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Review Article

Long-Term Survival of Korean Aortic Aneurysm Patients

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Abstract

The study aim is to determine factors affecting the long-term survival of subjects with Aortic Aneurysm (AA). The sample included 294 Korean patients aged ≥ 30 years who were hospitalized from 1994 through 2004. Diagnosis was confirmed in 294 AA subjects (18.4% in affected Coronary Artery Disease (CAD); 75.8% with abdominal only AA (AAA) and 24.2% with Thoracic AA (TAA)) by computed tomography angiography in Samsung Medical Center, Seoul, Korea. AA repair direct operation or percutaneous endovascular AA repair (Revascularized group) was performed for 60.3% of the patients. Death data were obtained from all participants between 1994 and 2009. The mean age of AA subjects was 68.7 (±8.1) years. The proportion of males was 82%. Five- and 10-year survival rates were 89.8% and 82.6%, respectively. The 5-and 10-year survival rates were 92.3% and 84.9% in revascularized group and 86.4% and 79.5% in non-revascularized group, respectively. Adjusted hazard ratios were 1.14 (95% Confidence Interval (CI) 1.06-1.22) in ages and 2.94 (95% CI 1.23-7.38) in smoking for AA. Age and smoking contributed to death in Korean AA patients. And the 10-year survival rate for AA patients in Korea was over 80%. Revascularized group shows higher survival rate than non-revascularized group.

Introduction

Atherosclerosis is the leading cause of Cardiovascular Disease (CVD) such as Coronary Artery Disease (CAD), Cerebrovascular Accident (CVA) and other atherosclerotic vascular disease. Mortality due to CAD and CVA has increased worldwide over the past few decades. The increase in mortality has been attributed to an increase in the elderly population, a westernized life style, and/or increased chronic disease incidence in Korea [1,2]. For the aforementioned reasons, more attention has recently been focused on the aortic disease [3]. Although the incidence of Aortic Aneurysm (AA) has increased with the increase in the elderly population [4], few studies have reported the long-term survival of subjects with AA in Korea. Our objective in this study was to analyze factors affecting the long-term survival of subjects with AA.

Methods

Study population and design

We reviewed the records of patients diagnosed with AA at the Cardiac and Vascular Center, Samsung Medical Center, Seoul, Korea from 1994 through 2004. Subjects consisted of patients with AA (n=267, male=82%) including Thoracic Aortic Aneurysm (TAA, n=52) and Abdominal Aortic Aneurysm (AAA, n=215) confirmed by Computed Tomography (CT) angiography. TAA and AAA were defined as follows: TAA was AA affecting the thoracic aorta, regardless of abdominal aorta, while AAA was AA affecting only the abdominal aorta. Genetic aorta diseases such as marfan syndrome and Loeys-Dietz syndrome were excluded. CAD in AA subjects was confirmed by cardiac catheterization, coronary CT, echocardiography, or positron emission tomography. AA repair direct operation or percutaneous endovascular AA repair (AA Revascularized group) (n=161) was performed. Information was obtained by reviewing electronic medical charts. This study was approved by the Samsung Medical Center institutional review board; informed consent was waived for this retrospective study.

Diagnostic criteria

Cardiovascular risk factors: Subjects were defined as having Hyper Tension (HT) if they were taking an anti-hypertensive agent, had been clinically diagnosed with HT, or had either a Systolic Blood Pressure (SBP) ≥ 140 mmHg or a Diastolic Blood Pressure (DBP) ≥ 90 mmHg. Subjects who met one of the following requirements were defined as having Diabetes Mellitus (DM): taking an oral hyperglycemic agent, using insulin, clinical diagnosis of diabetes, or a fasting plasma glucose > 125 mg/dL. Subjects were defined as dyslipidemia if they met one of the following requirements: diagnosis of hypercholesterolemia or medication history for lipid lowering history or Total Cholesterol (TC) > 200 mg/dL or Low Density Lipoprotein (LDL) > 130 mg/dL. Anti-coagulants agents' data also was collected. The criterion for obesity based on Body Mass Index (BMI) was

Table 1: General and clinical characteristics of subjects with aortic aneurysm (n=267).

