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# Usefulness of the Suita Score in predicting Deaths from Aortic Aneurysm Rupture and Aortic Dissection in the Japanese General Population

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## Abstract

**Background:** Aortic aneurysm rupture and aortic dissection are the major causes of sudden death in Japan. The Suita score (developed in Japan) and the Framingham risk score are associated with ischemic heart disease deaths. However, it is unclear whether the Suita score is associated with aortic aneurysm rupture and aortic dissection deaths in the Japanese general population. This study aimed to examine whether the Suita score can predict aortic aneurysm rupture and aortic dissection deaths in the Japanese general population.

**Methods and Results:** We used data on 534,414 subjects (aged 40–75 years) who participated in the annual "Specific Health Check and Guidance in Japan" checkup between 2008 and 2013. Univariate and multivariate Cox proportional hazard regression analyses demonstrated that the Suita score was associated with aortic aneurysm rupture and aortic dissection deaths after adjusting for confounding risk factors. The C indices in the Suita score for aortic aneurysm rupture deaths, aortic dissection deaths, and ischemic heart disease deaths were 0.8295, 0.6689, and 0.7039, respectively. The C indices in the Suita score were significantly greater than those in the Framingham risk score for predicting aortic aneurysm rupture and aortic dissection deaths.

**Conclusion:** The Suita score was superior to the Framingham risk score and a feasible marker for aortic aneurysm rupture and aortic dissection deaths in the Japanese general population, indicating that can be used to identify individuals at high risk of aortic aneurysm rupture, aortic dissection, and ischemic heart disease.

## Introduction

Aortic diseases, such as aortic artery dissection and aortic aneurysm rupture, are the major causes of sudden death [1, 2]. Aortic diseases are the third leading cause of sudden death according to autopsy data in Japan [3]. According to the guidelines for the diagnosis and treatment of aortic aneurysm and aortic dissection, it is difficult to prevent death after the onset of aortic diseases since almost all people who suffer from aortic diseases die before hospital arrival [4]. Furthermore, the mortality rate associated with aortic diseases 1 month after symptom onset reaches approximately 50% despite treatment [5, 6]. Therefore, it is important to identify high-risk individuals and prevent the development of aortic diseases in the general population through health checkups.

Several risk scores for ischemic heart disease (IHD) have been developed, such as the Framingham risk score in the United States [7], the European Society of Cardiology-Systemic Coronary Risk Evaluation (ESC-SCORE) in Western countries [8], and the Suita score in Japan. However, the usefulness of these risk scores in predicting aortic aneurysm rupture and aortic dissection deaths has never been examined. The Suita score is an IHD-predictive model score based on the Suita study, a prospective cohort study evaluating new-onset IHD in Suita city, Osaka, Japan [9]. The Suita score low-density lipoprotein cholesterol (LDL-C) version comprises age, sex, smoking, diabetes mellitus, blood pressure, LDL-C, and high-density lipoprotein cholesterol (HDL-C) levels, and chronic kidney disease (CKD) and has a superior prognostic value to the Framingham risk score for IHD. The components of Suita score, excluding diabetes mellitus, are risk factors for aortic aneurysm [10, 11]. IHD is a major risk factor for the presence of an abdominal aortic aneurysm [12, 13]. Thus, we hypothesized that the Suita score can identify individuals at a high risk of aortic diseases and IHD among the general population in Japan.

This study aimed to compare the prognostic value of the Framingham risk score to that of the Suita score and examine whether the Suita score can predict aortic aneurysm rupture and aortic dissection deaths in the Japanese general population.

## Methods

The manuscript was drafted in accordance with the STROBE statement for observational studies [14].

### Study population

This study is a part of the ongoing Research on Design of the Comprehensive Health Care System for Chronic Kidney Disease (CKD), based on individual risk assessments by specific health checkups for all inhabitants of Japan aged between 40 and 74 years and is covered by the Japanese national health insurance. We used data obtained from the following 16 prefectures: Hokkaido, Tochigi, Saitama, Chiba, Nagano, Niigata, Ishikawa, Fukui, Gifu, Hyogo, Tokushima, Fukuoka, Saga, Nagasaki, Kumamoto, and Okinawa. We collected data from 284,321 men and 380,606 women (total, 664,927; age range, 40–74 years) who underwent health checkups during 2008–2013. Among the 664,927 subjects, 110,485 were excluded because of a lack of essential data, including serum creatinine level, proteinuria, and medications. Therefore, 229,927 men and 304,487 women (total, 534,414) were included. A flow chart of the study selection process is shown in (Figure 1).

