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Sustained progression and loss of the gender-related difference in atherosclerosis in the very old: A pathological study of 1074 consecutive autopsy cases

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Abstract

Introduction: Epidemiological surveys show decrease or reversal of male predominance in cardiovascular mortality in the very old, but the actual condition of atherosclerosis in the very old is largely unknown. The objective of this paper is to reveal whether the atherosclerosis continues to progress, or the gender-related difference exists in the very old.
Methods: The subjects were 1074 consecutive autopsy cases of in-hospital death. The male:female ratio was 1.1:1 and the average age was 80 years. Macroscopic evaluation was performed on the degree of atherosclerosis in 10 arteries including the intracranial arteries, carotid artery, aorta, coronary artery, and femoral artery.
Results: The severity of atherosclerosis differed greatly among arteries. The age-related increase of the atherosclerotic degree was evident, even after 80 years of age. The atherosclerosis was more severe in males than in females in their 60s, but this male predominance decreased with ageing and finally disappeared in their 90s.
Conclusion: The sustained progression of atherosclerosis and loss of the gender-related difference probably account for the increase of cardiovascular mortality in very old females. They also suggest that the prevention of the atherosclerotic progression is still important in the seventh and eighth decade of life.

Keywords: Aging; Atherosclerosis; Pathology; Autopsy; Gender-difference

1. Introduction

Atherosclerosis causes a large number of complications, such as cerebrovascular disease, coronary heart disease, ischemic bowel disease, renovascular hypertension, Leriche syndrome, peripheral arterial disease, and aneurysms. Chronic disseminated intravascular coagulation and elevated inflammatory markers, such as highly sensitive C-reactive protein, are reported to be other manifestations of atherosclerosis. Atherosclerosis, however, is also a sub-

Abbreviations: CHD, coronary heart disease; CSI, coronary stenotic index; CT, computer tomography; ICAI, intracranial atherosclerotic index; JG-SNP, the Japanese SNP database for geriatric research; MRI, magnetic resonance imaging; PAI, pathological atherosclerotic index.

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clinical entity because it does not always result in these complications even in cases with severe atherosclerosis. It is, therefore, difficult to speculate on the severity of atherosclerosis only from the presence of these complications. The clinical assessment of atherosclerosis is a challenging subject and the pathological study by autopsy is still the most reliable assessment method of systemic atherosclerosis.

Although several pathological studies have been reported regarding the severity of atherosclerosis [1–8], very little information was available about atherosclerosis in the elderly, especially in people of more than 80 years of age. It is still unknown whether atherosclerosis continues to progress in the very old, or whether the gender-related difference exists in the elderly because decades have passed since the menopause in female subjects. Recent epidemiological surveys showed decrease or reversal of the male predominance in cardiovascular mortality in the very old both in Japan and the U.S. [9,10], but the exact cause was unspecified. To address these issues, we performed a comprehensive pathological study in more than 1000 consecutive autopsy cases. This is the first pathological report analyzing the gender-specific, age-related changes of atherosclerosis in the very elderly.

2. Subjects and methods

2.1. Subjects

The subjects were 1074 consecutive elderly autopsy cases performed at Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan from 1995 to 2000. The details of the subjects including major clinical diagnosis and direct causes of death examined by autopsy are summarized in Table 1. We have been presenting our autopsy cases on an Internet-based database on the web since April 2003, which was named "The Japanese SNP database for geriatric research (JG-SNP)" located at http://www.tmgh.metro.tokyo.jp/jg-snp/english/E_top.html, as was previously reported [11]. The JG-SNP included all the subjects used in this study. The subjects did not include any medicolegal cases.

Tokyo Metropolitan Geriatric Hospital is a community-based general hospital for the aged and has all medical departments except Obstetrics and Pediatrics. Over 90% of the outpatients come from the neighboring wards or cities of Tokyo. The average day of hospitalization had decreased during the observation period from 45.6 days in 1995 to 24.3 days in 2000. The average autopsy rate in this period was 40% in whom the brain was available in 85%.

2.2. Pathological assessment of atherosclerosis

The method of the pathological assessment of atherosclerosis was recently reported [12]. Briefly, the varying degree of atherosclerosis in eight large arteries was evaluated by macroscopic examination of the luminal surface in the formalin-fixed arteries. The eight large arteries included the common carotid artery, subclavian artery, aorta, splenic artery, superior mesenteric artery, common iliac artery, external iliac artery, and left femoral artery. The atherosclerotic degree was scored according to the ratio of the occupying atheroma to the entire intimal area: from 0 (absent, less than 1/20 of the intimal areas occupied by the atheroma), 2 (minimal, 1/20–1/6), 4 (mild, 1/6–1/3), 6 (moderate, 1/3–2/3) to 8 (severe, 2/3–1). A comparison was made to the standard grading method proposed by the American Heart Association in 1968 [13]. The grading panel of AHA and corresponding scores in our scale are shown in Fig. 1.

The pathological atherosclerotic index (PAI) was defined as the average atherosclerotic degree of these eight arteries. The coronary stenotic index (CSI) was studied according to the previous report [14]. Examination of the coronary scle-

Table 1
Clinical summary of the patients

Gender	Males	Females
Number of cases	565	509
Age at death (year)		
45–59	5	7
60–69	63	41
70–79	220	144
80–89	217	203
90–104	60	114
Mean age[a]	79.2 ± 8.1 (52–102)	81.8 ± 9.5 (47–104)
Body mass index (kg/m^2)[a]	16.9 ± 3.4 (10.7–28.4)	17.2 ± 4.0 (8.4–37.9)
History of smoking	382/519 (73.6%)	98/445 (22.0%)
Clinical diagnoses (%)		
Cerebrovascular disease[b]	187 (33.1%)	157 (30.8%)
Coronary heart disease[c]	96 (17.0%)	77 (15.1%)
Aneurysm	27 (4.8%)	17 (3.3%)
Peripheral arterial disease	24 (4.2%)	17 (3.3%)
Hypertension	131 (23.2%)	134 (26.3%)
Diabetes mellitus	78 (13.8%)	63 (12.4%)
Hyperlipidemia	11 (1.9%)	6 (1.2%)
Direct causes of death (%)[d]		
Cardiovascular events	70 (15.3%)	76 (18.3%)
Cerebral infarctions or hemorrhages	14 (3.1%)	24 (5.8%)
Myocardial infarction	43 (9.4%)	37 (8.9%)
Other events[e]	13 (2.8%)	15 (3.6%)
Pneumonia	141 (30.8%)	71 (17.1%)
Malignancy	160 (34.9%)	138 (33.3%)

[a] The figures are the averages ± S.D. and ranges in parentheses.
[b] The clinical diagnosis of cerebrovascular disease was based on neurological signs and symptoms usually with radiological evidences, which includes transient ischemic attack, reversible ischemic neurological deficit, subarachnoid hemorrhage, cerebral hemorrhage, and cerebral infarction.
[c] The coronary heart disease includes angina pectoris and myocardial infarction.
[d] The direct causes of death are determined by autopsy findings of 872 cases (458 males and 414 females) among the subjects.
[e] The other cardiovascular events include aneurysmal rupture, intestinal infarction, and severe peripheral arterial disease.

