a study, which measured the proportion of individuals with hypertension due to the same BMI level as ours (BMI 25.0 kg/m^2) among total hypertensives in a Western country. Wilson et al. [27] reported that 26% of male hypertensives and 28% of female hypertensives in a population in the United States had hypertension which was attributed to BMI $\geq$ 25.0 kg/m^2 in a 44-year follow-up study from 1948. Consequently, the proportion of individuals with hypertension due to BMI $\geq$ 25.0 kg/m^2 among total hypertensives in Japan should be lower than the corresponding proportion in the United States.

The number of Japanese participants with 25.0 $\leq$ BMI < 30.0 kg/m^2 was approximately eight times greater than that with BMI $\geq$ 30.0 kg/m^2 for both sexes in the present study. Approximately 80–90% of the Japanese participants with hypertension due to BMI $\geq$ 25.0 kg/m^2 were in the 25.0 $\leq$ BMI < 30.0 kg/m^2 category for both sexes. Japanese in the 25.0 $\leq$ BMI < 30.0 kg/m^2 category contributed more significantly to the high prevalence of hypertension in Japan rather than Japanese with BMI 30.0 kg/m^2. Therefore, in order to reduce the prevalence of hypertension in Japan, more attention should be paid to Japanese in the 25.0 $\leq$ BMI < 30.0 kg/m^2 category who account for the majority of the obese in the Japanese population (BMI $\geq$ 25.0 kg/m^2) [35–38]. However, according to Wilson's study [27], in the United States, approximately 60–70% of individuals with hypertension due to BMI $\geq$ 25.0 kg/m^2 could be attributed to the 25.0 $\leq$ BMI < 30.0 kg/m^2 category, whereas approximately 30–40% could be attributed to the BMI $\geq$ 30.0 kg/m^2 category.

The prevalence of hypertension among Japanese has remained unchanged from 1980 to 1990 (approximately 50% for men and 40% for women). However, the proportion of individuals with obesity-induced hypertension among total hypertensives in Japan increased, as the prevalence of obesity among Japanese has increased. As for the increased prevalence of obesity, it is notable that the mean body weight remarkably increased between 1980 and 1990, although the mean body height also somewhat increased. High sodium intake has been a more important factor for hypertension in the Japanese population, compared to Western populations [1–5]. Some previous studies suggest the mean value of sodium intake in the Japanese population has remained unchanged or slightly decreased between 1980 and 1990this is lower than in the mid-1970s or beforē[1–5, 39], although we could not confirm such a trend by using this data because of lack of information on sodium intake. Furthermore, high alcohol intake also has been important among Japanese men, although the prevalence of drinkers among Japanese women is very low [2, 4, 6–8]. We confirmed the decreased prevalence of current daily drinkers among men over the decade using this data (74.3% in 1980 and 57.7% in 1990). These findings possible imply that high sodium and alcohol intake play a less important role in the high prevalence of hypertension in Japan than it did before. Therefore, we propose that the increased prevalence of obesity has compensated for reduced sodium and alcohol intake with regards to the high prevalence of hypertension in Japan. Moreover, we assume that the pandemic of obesity in Japan may have affected not only the prevalence of hypertension but also the prevalence of other obesity-related cardiovascular risks (e.g., type 2 diabetes) in Japan [29, 31, 40].

BMI is a widely used surrogate measurement of total body fat [41]. Recently, obesity has been quantified not only by BMI but also by other anthropometric parameters (e.g., waist circumference, fat distribution). However, other anthropometric parameters were not available in the present study. Sakurai et al. [42] suggested that among four anthropometric parameters of obesity (i.e., BMI, waist circumference, waist-to-hip ratio, and waist-to-height ratio), BMI has the strongest association with blood pressure and the prevalence of hypertension for middle-aged Japanese women. Additionally, there is little difference among the four anthropometric parameters in the strength of association with blood pressure or the prevalence of hypertension for middle-aged Japanese men, although BMI is ranked third among these four parameters [42]. Therefore, our results for the proportion of individuals with obesity-induced hypertension quantified by BMI among total hypertensives in Japan are reasonable.

The present study has some limitations. First, our results were estimated by using cross-sectional data in which reverse causality is occasionally observed. For example, the participants with obesity-induced hypertension may have attempted to reduce their body weight prior to the surveys, and this would results in a decreased prevalence of obesity in the study population. However, blood pressure levels also might have decreased after body weight reduction among the participants with obesity-induced hypertension [36–38]. Therefore, our results may show the prevalence of obesity and hypertension in the study population on the basis of the well-established causality between obesity and hypertension [26–32]. Finally, blood pressure-related social factors (e.g., stress, irregular lifestyle) and dietary factors (e.g., sodium intake, potassium intake) were not available in the present study. Especially, adjustment for sodium intake is significant to assess the risk for hypertension among Japanese because of its importance [1–5]. However, in addition to the trend of unchanged or slightly decreased sodium intake among Japanese between 1980 and 1990 [3–5, 39], Mikawa et al. [13] observed there was little difference in the sodium/potassium intake ratio between obese and non-obese Japanese in 1985. Consequently, the lack of adjustment for

sodium intake perhaps may have little impact on the result of increased proportion of hypertensives due to obesity over the decade.

In conclusion, Japan has witnessed a progressive rise in the proportion of individuals with obesity-induced hypertension among total hypertensives between 1980 and 1990 in both sexes. Obesity now plays a more important role in the high prevalence of hypertension in Japan than it did before. In order to reduce the proportion of individuals with obesity-induced hypertension among total hypertensives in Japan, an appropriate strategy to encourage the population to adopt healthy dietary habits and to increase their physical activity should be considered.

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Appendix

List of the NIPPON DATA80, 90 Research group.

NIPPON DATA80, 90: "National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged."

Chairman: Hirotsugu Ueshima (Department of Health Science, Shiga University of Medical Science, Otsu, Shiga).

Consultant: Osamu Iimura (Hokkaido JR Sapporo Hospital, Sapporo, Hokkaido), Teruo Omae (Health C&C Center, Hisayama, Kasuya, Fukuoka), Kazuo Ueda (Murakami Memorial Hospital, Nakatsu, Oita), Hiroshi Yanagawa (Saitama Prefectural University, Koshigaya, Saitama), Hiroshi Horibe (Aichi Medical University, Nagakute, Aichi).

Participating Researchers: Akira Okayama (The First Institute of Health Service, Japan Anti-Tuberculosis Association, Chyioda-ku, Tokyo), Kazunori Kodama, Fumiyoshi Kasagi (Department of Epidemiology, Radiation Effects Research Foundation, Hiroshima, Hiroshima), Tomonori Okamura, Yoshikuni Kita (Department of Health Science, Shiga University of Medical Science, Otsu, Shiga), Takehito Hayakawa (Department of Hygiene and Preventive Medicine, Fukushima Medical University, Fukushima, Fukushima), Shinichi Tanihara (Department of Hygiene and Preventive Medicine, Fukuoka University School of Medicine, Fukuoka, Fukuoka), Shigeyuki Saito (Second Department of Internal Medicine, Sapporo Medical University School of Medicine, Sapporo, Hokkaido), Kiyomi Sakata (Department of Hygiene and Preventive Medicine, Iwate Medical University School of Medicine, Morioka, Iwate), Yosikazu Nakamura (Department of Public Health, Jichi Medical University School of Medicine, Shimotsuke, Tochigi), Fumihiko Kakuno (Higashiomi Public Health Center, Higashiomi, Shiga).