**Figure 1**

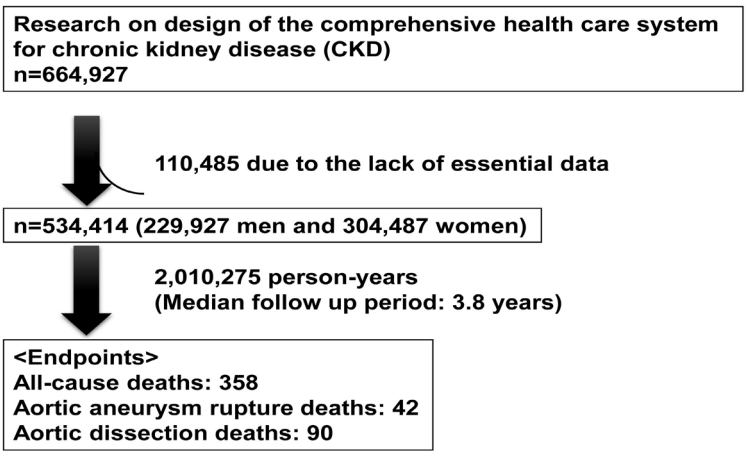


Figure 1. A flow chart of the study selection process

### Definition of cardiovascular risk

Hypertension was defined as a systolic blood pressure of ≥140 mmHg, a diastolic blood pressure of ≥90 mmHg, or antihypertensive medication use. Diabetes mellitus was defined as a fasting blood glucose level of ≥126 mg/dL, a glycosylated hemoglobin A1c level of ≥6.5% (National Glycohemoglobin Standardization Program), or antidiabetic medication use. Dyslipidemia was defined as the HDL-C level of<40 mg/dL, and LDL-C level of ≥140 mg/dL, a triglyceride level of ≥150 mg/dL, or lipid-lowering medication use.

### Definition of chronic kidney disease

The serum creatinine level was measured using an enzymatic method, while the estimated glomerular filtration rate (eGFR) was calculated using the modification of diet in renal disease equation with the Japanese coefficient [15]. The urinalysis consisted of the dipstick measurement of a single spot urine specimen collected at the health checkup. The results were recorded as negative, trace, 1+, 2+, or 3+. Proteinuria was defined as a value of ≥1+. CKD was defined as a reduced eGFR (<60 mL/min/1.73 m2) or the presence of proteinuria according to Kidney Disease Improving Global Outcomes guidelines.

### Measurements

Fasting blood sugar, glycosylated hemoglobin A1c, HDL-C, LDL-C, and triglyceride levels were measured. All blood and urine analyses were performed at the local laboratories. The analytical methods were not standardized between laboratories. However, the analyses were based on the Japan Society of Clinical Chemistry-recommended methods for laboratory tests, which have been widely accepted by laboratories across Japan.

### Suita score

The Suita score LDL-C version was calculated using age, sex, HDL-C and LDL-C levels, systolic blood pressure, diastolic blood pressure, smoking, diabetes mellitus, and eGFR according to a previous report [9]. A high Suita score was defined as a Suita score ≥56, which represents a high risk for IHD.

### Endpoint and follow-up

After obtaining permission from the Ministry of Health, Labour, and Welfare, we accessed the database containing death certificates for all deaths occurring from 2008 to 2015. All subjects were prospectively followed for a median period of 1,450 days (interquartile range, 967–1,828 days). The endpoint was aortic aneurysm rupture or aortic dissection death. To validate the usefulness of the Suita score in this population, we also examined IHD deaths. The cause of death was determined by reviewing the death certificates and classified based on the death code (International Classification of Diseases, 10th Revision). Aortic aneurysm rupture death was defined as the death code [I71.1], [I71.3], or [I71.8]. Aortic dissection death was defined as the death code [I71.0]. IHD death was defined as the death codes [I20.9],[I21.0],[I21.1],[I21.2],[I21.3],[I21.9],[I22.9],[I24.8],[I24.9],[I25.1],[I25.2],[I25.5],[I25.8], and [I25.9].