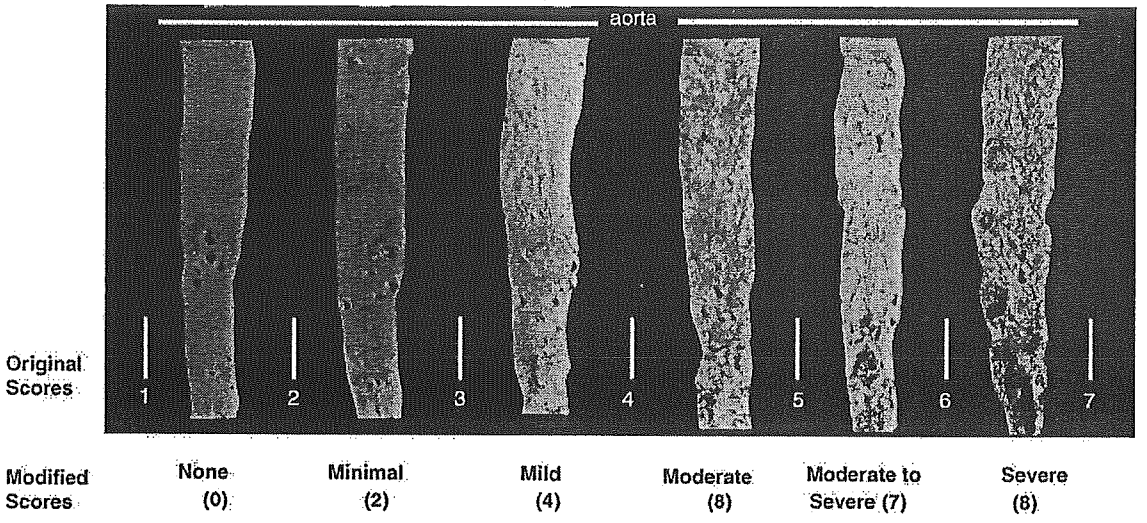

Fig. 1. Grading panel for atherosclerotic lesions, issued by the Committee on grading lesion, Council of Atherosclerosis, American Heart Association. The photographs show the aorta with different grades of atherosclerosis. Corresponding modified scores of our scale are shown beneath the original scores from 0 to 8. Reprint from the article by McGill et al. [9] with permission.

rosis was made by transverse section at 5 mm intervals. The degree of coronary stenosis was scored from 0 to 5: 0 in no sclerosis, 1 in slight stenosis, 2 in 25% stenosis, 3 in 50%, 4 in 75%, and 5 in 100% obstruction. The CSI was the sum of the stenotic scores of the three branches; left anterior descending branch, left circumflex branch, and right coronary artery. The intracranial atherosclerotic index (ICAI) was examined as previously reported [15]. The cut sections of the intracranial arteries were observed and the degree of stenosis was scored from 0 to 3: 0 in no stenosis, 0.5 in the cases only with fatty streaks, 1 in less than 50% stenosis, 2 in 50% to 90% stenosis, and 3 in 90% stenosis to occlusion. The ICAI was the sum of the stenotic scores of the left and right middle cerebral arteries and basilar artery.

2.3. Interobserver and intraobserver variations

The Bland–Altman analysis was performed for statistical analysis of interobserver and intraobserver variations, as shown in Fig. 2 [16]. The assessment was performed by two of the authors on 180 arteries derived from 15 cases. The mean difference was 0.5 (95% confidence interval; 0.3–0.7), while the upper and lower 95% limits of agreement were 3.3 (3.3–3.7) and −2.3 (−2.7 to −2.0), respectively. The standard deviation of intraobserver differences was 1.3. Considering the range from zero to eight of the atherosclerotic degree, the interobserver and intraobserver variations seemed acceptable.

2.4. Statistical analysis

A Mann–Whitney test was performed to compare the atherosclerotic degrees in the individual arteries between genders. The interobserver and intraobserver variations were assessed by the Bland and Altman plot analysis [16]. The difference between the atherosclerotic degrees assessed by the different observer against their mean was plotted to examine the interobserver variation. Repeatability was similarly

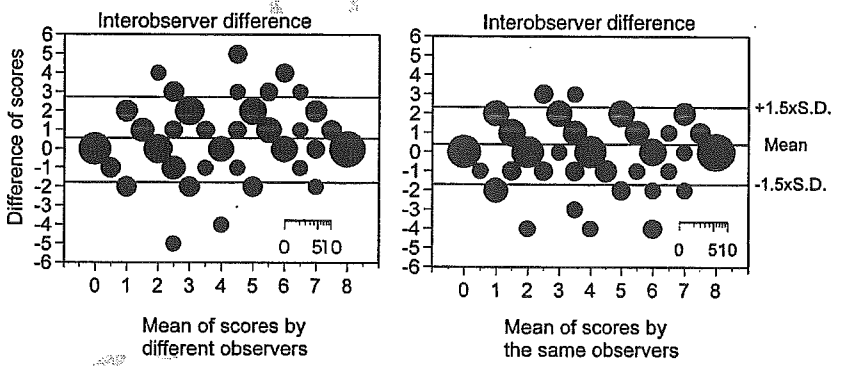

Fig. 2. Bland–Altman plot for statistical analysis of interobserver and intraobserver differences. The assessment was performed on 180 arteries derived from 15 cases. The areas of the circles represent the number of the cases.

assessed by plotting the difference between the atherosclerotic degrees assessed by the same observer against their mean. The statistical significance level was set at 0.05. The SAS system for Windows (Version 8.1) and JMP (Version 5.1) (SAS Institute Inc., NC) were used for the statistical analyses.

2.5. Ethical considerations

Written informed consent was obtained from the bereaved family of each of the patients prior to the autopsy examination. The use of autopsy materials for medical education and research is generally permitted by the Act of Postmortem Examinations of Japan.

3. Results

3.1. Distribution of the atherosclerotic degrees

Fig. 3 shows the distribution of the atherosclerotic degrees of the eight large arteries, PAI, CSI, and ICAI. The medians were high in the common iliac artery and aorta, while they were low in the splenic and superior mesenteric arteries. Variations in the degree of atherosclerosis were large in the external iliac and femoral arteries. The average (±S.D.) of the PAI, CSI, and ICAI were 3.9 (±1.5), 8.2 (±3.5), and 2.8 (±2.1), respectively. The atherosclerotic degree of the subclavian artery, PAI, and CSI followed a Normal distribution (Gaussian).

3.2. Gender-specific, age-related changes of the atherosclerotic degrees

The age-related increase in the degree of atherosclerosis was evident in both genders, as shown in Fig. 4. The atherosclerotic degree is the highest in the aorta, followed by the femoral artery, common carotid artery, and superior mesenteric artery. For subjects in their 60s and 70s, the degree of atherosclerosis is statistically higher in males than in females in most arteries, but no statistical differences are observed when subjects reach their 90s. Namely, the gender-related differences subsequently reduced with ageing and finally disappeared in their 90s. The changing rate of the age-related increase in the degree of atherosclerosis, namely the slope of the line graphs, was especially high in the femoral artery.

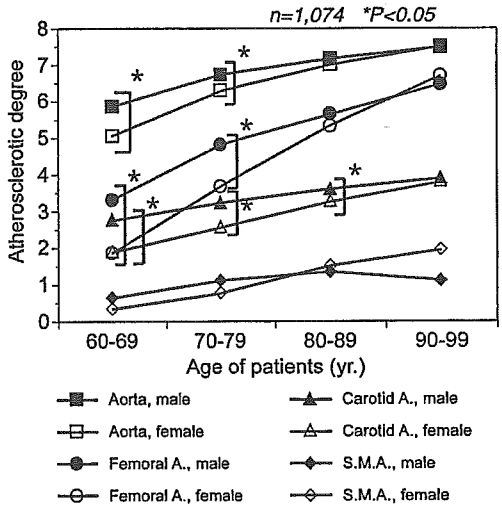

Fig. 4. Gender-specific, age-related changes of the degree of atherosclerosis in the individual arteries. S.M.A.; superior mesenteric artery. (■) Aorta, male; (□) aorta, female; (●) femoral A., male; (○) femoral A., female; (▲) carotid A., male; (△) carotid A., female; (♦) S.M.A., male; (◇) S.M.A., female.

The average CSI was statistically higher in males than in females in their 60s and 70s, as shown in Fig. 5. The age-

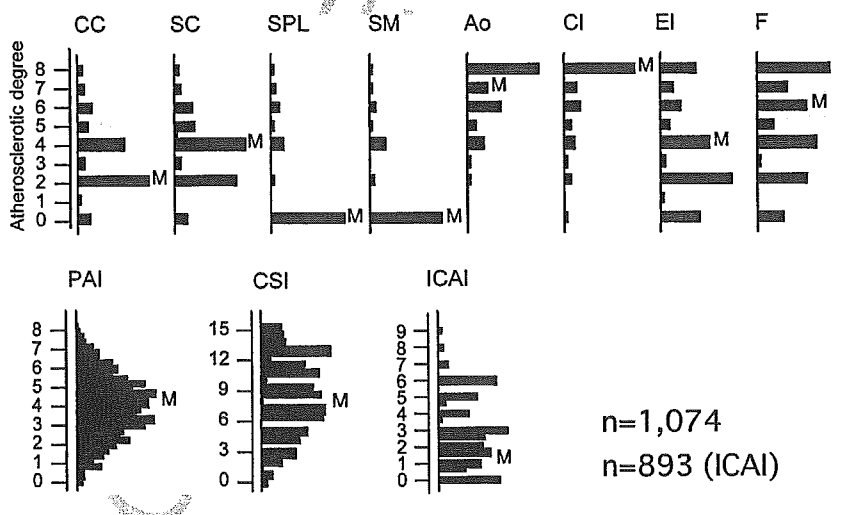

Fig. 3. Severity of atherosclerosis in the individual arteries. Ao, aorta; CC, common carotid artery; CI, common iliac artery; CSI, coronary stenotic index; EI, external iliac artery; F, femoral artery; ICAI, intracranial atherosclerotic index; M, median of the atherosclerotic degrees or indices; PAI, pathological atherosclerotic index; SC, subclavian artery; SM, superior mesenteric artery; SPL, splenic artery.