Participating Research Associates: Toshihiro Takeuchi, Mitsuru Hasebe, Fumitsugu Kusano, Takahisa Kawamoto and members of 300 Public Health Centers in Japan, Masumi Minowa (Faculty of Humanities, Seitoku University, Matsudo, Chiba), Minoru Iida (Kansai University of Welfare Sciences, Kashiwara, Osaka), Tsutomu Hashimoto (Kinugasa General Hospital, Yokosuka, Kanagawa), Shigemichi Tanaka (Department of Cardiology, Cardiovascular Center, Teine Keijinkai, Sapporo, Hokkaido), Atsushi Terao (Health Promotion Division, Department of Public Health and Welfare, Shiga Prefecture, Otsu, Shiga), Katsuhiko Kawaminami (Department of Public Health Policy, National Institute of Public Health, Wako, Saitama), Koryo Sawai (The Japanese Association for Cerebro-cardiovascular Disease Control, Tokyo), Shigeo Shibata (Clinical Nutrition, Kagawa Nutrition University, Sakado, Saitama).

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中高年日本人一般住民の心房細動による死亡リスク上昇について、NIPPON DATA80　19年間の追跡調査結果より

研究協力者　大澤　正樹　岩手医科大学衛生学公衆衛生学講座　講師
分担研究者　岡山　明　　財団法人結核予防会第1健康相談所　所長
研究協力者　小野田敏行　岩手医科大学衛生学公衆衛生学講座　講師
分担研究者　坂田　清美　岩手医科大学衛生学公衆衛生学講座　教授
主任研究者　上島　弘嗣　滋賀医科大学社会医学講座福祉保健医学　教授

要約

心房細動は、心不全発症、脳卒中発症の強いリスク要因であり、また心房細動が原因で発症する心原性脳塞栓症は重症で予後不良の転帰を辿ることから、脳卒中死亡にも大きく関わる。欧米では、心房細動患者数が人口の高齢化とともに増加し続けていることが示されている。日本は世界で最も急速に高齢化が進んでいる国であり、心房細動有病率も増加していることが示されている。日本でも欧米と同様あるいはそれ以上に今後心房細動が国民の予後に与える影響力は益々大きくなることが予想される。したがって、日本国民を対象として、心房細動が総死亡、循環器疾患死亡、脳卒中死亡にどの程度の影響力を持つのかを知ることはたいへん重要なことと考えられる。そこで本研究では、NIPPON DATA80の研究対象者のデータを用いて心房細動が日本人一般住民の死亡率にどのような影響を与えているのかを検討した。対象者はNIPPON DATA80参加者9,638名である。心房細動の死亡リスクを求めるに当たり、心筋梗塞の既往を有する者（45名）、脳卒中の既往を有する者（110名）を除外し、最終的には9,483名（男性4154名、女性5329名)を解析対象とした。心房細動による死亡リスクへの影響度をみるために、コックス比例ハザードモデルを用いて多変量調整ハザード比を求め、これを相対危険率として解釈した。説明変数には、年齢、BMI、収縮期血圧、血清総コレステロール値、血糖値、心臓弁膜疾患の有無、左室肥大の有無, 現在喫煙、飲酒を用いた。対象者の心房細動有病率は0.64%（男性0.65%、女性0.62%)であった。追跡調査の総観察人年は163,679であった。心房細動群の死亡の相対危険度（ハザード比）は、脳卒中死亡で2.69倍、循環器疾患死亡で2.76倍、総死亡で1.88倍であり、いずれも有意に死亡リスクが上昇していた。対象者を男性に限ると、それらは1.27倍、1.38倍、1.39倍であり、死亡リスクの上昇は有意ではなかった。女性では3.75倍、3.96倍、2.28倍のリスク上昇が認められ、これらはいずれも統計的に有意であった。対象者を研究参加当時の年齢で65歳未満と65歳以上に分けて解析をすると、心房細動による死亡リスク上昇は65歳未満でより明確となり、相対危険度も高かった。65歳未満の対象者では、特に脳卒中死亡リスクの上昇が顕著であり、男性では9倍、女性では19倍のリスク上昇が認められた。

NIPPON DATA80に参加した日本人一般住民を対象として解析した結果、心房細動は日本人の総死亡率を1.88倍高めていることが判明した。心房細動は欧米のみならず日本人にとっても予後を悪化させる重要な危険因子であり、十分な対策が必要である。

Mortality Risk Attributable to Atrial Fibrillation in Middle-Aged and Elderly People in the Japanese General Population

— Nineteen-Year Follow-up in NIPPON DATA80 —

Masaki Ohsawa, MD; Akira Okayama, MD*; Tomonori Okamura, MD**; Kazuyoshi Itai, PhD; Motoyuki Nakamura, MD†; Kozo Tanno, MD; Karen Kato, MD; Yumi Yaegashi, MA; Toshiyuki Onoda, MD; Kiyomi Sakata, MD; Hirotsugu Ueshima, MD**
for the NIPPON DATA80 Research Group

Background The extent to which atrial fibrillation (AF) contributes to mortality in the Japanese general population has not been clarified.

Methods and Results A randomly sampled general population from all over Japan (4,154 men, 5,329 women; age ≥30 years) was enrolled. Single electrocardiogram recordings were taken in the baseline survey. Stroke death, cardiovascular deaths and all-cause deaths during the subsequent 19 years were analyzed by the presence of AF at baseline. Cox's regression analysis was carried out to estimate the hazard ratios (HRs) of each cause of death attributable to AF after adjusting for other risk factors. Prevalence of AF was 0.64% in the study. The observed person-years were 162,980 among persons without AF and 699 among persons with AF. There were 1,919 deaths. Multivariate adjusted HRs for stroke death, cardiovascular death and all-cause death were 2.69, 2.76 and 1.88, respectively ($p<0.05$). These HRs were 14.7, 9.63 and 4.00 among persons aged 64 years or younger ($p<0.05$).

Conclusion AF affects stroke mortality, cardiovascular mortality and all-cause mortality in the Japanese general population. Careful attention should be paid to persons with AF in order to prevent future cardiovascular events. (*Circ J* 2007; **71:** 814–819)

Key Words: Atrial fibrillation; Japanese; Mortality; Stroke

Atrial fibrillation (AF) is a strong risk factor for death, especially from stroke[1] and ischemic stroke associated with AF frequently results in a serious outcome[2] Thus, AF contributes not only to an increase in mortality risk but also to the burden of disability, which combined with the medical costs associated with AF has become a critical issue[3]

The prevalence of AF among patients with ischemic stroke has been reported to be approximately 15%[4] and has been increasing over the past 2 decades[5] because of the aging population[6] and the age-specific prevalence of AF has been increasing in Western countries, especially among men[7,8]

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*Department of Hygiene and Preventive Medicine, School of Medicine, Iwate Medical University, Morioka, *Department of Preventive Cardiology, National Cardiovascular Center, Suita, **Department of Health Science, Shiga University of Medical Science, Otsu and †Department of Internal Medicine II, School of Medicine, Iwate Medical University, Morioka, Japan*
Members of the NIPPON DATA80 Research Group are listed in Appendix 1.
Mailing address: Masaki Ohsawa, MD, Department of Hygiene and Preventive Medicine, Iwate Medical University, 19-1 Uchimaru, Morioka 020-8505, Japan. E-mail: masakio@iwate-med.ac.jp

Stroke incidence and mortality rates are higher than for coronary artery disease in Japanese people compared with Westerners[9–12] AF is an independent risk factor for stroke, resulting in an approximately 3- to 5-fold excess risk in the Japanese general population[13] and Japan has the most rapidly aging population in the world. The estimated number of Japanese adults with AF was 391,000 in 1980 and 729,000 in 2000, and in 2030 it is predicted to be 1,081,000[14] Consequently, there are expected increases in mortality, morbidity and the burden of disability associated with AF.