Variables	mean±SD or percentage
Age, years	68.7±8.1
45-64 years	29.2
≥65 years	70.8
Gender, male	82.0
Hypertension	63.7
Diabetes	21.7
Dyslipidemia	41.6
Body mass index	23.0±3.21
Obese	25.5
Smoking, current	40.8
Chronic kidney disease	35.4
Coronary artery disease presence	19.9
Aortic aneurysm type	
Only abdominal aorta affected	80.5
Thoracic aorta affected	19.5
Aortic aneurysm operation or stent insertion	60.3
Aortic aneurysm maximum size, mm	55.5±16.2
Systolic blood pressure, mmHg	134.8±22.5
Diastolic blood pressure, mmHg	79.2±13.7
Fasting plasma glucose, mg/dl	118.5±43.0
Cholesterol, mg/dl	
Total cholesterol (normal range 110-240)	183.0±42.5
Triglyceride (normal range 50-200)	140.9±87.8
Low density lipoprotein (normal range 40-130)	118.5±41.6
High density lipoprotein (normal range 45-65)	42.5±16.0
Creatinine, mg/dl (normal range 0.7-1.3 in male, 0.6-1.1 in female)	1.24±0.74
eGFR, mL/min/1.73m^2 (normal range 60-90)	65.2±20.3
Medication	
Anti-coagulants agents	54.0
Anti-hypertensive agents	62.2
Oral hyperglycemic agents or insulin	2.90
Lipid lowering agents	40.7

AA Aortic Aneurysm; eGFR estimated Glomerular Filtration Rate.

BMI ≥ 25 [5]. A patient who had smoked within a year prior to the study was defined as a smoker. The estimated Glomerular Filtration Rate (eGFR), which is used as an indicator of kidney function, was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. The CKD-EPI equation is eGFR $=141\times\min(\text{serum Cr}/\kappa; 1)^{\alpha} \times \max(\text{serum Cr}/\kappa, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018$ [if female], where κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of serum Cr /κ or 1, and max indicates the maximum of serum Cr /κ or 1. Multiplication factors for race and sex are incorporated into the intercept, which results in different intercepts for different age and sex combinations. The National Kidney Foundation Kidney Disease Outcome Quality Initiative defines Chronic Kidney Disease (CKD) as an eGFR < 60 mL/min/1.73m^2.

Table 2: Associations between clinical variables and overall hazard ratios.

Variables	Crude Hazard Ratio and 95% CI	p-value	Adjusted Hazard Ratio and 95% CI*	p-value
Age, years old	1.05 (1.01-1.09)	0.008	1.11 (1.04-1.21)	0.004
Gender, male vs. female	1.55 (0.69-4.72)	0.343	1.25 (0.39-4.79)	0.726
Systolic blood pressure, mmHg	1.00 (0.98-1.01)	0.707	1.00 (0.97-1.02)	0.855
Diastolic blood pressure, mmHg	1.01 (0.98-1.02)	0.598	1.01 (0.96-1.06)	0.527
Fasting plasma glucose, mg/dl	1.00 (0.99-1.01)	0.224	1.01 (0.99-1.01)	0.117
Triglyceride, mg/dl	0.99 (0.98-1.00)	0.116	0.99 (0.98-1.01)	0.247
High density lipoprotein, mg/dl	1.00 (0.97-1.02)	0.908	1.00 (0.97-1.02)	0.901
eGFR, mL/min/1.73m^2	0.99 (0.97-1.01)	0.297	1.00 (0.98-1.03)	0.693
Smoking, current	1.75 (0.96-3.22)	0.068	3.07 (1.26-7.90)	0.017
Body mass index	0.99 (0.89-1.11)	0.941	1.13 (0.98-1.32)	0.084
AA revascularized group	0.65 (0.35-1.19)	0.173	0.99 (0.95-1.02)	0.584
Aortic aneurysm max size, mm	1.00 (0.98-1.02)	0.866	0.58 (0.21-1.65)	0.321

eGFR estimated Glomerular Filtration Rate.

*Estimated by cox proportional hazard model analysis using the variables indicated in the table.

Statistical analysis: General and clinical characteristics of AA subjects are reported as means ± standard deviations (SD) for continuous variables and percentages for categorical variables. Kaplan-Meier analysis was used to plot survival curves for AA subjects. Kaplan-Meier method was also used to compare survival among patients with AA at different sites or in the presence of CAD using log-rank tests. Multiple cox proportional hazards analysis was carried out using the variables of age, gender, SBP, DBP, fasting plasma glucose, triglyceride, high density lipoprotein, eGFR, smoking, BMI, AA Revascularized group, and AA maximum size.