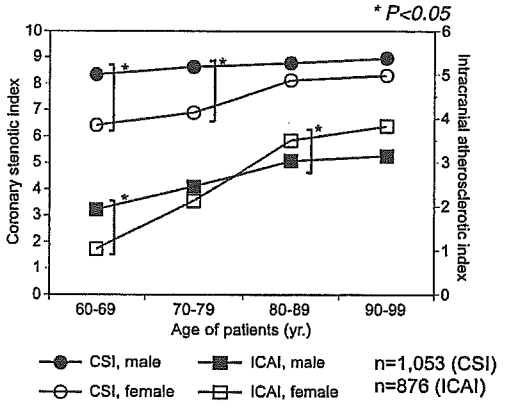

Fig. 5. Gender-specific, age-related changes of the coronary stenotic index (CSI) and intracranial atherosclerotic index (ICAI). (●) CSI, male; (■) ICAI, male; $n = 1053$ CSI; (○) CSI, female; (□) ICAI, female; $n = 1053$ ICAI.

related increase of ICAI was larger in females than in males. In their 80s, the ICAI was statistically even higher in females than in males.

4. Discussion

4.1. Distribution of the atherosclerotic degrees

The present study revealed the severity of atherosclerosis differed by the arterial segments. The aorta and arteries of the lower extremities were severely affected, while the abdominal arteries, such as the splenic and superior mesenteric arteries, were mildly affected. These results were consistent with previous reports stating the abdominal aorta and common iliac arteries were the most severe sites of atherosclerotic involvement [1,2,4].

4.2. Gender-specific, age-related changes of the atherosclerotic degrees

Atherosclerosis continued to progress in the elderly in most arteries except for the coronary artery in males. Males in their 60s were more severely affected by atherosclerosis than age-matched females, but this gender-related difference reduced with ageing and finally disappeared in subjects in their 90s. In the case of the intracranial arteries and superior mesenteric artery, atherosclerosis was even more severe in females than in males in their 80s or 90s. The loss of the gender difference of atherosclerosis in the very old seems to influence the mortality. In Japan, the mortalities from heart diseases and cerebrovascular diseases are higher in males than in females in all age groups [9] and the gender differences in mortality increase with ageing, peak at 85–89 years and decrease thereafter in both diseases. A similar trend is present in the death rates from heart diseases in the U.S. [10]. The death rates from cerebrovascular diseases in the U.S. are almost even in each age group except for that of 85 years and over, in whom female predominance is evident. The loss of the gender-related difference in atherosclerosis in the very old seems responsible for the decrease or reversal of male predominance in cardiovascular mortality in the very old. Our results also suggest that the prevention of the atherosclerotic progression is still necessary in the very old, especially in females.

4.3. Limitations of the study

The subjects of this study were autopsy cases of the patients in a geriatric hospital. Therefore, we need to evaluate whether the subjects represent a hospitalized population or the demographics in Japan. The general prevalence of the major underlying diseases over 70 years of age was as follows: 29.5% in males versus 28.5% in females in hypertension (systolic blood pressure $\geq$160 Torr or diastolic blood pressure $\geq$95 Torr), 11.6% versus 21.3% in diabetes mellitus (under diabetic control or HbA1c $\geq$ 6.1%), and 15.8% versus 38.5% in hyperlipidemia (total cholesterol $\geq$ 220 mg/dl) [17]. The figures were similar to those of our results except for hyperlipidemia. Considering the low average BMI of the subjects (17 kg/m^2), the undernourished conditions seemed to contribute to the low incidence of hyperlipidemia. The death rates per 100,000 over 75 years of age in Japan were as follows: 1027.6 in males versus 860.1 in females in the cerebrovascular diseases, 537.9 versus 398.5 in ischemic heart disease, 1017.6 versus 571.4 in pneumonia, and 2085.7 versus 980.0 in malignancy [9]. The frequency of cerebrovascular diseases seems higher than our autopsy data. Since the subjects comprised entirely of the Japanese race except for one Korean and the national health insurance covers the whole population in Japan, the selection bias from the racial and socioeconomic differences of the subjects seems minimal. Altogether our subjects may represent the general population in Japan.

4.4. Perspectives

Atherosclerosis is a multifactorial disease and 30–66% of the variation of the atherosclerosis could be explained by the genetic factors [18–20]. In this context, the roles of the genetic polymorphism have been extensively studied to identify the most responsible genes for atherosclerosis. Since the postmortem pathological evaluation of the atherosclerosis is more accurate than other clinical methods, a few autopsy studies have been conducted for the genetic studies, including Helsinki Sudden Death Study [21,22] and Pathological Determinants of Atherosclerosis in Youth Study [23,24]. Both studies examined the aortic and coronary atherosclerosis in large numbers of forensic autopsy cases of sudden death and analyzed the correlations between the genetic polymorphism and the pathologically verified atherosclerosis. We also have been engaged in the researches of the genetic polymorphism of atherosclerosis, based on the autopsy cases used in this study. In the course of our study, we have obtained several

interesting results, including those appeared in this paper. We hope to identify relevant genetic polymorphic sites of the candidate genes for atherosclerosis.

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References

[1] Roberts JC, Moses C, Wilkins RH. Autopsy studies in atherosclerosis. I. Distribution and severity of atherosclerosis in patients dying without morphologic evidence of atherosclerotic catastrophe. Circulation 1959;20:511–9.

[2] Roberts JC, Wilkins RH, Moses C. Autopsy studies in atherosclerosis. II. Distribution and severity of atherosclerosis in patients dying with morphologic evidence of atherosclerotic catastrophe. Circulation 1959;20:520–6.

[3] Strong JP, McGill Jr HC. The natural history of aortic atherosclerosis: relationship to race, sex, and coronary lesions in New Orleans. Exp Mol Pathol 1963;52(1):15–27. Suppl.

[4] Solberg LA, McGarry PA, Moossy J, Strong JP, Tejada C, Löken AC. Severity of atherosclerosis in cerebral arteries, coronary arteries, and aortas. Ann N Y Acad Sci 1968;149:956–73.

[5] Bjurulf P. Atherosclerosis in different parts of the arterial system. Am Heart J 1964;68:41–5.

[6] Reiner L, Jimenez FA, Rodriguez FL. Atherosclerosis in the mesenteric circulation. Observations and correlations with aortic and coronary atherosclerosis. Am Heart J 1963;66:200–9.

[7] Larsen E, Johansen AA, Andersen D. Gastric arteriosclerosis in elderly people. Scand J Gastroenterol 1969;4(4):387–9.

[8] Jävinen O, Laurikka J, Sisto T, Salenius J-P, Tarkka MR. Atherosclerosis of the visceral arteries. Vasa 1995;24:9–14.

[9] Statistics and Information Department, Ministry of Health, Labour and Welfare, Japan. Vital Statistics, Abridged Life Tables for Japan; 2003. Available at http://www.mhlw.go.jp/english/database/db-hw/index.html (in English) or http://www.mhlw.go.jp/toukei/saikin/hw/jinkou/geppo/nengai03/index.html (in Japanese). Accessed on July 10, 2005.

[10] U.S. Census Bureau. Statistical Abstract of the United States 2004–2005, Section 2. Vital Statistics, Table No. 107 and 108; 2005. Available at: http://www.census.gov/prod/www/statistical-abstract-03.html. Accessed on July 10, 2005.