Therefore, determining the relative risk for mortality attributable to AF in Japan is an urgent task, but the extent to which AF contributes to mortality in the Japanese general population has not been clarified. In this study, we investigated the relative risks for stroke death, cardiovascular death and all-cause death attributable to AF in a representative Japanese population.

Methods

Subjects

The National Survey on Circulatory Disorders 1980 investigated household members aged 30 years or older (n=13,771) in 300 districts from all over Japan using the stratified random sampling method based on the national

Table 1 Baseline Characteristics of Participants With/Without AF in NIPPON DATA80

	Men		Women	
	Non-AF	AF	Non-AF	AF
n	4,127	27	5,296	33
Age (years)	50.6 (13.2)	63.4 (15.5)**	50.3 (13.1)	68.8 (10.3)**
BMI (kg/m²)	22.5 (2.9)	23.0 (2.9)	22.9 (3.4)	23.4 (4.0)
SBP (mmHg)	138.4 (20.8)	141.3 (21.9)	133.9 (21.4)	145.2 (21.5)*
DBP (mmHg)	83.5 (12.3)	83.5 (10.7)	79.5 (11.8)	85.7 (16.5)
TC (mg/dl)	186.1 (32.8)	181.0 (36.8)	190.9 (34.1)	198.6 (32.6)
PG (mg/dl)	130.8 (38.1)	145.3 (49.2)	29.2 (33.7)	142.9 (38.5)
HT	2,066 (50.1%)	17 (63.0%)	2,193 (41.4%)	23 (69.7%)†
DM	285 (6.9%)	5 (18.5%)	216 (4.1%)	4 (12.1%)†
VHD	20 (0.5%)	3 (11.1%)‡	31 (0.6%)	6 (18.2%)‡
LVH	621 (15.0%)	4 (14.8%)	253 (4.8%)	5 (15.2%)
Smoker	2,612 (63.3%)	10 (37.0%)†	469 (8.9%)	0 (0.0%)
Drinker	1,978 (47.9%)	12 (44.4%)	150 (2.8%)	1 (3.0%)

Data are means (standard deviations) or numbers of persons (percentages).
P values were obtained by Student's t-test, chi-square test.
**p<0.05, **p<0.01 by Student's t-test; †p<0.05, ‡p<0.01 by chi-square test.*
AF, atrial fibrillation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; PG, plasma glucose; HT, hypertension; DM, diabetes mellitus; VHD, valvular heart disease; LVH, left ventricular hypertrophy; Smoker, current smoker; Drinker, regular drinker.

census in 1975. A total of 10,897 persons (response rate: 79.4%) participated in the survey![5]

A study group was formed in 1994 to conduct a follow-up study of 10,546 participants in the Survey under the auspices of the Ministry of Health and Welfare (The National Integrated Project for Prospective Observation of Non-communicable Diseases and Its Trends in the Aged: NIPPON DATA80)![16,17]

Initial Investigation

The initial investigations in the National Survey on Circulatory Disorders 1980 were conducted by public health centers and consisted of a questionnaire, measurements of blood pressure and anthropometric data, blood and urine tests, and a resting electrocardiogram (ECG). Public health nurses confirmed information on smoking and drinking habits, and present and past histories of myocardial infarction, stroke, valvular heart disease, hypertension (HT) and diabetes mellitus (DM) using questionnaires. Participants were asked to record whether they were current smokers, ex-smokers or non-smokers. Smokers were asked to note the number of cigarettes smoked per day. All participants were asked to record whether they were non-drinkers, ex-drinkers or current drinkers. Regular drinking was defined as a current drinker consuming alcohol every day or occasionally.

Participants were asked to avoid eating or exercise for 30 min before the measurements. Body weight was measured while the participants wore light clothing and no shoes, and the body mass index (BMI) was calculated. Single blood pressures and pulse rates were measured by a trained public health nurse in each public health center using a standard sphygmomanometer on the right arm of the seated subject after a 5-min rest.

Non-fasting blood samples were drawn and then centrifuged within 60 min of collection and stored at −70°C until analyses. Serum total cholesterol (TC) levels were analyzed in a sequential autoanalyzer (SMA12; Technicon, Tarrytown, USA) by the Liebermann-Burchard direct method at a laboratory (Osaka Medical Center for Health Science and Promotion). Casual blood glucose levels were determined in the same laboratory using the neocaprotine-copper method. Therefore, determined glucose levels in this survey tended to be 20–30 mg/dl higher than those measured by the deoxidized method. The laboratory belonged to the Cholesterol Reference Method Laboratory Network (CRMLN), and the measurement precision and accuracy for serum cholesterol were certified in the lipid Standardization Program administered by the Centers for Disease Control and Prevention in the United States. Details have been published elsewhere![16,17]

HT was defined as systolic blood pressure (SBP) ≥140, diastolic blood pressure (DBP) ≥90 mmHg, use of antihypertensive agents or a combination of these. DM was defined as serum glucose level ≥200 mg/dl, a past history of diabetes, or both.

The ECG findings were independently evaluated by 2 trained doctors in each of 12 institutes (Department of Health Science, Jichi Medical School; Department of Public Health Science, Dokkyo Medical University; Fourth Department of Internal Medicine, Tokyo University; Tokyo Metropolitan Institute of Gerontology; National Institute of Public Health; Chiba University School of Nursing; Saku Central Hospital; Nagoya University Faculty of Medicine; Aichi Medical University; Department of Epidemiology, National Cardiovascular Center; Department of Preventive Cardiology, National Cardiovascular Center) according to the Minnesota Code. In cases of inconsistent judgments, the final judgments were made by the Approval Committee on Coding. AF was defined as 8-3 and left ventricular hypertrophy (LVH) was defined as 3-1 according to the Minnesota Code![5]

Follow-up Surveys and Determination of Causes of Death

Follow-up surveys were performed in 1994 and 1999 to ascertain the status of each of the participants: 9,638 (91.4%) of the 10,546 original respondents were available. For longitudinal analyses, we excluded an additional 155 persons because they had a history of stroke (110 persons) or myocardial infarction (45 persons). Finally, the data from 9,483 subjects (4,154 men, 5,329 women) were used for the analyses.

National Vital Statistics were used to clarify the underlying causes of death. In accordance with Japan's Family

Table 2 Person-Years, Numbers of Deaths and Age-Adjusted Mortality Rate (per 100,000 Person-Years) and RR for Stroke Death, Cardiovascular Death and All-Cause Death by 19-Year Follow-up of NIPPON DATA80

	Non-AF	*AF*	*RR (95%CI)*
Men and women			
Total number	*9,423*	*60*	
Person-years	*162,980*	*699*	
Stroke death	*308 (115)*	*10 (342)*	*2.51 (1.37–4.62)*
Cardiovascular death	*674 (249)*	*24 (1,342)*	*2.76 (1.87–4.08)*
All-cause death	*1,878 (713)*	*41 (2,173)*	*1.87 (1.38–16.2)*
Men			
Total number	*4,127*	*27*	
Person-years	*69,915*	*356*	
Stroke death	*163 (156)*	*2 (227)*	*0.99 (0.25–3.98)*
Cardiovascular death	*343 (328)*	*5 (366)*	*1.24 (0.51–2.99)*
All-cause death	*1,014 (983)*	*15 (1,429)*	*1.37 (0.82–2.27)*
Women			
Total number	*5,296*	*33*	
Person-years	*93,065*	*343*	
Stroke death	*145 (100)*	*8 (689)*	*5.43 (2.89–10.2)*
Cardiovascular death	*331 (217)*	*19 (5,711)*	*5.41 (3.59–8.15)*
All-cause death	*864 (587)*	*26 (6,398)*	*4.59 (2.19–37.7)*

Data are number of deaths (age-adjusted mortality rates) and RR (95%CI).
Direct age adjustment was performed based on the Japan standard population of 1985.
Age-adjusted RR and 95%CI were estimated by the Mantel-Haenszel procedure.
RR, relative risks; CI, confidence intervals. Other abbreviation see in Table 1.

