2009年度の研究成果

（公表論文）

30年間の死亡追跡に基づく生物学的評価指標と死亡率の関係：放射線影響研究所成人健康調査

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Biological Score and Mortality Based on a 30-year Mortality Follow-up: Radiation Effects Research Foundation Adult Health Study

Kasagi F, Yamada M, Sasaki H, Fujita S.

J Gerontol A Biol Sci Med Sci. 64: 865-70, 2009.

要約

この研究の目的は生物学的機能の評価指標が個人の生命予後を予測するかを調べ、死因や時間の経過で区分した解析で、死亡のリスクを比較検討することである。加齢に関連した5つの生理機能検査（握力、聴力、振動感覚検査、皮膚弾性、閃光反応時間）の第一主成分スコアを生物学的機能評価指標として用いた。調査対象者は1970-72年の調査開始時に35-74歳であった4874人で、1999年までの生存状況ならびに死因を追跡した。追跡期間中に2,475人の死亡が確認され、1000人年当たりの粗死亡率は23.3であった。Cox比例ハザード解析で生物学的評価指標による死亡予測の程度を評価した。性・年齢（10歳区分）別の解析ではいずれの群においても年齢、収縮期血圧、BMI、総コレステロール、喫煙、飲酒、被曝線量等のリスク要因の調整後に、生物学的評価指標の増加に伴う全死亡の増加が認められた。死亡の予測における生物学評価指標の妥当性は全調査期間を通じて有意であった。がんを除くさまざまな疾患においてベースライン時の生物学的評価指標と死亡の有意な関係が認められた。結論として中高年齢からなる日本人集団の大規模前向き調査において生物学的評価指標は妥当な生命予後予測要因であった。

原爆被爆者における認知症発症率—放射線影響研究所成人健康調査において

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Incidence of dementia among atomic bomb survivors - Radiation Effects Research Foundation Adult Health Study.

Yamada M, Kasagi F, Mimori Y, Miyachi T, Ohshita T, Sasaki H.

J Neurol Sci. 281:11-14, 2009.

要約

放射線治療が神経心理機能障害の原因となることが報告されている。この研究では原爆被爆者とその対照からなる成人健康調査対象者2286人について原爆被曝が認知症の発症に影響したか否かを調査した。1945年時に13歳以上で、放射線治療の線量と比較して相対的に低い線量（4Gy以下）を被曝し、認知症調査のベースライン調査時(1992－1996年)に60歳以上で認知症のなかった者を調査対象とした。認知症の診断は2年毎の健診の際に2段階法（スクリーニング検査と精査）に基づいて行った。認知症の診断にはDSM-IVの診断基準、アルツハイマー病にはNINCDS-ADRDAの診断基準、血管性認知症にはNINDS-AIRENの診断基準を用いた。認知症発症における放射線の影響を評価するため、ポワソン回帰解析を用いた。1000人年あたりの発症率は被曝線量5mGy以下群では16.3、5-499mGy群では17.0、500mGy以上群では15.2であった。いずれの被曝線量群においてもアルツハイマー病が認知症のタイプとして優位であった。全認知症とタイプ別認知症のいずれでも考慮された危険因子の調整後に認知症の発症に放射線被曝の影響は認められなかった。認知症患者には過去に頭部への放射線治療の既往を持つ者はいなかった。今回の縦断的研究では13歳以上で被曝した被爆者において放射線被曝と認知症の関係は認められなかったが、被爆者では早期に死亡するリスクが高いことを考慮すべきである。

日本人女性における認知症の発症率とリスク因子：成人健康調査において

山田美智子[1]、笠置文善[2]、三森康世[3]、宮地隆文[4]、大下智彦[4]、佐々木英夫[5]
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[3]広島国際大学　保健医療学部、
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Incidence of dementia among atomic bomb survivors - Radiation Effects Research Foundation Adult Health Study.

Yamada M, Kasagi F, Mimori Y, Miyachi T, Ohshita T, Sasaki H.

J Neurol Sci. 281:11-14, 2009.