[11] Sawabe M, Arai T, Kasahara I, et al. Development of a geriatric autopsy database and internet-based database of Japanese single nucleotide polymorphisms for geriatric research (JG-SNP). Mech Ageing Dev 2004;125:547–52.

[12] Sawabe M, Takahashi R, Matsushita S, et al. Aortic pulse wave velocity and the degree of atherosclerosis in the elderly: a pathological study based on 304 autopsy cases. Atherosclerosis 2005;179:345–51.

[13] McGill Jr HC, Brown BW, Gore I, et al. Report of Committee on grading lesions, council on arteriosclerosis, American Heart Association. Grading human atherosclerotic lesions using a panel of photographs. Circulation 1968;37:455–9.

[14] Chida K, Ohkawa S, Watanabe C, Shimada H, Ohtsubo K, Sugiura M. A morphological study of the normally aging heart. Cardiovasc Pathol 1994;3:1–7.

[15] Koyama S, Saito Y, Yamanouchi H, et al. Marked decrease of intracranial atherosclerosis in contrast with unchanged coronary artery stenosis in Japan. Nippon Ronen Igakkai Zasshi 2003;40:267–73 (in Japanese with English abstract).

[16] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.

[17] Ministry of Health, Labour and Welfare, Japan. The National Nutrition Survey in Japan. Tokyo: Dai-ichi Shuppan Publishing Co. Ltd.; 2004 (In Japanese).

[18] Duggirala R, Gonzalez Villalpando C, O'Leary DH, Stern MP, Blangero J. Genetic basis of variation in carotid artery wall thickness. Stroke 1996;27:833–7.

[19] Zannad F, Visvikis S, Gueguen R, et al. Genetics strongly determines the wall thickness of the left and right carotid arteries. Hum Genet 1998;103(2):183–8.

[20] O'Donnell CJ, Chazaro I, Wilson PW, et al. Evidence for heritability of abdominal aortic calcific deposits in the Framingham Heart Study. Circulation 2002;106(3):337–41.

[21] Ilveskoski E, Perola M, Lehtimäki T, et al. Age-dependent association of apolipoprotein E genotype with coronary and aortic atherosclerosis in middle-aged men: an autopsy study. Circulation 1999;100(6):608–13.

[22] Pöllänen PJ, Lehtimäki T, Mikkelsson J, et al. Matrix metalloproteinase3 and 9 gene promoter polymorphisms: joint action of two loci as a risk factor for coronary artery complicated plaques. Atherosclerosis 2005;180(1):73–8.

[23] Strong JP, Malcom GT, McMahan CA, et al. Prevalence and extent of atherosclerosis in adolescents and young adults: implications for prevention from the pathobiological determinants of atherosclerosis in youth study. JAMA 1999;281(8):727–35.

[24] Scheer WD, Boudreau DA, Hixson JE, et al. ACE insert/delete polymorphism and atherosclerosis. Atherosclerosis 2005;178(2):241–7.

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Original Article

Standard organ weights among elderly Japanese who died in hospital, including 50 centenarians

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The present study was conducted to determine standard organ weights among the elderly, because little has been reported on this subject. To analyze the human aging process in terms of organ weights, age-associated changes and correlations among organ weights and the contributions of age and nutrition to organ weights were also examined. The subjects included 1615 consecutive autopsy cases of patients aged 60–99 years who died between 1995 and 2003, and cases of 50 centenarians who died between 1973 and 2005. The weights of nine organs were measured before formalin fixation. If affected by serious diseases, such as cancer, the organs were excluded from the study. Values beyond 99% of the bilateral measurement limits were also excluded. In this manner the standard organ weights were obtained. The organ weights decreased significantly according to age in all organs except for the heart in men and the lungs in both genders. Undernutrition strongly contributed to organ weight except for the hypophysis, and was especially apparent in the heart and liver. In conclusion, the standard organ weights of elderly patients who died while hospitalized were determined. Undernutrition contributed significantly to a reduction in organ weights.

Key words: aging, autopsy, elderly, organ weight, undernutrition

Few reports are available on normal organ weights in the elderly.[1–3] Inoue and Otsu examined 1000 consecutive autopsy cases (of patients between the ages of 60 and 99 years) performed at the Tokyo Metropolitan Geriatric Hospital between 1972 and 1977 and published an article in this journal in 1987.[1] Because no subsequent reports have been published, to the best of our knowledge the Inoue and Otsu report seemed to be the de facto standard for organ weights in the elderly. The present report partially revises their report, based on data for 1615 consecutive autopsy cases performed between 1995 and 2003. Because no data are available on organ weight in centenarians, data from 50 centenarians were also added to the present report.

Organs in the elderly generally show marked atrophy with loss of weight, and the small brown heart and liver frequently seen in the very elderly are described as 'brown atrophy'. The major causes of atrophy are listed in textbooks as decreased workload (disuse), loss of innervation, diminished blood supply, inadequate nutrition, reductions in endocrine stimulation, and aging. The mechanism of senile atrophy is not clear, and all of the aforementioned factors seem to work simultaneously in the elderly. In the present paper, age-associated changes, correlations among organ weights, and the contribution of malnutrition to the loss of organ weight were studied to analyze the process of senile atrophy in terms of organ weight.

MATERIALS AND METHOD

Study subjects

The subjects consisted of two groups: (i) 1615 consecutive autopsy cases performed at the Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan, between January 1995 and November 2003; and (ii) 50 centenarian autopsy cases performed at the same hospital between January 1973 and March 2005. No medicolegal autopsy cases were included. The average autopsy rate for in-hospital deaths was 35.7% between 1995 and 2003, and the brain was available in 82.2% of the cases. The 1665 cases were composed of 896 men and 769 women.

The autopsy cases in group (i) are registered in the Japanese SNP database for Geriatric Research, which is available on the web at http://www.tmgh.metro.tokyo.jp/jg-snp/english/E_top.html.[4] This database was developed by

the Prime Minister's Millennium Project and the Database Development Program of the Japan Science and Technology Agency in collaboration with Tokyo Metropolitan Geriatric Hospital. The original data of organ weights and a brief summary will be given on the web site.

Measurement of organ weights and exclusion criteria

The bodyweight and height were measured at the time of autopsy, and the body mass index (BMI; bodyweight (kg)/height(m^2)) was calculated. The weights of nine organs (brain, heart, lungs, liver, kidneys, spleen, hypophysis, thyroid, and adrenals) were measured before formalin fixation. The weights of the brain, heart, lungs, liver, kidneys, and spleen were measured by an electric balance in grams, while those of the hypophysis, thyroid, and adrenals were measured in milligrams. The heart weight was measured after removing blood clots within the cardiac chambers, and the liver weight was measured after emptying the bile from the gallbladder.

When the organs were affected by serious diseases, such as cancer, these abnormal organ weights were excluded from the study. Namely, the weights of any organs with malignant tumors, either primary or metastatic, were excluded. The weights of the following organs with specified diseases were also excluded: lungs with pneumonia, diffuse alveolar damage or aspergillosis; kidneys with pyelonephritis; adrenals with hyperplasia or adenomas; and thyroid with hyperplasia, thyroiditis or adenomas. After these primary exclusions, organs with off-limit values beyond 99% of the bilateral limits were secondarily excluded.

Statistical analysis

The summary statistics of the body indices (bodyweight, body height and BMI) and organ weights were calculated according to gender-specific age groups. A regression analysis was done to compare age-related changes in the measured values between genders, using age and gender as independent variables and each measurement as a dependent variable. The Pearson correlation coefficients were calculated for the body indices and organ weights. Another regression analysis was done to clarify the contributions of standardized age and nutrition (bodyweight) to the organ weights, employing age and bodyweight as independent variables and each organ weight as a dependent variable. The standardized age and bodyweight were calculated by (measurement–mean)/SD. The SAS system for Windows (ver. 8.1) and JMP (ver. 5.1; SAS Institute Japan, Tokyo, Japan) were used for the statistical analyses, and the significance level was set at 0.05.

Ethical considerations

Written informed consent was obtained from the bereaved family of each of the patients prior to the autopsy examination. The use of autopsy materials for medical education and research is generally permitted by the Act of Postmortem Examinations of Japan.