Registration Law, all death certificates issued by medical doctors are forwarded centrally to the Ministry of Health and Welfare via the public health centers in the area of residency. From 1980 to 1994 the underlying causes of death were coded according to the International Classification of Diseases (ICD) 9th Revision and from 1995 to 1999 were coded according to the ICD 10th Revision.

We confirmed deaths by computer matching of data from the Vital Statistics, using area, sex, dates of birth and death as key codes[16] Death from stroke was defined as ICD 9 code numbers 430–438 or ICD 10 code numbers I60–I69. Death from cardiovascular disease was defined as ICD 9 code numbers 390–459 or ICD 10 code numbers I00–I99.

Permission to use the National Vital Statistics was obtained from the Management and Coordination Agency, the Government of Japan. Approval for this study was obtained from the Institutional Review Board of Shiga University of Medical Science for ethical issues (No. 12-18, 2000).

Statistical Analysis

Student's t-test was used to test differences of several parameters between 2 groups. The chi-square test was used to compare the frequencies among the categories. Age-adjusted mortality rates were calculated by the direct method using the Japanese standard population of 1985. Age-adjusted relative risks and 95% confidence intervals were calculated using the Mantel-Haenszel procedure. Multivariate adjusted relative risks attributable to AF for all-cause mortality and cause-specific mortality were calculated using Cox's proportional hazard model with adjustments for age, SBP, BMI, serum TC levels, plasma glucose levels, presence of valvular heart disease or LVH on ECG, current smoking and regular drinking. All probability values were 2-tailed, and values less than 0.05 were considered to be statistically significant. The Statistical Package for Social Sciences (SPSS Japan Inc version 11.0 Tokyo, Japan) was used for the analyses.

Results

The prevalence of AF was 0.64% in this study (0.65% among men and 0.62% among women). Table 1 shows the baseline characteristics of participants with AF (AF group) and those without AF (non-AF group). Mean ages in the male and female AF groups (63.4 years and 68.8 years, respectively) were significantly higher than those in the non-AF groups (50.6 years and 50.3 years, respectively). In women, mean SBP and the percentages of participants with LVH or HT in the AF group were significantly higher than those in the non-AF group (SBP: 145.2 vs 133.9; LVH: 15.2% vs 4.8%; HT: 69.7% vs 41.4%). The proportion of subjects with valvular heart disease in the AF groups was significantly higher than in the non-AF group in both men and women (11.1% vs 0.5% in men; 18.2% vs 0.6% in women). Prevalence of current smokers in the male AF group was significantly lower than in the male non-AF group (37.0% vs 63.3%).

Table 2 shows the results of age-adjusted mortality rates based on the Japan standard population of 1985 (per 100,000 person-years) and relative risks for stroke death, cardiovascular death and all-cause death. The observed person-years were 163,679. A total of 1,919 deaths occurred during this period (1,878 in the non-AF group and 41 in the AF group). Age-adjusted mortality rates in both sexes were 713 in the non-AF group and 2,173 in the AF group. Age-adjusted relative risks in both sexes attributable to AF for stroke death, cardiovascular death and all-cause death were 2.51, 2.76 and 1.87, respectively.

Among men, age-adjusted mortality rates were 983 in the non-AF group, 1,429 in the AF group. Age-adjusted relative risks attributable to AF for stroke death, cardiovascular death and all-cause death were 0.99, 1.24 and 1.37, respectively (NS).

On the other hand, age-adjusted relative risks attributable to AF for stroke death, cardiovascular death and all-cause death among women were 5.43, 5.41 and 4.59, respectively (all p values <0.05).

Table 3 shows the results of Cox's regression analysis

Table 3 Multivariate Adjusted RR (95% CI) Attributable to AF by Cox's Regression Analysis, NIPPON DATA80, 19-Year Follow-up

	All participants RR (95%CI)	<65 years RR (95%CI)	≥65 years RR (95%CI)
Men and women	9,483 (60†)	7,922 (24†)	1,561 (36†)
Stroke death	2.69 (1.42–5.10)	14.7 (4.59–47.2)	1.93 (0.90–4.14)
CVD death	2.76 (1.81–4.20)	9.63 (4.30–21.6)	2.06 (1.26–3.39)
All-cause death	1.88 (1.37–2.58)	4.00 (2.21–7.25)	1.47 (1.01–2.13)
Men	4,154 (27†)	3,477 (12†)	677 (15†)
Stroke death	1.27 (0.31–5.18)	9.31 (1.24–70.1)	0.67 (0.09–4.85)
CVD death	1.38 (0.56–3.43)	3.44 (0.47–25.0)	1.09 (0.39–3.05)
All-cause death	1.39 (0.82–2.35)	2.83 (1.05–7.63)	1.10 (0.59–2.05)
Women	5,329 (33†)	4,445 (12†)	863 (21†)
Stroke death	3.75 (1.80–7.82)	19.0 (4.41–82.1)	2.83 (1.21–6.60)
CVD death	3.96 (2.46–6.37)	10.8 (3.80–30.9)	2.87 (1.62–5.08)
All-cause death	2.28 (1.53–3.38)	5.00 (2.16–11.6)	1.73 (1.07–2.78)

Data are multivariate adjusted RR (95%CI).
Multivariate adjusted RR (exponential β) and 95%CI were estimated by Cox's regression analysis after adjusting for age, body mass index, systolic blood pressure, blood glucose level, total cholesterol level, history of valvular heart disease, existence of left ventricular hypertrophy, regular drinking and current smoking status.
†Number of participants with atrial fibrillation.
CVD, cardiovascular disease. Other abbreviation see in Tables 1,2.