### Statistical analysis

Continuous and categorical variables were compared using the t-test and chi-square test, respectively. Survival curves were constructed using the Kaplan–Meier method and compared using the log-rank test. A Cox proportional hazard analysis was performed to determine independent predictors for aortic aneurysm rupture and aortic dissection deaths, and Framingham risk score, waist circumference, alcohol consumption, and CKD were entered in the multivariate analysis. Receiver operating characteristics (ROC) curves for IHD, aortic aneurysm rupture, and aortic dissection deaths were constructed and used to measure the predictive accuracy of the Suita score for IHD, aortic aneurysm rupture, and aortic dissection deaths. A P value <0.05 was considered statistically significant. All statistical analyses were performed using standard statistical program packages (JMP version 12, SAS Institute Inc., Cary, NC, USA; and R 3.0.2 with additional packages including Rcmdr, Epi, and pROC).

## Results

### Baseline characteristics and comparison of clinical characteristics between subjects with high and low Suita scores

The subjects' baseline characteristics are shown in (Table 1). Hypertension, dyslipidemia, and diabetes mellitus were identified in 231,126 (43%), 298,946 (56%), and 62,189 (12%) subjects, respectively. The mean Suita and Framingham risk scores were 46 and 6.6, respectively. Since a Suita score ≥56 was considered indicative of a high risk of coronary artery disease, the subjects were divided into a high score group (Suita score ≥56) and a low group (Suita score <56). Subjects with a high Suita score were older and more likely to be male; more likely to have hyper tension, dyslipidemia, diabetes mellitus, proteinuria, and CKD; more likely to be a current smoker; and more likely to be taking antihypertensive, antidiabetic, and antidyslipidemia drugs than those with a low Suita score. Further, subjects with a high Suita score showed a higher Framingham risk score; body mass index; waist circumference; systolic and diastolic blood pressure; and glycosylated hemoglobin A1c, fasting blood sugar, total cholesterol, triglyceride, and LDL-C levels and a lower eGFR and HDL-C levels than those with a low Suita score (Table 2).

| Variables | All subjects n = 534,414 |
|---|---|
| Age, years | 63 ± 6 |
| Male, n (%) | 229,927(43%) |
| Suita score | 46 ± 10 |
| Framingham risk score | 6.6 ± 2.9 |
| BMI, kg/m$^2$ | 23.5 ± 3.4 |
| Waist circumference, cm | 84 ± 9 |
| Hypertension, n (%) | 231,126 (43%) |
| Systolic BP, mmHg | 129 ± 16 |
| Diastolic BP, mmHg | 76 ± 11 |
| Dyslipidemia, n (%) | 298,946 (56%) |
| Diabetes mellitus, n (%) | 62,189 (12%) |
| Smoking, n (%) | 82,391 (15%) |
| *Biochemical data* | |
| eGFR, ml/min/1.73m$^2$ | 76 ± 17 |
| HbA1c, % | 5.4 ± 0.7 |
| FBS, mg/dL | 98 ± 21 |
| Total cholesterol, mg/dL | 211 ± 35 |
| Triglyceride, mg/dL | 125 ± 89 |
| HDL-C, mg/dL | 61 ± 15 |
| LDL-C, mg/dL | 125 ± 30 |
| Proteinuria, n (%) | 31,498 (6%) |
| CKD, n (%) | 98,816 (18%) |
| *Medications* | |
| Anti-hypertensive drug, n (%) | 159,140 (30%) |
| Anti-diabetic drug, n (%) | 29,307 (5%) |
| Anti-dyslipidemia drug, n (%) | 79,149 (15%) |

Table 1. Baseline characteristics of all subjects.

Data are expressed as mean ± SD, number (percentage).
BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FBS, fasting blood sugar; HbA1c, glycosylated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

### The Suita score and aortic diseases-related deaths

All subjects were prospectively followed for a median period of 1,450 days (interquartile range, 967–1,828 days). During the follow-up period, there were 385 IHD deaths, 42 aortic aneurysm rupture deaths, and 90 aortic dissection deaths. The Kaplan–Meier analysis demonstrated that subjects with a high Suita score had higher rates of IHD, aortic aneurysm rupture, and aortic dissection deaths than those with a low Suita score (Figure 2).