RESULTS

Age-related changes of the body indices and organ weights

Table 1 shows the summary statistics of the body indices (body height, weight, and BMI) and organ weights. The number of lung weight measurements was relatively small because many autopsy cases with pneumonia were excluded from the study. The body indices and organ weights followed normal distributions. The means of the body indices and organ weights were significantly higher in men than in women, except for the BMI. The coefficient of variation (CV), standard deviation divided by mean, was calculated to compare the relative variation among the measurements. The spleen weight varied greatly with a CV >0.6, while the body height and brain weight varied little, with a CV <0.1.

Tables 2 and 3 show the gender- and age-specific standard values of the body indices and organ weights. The means of all measurements significantly decreased with advancing age both in men and in women, except for the heart in men and the lungs in both genders ($P < 0.05$). Figure 1 shows the age-related changes of the relative means of the measurements when the values for patients aged 60–69 years were set to 1. The body heights decreased by 6–9% between the 7th and 11th decades in both genders. The bodyweights of women showed a marked linear decrease by 35% among the centenarians, while the decrease was milder (26%) among male centenarians. The decrease in BMI was milder than that of bodyweight because of the concomitant decrease in body height. The brain weights showed a mild decrease by 9–15% in the centenarians. The age-related changes in heart weight were inconsistent, but a 12% decrease was noted in female centenarians. The organ weights of the liver, kidneys and spleen decreased by more than 30% and in a strong linear fashion. The decrease in the splenic weight of women was the most severe, with a mean of 39 g among centenarians; this corresponds to 43% of the weight in the 7th decade. The age-related decreases in body height, bodyweight, BMI, heart weight, and pituitary weight were significantly more severe in women than in men ($P < 0.05$).

Correlations among body indices and organ weights

Table 4 shows the Pearson correlation coefficients and *P* under a null hypothesis of zero among the measurements. The correlation between bodyweight and each organ weight was stronger than that between body height (or BMI) and each organ weight, except for the brain. The correlation between body height and brain weight was stronger than that between bodyweight (or BMI) and brain weight. The organ weights of the heart, liver, kidneys and spleen had high correlation coefficients ($r = 0.4$) for bodyweight in both genders. The correlations between organ weights were high ($r = 0.4$) for the heart and liver, the liver and kidneys, and the liver and spleen in both genders and between the kidney and spleen in women. The correlations were generally low between the thyroid (or adrenals) and other organs. The lowest correlations were observed between the hypophysis and other organs ($r = 0.21$).

Regression analysis of the organ weights

The regression coefficients for standardized age and bodyweight to the organ weights are shown in Table 5. Age negatively affected the organ weights, except for the heart and hypophysis. The regression coefficients between bodyweight and organ weight were high for most organs except for the hypophysis, and were highest in the heart and liver.

DISCUSSION

Previous reports on normal organ weights in the elderly

The standard organ weights of elderly Japanese who died while hospitalized were determined in the present study. There have been several reports on the normal values of organ weights among Japanese autopsy patients who died from external causes.[5–9] In these reports, however, the age of the subjects ranged from neonates to the elderly, and the analyses usually focused on changes in the organ weights during the developmental period. The number of subjects over the age of 90 years was also small. None of these reports focused on senescent changes in organ weights. Meanwhile, a few papers have been published on organ weights in the elderly based on autopsies of patients who died while hospitalized.[1–3,10–14] The present report is the second study to examine this topic after the Inoue and Otsu report, and both reports analyzed consecutive autopsy cases performed at the same hospital. The subjects of the Inoue and Otsu report were autopsied between 1972 and 1977, while the present subjects were autopsied between 1995 and 2003; thus, the interval between these reports is approximately 25 years. The body height and weight in women, the heart weight in men, and the splenic weights in both genders significantly increased in the present study, compared with those in the Inoue and Otsu report, as shown in Table 6. These increases may be ascribed to nutritional improvements during the past 25 years. The reason for the decrease in renal weights is unclear. The standard organ weights of the lungs, hypophysis, thyroid and adrenals, which were not described in the Inoue and Otsu report, are given in the present report.

Nutrition and organ weights

Although the precise mechanism of senile atrophy is unclear, the decrease in organ weights in the elderly can be simply ascribed to aging. Many factors, such as disuse, undernutrition, arteriosclerosis, or reductions in endocrine activity, may cause the loss of organ weights in the elderly. The present report shows that undernutrition was a significant cause of senile atrophy. In undernourished patients, the glycogen and neutral fat contents decrease in the parenchymal cells of the liver, heart and kidneys, and the volume of adipose tissue diminishes in the interstitium of the organs. Tanaka *et al.* conducted a unique study comparing organ weights between the years of starvation immediately after World War II and the years of improved nutrition from 1970 to 1980.[6] The organ weights of the heart, kidneys, spleen and adrenals increased by 15–20%, and the liver weight increased by 8%. These organs seem to be strongly affected by nutritional state.

Individual organ weights

Age-related physiological and pathological conditions (geriatric diseases) may contribute to the loss of organ weight.

Age-related reductions in brain weight were mild, and the brain was the sole organ in which the correlation with body height was stronger than that with bodyweight.[15,16] Undernutrition in the elderly had a relatively small effect on brain weight, probably because the brain contains only very small amounts of glycogen and neutral fat. Neuronal death typically seen in Alzheimer disease may also have contributed to the loss of brain weight in some cases. Longitudinal CT studies showed significantly larger reduction of brain volume in patients with Alzheimer disease than controls.[17,18] A report from Tokyo Metropolitan Geriatric Hospital also indicated accelerated brain atrophy and ventricular dilatation in pathologically verified autopsy cases of Alzheimer disease.[19]

The heart was an exceptional organ in that the heart weight was almost constant or even increased with age. This phenomenon is also observed during middle age and has attracted the attention of researchers.[1,20,21] Systolic

hypertension is frequently seen in the middle-aged and elderly, mainly accounting for the increase in heart weight. Although hypertension was frequent in the present subjects (33% of the cases), undernutrition seemed to suppress the increase in heart weight.

The organ weights of the liver, spleen and kidneys decreased prominently with age. Tauchi *et al.* reported that in livers with senile atrophy, both the number and volume of the individual hepatocytes decreased.[22] In benign nephrosclerosis, the alteration of vascular structures, such as atherosclerosis, hyaline arteriosclerosis, and glomerular sclerosis may lead to renal weight loss.[23–25]

The hypophysis, an upstream endocrine organ of the thyroid and adrenals, did not show any age-related changes but did exhibit a gender-related difference. Because the significant figure for pituitary weight was two digits and the specimens often contained a small piece of adjacent structures, such as the diaphragm, pituitary weight seemed to be less reliable than those of the other organs. Nevertheless, another study in which male hypophysis was carefully prepared and weighed in milligrams revealed that pituitary weight increased with age in cases with prostatic hypertrophy and decreased in cases with a normal prostate; therefore, the pituitary weight was almost constant up to 80 years of age.[26] Because of this, the serum concentration (level) of pituitary hormones such as growth hormone or gonadotropins does not change significantly throughout adulthood or in the elderly.

Limitations of the present study

The National Nutritional Survey in Japan (1995) showed the mean BMI in the 7th decade and in subjects over 70 years of age to be 23.1 and 22.0 in men and 23.6 and 22.9 in women, respectively.[27] Considering the average BMI of 17.8 in men and 19.0 in women in their 7th decade, the present subjects were apparently undernourished. The nutritional state was proved to contribute significantly to organ weight. Thus, the present results may not represent the normal organ weights of healthy elderly people. But the very elderly are often frail; 52.3% of people aged 85–89 years and 72.1% of people over 90 years are eligible to receive Elderly Health Insurance in Japan (2005).[28,29] Even if they are neither covered by health care, nor attend a hospital, they frequently suffer from chronic diseases. Therefore, the present results could probably be used as the normal values for the 10th and 11th decades of life, for which data on organ weights are scarce.