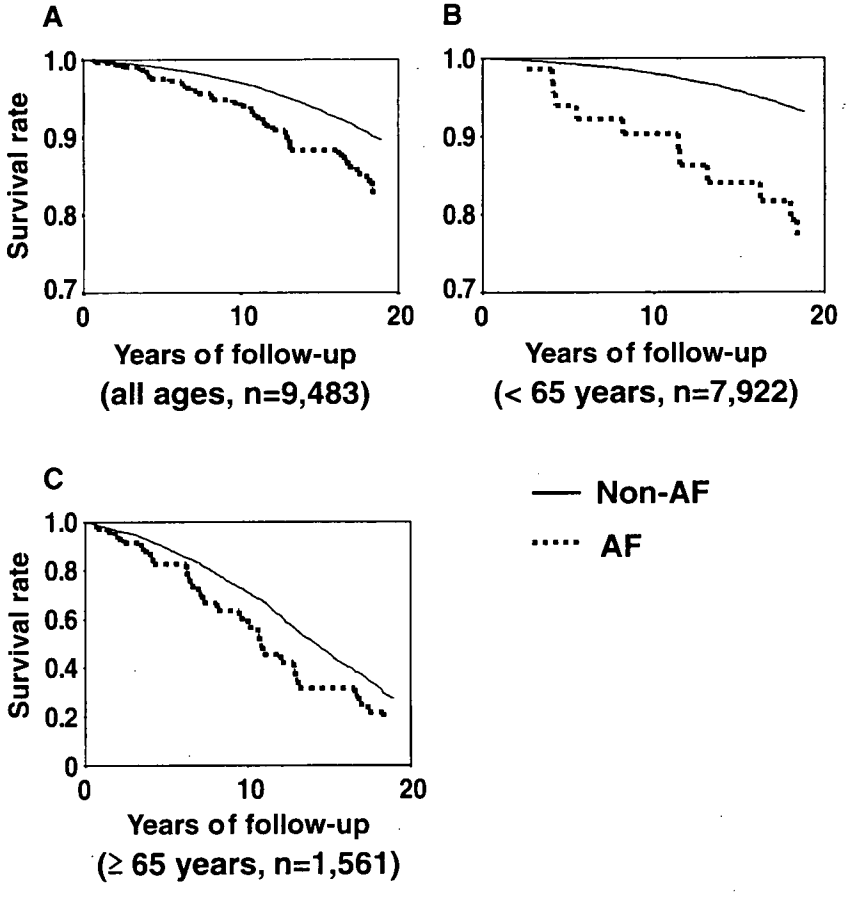

Fig 1. Cox's regression survival curves for subjects with and without atrial fibrillation (AF) in the 19-year follow-up of NIPPON DATA80. Survival curves were determined by Cox's regression analysis stratified by existence of AF after adjusting for age, body mass index, systolic blood pressure, blood glucose level, total cholesterol level, history of valvular heart disease, existence of left ventricular hypertrophy, regular drinking, and current smoking status. Cox's regression curves for (A) subjects of all ages, (B) subjects aged 64 years or younger, (C) subjects aged 65 years or older.

with adjustments for other risk factors. At all ages, multivariate adjusted relative risks for both sexes attributable to AF for stroke death, cardiovascular death and all-cause death were 2.69, 2.76 and 1.88, respectively (all p values <0.05). These were 1.27, 1.38 and 1.39 among men (NS) and 3.75, 3.96 and 2.28 among women (all p values <0.05). Among persons aged 64 years or younger, relative risks for stroke death, cardiovascular death and all-cause death attributable to AF were higher than among participants of all ages. Relative risks for stroke death were notably high in both men and women. Among persons aged 65 years or older, relative risks for death from each cause were lower than among participants of all ages.

Fig 1 shows the Cox's regression survival curves for subjects with or without AF. The survival curve in the AF group was below that in the non-AF group (Fig 1A). The difference between survival rates in the AF group and the non-AF group was more evident among persons aged 64

years or younger (Fig 1B), with the difference being somewhat vague among persons aged 65 years or older (Fig 1C).

Discussion

This study shows that AF contributes to stroke mortality, cardiovascular mortality and all-cause mortality in both sexes of the Japanese general population, especially the young generation (<65 years old). Although the prognosis of AF has been reported for Westerners, the extent to which AF contributes to mortality in the Japanese general population has not been fully elucidated. Some researchers tried to reveal the difference in Japanese subjects between the prognosis of patients with sustained AF and that of patients without AF after cardioversion; however, those studies did not determine whether AF contributes to mortality in Japanese people[18,19] Moreover, the difference in mortality attributable to AF in elderly and middle-aged people has not been addressed in a representative Japanese general population until now.

The framingham Heart Study showed that AF contributed to an increase in stroke incidence, even in elderly people[20] and so careful attention is needed to interpret the result that suggested a low relative risk for mortality attributable to AF among elderly persons in the present study. Because the prevalence of AF has been reported to be less than 1% among Japanese persons aged less than 70 years;[14] participants aged less than 65 years at the time of registration would be less likely to develop AF and elderly persons more likely to develop AF during the follow-up period. This would attenuate the relative risk for death from each cause attributable to AF among the elderly.

The present study also showed obvious sex difference in the risk for death from each cause attributable to AF. A significant interaction between AF and sex certainly exists. In the Framingham Heart Study, AF was no longer significantly associated with increased mortality among men after elimination of 30-day mortality, in contrast to the results for women?[21] Other studies also showed that AF was a greater risk for mortality in women than in men?[22–24] In a recent study the greater risk for ischemic stroke attributable to AF in women than in men was also confirmed, as well as the risk for mortality?[25] The reason why a sex difference exists in the relationship between AF and mortality and in the relationship between AF and ischemic stroke is unknown.

We estimated age-adjusted mortality rates using direct age adjustment based on the Japanese standard population of 1985. All-cause mortality in female participants with AF exceeded 6,000 per 100,000 person-years, which seems to be an overestimation of the actual status, although the relative risk determined by using the Mantel-Haenszel procedure was similar to the multivariate adjusted relative risk estimated by Cox's regression analysis. The small number of subjects with AF, especially in the female younger generation, may have distorted the results and caused overestimation of the mortality rate. Analysis of a small number of subjects with AF may also lack robustness, because a different result would be obtained if several cases had other outcomes.

Study Limitations

Since the original survey in 1980 was not designed for a prospective study, retrospective analyses of the data have several limitations. Risk factors were only observed once at baseline and changes in lifestyle or risk factor levels were not considered. The risk attributable to risk factors may have been underestimated and confounding effects of risk factors may not have been fully adjusted. Assessment of relative risks attributable to AF for mortality analyzed by the presence of AF based on a single recording of ECG at baseline does not take into account subsequent development of AF and, therefore, tolerates underestimation of the relative risks. A follow-up study of the incident cases is preferable for estimating the actual risks for mortality attributable to diseases such as AF, which have an age-dependent prevalence. Paroxysmal AF can not be always detected by a single recording of ECG, so the lack of cases of paroxysmal AF results in underestimation of the relative risks for mortality attributable to AF. Lack of information on the history of anticoagulant therapy also seems to be a study limitation.

Persons with AF may have impaired cardiac function and therefore already have developed asymptomatic organic heart disease. Although we estimated the mortality risk after adjusting for other risk factors, including presence of valvular heart disease or LVH, this analytical procedure may not have been fully adjusted for the effect of heart failure on prognosis.

We estimated the relative risks for mortality attributable to AF using data from the Vital Statistics, but we did not estimate relative risks for cardiovascular morbidity attributable to AF. AF is an important predisposing factor for both heart failure[26] and hospital admission?[27] Whether AF affects cardiovascular morbidity among Japanese people remains to be determined.

Despite its several limitations, this study has some strong points. One is the representative Japanese population randomly selected from throughout Japan in the 1980s. Therefore, the total mortality rate and cause-specific mortality rate in this study should be considered as representing the actual status of Japanese adults living in the 1980s and may reflect results from the era before anticoagulant therapy became widespread. Another strong point of this study is the high follow-up rate despite a long follow-up period. There were 163,679 person-years and the mean follow-up period exceeded 17.

Conclusions

AF affects stroke mortality, cardiovascular mortality and all-cause mortality in the Japanese general population. Careful attention should therefore be paid to persons with AF in order to prevent future cardiovascular events.

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Appendix 1

The NIPPON DATA80 Research Group

Chairman: Hirotsugu Ueshima (Department of Health Science, Shiga University of Medical Science, Otsu).

Consultants: Osamu Iimura (Hokkaido JR Sapporo Hospital, Sapporo), Teruo Omae (National Cardiovascular Center, Suita), Kazuo Ueda (School of Health Science, Kyusyu University, Fukuoka), Hiroshi Yanagawa (Saitama Prefectural University, Koshigaya).