We performed univariate and multivariate Cox proportional hazard regression analyses to determine the risk factors for predicting aortic aneurysm rupture and aortic dissection deaths. In the univariate analysis, the Suita score was significantly associated with aortic aneurysm rupture and aortic dissection deaths (Table 3). The Framingham risk score and waist circumference were also associated with aortic aneurysm rupture and aortic dissection deaths. Alcohol consumption was related to aortic aneurysm rupture deaths. The multivariate Cox proportional hazard regression analysis demonstrated that the Suita score was an independent predictor of aortic aneurysm rupture and aortic dissection deaths after adjusting for waist circumference, alcohol consumption, and CKD (Table 4). In contrast, the multivariate Cox proportional hazard regression analysis demonstrated that the Framingham risk score was not significantly associated with aortic dissection deaths after adjusting for waist circumference, alcohol consumption, and CKD (Table 4).

### Prognostic ability of the Suita score versus the Framingham risk score

To compare the prognostic abilities of the Suita score to those of the Framingham risk score, ROC curves were used (Figure 3). The C indices in the Suita score for IHD, aortic aneurysm rupture, and aortic dissection deaths were 0.7039, 0.8295, and 0.6689, respectively. The abnormal cutoff values of the Suita score for IHD, aortic aneurysm rupture, and aortic dissection deaths were 51, 50, and 48, respectively. The C indices in the Framingham risk score for IHD, aortic aneurysm rupture, and aortic dissection deaths were 0.6175, 0.7412, and 0.5772, respectively. The abnormal cutoff values of the Framingham risk score for IHD, aortic aneurysm rupture, and aortic dissection deaths were 7, 9, and 7, respectively. The C indices for IHD, aortic aneurysm rupture, and aortic dissection deaths in the Suita score were significantly greater than those in the Framingham risk score.

## Discussion

The main findings of the present study were as follows: (1) the Kaplan–Meier analysis demonstrated that subjects with a high Suita score had higher rates of aortic aneurysm rupture and aortic dissection deaths than those with a low Suita score; (2) the multivariate analysis demonstrated that the Suita score was an independent predictor of aortic aneurysm rupture and aortic dissection deaths; and (3) the ROC analysis demonstrated that the Suita score had superior prognostic value to the Framingham risk score for aortic aneurysm rupture, aortic dissection, and IHD deaths.

### The Suita score and Framingham risk score

The European guidelines recommended the use of the ESC-SCORE to assess risk in the primary prevention of IHD,

| Variables | Low Suita score n = 448,223 | High Suita score n = 86,181 | P value |
|---|---|---|---|
| Age, years | 62 ± 9 | 69 ± 4 | <0.0001 |
| Male, n (%) | 154,752(29%) | 75175 (87%) | <0.0001 |
| Framingham risk score | 6.0 ± 3.6 | 9.9 ± 2.4 | <0.0001 |
| BMI, kg/m$^2$ | 23.2 ± 3.5 | 24.5 ± 3.2 | <0.0001 |
| Waist circumference, cm | 84 ± 10 | 88 ± 8 | <0.0001 |
| Hypertension, n (%) | 166,153 (37%) | 64,973 (75%) | <0.0001 |
| Systolic BP, mmHg | 127 ± 17 | 139 ± 18 | <0.0001 |
| Diastolic BP, mmHg | 76 ± 11 | 80 ± 11 | <0.0001 |
| Dyslipidemia, n (%) | 237,225 (53%) | 61,721 (72%) | <0.0001 |
| Diabetes mellitus, n (%) | 33,075 (7.4%) | 29,114 (34%) | <0.0001 |
| Smoking, n (%) | 56,385 (13%) | 26,006 (30%) | <0.0001 |
| *Biochemical data* | | | |
| eGFR, ml/min/1.73m$^2$ | 77 ± 17 | 68 ± 18 | <0.0001 |
| HbA1c, % | 5.3 ± 0.6 | 5.8 ± 1.0 | <0.0001 |
| FBS, mg/dL | 96 ± 18 | 110 ± 31 | <0.0001 |
| Total cholesterol, mg/dL | 211 ± 36 | 216 ± 37 | <0.0001 |
| Triglyceride, mg/dL | 121 ± 89 | 148 ± 94 | <0.0001 |
| HDL-C, mg/dL | 63 ± 16 | 53 ± 14 | <0.0001 |
| LDL-C, mg/dL | 123 ± 31 | 134 ± 32 | <0.0001 |
| Proteinuria, n (%) | 20,381 (4.6%) | 11,117 (13%) | <0.0001 |
| CKD, n (%) | 64,008 (14%) | 34,808 (40%) | <0.0001 |
| *Medications* | | | |
| Anti-hypertensive drug, n (%) | 113,247 (25%) | 45,893 (53%) | <0.0001 |
| Anti-diabetic drug, n (%) | 15,425 (3.4%) | 13,882 (16%) | <0.0001 |
| Anti-dyslipidemia drug, n (%) | 65,270 (15%) | 13,879 (16%) | <0.0001 |