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REFERENCES

1 Inoue T, Otsu S. Statistical analysis of the organ weights in 1000 autopsy cases of Japanese aged over 60 years. *Acta Pathol Jpn* 1987; **37**: 343–59.
2 Ueda K, Omae T, Fujishima M. Physiological and biochemical changes in ageing: Based on a population survey in a Japanese community, Hisayama. *Ann Acad Med Singapore* 1987; **16**: 35–41.
3 Howell TH. Organ weights in nonagenarians. *J Am Geriatr Soc* 1978; **26**: 385–90.
4 Sawabe M, Arai T, Kasahara I *et al.* Developments of geriatric autopsy database and Internet-based database of Japanese single nucleotide polymorphisms for geriatric research (JG-SNP). *Mech Ageing Dev* 2004; **125**: 547–52.
5 Tanaka GI, Kawamura H, Nakahara Y. Reference Japanese man – I. mass of organs and other characteristics of normal Japanese. *Health Phys* 1979; **36**: 333–46.
6 Tanaka G, Nakahara Y, Nakazima Y. Japanese reference man 1988-IV. Studies on the weight and size of internal organs of Normal Japanese. *Nippon Igaku Hoshasen Gakkai Zasshi* 1989; **49**: 344–64 (in Japanese with English abstract).
7 Xxxxxxxxxx. Reports on medico-legal data from massive investigation performed by the Medico-Legal Society of Japan: Weight and size of internal organs of normal Japanese today. *Nippon Hoigaku Zasshi* 1992; **46**: 225–35 (in Japanese with English abstract).
8 Ogiu N, Nakamura Y, Ijiri I, Hiraiwa K, Ogiu T. A statistical analysis of the internal organ weights of normal Japanese people. *Health Phys* 1997; **72**: 368–83.
9 Furutani A, Noda H, Yamaguchi M, Tatsumi S, Yasui M, Sugiyama S. Standard weight of the normal brain, spleen and pancreas in Japanese. *Acta Med Kinki Univ* 1999; **24**: 19–25.
10 Howell TH. Heart weights among octogenarians. *J Am Geriatr Soc* 1981; **29**: 572–5.
11 Howell TH. Brain weights in octogenarians. *J Am Geriatr Soc* 1981; **29**: 450–52.
12 Howell TH. Brain weights in septuagenarians. *J Am Geriatr Soc* 1982; **30**: 754–5.
13 Spencer RP. Organ/body weight loss with aging: Evidence for co-ordinated involution. *Med Hypotheses* 1996; **46**: 59–62.
14 Okudaira M, Ikawa N, Yasuhara M, Kumagai T, Kurosu K. Liver weight of adult Japanese, especially recent weight values. *Hepatol Res* 2000; **18**: 95–103.
15 Chrzanowska G, Beben A. Weight of the brain and body height in man between the ages of 20 and 89 years. *Folia Morphol (Warsz)* 1973; **32**: 391–406.

16 Dekaban AS. Changes in brain weights during the span of human life: Relation of brain weights to body heights and body weights. *Ann Neurol* 1978; **4**: 345–56.
17 Gado M, Hughes CP, Danziger W, Chi D. Aging, dementia, and brain atrophy: A longitudinal computed tomographic study. *Am J Neuroradiol* 1983; **4**: 699–702.
18 Shear PK, Sullivan EV, Mathalon DH *et al.* Longitudinal volumetric computed tomographic analysis of regional brain changes in normal aging and Alzheimer's disease. *Arch Neurol* 1995; **52**: 392–402.
19 Yamada S, Asano T, Enomoto M *et al.* Ventricular dilatation and brain atrophy of normal elderly individuals and patients with Alzheimer-type dementia: A retrospective longitudinal computed tomographic study of autopsy cases. *Neuropathology* 1998; **18**: 261–9.
20 Kitzman DW, Scholz DG, Hagen PT, Ilstrup DM, Edwards WD. Age-related changes in normal human hearts during the first 10 decades of life. Part II (Maturity). A quantitative anatomic study of 765 specimens from subjects 20–99 years old. *Mayo Clin Proc* 1988; **63**: 137–46.
21 Adebo OA, Lun KC, Lee CN, Chao TC. Age-related changes in normal Chinese hearts. *Chin Med J (Engl)* 1994; **107**: 88–94.
22 Tauchi H, Sato T, Ito Y. Morphological aspects of aging liver: Half a century of progress in Japan. *Arch Gerontol Geriatr* 1994; **19**: 135–44.
23 Ueda K, Omae T, Hirota Y, Takeshita M, Hiyoshi Y. Epidemiological and clinco-pathological study on renal diseases observed in the autopsy cases in Hisayama population, Kyushu Island, Japan. *J Chronic Dis* 1976; **29**: 159–73.
24 Hoy WE, Douglas-Denton RN, Hughson MD, Cass A, Johnson K, Bertram JF. A stereological study of glomerular number and volume: Preliminary findings in a multiracial study of kidneys at autopsy. *Kidney Int Suppl* 2003; **63**: S31–S37.
25 Kubo M, Kiyohara Y, Kato I *et al.* Risk factors for renal glomerular and vascular changes in an autopsy-based population survey: The Hisayama study. *Kidney Int* 2003; **63**: 1508–15.
26 Haugen OA. Pituitary weight and the histology of the prostate in elderly men. An analysis in an autopsy series. *Acta Pathol Microbiol Scand* [*A*] 1973; **81**: 204–12.
27 *National Nutrition Survey (NNS).* Tokyo: National Institute of Health and Nutrition. (Cited by 15 January 2006). Available from http://nihn-jst.nih.go.jp:8888/nns/owa/nns_main_e.hm01
28 *The Portal Site of Statistical Data in Japan.* Tokyo: Statistics Bureau of Japan. (Cited 15 January 2006). Available from http://portal.stat.go.jp/Pubstat/topE.html
29 *Forum of National Health Insurance.* Tokyo: All-Japan Federation of National Health Insurance Organization. (Cited 15 January 2006). Available from http://www.kokuho.or.jp/english/index.htm

Figure 1 Ratio of body indices and organ weights to those for subjects aged 60–69 years. The weights of the left lung, kidney and adrenal are used for the analysis. Age-related decreases in body height, weight, body mass index (BMI), and heart and pituitary weights are significantly more severe in women than in men (*$P < 0.05$). (**a**) body height (BH; ■, men; □, women), bodyweight (BW; ●, men; O, women) and BMI (s, men; ▵, women); (**b**) brain (■, men; □, women), heart (●, men; O, women) and lung (s, men; ▵, women); (**c**) liver (■, men; □, women), kidney (●, men; O, women) and spleen (s, men; ▵, women); (**d**) hypophysis (■, men; □, women), thyroid (●, men; O, women) and adrenal (s, men; ▵, women).

Table 1 Body indices and organ weights

	<ts3>Men			<ts3>Women		
	n	Mean ± SD	CV	*n*	Mean ± SD	CV
Body height (cm)	890	161.1 ± 6.9	0.04	764	147.4 ± 7.2	0.05
Bodyweight (kg)	891	44.3 ± 9.9	0.22	764	38.0 ± 10.0	0.26
BMI (kg/m^2)	891	17.0 ± 3.4	0.20	764	17.4 ± 3.9	0.22
Brain (g)	673	1275.5 ± 116.1	0.09	597	1140.7 ± 113.7	0.10
Heart (g)	880	342.0 ± 89.9	0.26	753	312.3 ± 83.0	0.27
Lung, left (g)	225	404.2 ± 159.6	0.39	312	284.8 ± 106.3	0.37
Lung, right (g)	227	474.2 ± 179.6	0.38	313	351.9 ± 134.0	0.38
Liver (g)	668	920.3 ± 283	0.31	589	794.7 ± 251.7	0.32
Kidney, left (g)	871	120.8 ± 36	0.30	740	98.9 ± 31.1	0.31
Kidney, right (g)	873	113.6 ± 34.2	0.30	745	94.3 ± 29.6	0.31
Spleen (g)	779	80.7 ± 51.8	0.64	694	62.8 ± 41.5	0.66
Hypophysis (g)	718	0.55 ± 0.13	0.24	608	0.65 ± 0.16	0.25
Thyroid (g)	807	13.5 ± 5.1	0.38	626	11.6 ± 5.1	0.44
Adrenal, left (g)	780	5.6 ± 1.7	0.30	676	4.9 ± 1.5	0.31
Adrenal, right (g)	780	5.1 ± 1.5	0.29	686	4.6 ± 1.3	0.28

BMI, body mass index; CV, coefficient of variation (SD/mean).