Research Members: Akira Okayama (Department of Preventive Cardiology, National Cardiovascular Center, Suita), Kazunori Kodama, Fumiyoshi Kasagi (Radiation Effects Research Foundation, Hiroshima), Tomonori Okamura, Yoshikuni Kita (Department of Health Science, Shiga University of Medical Science, Otsu), Shigeyuki Saito (Internal Medicine II, Cardiology and Nephrology, Sapporo Medical University, Sapporo), Kiyomi Sakata (Department of Hygiene and Preventive Medicine, School of Medicine, Iwate Medical University, Morioka), Takehito Hayakawa, Shinichi Tanihara (Department of Public Health, School of Medicine, Shimane University, Izumo), Yoshikazu Nakamura (Department of Public Health, Jichi Medical School, Minamikawachi), Hiroshi Horibe (Keisen Clinic, Akashi), Masumi Minowa (Department of Epidemiology, National Institute of Public Health, Wako).

Research Associate Members: Toshihiro Takeuchi, Mitsuru Hasebe, Fumitsugu Kusano and members of 300 public health centers in Japan, Minoru Iida (Kansai University of Welfare Science, Osaka), Katsuhiko Kawaminami (Department of Public Health Policy, National Institute of Public health, Wako), Sohel R Choundhury (Department of Community Medicine, School of Medical Sciences University Sains Malaysia), Yutaka Kiyohara (Department of Medicine and Clinical Science, Kyusyu University, Fukuoka), Tsutomu Hashimoto (Wakayama Red Cross Blood Center, Wakayama), Atsushi Terao (Hikone Public Health Center, Hikone), Koryo Sawai (The Japanese Association for Cerebro-cardiovascular Disease Control, Tokyo), Shigeo Shibata (Clinical Nutrition, Kagawa Nutrition University, Saitama).

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1	著者名	Yamamoto T, Nakamura Y, Hozawa A,Okamura T, Kadowaki T, Hayakawa T, Murakami Y, Kita Y, Okayama A, Robert D. Abbott, Ueshima H. for the NIPPON DATA80 Research Group
	論文題目	Cause-specific and all-cause mortality in individuals with low risk status for cardiovascular disease among the Japanese population: NIPPON DATA80, 1980-99
	雑誌名	Circulation Journal 2007 (in press)
2	著者名	Kadowaki S, Okamura T, Hozawa A, Kadowaki T, Kadota A, Murakami Y, Nakamura K, Saitoh S, Nakamura Y, Hayakawa T, Kita Y, Okayama A, and Ueshima H. for the NIPPON DATA Research Group
	論文題目	Relationship of elevated casual blood glucose level with coronary heart disease, cardiovascular disease, and all-cause mortality in a japanese represent ative population-
	雑誌名	Diabetologia 2007 (in press)
3	著者名	Okamura T, Hayakawa T, Hozawa A, Kadowaki T, Murakami Y, Kita Y, Robert D. Abbott, Okayama A, and Ueshima H. for the NIPPON DATA80 Research Group
	論文題目	Lower levels of serum albumin and total cholesterol were associated with decline in activities of daily living and excess mortality in a 12-year cohort study of elderly Japanese
	雑誌名	the Journal of the American Geriatrics Society 2008;56:529-535
4	著者名	Hozawa A, Okamura T, Kadowaki T, Murakami Y, Nakamura K, Hayakawa T, Kita Y, Nakamura Y, Okayama A. and Ueshima H. for NIPPON DATA80 Research group
	論文題目	Is weak association between cigarette smoking and cardiovascular disease mortality observed in Japan explained by low total cholesterol?-NIPPON DATA80
	雑誌名	International Journal of Epidemiology 2007;36:1060-1067
5	著者名	Hozawa A, Okamura T, Murakami Y, Kadowaki T, Nakamura K, Hayakawa T, Kita Y, Nakamura Y, Robert D.Abbott, Okayama A, Ueshima H. -The NIPPON DATA80 RESEARCH GROUP
	論文題目	Joint Impact of Smoking and Hypertension on Cardiovascular Disease and All-Cause Mortality in Japan: NIPPON DATA80, a 19-Year Follow-Up
	雑誌名	Hypertension Research 2007;30(12):1169-1175
6	著者名	Nakamura K, Okamura T, Hayakawa T, Hozawa A, Kadowaki T, Murakami Y, Kita Y, Okayama A, Ueshima H. for the NIPPON DATA80, 90 Research Group
	論文題目	The proportion of individuals with obesity-induced hypertension among total hypertensives in a general Japanese population: NIPPON DATA80, 90
	雑誌名	Eur J Epidemiol. 2007;22:691-698
7	著者名	Ohsawa M, Okayama A, Okamura T, Itai K, Nakamura M, Tanno K, Kato K, Yaegashi Y, Onoda T, Sakata K, Ueshima H; The NIPPON DATA80 Research Group.
	論文題目	Mortality Risk Attributable to Atrial Fibrillation in Middle-Aged and Elderly People in the Japanese General Population.
	雑誌名	Circulation Journal 2007;71(6):814-819
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9	著者名	Nishi N, Sugiyama H, Kasagi F, Kodama K, Hayakawa T, Ueda K, Okayama A, Ueshima H.
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新聞報道

1	タイトル 新聞名 発行所	喫煙、寿命3．5年縮める リスク値 明らかに 厚労省研究班 40歳男性追跡調査 読売新聞 朝刊 2007年5月9日 読売新聞東京本社
2	タイトル 新聞名 発行所	40歳男性 喫煙で余命3．5年短く 厚労省研究班調査 禁煙で延長効果も 日本経済新聞 夕刊 2007年5月9日 日本経済新聞社
3	タイトル 新聞名 発行所	メタボじゃなくてもご用心 高血圧・高血糖ならやせている方が危険 朝日新聞 朝刊 2007年5月28日 朝日新聞東京本社
4	タイトル 新聞名 発行所	禁煙デーを機に 40歳で吸う男性 余命3．5年短い 朝日新聞 夕刊 2007年5月31日 朝日新聞東京本社
5	タイトル 新聞名 発行所	元気のひけつ コレステロール 運動して「善玉」増やそう 朝日新聞 朝刊 2007年10月21日 朝日新聞大阪本社

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(一面トップ)

喫煙、寿命3.5年縮める

リスク値 明らかに

厚労省研究班

40歳男性追跡調査

たばこを吸う男性は、吸わない男性に比べて40歳以降の余命が約3・5年短くなることが、厚生労働省研究班(研究班長・上島弘嗣滋賀医大教授)の大規模な疫学調査でわかった。寿命に対する喫煙の影響が、具体的な数値として明らかになったのは国内で初めて。喫煙対策の重要性を示す研究として注目される。

1980年に、全国30か所の保健所で健診を受けた男女約1万人(平均年齢約50歳)を対象に、喫煙習慣の有無や喫煙量を質問し、1999年まで追跡調査。亡くなった約2000人の年齢と喫煙習慣から平均余命を算出した。

その結果、80年時点でたばこを吸っていた男性の場合、40歳時の平均余命は38・6年で、吸わない男性の42・1年に比べ、3・5年短かった。1日に2箱以上吸う男性の余命は38・1年で、非喫煙者との差が4年に拡大した。

65歳男性では、喫煙者の余命は16・8年で非喫煙者は19・3年。女性の場合、吸う人の40歳時の余命は43・4年、吸わない人は45・6年で、いずれも喫煙者が短くなった。