Table 2.Comparison of clinical characteristics between subjects with high and low Suita score.

Data are expressed as mean ± SD, number (percentage).
BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FBS, fasting blood sugar; HbA1c, glycosylated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

which has been validated in a large cohort of patients and ethnicities and the endpoint of cardiovascular mortality [16]. However, the ESC-SCORE has not been validated in Asians. Therefore, in this study, we compared the Framingham risk score and the Suita score and demonstrated the superior prognostic value of the latter. Since the Suita score was developed in Japan and applied to the Japanese general population to predict IHD, it is plausible that the Suita score is also superior to the Framingham risk score for predicting aortic diseases in the Japanese general population. Another explanation may be the difference in the score components. The difference between the two scores is the incorporation of CKD, which is closely associated with the presence of an aortic aneurysm in the general population [17]. Therefore, the Suita score may be superior to the Framingham risk score for predicting aortic aneurysm rupture and aortic dissection deaths in the Japanese general population.

## The Suita score and aortic diseases

Another important finding of the present study was that the Suita score is a useful predictor for aortic aneurysm rupture and aortic dissection death in the general population. Its C index for aortic aneurysm rupture death was 0.8296, suggesting the excellent predictive capacity of the Suita score for aortic aneurysm rupture deaths in the general population. The estimated incidence of IHD in 10 years was about 5% in subjects with a Suita score ≥51. The prevalence of aortic aneurysm in patients with IHD is 10%–15% [18, 19], suggesting that aortic aneurysm does not necessarily coexist with IHD. The relationship between ath-

**Figure 2**

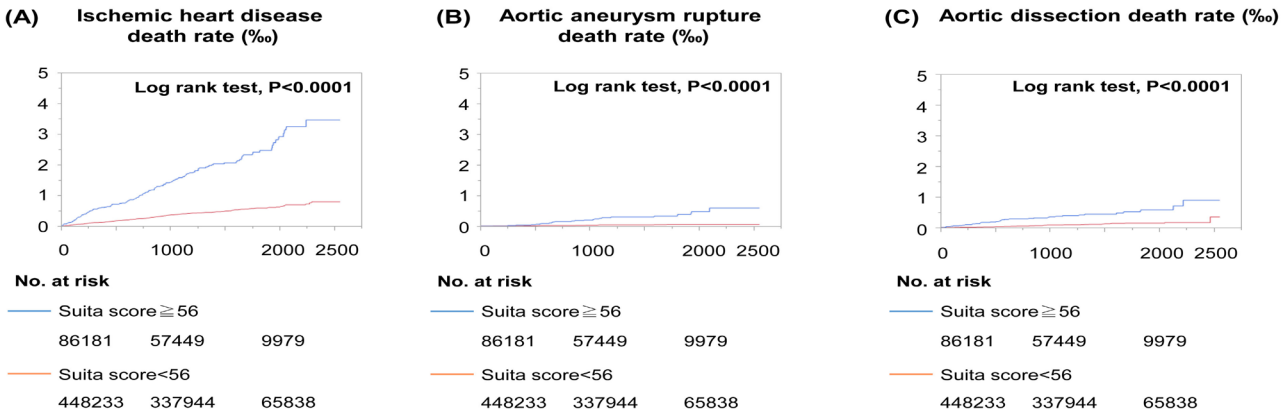


Figure 2. Kaplan–Meier analysis of deaths of ischemic heart disease (A), aortic aneurysm rupture (B), and aortic dissection (C) for subjects with a high and low Suita score.