Table 2 Standard body indices and organ weights in men (n = 896)

	Age (years)	n	Mean ± SD	CV	Range
Body height (cm)	60–69	96	164.1 ± 5.9	0.036	145–180
	70–79	369	162.5 ± 6.3	0.039	146–180
	80–89	317	159.9 ± 7.0	0.044	137–176
	90–99	97	158.0 ± 6.8	0.043	139–170
	100–	11	153.9 ± 8.0	0.052	138–165
Bodyweight (kg)	60–69	96	48.1 ± 10.3	0.215	28.5–75.5
	70–79	370	44.8 ± 10.1	0.226	26.5–83.0
	80–89	317	43.2 ± 9.4	0.217	23.0–79.5
	90–99	97	42.9 ± 8.7	0.203	25.0–67.5
	100–	11	35.7 ± 7.0	0.195	23.0–47.0
BMI (kg/m^2)	60–69	96	17.8 ± 3.4	0.193	11.2–27.7
	70–79	370	17.0 ± 3.6	0.212	10.6–28.4
	80–89	317	16.9 ± 3.4	0.200	10.8–27.8
	90–99	97	17.1 ± 3.1	0.180	11.8–24.5
	100–	11	14.9 ± 2.0	0.135	12.1–19.3
Brain (g)	60–69	68	1339.2 ± 123.1	0.092	1060–1600
	70–79	267	1289.7 ± 118.9	0.092	920–1690
	80–89	250	1263.2 ± 104.6	0.083	920–1570
	90–99	77	1219.3 ± 104.8	0.086	970–1550
	100–	11	1212.3 ± 83.6	0.069	1080–1350
Heart (g)	60–69	91	351.7 ± 92.4	0.263	210–607
	70–79	368	336.5 ± 91.8	0.273	175–628
	80–89	313	343.2 ± 87.2	0.254	171–650
	90–99	97	350.5 ± 90.8	0.259	205–627
	100–	11	338.3 ± 76.1	0.225	240–470
Lung, left (g)	60–69	26	479.9 ± 205.2	0.428	235–1030
	70–79	100	397.3 ± 156.7	0.394	170–930
	80–89	65	375.7 ± 139.0	0.370	165–875
	90–99	32	410.8 ± 151.6	0.369	147–787
	100–	2	350.0 ± 56.6	0.162	310–390
Lung, right (g)	60–69	27	546.8 ± 231.7	0.424	230–1100
	70–79	101	472.1 ± 170.0	0.360	200–980
	80–89	66	435.0 ± 157.2	0.361	185–890
	90–99	31	499.5 ± 211.0	0.422	182–1025
	100–	2	395.0 ± 35.4	0.090	370–420
Liver (g)	60–69	58	1158.4 ± 309.6	0.267	620–1850
	70–79	269	972.3 ± 294.9	0.303	450–2055
	80–89	243	865.0 ± 245.3	0.284	430–2000
	90–99	87	781.3 ± 188.5	0.241	412–1355
	100–	11	716.4 ± 110.1	0.154	550–970
Kidney, left (g)	60–69	89	150.5 ± 38.7	0.257	76–240
	70–79	365	125.1 ± 37.2	0.297	35–246
	80–89	311	113.3 ± 28.7	0.253	41–204
	90–99	95	103.9 ± 31.8	0.306	40–200
	100–	11	97.2 ± 27.3	0.281	55–140
Kidney, right (g)	60–69	91	140.6 ± 35.5	0.252	70–220
	70–79	364	119.3 ± 35.5	0.297	35–232
	80–89	310	105.4 ± 27.4	0.260	45–200
	90–99	97	96.6 ± 28.4	0.294	35–180
	100–	11	83.4 ± 25.6	0.308	40–110
Spleen (g)	60–69	82	99.9 ± 59.9	0.599	10–319
	70–79	313	87.8 ± 55.4	0.631	10–430
	80–89	279	73.7 ± 47.4	0.643	10–335
	90–99	94	64.0 ± 35.0	0.548	15–200
	100–	11	56.8 ± 27.3	0.481	25–100

Hypophysis (g)	60–69	71	0.5 ± 0.1	0.221	0.3–1.0
	70–79	294	0.5 ± 0.1	0.249	0.3–1.0
	80–89	263	0.6 ± 0.1	0.237	0.3–1.0
	90–99	79	0.6 ± 0.2	0.261	0.3–1.0
	100–	11	0.6 ± 0.1	0.145	0.5–0.8
Thyroid (g)	60–69	87	15.0 ± 5.3	0.353	6.2–31
	70–79	340	13.6 ± 5.1	0.372	5.3–38
	80–89	281	13.3 ± 5.4	0.403	5.5–35
	90–99	88	12.0 ± 3.9	0.326	6.2–25
	100–	11	11.8 ± 4.7	0.400	7.1–21
Adrenal, left (g)	60–69	77	6.5 ± 1.9	0.296	2.6–12.8
	70–79	318	5.6 ± 1.6	0.279	2.4–12.3
	80–89	286	5.5 ± 1.7	0.311	2.0–11.7
	90–99	88	5.0 ± 1.7	0.346	2.0–13.5
	100–	11	4.3 ± 1.3	0.309	1.9–6.5
Adrenal, right (g)	60–69	76	5.7 ± 1.5	0.257	3.4–9.4
	70–79	321	5.1 ± 1.4	0.278	2.3–10.2
	80–89	286	5.0 ± 1.6	0.311	2.0–11.3
	90–99	86	4.5 ± 1.4	0.314	2.4–8.8
	100–	11	3.9 ± 0.9	0.237	2.0–5.0

BMI, body mass index; CV, coefficient of variation (SD/mean).

Table 3 Standard body indices and organ weights in women (n = 769)

	Age (years)	n	Mean ± SD	CV	Range
Body height (cm)	60–69	53	152.1 ± 7.1	0.047	126–162
	70–79	220	150.0 ± 6.1	0.041	129–164
	80–89	297	147.2 ± 7.2	0.049	120–165
	90–99	155	145.0 ± 5.7	0.039	129–162
	100–	39	138.6 ± 7.0	0.050	115–152
Bodyweight (kg)	60–69	53	44.2 ± 12.1	0.274	24.5–74
	70–79	220	41.3 ± 10.4	0.252	20.5–82
	80–89	297	37.6 ± 9.5	0.252	20.5–91
	90–99	155	34.0 ± 6.8	0.199	21–60
	100–	39	28.9 ± 5.6	0.192	17.5–41
BMI (kg/m^2)	60–69	53	19.0 ± 4.7	0.246	11.5–30.8
	70–79	220	18.3 ± 4.2	0.229	8.4–32.2
	80–89	297	17.3 ± 3.8	0.217	9.8–37.9
	90–99	155	16.2 ± 2.9	0.179	10.7–24.7
	100–	39	15.0 ± 2.4	0.159	10.4–20.6
Brain (g)	60–69	31	1239.4 ± 112.7	0.091	1075–1470
	70–79	155	1171.1 ± 108.4	0.093	800–1490
	80–89	234	1136.3 ± 106.5	0.094	880–1470
	90–99	139	1116.0 ± 112.5	0.101	890–1550
	100–	38	1054.0 ± 91.4	0.087	850–1260
Heart (g)	60–69	53	315.5 ± 93.6	0.297	160–530
	70–79	216	320.9 ± 89.1	0.278	157–598
	80–89	290	315.1 ± 84.3	0.268	165–600
	90–99	155	303.1 ± 69.7	0.230	155–525
	100–	39	277.3 ± 59.6	0.215	160–415
Lung, left (g)	60–69	16	311.6 ± 101.0	0.324	215–655
	70–79	92	307.7 ± 125.1	0.407	125–670
	80–89	126	293.9 ± 106.8	0.363	135–660
	90–99	64	251.3 ± 77.4	0.308	120–460
	100–	14	205.7 ± 47.8	0.361	120–280
Lung, right (g)	60–69	16	389.1 ± 139.5	0.358	250–730
	70–79	92	378.5 ± 150.3	0.397	160–830
	80–89	127	362.2 ± 132.5	0.366	147–830
	90–99	64	307.3 ± 115.7	0.376	160–825
	100–	14	275.4 ± 71.3	0.259	130–370
Liver (g)	60–69	35	1006.6 ± 295.2	0.293	500–1960
	70–79	152	912.9 ± 251.2	0.275	360–1600
	80–89	227	799.4 ± 231.8	0.290	380–1760
	90–99	140	664.5 ± 173.3	0.261	350–1340
	100–	35	571.2 ± 141.3	0.251	340–920
Kidney, left (g)	60–69	52	125.3 ± 34.9	0.279	45–210
	70–79	211	107.0 ± 28.5	0.284	30–188
	80–89	289	98.4 ± 28.6	0.291	40–207
	90–99	153	80.0 ± 21.2	0.265	38–210
	100–	35	77.3 ± 23.3	0.306	45–140
Kidney, right (g)	60–69	51	119.4 ± 31.4	0.263	44–177
	70–79	213	110.6 ± 30.4	0.275	50–213
	80–89	293	93.1 ± 27.7	0.297	23–176
	90–99	153	76.9 ± 19.6	0.255	23–136
	100–	35	70.3 ± 20.2	0.288	35–115
Spleen (g)	60–69	46	89.8 ± 59.1	0.658	27–262
	70–79	183	74.3 ± 44.5	0.600	14–220
	80–89	280	63.1 ± 40.9	0.649	13–259
	90–99	147	45.7 ± 22.3	0.488	12–117
	100–	38	39.0 ± 20.2	0.512	10–110