80年の時点では、調査した男性の喫煙率は62%と高く、その後も高率で喫煙を続けたとみられる。一方、途中で禁煙に転じた人がいる可能性もあり、研究班では、仮に誰も禁煙しなかったら余命格差はさらに広がったとみている。

調査時、「禁煙した」と答えた人の余命は、大半の世代で喫煙者と非喫煙者の間の値となり、禁煙が余命を延ばす効果も確認された。

喫煙が寿命を縮めるのは、肺がんや脳卒中、心筋梗塞(こうそく)による死亡率が高まるためで、研究を主導した村上義孝・滋賀医大特任講師は「平均寿命が3・5年短くなることは、ほぼ20年前の寿命に逆戻りしたことに匹敵する。たばこの影響は大きい」と話している。

海外では、喫煙が寿命を短くする数値を示した研究がある。日本では、喫煙で肺がん、心筋梗塞の死亡率が高まるとの報告はあるが寿命への影響を調べた研究はなかった。2005年、日本人の喫煙と寿命の関係についてただした民主党衆院議員の質問主意書に対し、政府は「数値等の資料がないため、回答は困難」と答弁書を出している。

国の調査では、2005年の日本人の平均寿命(0歳時の平均余命)は男性78・56歳、女性85・52歳。この差にも、喫煙習慣の男女差が大きく影響していると研究班ではみている。

たばこと男性の平均余命の関係

	40歳	50歳	60歳
吸わない人	42.1	32.6	23.8
禁煙した人	40.4	30.9	22.1
吸う人	38.6	29.4	20.7
(うち1日2箱以上)	38.1	28.7	20.4

(厚生労働省研究班調べ。数字は年)

日本経済新聞（夕刊）
2007年（平成19年）5月9日（水曜日）

40歳男性

喫煙で余命3.5年短く

厚労省研究班調査 禁煙で延長効果も

たばこを吸う男性は、吸わない男性よりも四十歳以降の余命が三・五年短いことが九日、厚生労働省研究班（主任研究者・上島弘嗣滋賀医大教授）の大規模疫学調査で分かった。

たばこの健康への影響に関してはさまざまな研究があるが、日本人の寿命との関係が明確に数値で示されたのは初めて。

研究班は一九八〇年、全国から無作為に抽出した三十歳以上の男女約一万人（平均年齢約五十歳）を対象に、喫煙の有無や本数などを調査。男性の喫煙率は六二・九％、女性は八・八％で、九九年まで追跡し、この間の年齢層ごとの死亡率から各年齢の余命を試算した。

この結果、たばこを吸わない男性の四十歳時の平均余命は四十二・一年なのに対し、吸う男性は三十八・六年と、三・五年の差が開いた。

以前吸っていて調査時までに禁煙した人は四十・四年。他の年齢でも同じ傾向となり、禁煙による寿命延長効果が示された。

朝日新聞
1　14版　2007年(平成19年)5月28日　月曜日

メタボじゃなくてもご用心

心臓病・脳卒中

高血圧・高血糖なら やせている方が危険

高血圧や高血糖といった生活習慣病の危険要因を同時に抱えると、心筋梗塞や脳卒中を起こす危険が高まるが、その程度は、太っているよりもやせている人の方が高くなりやすいことが、厚生労働省研究班（主任研究者＝上島弘嗣・滋賀医科大教授）の調査でわかった。来年度から、生活習慣病予防のための特定健康診査（特定健診）が始まるが、その柱となる「メタボリック症候群（内臓脂肪症候群）」の診断基準が、やせた人たちのリスクを見逃してしまう可能性を示したものだ。（田村建二）

同症候群は心筋梗塞や脳卒中など循環器病とかかわりが深い。危険要因として、肥満、高血圧、高血糖、高中性脂肪、低HDLコレステロールが挙げられ、欧米では基本的に、うち三つ以上の値が一定値を超えると、「あなたはメタボ」などと診断される。

日本の診断基準では特に肥満が重視されており、ウエストサイズが一定以上であることが必須条件。例えば血糖値がかなり高くても、太っていなければ同症候群には該当しないことになる。

ところが上島教授らの調査で、この診断基準では、そんな人たちのリスクを見落とす可能性があることがわかった。

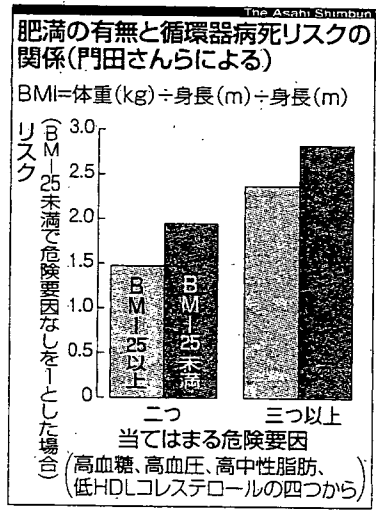
上島教授は、90年に全国の保健所で健診を受けた男女約7200人を約10年間追跡し、死亡原因などを調べた。

肥満の指標となるBMI（体格指数）が25以上の太った人が循環器病で死亡するリスクは、肥満でなくほかの危険要因もない人と比べると、危険要因が肥満以外に二つの場合は1・5倍。三つ以上だと2・4倍だった。

一方、BMIが25未満の人で同じ比較をすると、それぞれ2倍、2・8倍となり、肥満傾向の人よりも高かった。

やせた人でも、体質的に高血糖や高血圧などを起こしやすい人がおり、そういう人は太っている人よりむしろリスクが高まりやすいらしい。

調査をまとめた滋賀医科大の門田文（あや）医師は「日本の基準にあてはまらない人にも高リスクの人がいることに、注意を払うべきだ」としている。



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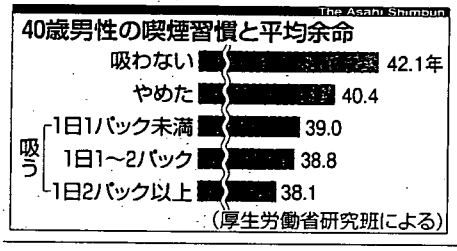
禁煙デーを機に

31日は世界禁煙デー。喫煙習慣が、平均余命や乳幼児の突然死にも影響するといった研究報告が相次いでいる。

40歳で吸う男性 余命3.5年短い



厚生労働省研究班（主任研究者＝上島弘嗣・滋賀医科大教授）の調査で、40歳時点での平均余命が、たばこを吸う男性は吸わない男性より3年半短かったことがわかった。余命への影響が確認されたのは国内で初めてだという。

80年に全国の保健所で健診を受けた男女約1万人を、99年まで追跡調査した。80年の調査で、男性の喫煙率は62・9％、女性は8・8％。当時の調査時に、たばこを吸わないと答えた40歳男性の平均余命は42・1年、吸う男性は38・6年だった。当時、1日2パック以上吸っていた男性に限ると、38・1年とさらに短かった。一方、調査時点でたばこをやめたと答えた男性は40・4年で、喫煙者より長かった。

女性は、たばこを吸わない女性の平均余命が45・6年に対し、吸う女性は43・4年と、やはり短い傾向がみられた。

喫煙者が80年以降に禁煙したかどうかまでは調べていないため、影響が明確でない面もあるが、同医科大の村上義孝・特任講師は「吸い続けた人に限って解析できれば、吸わない人との差はさらに広がったはず」とみている。

（田村建二）

元気のひけつ

コレステロール

運動して「善玉」増やそう

動脈硬化を招くからと、健康の目の敵にされやすいコレステロール。でも、細胞膜やホルモンの材料として、体に欠かせないのも事実です。低ければいい、とは限りません。むしろたくさんあった方がいいコレステロールもあります。