要約

背景と目的：認知症は高齢者に身体障害をもたらす主要な疾患の一つである。日本人女性は世界で最も長寿であるため、認知症への対策は必要不可欠である。放射線影響研究所の成人健康調査では認知症に関する前向きコホート研究を実施し、認知症の発症率とリスク要因について調べた。方法：調査開始時年齢が60歳以上で認知症のなかった女性1637人が2年毎の検査で神経内科により診断された。ベースライン時調査は1992-1996年に実施された。平均追跡期間は5.9年であった。認知症、アルツハイマー病（AD）、血管性認知症（VaD）の診断は各々、DSM IV, NINCDS-ADRDA, NINDS-AIRENの診断基準に準拠した。結果：161人が新たに認知症と診断され、1000人あたりの発症率は16.6であった。ADは109症例、VaDは56症例でその内17症例はPossible ADとPossible VaDの両方の診断を受けていた。性、年齢、教育歴、初潮年齢、閉経年齢、糖尿病既往、脳卒中既往含む要因について認知症のリスクを解析した。全認知症は性、年齢、教育歴、脳卒中既往との関連を示し、ADは年齢と教育歴、VaDは性、年齢、血圧、脳卒中既往と関連していた。中年期から老年期の握力変化を体力の指標として認知症への影響を解析したところ、握力低下と認知症の発症には関連が認められた。結論：血圧のコントロールや体力向上が認知症予防のために重要である。

厚生労働科学研究費補助金（循環器疾患等生活習慣病対策総合研究事業）
分担研究報告書

国内循環器疫学エビデンスのより広い周知に向けて：Mindsと提携した構造化抄録の提供システムの構築

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研究要旨：
わが国の地域を基盤とした循環器疫学のエビデンスを国内でより広く周知するため、代表的論文の日本語構造化抄録を作成し、財団法人日本医療機能評価機構 Minds と連携して、広く一般に公開するシステムを構築した。この取り組みの結果、Minds の「関連サービス」として、65 論文の構造化抄録が閲覧可能となった。

A．目的

診療ガイドラインとは米国 IOM により「特定の臨床状況において、適切な判断を行なうために、臨床家と患者を支援する目的で系統的に作成された文書」と定義される。2002 年、財団法人日本医療機能評価機構の「医療情報サービス事業」、通称・"Minds" (Medical Information Network Distribution Service)が開設され、臨床家を中心とする診療ガイドライン関係者の間で重要な情報源として認識が定着しつつある（図 1)。

Minds では医療者向けの診療ガイドラインに加え、その領域の専門家による解説、診療ガイドラインに基づく一般向けの解説情報、コクラン共同計画によるシステマティック・レビューの抄録の翻訳、そして海外の重要論文の構造化抄録形式(Minds アブストラクト)が提供されている。

本課題では、疫学研究の認知を高めるため、Minds と連携してより広く一般へ周知するシステムを開発する。

B．方法

本班の班員が実施している国内疫学研究のエビデンスを構造化抄録として Minds を通して公開する。 構造化抄録の形式は、Minds アブストラクト形式に準拠する。
本班班員が関与する地域基盤の循環器疫学の代表的論文について各班員に構造化抄録作成を依頼し、作成された 65 件のファイルを html 化して Minds に提供した。

C．結果

Minds 事務局との協議の結果、Minds 独自のコンテンツとは別に、「Minds・関連サービス」を隣接したエリアに新たに設けられ（図 1)、構造化抄録 65 件が掲載された（図 2～4)。

D．考察

Mindsは国内で作成された根拠に基づく診療ガイドラインを中心とした情報センターとして発展している。Mindsの関連サービスとして本班関係の循環器疫学のエビデンスが広く公開されることで、下記の効果が期待される。

- 診療ガイドラインや関連情報の作成者、利用者に閲覧の機会を提供し、疫学への関係者の認知を高める契機となる。
- 診療ガイドライン作成者は、日本人を対象とした疫学研究の成果を効率よくレビューし、ガイドラインに反映出来るようになる。
- Mindsにとっては、関連サービスとして日本発の質の高い循環器疫学のコンテンツが充実する。
- 人間集団を対象とした研究方法論の専門家としての疫学研究者に対する関係者の認知が高まる。その結果、ガイドライン作成の取り組みに疫学研究者が参加し後見する機会が増えることが期待される。

E．結論

国内の代表的な循環器疫学65論文が構造化抄録化され、Minds関連サービスとして一般公開されるシステムが構築された。

F．健康危険情報

なし

G．研究発表

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4. Sakai M, Nakayama T, Shimbo T, Ueshima K, Kobayashi N, Izumi T, Sato N, Yoshiyama M, Yamashina A, Fukuhara S. Post-discharge depressive symptoms can predict quality of life in AMI survivors: A prospective cohort study in Japan. **International Journal of Cardiology.** 2009 Aug 26. [Epub ahead of print]