Results

The mean age of AA subjects (n=267; male: female = 8:2) was 68.7 (±8.1) years. The proportion of patients older than 65 years was 70.8%. The proportion of males was 82%. The proportion of cardiovascular risk factors in the patient population was as follows: 63.7% had HT, 41.6% had dyslipidemia, 40.8% had smokers, 35.4% had CKD, 21.7% had DM, and 25.5% had obese. The proportion of CAD comorbidity was 19.9% (Table 1).

Five- and 10-year survival rates for all subjects were 89.8% and 82.6%, respectively. The 5- and 10-year survival rates were 90.2% and 83.3% for AAA patients and 86.4% and 76.8% for TAA patients, respectively (p=.250). The 5- and 10-year survival rates were 88.7% and 81.9% in non-CAD subjects versus 92.6% and 86.6% in CAD subjects, respectively (p=.490). And for AA revascularized group versus non-revascularized group, the 5- and 10-year survival rates were 92.3% and 84.9 % in AA revascularized group versus 86.4% and 79.5% in non-revascularized group, respectively (p= .173) (Figures a-d).

Adjusted Hazard Ratios (HRs) of age was 1.14 (95% Confidence Interval (CI) 1.06-1.22) in ages and adjusted HRs of smoking was 2.94 (95% CI 1.23-7.38) for AA subjects (Table 2). However, adjusted

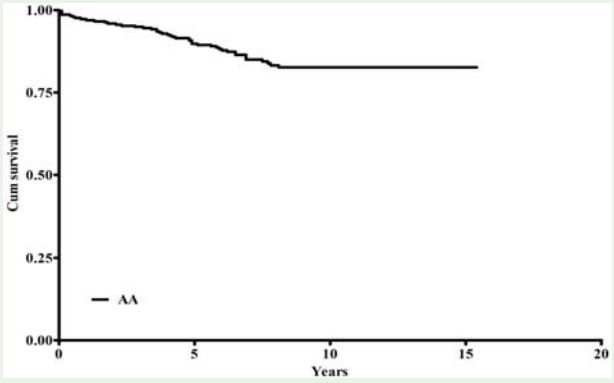

Figure a: Kaplan-Meier curves of cumulative survival rate of all AA subjects.

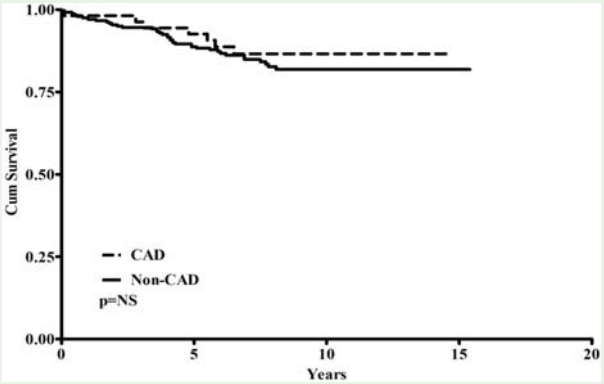

Figure c: Cumulative survival rate of TAA and AAA subjects (p=NS).

HRs of gender, SBP, DBP, fasting plasma glucose, triglyceride, high density lipoprotein, eGFR, BMI, AA revascularized group, and AA maximum size was not significant association.

Discussion

We found that older age and current smoking were shown high risk for death in Korean AA patients. To long term survival of AA patients, they must quit smoking. These findings are consistent with those of previous studies that smoking is a predictor for AA patients [6-9]. AA development was contributed endothelial cells [10]. Endothelial cells respond to a number of stimulating factors such as smoking [11]. Therefore, aggressive non-smoking education program should be applied in smoking AA patients. However, a study in an England cohort from 1997 through 2010 showed that smoking was not associated with cardiac death [12]. Mechanism of underlying the association between older age and development of AA might be related to aortic wall changes. With aging, the vascular wall will gradually lose its elasticity, resulting in aortic dilatation from which mechanical forces will be conveyed to collagen within the aortic wall. Subsequent changes in collagen due to remodeling will lead to a stiffer and less compliant vessel [13]. These findings differ from those for HT [7,8], DM [14], and BMI-defined obesity [8]. Dyslipidemia [15] and CKD may be involved in the pathophysiological mechanism of development due to AA. CVD risk factors did not show affected AA in this study. Because we think that these AA patients were given medical treatment and managed HT, DM, dyslipidemia, and/or CKD in this hospital.