■□■

日本動脈硬化学会は今春、血中の脂質を総コレステロール値でみるのをやめた。

脂質が増えるにつれて心筋梗塞などの恐れが高まるとされ、学会は「総コレステロール220」（単位はmg/dl）を基準値にしてきた。だが最近、女性では250程度までは心臓病などで死亡するリスクは上がらないと報告された。「NIPPON DATA」という、全国の1万近い人たちの健康状態を長年調べている調査だ。

ポイントは、何種類かあるコレステロールのうち、「善玉」と呼ばれるHDL－C（Cはコレステロール）らしい。このグループの別の調査で、HDL－Cが高いほど総死亡のリスクが低いこともわかっている＝グラフ。これが高ければ、総コレステロールが高くてもリスクが上がるとは限らない。学会はいま、「悪玉」と呼ばれるLDL－Cを重視するようになっている。

肝臓でできたコレステロールを体の隅々まで届けるのがLDLで、余った分を拾い集めて肝臓に戻すのがHDLの役目だ。日本医科大の及川眞一教授は「回収されたコレステロールは胆汁酸などの材料になる。HDLはいわば、コレステロールのリサイクル役です」と解説する。

HDL－Cは「HDLが運んでいるコレステロール」という意味で、血液検査ではこれの量を測る。少ないと余分なコレステロールを回収し切れず、残ったコレステロールが血管の壁にたまりやすくなる。その目安は40mg/dlグラム。これを下回ると、「低HDL－C血症」と診断される。

■□■

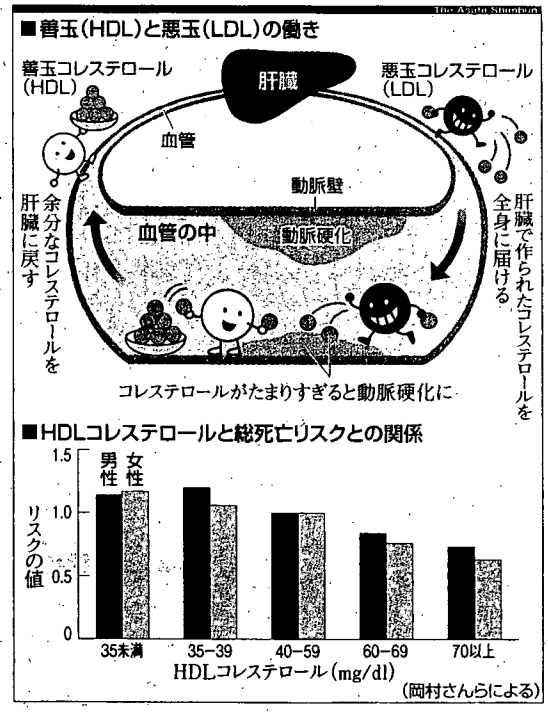
「NIPPON DATA」に携わる国立循環器病センターの岡村智教（ともり）・予防検診部長によると、運動をしない▽内臓に脂肪が多い▽たばこを吸う――人にHDL－Cが低い傾向があるという。不健康な生活の指標と言え、その改善がHDL－Cを増やすことにつながる。薬はいらない。

運動はどれくらいしたらいいのか。お茶の水女子大の曽根博仁・准教授たちが国内外の25の研究を詳しく分析すると、個人差はあるが、HDL－Cを増やすには「週に合計で120分以上の有酸素運動が必要。消費エネルギーなら900kcalカロリー以上」との結果が出た。

息がはずむ程度以上であれば、運動の強さはあまり関係がない。大切なのは時間で、1回あたり最低30分間は続けた方が効果が望めるという。一般に、体重60kgの人が1時間の速歩で消費するエネルギーは200kcalカロリー前後といわれている。

HDL－Cは飲酒でも上がる。1日あたり日本酒換算で約1・3合分を飲むと3・99mg/dlグラム増えると、海外の研究で報告されている。ただ体質の違う日本人でもあてはまるかは不明で、1日1合を超える飲酒はほかの病気のリスクを高めるともいわれる。健康にいいと早合点して飲み過ぎるのは禁物だ。

（田村建二）



プラスα

日本人は一般に、欧米人よりもHDL－Cが高めの人が多いといわれるが、なかには値が100mg/dlグラムを超えるほど高い人がいる。

遺伝子の変異がかかわっているとされ、こういう人の中には、心臓病などのリスクが下がらない人もいるので注意が必要だ。及川さんは「動脈硬化がないかを超音波で調べるなど定期的に医師の診察を受けるようにしてほしい」と助言する。

まとめと今後の課題

NIPPON DATA 80・90 は全国から無作為抽出された日本人を代表する集団（循環器疾患基礎調査および国民栄養調査の対象者）の長期追跡データとして極めて貴重なコホート研究である。本データベースから明らかとなる疫学的エビデンスは、日本人における健康寿命の延伸、介護予防、生活習慣病予防の対策立案や政策決定に直結する重要なものといえる。今回の研究班では特に国民栄養調査データとの結合に主眼をおき、日本人の食生活・栄養素摂取状況と健康寿命等、その後の健康状態との関連を明らかにするための作業が開始された。

本年度、昭和 55 年および平成 2 年実施の国民栄養調査データから、個人別栄養素・食品群摂取量の詳細な推定がほぼ完了し、NIPPON DATA との結合が行われた。従来発表されている国民栄養調査成績では性・年齢階級別の摂取量が明らかになっていないため、今回の推定作業で初めて当時の栄養摂取状況が明らかになったと言える。現状では摂取量が明らかとなった栄養素の種類が限られているが、来年度以降、主任研究者らがすでに作成しているインターマップ食品成分表を用いることによりさらに詳細な栄養素摂取量（各種脂肪酸、微量元素、アミノ酸、ショ糖、でんぷんなど）を明らかにすることができる。また、食品群については 110 分類に及ぶ摂取量が明らかであり、これら栄養素および食品群の摂取と健康寿命、ADL 低下、生活習慣病死亡リスクとの関連を順次明らかにし、最終的には食生活による健康寿命予測チャートの作成を目指す。

また、本年度から ADL の低下要因に関する分析が本格化し、血圧高値、喫煙、低栄養、低 HDL コレステロールが将来の ADL 低下と関連していることを明らかになった。また 60 歳の障害無し平均余命は喫煙者で約 1.3 歳、非喫煙者より短かったことも分かった。我が国における介護予防の対策立案において重要なエビデンスとなるだろう。

従来から進めてきた NIPPON DATA における総死亡リスクおよび循環器疾患死亡リスクの要因に関する解析も、本年度さらに発展を見せ、解析結果の論文発表が相次いだ。血圧、血清コレステロール、血糖値がすべて正常で、喫煙もしない低リスク者は、そうでない人と比べ循環器疾患死亡リスクが 3 分の 1 になることが明らかになった。また、喫煙と高血圧を合わせると男性の循環器死亡の 35%を説明できることが分かった。これらを含め、日本人を代表する本コホートから多くの新しい知見が論文公表された。

来年度以降、本研究班の計画を着実に進め、わが国国民の健康寿命延伸、介護予防、生活習慣病予防に資する質の高いエビデンスの提供を続けてゆくつもりである。

平成19年度厚生労働科学研究費補助金
長寿科学総合研究事業

食生活・栄養素摂取状況が高齢者の健康寿命に与える
影響に関する研究：NIPPON DATA80・90の追跡調査
報告書

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＜郵便番号 520-2192＞
滋賀県大津市瀬田月輪町
電話 077-548-2191　FAX 077-543-9732