Hypophysis (g)	60–69	35	0.7 ± 0.1	0.204	0.4–1.0
	70–79	161	0.7 ± 0.2	0.249	0.2–1.1
	80–89	236	0.6 ± 0.2	0.245	0.2–1.1
	90–99	137	0.6 ± 0.2	0.234	0.3–1.0
	100–	39	0.6 ± 0.2	0.258	0.2–0.8
Thyroid (g)	60–69	37	14.3 ± 5.5	0.386	6.9–31.3
	70–79	182	12.0 ± 4.7	0.395	3.7–31.0
	80–89	249	12.1 ± 5.3	0.438	4.0–38.0
	90–99	131	10.0 ± 4.2	0.416	3.7–34.0
	100–	27	9.2 ± 5.0	0.633	3.7–24.0
Adrenal, left (g)	60–69	48	5.4 ± 1.8	0.327	2.5–9.9
	70–79	186	5.4 ± 1.5	0.270	2.3–9.3
	80–89	266	4.9 ± 1.5	0.308	2.0–11.0
	90–99	139	4.5 ± 1.3	0.299	2.2–9.5
	100–	37	3.6 ± 0.8	0.237	2.0–5.0
Adrenal, right (g)	60–69	46	4.8 ± 1.5	0.305	2.5–8.5
	70–79	191	5.0 ± 1.5	0.294	2.1–10.0
	80–89	270	4.6 ± 1.3	0.276	2.1–9.7
	90–99	142	4.2 ± 1.1	0.255	2.3–8.5
	100–	37	3.6 ± 0.8	0.226	1.7–5.7

BMI, body mass index; CV, coefficient of variation (SD/mean).

Table 4 Correlations among body indices and organ weights in men (upper right) and women (lower left)

	BH	BW	BMI	Brain	Heart	Lung	Liver	Kidney	Spleen	Hypophysis	Thyroid	Adrenal
BH	1	**0.41****	0.01	0.23**	0.20**	0.20*	0.31**	0.29**	0.19**	0.09*	0.18**	0.25**
BW	**0.52****	1	**0.91****	0.22**	**0.55****	0.35**	**0.61****	**0.45****	**0.41****	0.11*	0.31**	0.37**
BMI	0.19**	**0.93****	1	0.15*	**0.52****	0.29**	**0.53****	0.36**	0.36**	0.07*	0.25**	0.30**
Brain	0.36**	0.29**	0.19**	1	0.11*	0.03	0.18**	0.27**	0.09*	0.09*	0.19**	0.18**
Heart	0.29**	**0.53****	**0.49****	0.17**	1	0.25*	**0.51****	0.25**	0.28**	0.12*	0.32**	0.31**
Lung	0.25**	0.32**	0.28**	0.23**	0.17*	1	0.31**	0.15*	0.20*	0.03	0.17*	0.12
Liver	**0.49****	**0.68****	**0.56****	0.37**	**0.53****	0.30**	1	**0.53****	**0.51****	0.08	0.35**	**0.41****
Kidney	**0.43****	**0.49****	0.39**	0.36**	0.27**	0.28**	**0.59****	1	0.35**	0.05	0.22**	0.34**
Spleen	0.32**	**0.49****	**0.43****	0.15*	0.36**	0.29**	**0.57****	**0.48****	1	0.09*	0.17**	0.25**
Hypophysis	0.11*	0.14*	0.11*	0.17**	0.14*	0.19*	0.21**	0.16*	0.14*	1	0.05	0.07
Thyroid	0.20**	0.36**	0.33**	0.17**	0.33**	0.15*	0.36**	0.21**	0.27**	0.13*	1	0.27**
Adrenal	0.34**	0.39**	0.31**	0.30**	0.18**	0.17*	0.39**	0.38**	0.23**	0.17**	0.27**	1

BH, body height; BMI, body mass index; BW, bodyweight.
The weights of the left lung, kidney and adrenal were used for the analysis.
Bold, correlation coefficient >0.4.
*$P < 0.05$; **$P < 0.0001$.

Table 5 Regression coefficients of standardized age and bodyweight on organ weight

	<ts3>Standardized age			<ts3>Standardized bodyweight		
	Estimates	SE	*P*	Estimates	SE	*P*
Brain	–0.278	0.026	<0.0001*	0.281	0.026	<0.0001*
Heart	0.112	0.021	<0.0001*	0.601	0.022	<0.0001*
Lung, left	–0.045	0.037	0.2225	0.412	0.041	<0.0001*
Liver	–0.266	0.020	<0.0001*	0.602	0.021	<0.0001*
Kidney, left	–0.307	0.021	<0.0001*	0.421	0.021	<0.0001*
Spleen	–0.164	0.024	<0.0001*	0.411	0.024	<0.0001*
Hypophysis	0.063	0.029	0.0267*	0.023	0.029	0.4158
Thyroid	–0.089	0.026	0.0006*	0.319	0.027	<0.0001*
Adrenal, left	–0.165	0.025	<0.0001*	0.364	0.025	<0.0001*

*$P < 0.05$.

Table 6 Comparison of body indices and organ weights between the Inoue and Otsu study and the present study

	Age (years)	<ts4>Men <ts4>Women Present study (Mean 1)	Inoue & Otsu[1] (Mean 2)	Relative increase (%)	$P^{\dagger}$	Present study (Mean 1)	Inoue & Otsu[1] (Mean 2)	Relative increase (%)	$P^{\dagger}$
Body height	70–79	162.5	159.3	2.0	<0.0001*	150.0	146.5	2.4	<0.0001*
	80–89	159.9	157.5	1.5	0.001*	147.2	144.5	1.8	<0.0001*
Bodyweight	70–79	44.8	44.3	1.1	0.540	41.3	38.8	6.4	0.013*
	80–89	43.2	42.5	1.6	0.433	37.6	36.0	4.6	0.049*
Brain	70–79	1290	1295	–0.4	0.640	1171	1170	0.1	0.925
	80–89	1263	1250	1.1	0.238	1136	1145	–0.8	0.400
Heart	70–79	336.5	332.0	1.4	0.524	320.9	317.0	1.2	0.680
	80–89	343.2	323.0	6.2	0.011*	315.1	303.5	3.8	0.116
Liver	70–79	972	1015	–4.2	0.091	913	900	1.4	0.597
	80–89	865	870	–0.6	0.835	799	775	3.2	0.273
Kidney, left	70–79	125.1	137.2	–8.8	<0.0001*	110.6	113.2	–2.3	0.363
	80–89	113.3	125.2	–9.5	<0.0001*	98.4	101.6	–3.1	0.226
Spleen	70–79	87.8	72.0	21.9	<0.0001*	74.3	64.6	14.9	0.009*
	80–89	73.7	69.2	6.5	0.299	63.1	56.6	11.4	0.069

Relative increase (%) = (mean 1 – mean 2)/mean 2.
[†]Student's *t*-test.
*$P < 0.05$.

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