The 5- and 10-year survival rates for Korean AA patients were over 80%. CAD, non-CAD, and AAA subjects also showed over 80% survival rate over 5 and 10 years. Patients with TAA had the lowest 10-year survival rate of 76.8%. Furthermore, the 5- and 10-year survival rates were 92.3% and 84.9% in AA revascularizaed group and 86.4% and 79.5% in non-revascularizaed group, respectively. In Korea, 21,301 echocardiography devices were available at 62,853 medical institutions registered with the National Health Insurance Service in 2013 [16]. This easy accessibility to clinics or hospitals and earlier health examination may have contributed to the higher AA survival rates in Korea. Also, it is important to educate patients and to follow AHA/ACC guidelines for secondary prevention, especially in those patients with coronary and other atherosclerotic vascular diseases in 2006 [17].

Our study showed the proportion of male patients was higher than that of female patients. This result is consistent with United States AAA study [18]. Their study showed that the ratio of male vs female was 4:1. In addition, they revealed that female is protected from AAA formation not only in human [19] but also in animal model [20,21].

This study had several limitations. First, the study was conducted retrospectively at a single center, which may have caused selection bias. We were also unable to eliminate the possibility of information bias when collecting medical records from the medical charts of the subjects and laboratory results. Second, we did not consider other CAD risk factors such as CRP [22], homocysteine [23], lipoprotein (a) [24], fibrinogen [25], physical activity, nutrition, socioeconomic

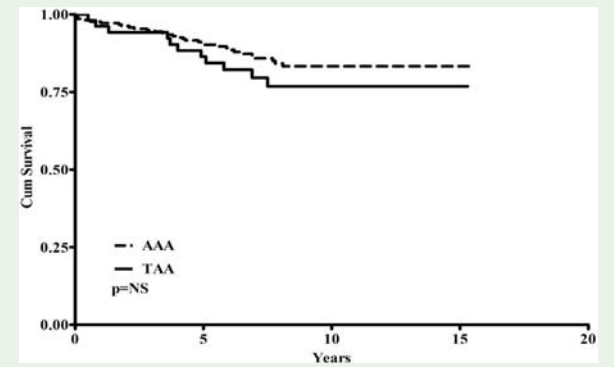

Figure b: Cumulative survival rates of AA patients with and without CAD (p=NS).

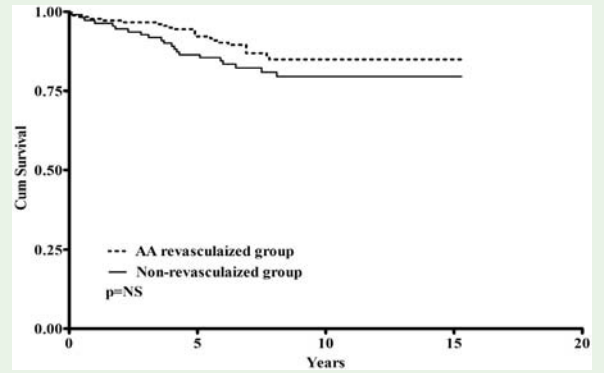

Figure d: Cumulative survival rate of AA patients with and without operation or stent (p=NS).

position, or health behavior variables in this study. Furthermore, we were unable to analyze smoking details because we grouped the patients only into current smoking and ex-smoker or none. Therefore, risk factors of atherosclerosis for prediction of CVD should be confirmed in further prospective cohort studies. We also suggest active non-smoking education program should be applied in smoking AA patients. Third, we could not separately analyze cox proportional hazard model for AAA and TAA due to their small sample size.

Conclusion

We found that age and smoking were associated with increased risk of death in AA patients in Korea. The proportion of male and older age was over two thirds, and the 10-year survival rate for AA patients in Korea was over 80%. Especially, the 10-year survival rates of AA revascularizaed group were over 85%.

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