JM, Giorgi R, Aymard T, Riberi A, Albat B, Chaptal PA, Mesana T. Clinical outcome after repair of acute type A dissection in patients over 70 years-old. European journal of cardio-thoracic surgery. 2002 Aug 1; 22(2):211-7.
16. Divchev D, Najjar T, Tillwich F, Rehders T, Palisch H, Nienaber CA. Predicting long-term outcomes of acute aortic dissection: a focus on gender. Expert review of cardiovascular therapy. 2015 Mar 4; 13(3):325-31.
17. Grubb KJ, Kron IL. Sex and gender in thoracic aortic aneurysms and dissection. InSeminars in thoracic and cardiovascular surgery 2011 Aug 31 (Vol. 23, No. 2, pp. 124-125). WB Saunders.
18. Cazzato M, Fellini P, Floris GP, Legittimo A, Rocco D, Sbenaglia E, di Quacquaro AS. Outcome of acute type A aortic dissection: single-center experience from 1998 to 2007. J prev med hyg. 2009;50:152-8.
19. Song JK, Kang SJ, Song JM, Kang DH, Song H, Chung CH, Lee JW, Song MG. Factors associated with in-hospital mortality in patients with acute aortic syndrome involving the ascending aorta. International journal of cardiology. 2007 Jan 31; 115(1):14-8.
20. Bachet J, Goudot B, Dreyfus G, Brodaty D, Dubois C, Delentdecker P, Teimouri F, Guilmet D. Surgery of acute type A dissection: what have we learned during the past 25 years?. Japanese Journal of Cardiovascular Surgery. 2000 Jul 15;29(4):211-20.
21. Meron G, Kürkciyan I, Sterz F, Tobler K, Losert H, Sedivy R, Laggner AN, Domanovits H. Non-traumatic aortic dissection or rupture as cause of cardiac arrest: presentation and outcome. Resuscitation. 2004 Feb 29;60(2):143-50.
22. von Bierbrauer, Dilger, Fink. Acute aortic dissection–vascular emergency with numerous pitfalls. Vasa. 2008 Feb 1;37(1):53-9.
23. Zhan S, Hong S, Shan-shan L, Chen-ling Y, Lai W, Dong-wei S, Chao-yang T, Xian-hong S, Chun-Sheng W. Misdiagnosis of aortic dissection: experience of 361 patients. The Journal of Clinical Hypertension. 2012 Apr 1; 14(4):256-60.
24. Kurabayashi M, Miwa N, Ueshima D, Sugiyama K, Yoshimura K, Shimura T, Aoyagi H, Azegami K, Okishige K, Isobe M. Factors leading to failure to diagnose acute aortic dissection in the emergency room. Journal of cardiology. 2011 Nov 30;58(3):287-93.
25. Asouhidou I, Asteri T. Acute aortic dissection: be aware of misdiagnosis. BMC research notes. 2009 Feb 20;2(1):25.
26. Blanco P, Aguiar FM, Blaivas M. Rapid Ultrasound in Shock (RUSH) Velocity-Time Integral A Proposal to Expand the RUSH Protocol. Journal of Ultrasound in Medicine. 2015 Sep 1; 34(9):1691-700.
27. Bagheri-Hariri S, Yekesadat M, Farahmand S, Arbab M, Sedaghat M, Shahlafar N, Takzare A, Seyedhossieni-Davarani S, Nejati A. The

impact of using RUSH protocol for diagnosing the type of unknown shock in the emergency department. Emergency radiology. 2015 Oct 1; 22(5):517-20.

28. Gaspari R, Weekes A, Adhikari S, Noble VE, Nomura JT, Theodoro D, Woo M, Atkinson P, Blehar D, Brown SM, Caffery T. Emergency department point-of-care ultrasound in out-of-hospital and in-ED cardiac arrest. Resuscitation. 2016 Dec 31; 109:33-9.