| | Univariate analysis | | |
|---|---|---|---|
| Variables | HR | 95%CI | P-value |
| *Aortic aneurysm rupture deaths* | | | |
| Suita score* | 4.605 | 3.281-6.466 | <0.0001 |
| Framingham risk score* | 1.926 | 1.496-2.481 | <0.0001 |
| Waist circumference | 1.046 | 1.016-1.077 | 0.0021 |
| Alcohol consumption | 2.094 | 1.093-4.011 | 0.0220 |
| *Aortic dissection deaths* | | | |
| Suita score* | 1.989 | 1.558-2.539 | <0.0001 |
| Framingham risk score* | 1.278 | 1.068-1.527 | 0.0067 |
| Waist circumference | 1.037 | 1.014-1.058 | 0.0009 |
| Alcohol consumption | 1.067 | 0.680-1.674 | 0.7760 |

Table 3. Univariate Cox proportional hazard analyses of predicting aortic aneurysm rupture and aortic dissection deaths.

| | Multivariate analysis | | |
|---|---|---|---|
| Variables | HR | 95%CI | P-value |
| *Aortic aneurysm rupture deaths* | | | |
| Suita score* | 4.342‡ | 3.014-6.257 | <0.0001 |
| Suita score* | 3.792# | 2.564-5.609 | <0.0001 |
| Framingham risk score* | 1.922‡ | 1.450-2.547 | <0.0001 |
| Framingham risk score* | 1.823# | 1.367-2.431 | <0.0001 |
| *Aortic dissection deaths* | | | |
| Suita score* | 1.992‡ | 1.524-2.602 | <0.0001 |
| Suita score* | 1.705# | 1.289-2.255 | 0.0002 |
| Framingham risk score* | 1.228‡ | 1.006-1.498 | 0.0433 |
| Framingham risk score* | 1.164# | 0.950-1.427 | 0.1416 |

Table 4. Multivariate Cox proportional hazard analyses of predicting aortic aneurysm rupture and aortic dissection deaths.
* Per 1-SD increase.
‡after adjustment for waist circumference and alcohol consumption.
#after adjustment for waist circumference, alcohol consumption, and chronic kidney disease.

CI, confidence interval; HR, hazard ratio.

**Figure 3**

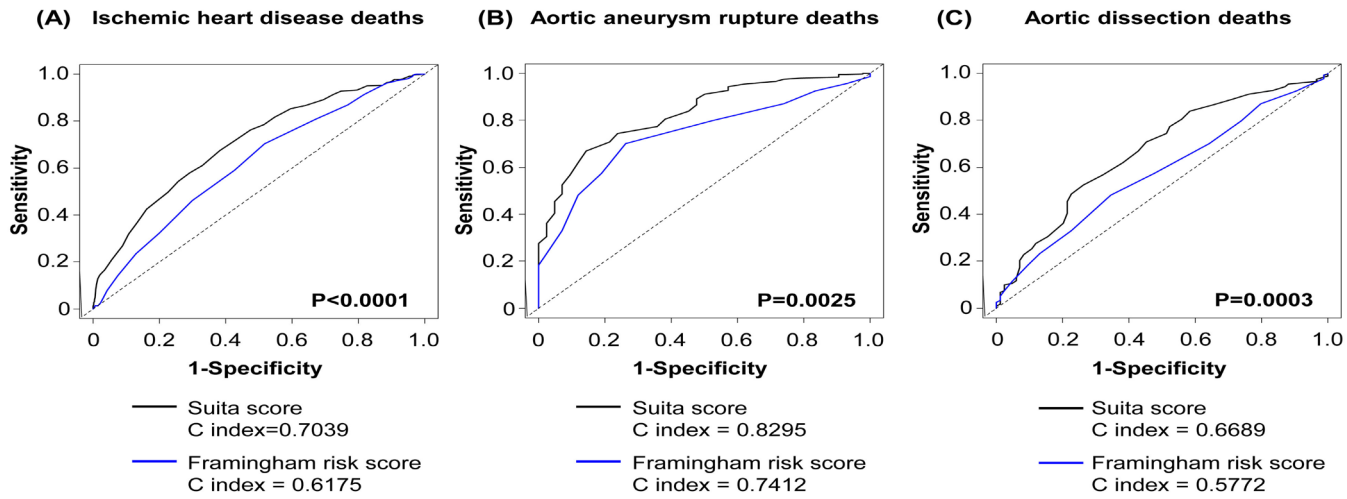


Figure 3. Comparisons of receiver operating characteristic curve analyses of deaths of ischemic heart disease (A), aortic aneurysm rupture (B), and aortic dissection (C) between the Suita score and the Framingham risk score.