図 1 財団法人日本医療機能評価機構 Minds ホームページ
(http://minds.jcqhc.or.jp/)

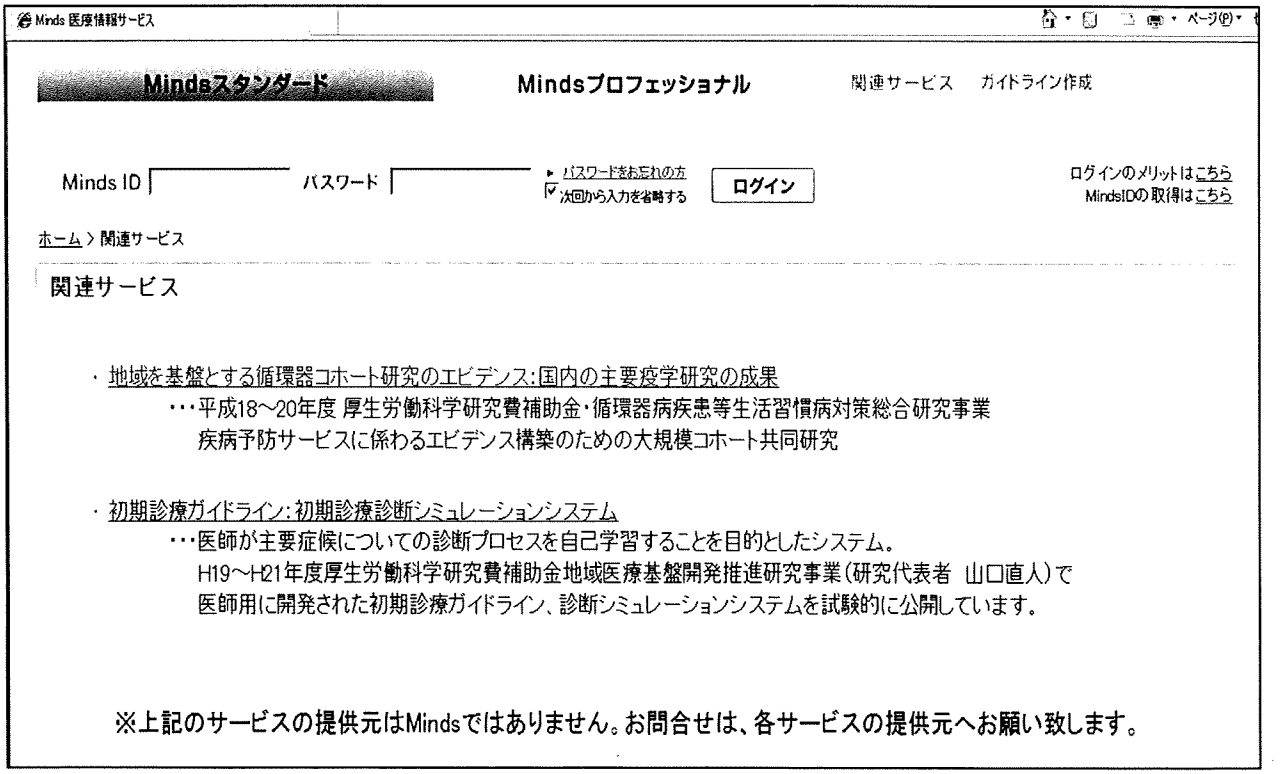

図 2 Minds 関連サービス

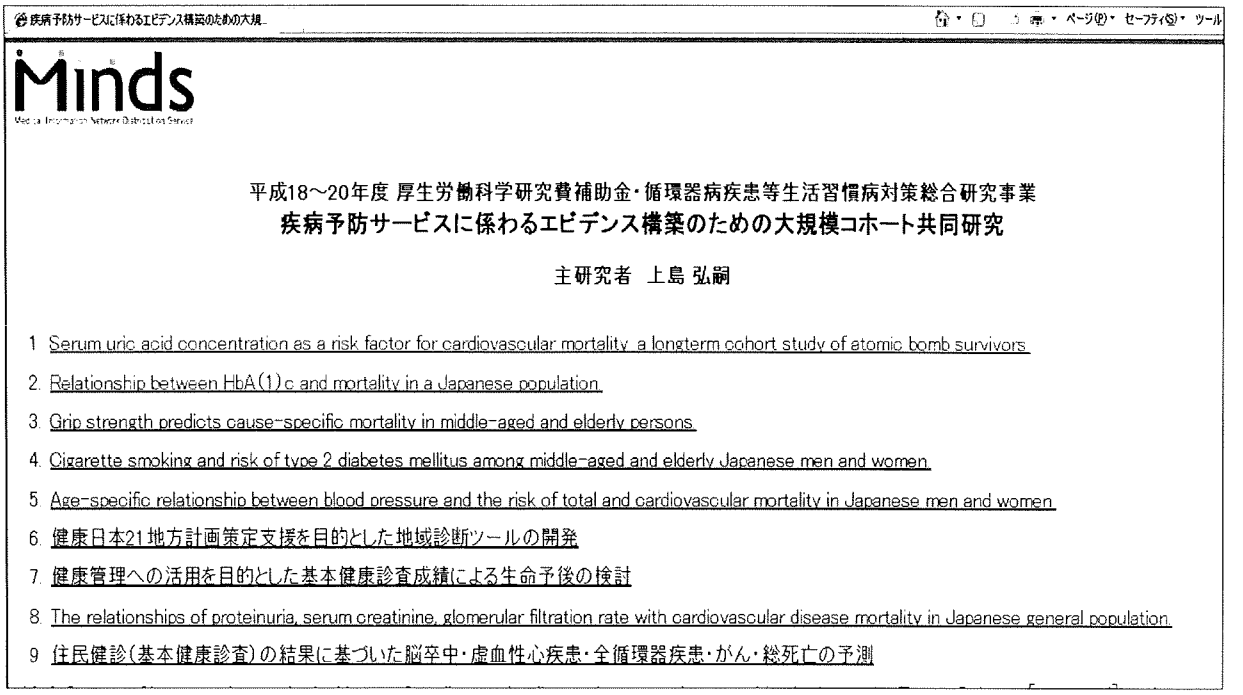

図 3.　Minds 関連サービスにおける循環器疫学エビデンス(65 論文)

図 4.　Minds 関連サービスにおける循環器疫学エビデンス:　構造化抄録の公開

Ⅲ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
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斎藤重幸	気管支喘息を有する高血圧	浦　信行	高血圧治療薬ハンドブック	羊土社	東京	2009	224-7
斎藤重幸	コレステロールの性差	寺本民夫	コレステロール－基礎から臨床へ	ライフサイエンス出版	東京	2009	103-8
斎藤重幸、島本和明	高齢者高血圧の疫学と生活習慣修正	日本老年医学会雑誌編集委員会編	老年医学Update2009-10	メディカルビュー社	東京	2009	9-18
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斎藤重幸	メタボリックシンドローム症候群を中心とした疫学	小川久雄、土師一夫	心血管イベントリスクファクターとその管理	文光堂	東京	2009	38-43

雑誌（英文）

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年	別刷記載ページ
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Ikehara S, Iso H, Date C, Kikuchi S, Watanabe Y, Wada Y, Inaba Y, Tamakoshi A; JACC Study Group.	Association of sleep duration with mortality from cardiovascular disease and other causes for Japanese men and women: the JACC study.	Sleep	32(3)	295-301	2009	162
Ryusuke Inoue, Takayoshi Ohkubo, Masahiro Kikuya, Hirohito Metoki, Kei Asayama, Atsuhiro Kanno, Taku Obara, Takuo Hirose, Azusa Hara, Haruhisa Hoshi, Kazuhito Totsune, Hiroshi Satoh, Yoshiaki Kondo, Yutaka Imai.	Stroke risk of blood pressure indices determined by home blood pressure measurement:The Ohasama Study.	Stroke	40	2859-61	2009	169

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Kei Asayama, Atsushi Sato, Takayoshi Ohkubo, Akira Mimura, Katsuhisa Hayashi, Masahiro Kikuya, Daisaku Yasui, Atsuhiro Kanno, Azusa Hara, Takuo Hirose, Taku Obara, Hirohito Metoki, Ryusuke Inoue, Haruhisa Hoshi, Hiroshi Satoh, and Yutaka Imai.	The association of masked hypertension and waist circumference as an obesity-related anthropometric index for metabolic syndrome: the Ohasama study.	Hypertension Research	32	438-43	2009	178
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Watanabe M, Okamura T, Kokubo Y, Higashiyama A, Okayama A.	Elevated serum creatine kinase predicts first-ever myocardial infarction: a 12-year population-based cohort study in Japan, the Suita study.	Int J Epidemiol.	38	1571-9	2009	223
Higashiyama A, Okamura T, Ono Y, Watanabe M, Kokubo Y, Okayama A.	Risk of smoking and metabolic syndrome for incidence of cardiovascular disease--comparison of relative contribution in urban Japanese population: the Suita study.	Circ J.	73	2258-63	2009	232
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C-reactive protein levels and risk of mortality from cardiovascular disease in Japanese: The JACC Study

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ABSTRACT

Objects: Limited evidence of association between C-reactive protein levels and cardiovascular disease has been produced for Japanese whose median protein levels are low by western standards.
Methods: We conducted a nested case-control study as part of the Japan Collaborative Cohort Study for evaluation of cancer risk (JACC Study). A total of 39,242 subjects 40–79 years of age provided serum samples at baseline between 1988 and 1990. During the 13-year follow-up, there were 525 deaths from total strokes (ICD10: I60–I69), 209 coronary heart diseases (I20–I25) and 939 total cardiovascular diseases (I00–I99). The control subjects were matched for sex, age, area of residence and year of serum storage, and analyses were conducted after further adjustment for cardiovascular risk factors. Serum high-sensitivity C-reactive protein (hs-CRP) levels were measured with ultra-sensitive latex-enhanced immunoassay.
Results: Median hs-CRP levels for controls were 0.40 mg/L for men and 0.41 mg/L for women. Hs-CRP levels were positively associated with risks of mortality from stroke, coronary heart disease, and total cardiovascular disease for men. The respective multivariable odds ratios (OR 95% CI) for the highest (≥0.85 mg/L) vs. lowest (<0.19 mg/L) quartiles of hs-CRP for men were 1.60 (0.90–2.85), 3.68 (1.02–13.3), and 2.31 (1.49–3.59). For women, positive associations with hs-CRP levels were weaker, reaching statistical significance only for total cardiovascular disease: OR = 1.69 (1.06–2.68). The positive association with total cardiovascular disease did not vary according to sex, age, smoking status, or body mass index.
Conclusions: Higher serum hs-CRP levels were associated with higher mortality from cardiovascular disease in Japanese.

1. Introduction

C-reactive protein, a marker of systemic inflammation, has been recognized as a risk factor for cardiovascular disease [1–3]. Follow-up studies of patients with diabetes mellitus, coronary atherosclerotic lesions or coronary heart disease showed that high sensitivity C-reactive protein (hs-CRP) was a significant predictor for cardiac events and mortality [4–8]. However, the data on general populations in Asia are limited to two prospective studies. The Hisayama cohort of approximately 2500 residents aged ≥40 years found positive associations between hs-CRP and risk of ischemic stroke for men but not for women [9], and risk of coronary heart disease for men and women combined [10]. In that study, however, the associations with coronary heart disease not examined by sex probably due to the small number of cases. The Iwate–Kenpoku cohort of 7901 men aged 40–79 years showed a positive association between hs-CRP and risk of ischemic stroke, but no data on coronary heart disease were reported [11].

Japanese have lower concentrations of CRP than western populations partly due to lower body mass index [10–14], and also show a different profile of cardiovascular disease, i.e., lower mortality from coronary heart disease and higher mortality from stroke [15,16].

To examine the impact of hs-CRP levels on risk of mortality from cardiovascular disease for an Asian population, we conducted a nested case-control study for approximately 40,000 men and women, who provided blood samples as part of the Japan Collaborative Cohort Study for evaluation of cancer risk (JACC Study). This study allowed us to examine sex-specific associations between hs-CRP and risk of mortality from stroke, stroke subtypes, coronary heart disease, and total cardiovascular disease. We also examined whether the contribution of hs-CRP to these risks was modified by

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age, smoking status and body mass index, i.e., major determinants of hs-CRP levels [10,12,13].

2. Methods

2.1. Survey population

We conducted a nested case-control study as part of the JACC Study sponsored by the then Ministry of Education (Monbusho), which was first conducted in 1988–1990 and involved 110,792 individuals (46,465 men and 64,327 women, age 40–79 years) living in 45 communities throughout Japan, who participated in municipal health screening examinations under the Health Law for the Aged with the population rate of 86–91%, and completed self-administered questionnaires about their lifestyles and medical histories of previous cardiovascular disease and cancer [17]. Informed consent was obtained from the participating individuals when they completed the questionnaire. In several communities, informed consent was obtained at community level after the study purpose, methods and data confidentiality had been explained to community leaders and mayors.