erosclerosis and aortic aneurysm remains to be elucidated [20]; however, atherosclerotic lesions are detected in aortic aneurysm [21]. Since a high Suita score reflects arteriosclerosis, the association between aortic aneurysm death and the Suita score could be explained by atherosclerosis. However, aortic dissection results from medial degeneration because of genetic collagen diseases, such as Marfan syndrome, Ehlers–Danlos syndrome, and Loeys–Dietz syndrome; advanced age; hypertension; and aortic aneurysm [22]. The different predictive capacity of the Suita score between aortic aneurysm rupture deaths and aortic dissection deaths may be because of the pathogenesis of these diseases.

An abnormal cutoff value for aortic diseases was almost equal to that of IHD. A Suita score ≥51 may be the potentially abnormal cutoff value for both IHD and aortic disease deaths.

### Clinical perspectives

Screening for the aortic disease has not been established in Japan. An aortic aneurysm is identified incidentally when subjects undergo echocardiography or computed tomography. Kazama et al have demonstrated the usefulness of transthoracic echocardiography for the detection of abdominal aortic aneurysm in patients with suspected cardiac disease [23]. The screening of elderly men using ultrasonography is recommended to reduce the death rate from abdominal aortic aneurysm rupture [24]. Therefore, ultrasonography screening of subjects with a high Suita score may enable the early identification of aortic aneurysm in the general population.

## Limitations

The strengths of the present study include its large sample size, prospective follow-up design, and nationwide data source. Therefore, our results are highly generalizable and reliable. However, there were some limitations as well. First, we assessed the Suita score at only one point. Since some components of the Suita score change with age, several subjects may have developed a high Suita score during the follow-up period. Second, we did not examine the development of aortic diseases and data on surgical and endovascular aortic repair. Although aortic diseases can be fatal, some subjects survived, probably because of treatment. Thus, we underestimated the impact of the Suita score on the development of aortic diseases. Third, we had no information about the prevalence of aortic diseases in the general population. Fourth, we had insufficient data to analyze the impact of the Suita score on aortic aneurysm rupture and aortic dissection deaths by aorta site and dissection type. Fifth, since we have no data regarding premature coronary artery disease, we could not compare the differences in prognostic ability between the Suita score in cases with and without premature coronary artery disease. Finally, we had no information about the medications used by this population.

## Conclusion

This study demonstrated that the Suita score was superior to the Framingham risk score and a feasible marker for aortic aneurysm rupture and aortic dissection deaths in a Japanese general population, indicating that it can be used to identify individuals at high risk of aortic aneurysm rupture, aortic dissection, and IHD.

## Acknowledgments

This work was supported by a Health and Labor Sciences Research Grant for Study on the Design of the Comprehensive Health Care System for Chronic Kidney Disease (CKD), based on the individual risk assessment by the specific health checkup, from the Ministry of Health, Labour and Welfare of Japan and a Grant-in-Aid for Research on Advanced Chronic Kidney Disease (REACH-J), Practical Research Project for Renal Disease from the Japan Agency for Medical Research and Development, AMED. We would like to thank Editage (www.editage.com) for English language editing.

## Ethical approval

All procedures performed in studies involving human participants were done so in accordance with the ethical institutional and/or national research committee at which the studies were conducted (Yamagata University, 2008, no. 103) and in compliance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

## Informed consent

This study was performed according to the Ethical Guidelines for Medical and Health Research Involving Human Subjects enacted by the Ministry of Health, Labour and Welfare of Japan (http://www.mhlw.go.jp/file/06-Seisakujouhou-10600000-Daijinkanboukouseikagakuka/0000069410.pdf;http://www.mhlw.go.jp/file/06-Seisakujouhou-10600000-Daijinkanboukouseikagakuka/0000080278.pdf). In the context of the guideline, the investigators shall not necessarily be required to obtain informed consent, but we publicized information concerning this study on the web (http://www.fmu.ac.jp/univ/sangaku/data/koukai_2/2771.pdf) and ensured opportunities for the research subjects to refuse the use of their personal information.

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