A total of 39,242 subjects (35.4% of the questionnaire respondents to the provided blood samples after giving individual informed consent [18]. After 557 men and 916 women with a history of cardiovascular disease or cancer at baseline had been excluded, a total of 37,769 subjects (13,282 men and 24,487 women) were enrolled in the study presented here, which was approved by the Ethics Committee of the University of Tsukuba, and Osaka University.

2.2. Mortality surveillance

The participants were followed up to determine mortality of cardiovascular disease by the end of 2003, except for four communities in which the follow-up had ended in 1999. For mortality surveillance in individual communities, investigators conducted systematic reviews of the death certificates, all of which were forwarded to the public health center in the area of residency. Mortality data were centralized at the Ministry of Health and Welfare, and the underlying cause of death was coded according to the *International Classification of Diseases (ICD)*, 9th revision, for deaths from 1988 to 1994, and the 10th revision for deaths from 1995 to 2003 as used for the National Vital Statistics. Registration of death is required by the Family Registration Law of Japan and is believed to be adhered to throughout Japan. All deaths occurring in the cohort were thus ascertained by death certificates from a public health center, except for subjects who died after moving away from their original community and were treated as censored cases.

The ICD 9th and 10th revisions were used to determine cause-specific mortality of cardiovascular disease as follows: total stroke (ICD 9th revision, codes 430–438, ICD 10th revision, codes I60–I69); coronary heart disease (410–414, I20–I25) and total cardiovascular disease (430–438, I60–I69). Further sub-groupings of total strokes were: intraparenchymal hemorrhage (431, I61), subarachnoid hemorrhage (430, I60) and ischemic stroke (433–434, I63). For each case, one control subject was selected randomly from among participants without mortality from stroke or coronary heart disease, and matched for sex, age (±5 years), community and year of blood drawing.

2.3. Determination of biochemical variables

Sera were prepared from blood samples as soon as possible after blood collection at laboratories in or near the surveyed municipalities. The serum from each participant was divided over 3–5 tubes (300 μl per tube), and stored at −80 °C until analysis. Hs-CRP levels were measured using an ultra-sensitive latex-enhanced immunoassay with an automatic analyzer (BN Prospec nephrometer; Dade Behring, Tokyo, Japan) at the Kotobikan Medical Laboratories Inc., Tsukuba, Japan. That laboratory took part in the quality control study in which each of the five samples was assayed in quadruplicate on 20 different days along with a single daily measurement of an internal quality control sample [14,15]. The inter-assay and intra-assay coefficients of variation (CV) were 1.3 and 1.4%, respectively, and the hs-CRP precision was satisfactory according to the AHA/CDC scientific criterion that the CV of hs-CRP should be <10% for a range of 0.3–10 mg/L [19].

Serum total and high-density lipoprotein (HDL)-cholesterol was measured using the enzymatic method with an automatic analyzer (Hitachi 7600-210; Hitachi Medical Corp., Tokyo, Japan) at Kotobiken Medical Laboratories, Inc. The standardization of lipid measurement was performed with the aid of the Osaka Medical Center for Health Science and Promotion, an international member of the US National Cholesterol Reference Method Laboratory Network (CRMLN) [20].

2.4. Statistical analysis

The paired Student's *t*-test was used to compare the mean values of baseline cardiovascular risk factors and hs-CRP levels for mortality cases and control subjects. The χ^2 test was used to compare percentages of cases and control subjects. The odds ratios for total stroke, stroke subtype and coronary heart disease were estimated according to sex-specific quartiles of hs-CRP levels and 1-SD increment of log hs-CRP (2.9 mg/L for men and 3.0 mg/L for women), and by means of conditional logistic regression models. Adjustments were made for sex-specific quartiles of body mass index (kg/m^2) based on actual measurement of height and weight, serum total and HDL-cholesterol levels (mmol/L), cigarette smoking status (never, former, and current), ethanol intake (never-, ex-, and current), quartiles of n-3polyunsaturated fat intake (g/day), walking (rarely, <30, 30–59 and ≥60 min/day), sports (rarely, 1–2, 3–4 and ≥5 h/week), and self-reported histories of physician's diagnosis hypertension and diabetes mellitus (yes vs. no) as well as matching for sex, age, community and year of blood drawing. Linear regression was employed to test for linear trends across the hs-CRP categories by using a median variable of hs-CRP for each hs-CRP category. The analyses were repeated, stratified by sex, age (40–64 and 65–79 years), smoking status (non-current vs. current smoker), and body mass index (high vs. low compared with median). The significance of the interactions for smoking status and body mass index was tested using cross-product terms of age, smoking and body mass index with hs-CRP levels.

All *p*-values for statistical tests were two-tailed and values <0.05 were considered to represent represented statistical significance. The SAS statistical package version 9.1 (Statistical Analysis System Inc., Cary, NC) was used for analyses.

3. Results

During the 13-year follow-up, we identified 525 deaths due to stroke, 209 deaths due to coronary heart disease, and 939 deaths due to total cardiovascular disease. Total stroke comprised 214 hemorrhagic strokes (119 intraparenchymal and 95 subarachnoid hemorrhages) and 294 ischemic strokes.

Table 1 shows sex-specific risk characteristics of cardiovascular disease for cases compared with control subjects. The average age was 66–67 years for total stroke to 64–68 years for coronary heart disease, varying from 63 to 64 years for hemorrhagic stroke to 67–70 years for ischemic stroke in both men and women. The prevalence of hypertension and current smokers was higher in men with total stroke, either ischemic or hemorrhagic, and total

Table 1
Sex-specific baseline characteristics by case and control status.

	No.	Age (year)	Hypertension (%)	Diabetes mellitus (%)	BMI (kg/m^2)	Alcohol intake (g/day)	Current smokers (%)	Total cholesterol (mmol/L)	HDL–cholesterol (mmol/L)	n-3polyunsaturated fat intake (g/day)	Sports ≥3 h/week (%)	Walking ≥0.5 h/day (%)	Median hs-CRP (mg/L)
Men													
Stroke													
Cases	268	66.0 (0.5)	42.9‡	8.1	22.4 (0.2)	20.8 (1.5)	53.7*	4.76 (0.06)	1.14 (0.03)	2.03 (0.06)	8.7	68.6*	0.49
Controls	268	65.1 (0.4)	25.1	6.8	22.3 (0.2)	17.9 (1.5)	42.2	4.90 (0.06)	1.20 (0.03)	1.89 (0.06)	12.6	79.1	0.40
Ischemic stroke													
Cases	173	67.4 (0.5)	45.7†	9.9	22.5 (0.2)	19.0 (1.7)	54.9*	4.81 (0.07)	1.13 (0.03)*	2.10 (0.08)	8.1	68.3	0.54
Controls	173	66.4 (0.5)	28.4	8.1	22.3 (0.2)	18.2 (1.8)	43.9	4.87 (0.07)	1.23 (0.03)	1.91 (0.08)	11.4	78.3	0.38
Hemorrhagic stroke													
Cases	89	63.3 (0.9)	35.7*	4.9	22.2 (0.3)	24.8 (3.1)	51.7	4.67 (0.12)	1.15 (0.05)	1.92 (0.10)	9.0	71.2	0.44
Controls	89	62.7 (0.8)	19.1	2.4	22.4 (0.3)	18.3 (2.7)	38.2	4.94 (0.10)	1.15 (0.04)	1.86 (0.11)	15.3	80.3	0.40
Coronary heart disease													
Cases	113	64.2 (0.9)	37.7	9.7	22.7 (0.3)	17.6 (2.3)	54.0	5.15 (0.09)	1.15 (0.04)	1.70 (0.10)	8.8	62.8	0.60*
Controls	113	63.7 (0.8)	25.7	8.0	22.8 (0.3)	16.7 (2.1)	48.7	4.97 (0.09)	1.13 (0.04)	1.54 (0.09)	8.2	70.4	0.39
Total cardiovascular disease													
Cases	484	66.0 (0.4)	43.1‡	8.4	22.4 (0.1)	19.3 (1.1)	53.5†	4.89 (0.05)	1.14 (0.02)	1.91 (0.05)	8.6	66.8*	0.55
Controls	484	65.1 (0.3)	26.4	7.0	22.4 (0.1)	17.0 (1.0)	42.4	4.94 (0.04)	1.16 (0.02)	1.80 (0.05)	12.7	75.7	0.38
Women													
Stroke													
Cases	257	67.0 (0.5)	44.9*	6.6	22.7 (0.2)	1.20 (0.4)	5.1	5.27 (0.07)†	1.13 (0.02)	1.73 (0.06)	6.7	71.5	0.34
Controls	257	66.9 (0.5)	34.0	4.1	23.0 (0.2)	1.14 (0.3)	3.9	5.55 (0.06)	1.17 (0.02)	1.67 (0.05)	9.1	85.7	0.41
Ischemic stroke													
Cases	121	70.0 (0.6)	41.3	8.8	22.4 (0.4)	0.71 (0.3)	6.6	5.29 (0.12)	1.16 (0.04)	1.77 (0.09)	8.7	75.0	0.38
Controls	121	69.8 (0.6)	38.3	5.2	22.6 (0.3)	1.39 (0.5)	5.7	5.52 (0.09)	1.18 (0.04)	1.67 (0.08)	12.1	77.4	0.37
Hemorrhagic stroke													
Cases	125	63.7 (0.8)	46.6†	5.3	22.8 (0.3)	1.75 (0.9)	4.0	5.25 (0.09)*	1.12 (0.03)	1.68 (0.08)	5.4	71.4	0.32
Controls	125	63.8 (0.8)	28.8	2.6	23.2 (0.3)	0.80 (0.3)	2.4	5.56 (0.10)	1.15 (0.03)	1.67 (0.07)	6.1	72.3	0.37
Coronary heart disease													
Cases	96	67.7 (0.7)	51.8	19.8*	23.9 (0.4)	1.30 (0.6)	14.6	5.73 (0.13)	1.03 (0.03)*	1.49 (0.10)	2.9	65.5	0.66
Controls	96	67.7 (0.7)	41.2	7.0	23.3 (0.3)	0.98 (0.5)	7.2	5.58 (0.11)	1.15 (0.04)	1.72 (0.07)	4.2	74.6	0.43
Total cardiovascular disease													
Cases	455	67.5 (0.4)	48.4‡	9.5*	23.1 (0.2)	1.02 (0.3)	7.5	5.45 (0.05)	1.10 (0.02)*	1.67 (0.05)	7.6	71.8	0.48
Controls	455	67.4 (0.4)	35.9	5.5	23.1 (0.2)	1.02 (0.2)	5.0	5.55 (0.05)	1.15 (0.02)	1.68 (0.04)	7.7	74.5	0.41

Difference between cases and controls: standard errors shown in parentheses.

* $p<0.05$.

† $p<0.01$.

‡ $p<0.001$.

Table 2
Sex-specific odds ratios (95% confidence intervals) of cardiovascular disease according to quartiles of serum hs-CRP levels.

	Quartiles of serum hs-CRP (mg/L)				*p* for trend	OR for 1-SD increment of log hs-CRP
	1 (low)	2	3	4 (high)		
Men						
Serum hs-CRP						
Median (mg/L)	0.16	0.28	0.55	1.47		
Range (mg/L)	0.04–0.18	0.19–0.37	0.38–0.84	0.85–2.74		
Total stroke						
No. of cases	58	55	66	89		
No. of controls	68	62	69	69		
Age and community-matched OR	1.00	1.07 (0.63–1.81)	1.14 (0.68–1.92)	1.56 (0.95–2.56)	0.05	1.18 (0.99–1.41)
Multivariable OR[a]	1.00	1.10 (0.60–2.00)	1.09 (0.59–2.02)	1.60 (0.90–2.85)	0.08	1.14 (0.93–1.40)
Ischemic stroke						
No. of cases	34	36	41	62		
No. of controls	45	42	38	48		
Age and community-matched OR	1.00	1.20 (0.62–2.34)	1.51 (0.77–2.95)	1.80 (0.97–3.36)	0.07	1.25 (1.00–1.56)
Multivariable OR[a]	1.00	1.28 (0.59–2.79)	1.33 (0.59–2.99)	2.04 (0.95–4.37)	0.08	1.20 (0.92–1.57)
Hemorrhagic stroke						
No. of cases	23	16	25	25		
No. of controls	23	19	28	19		
Age and community-matched OR	1.00	0.83 (0.34–2.04)	0.86 (0.36–2.04)	1.35 (0.56–3.24)	0.35	1.04 (0.84–1.27)
Multivariable OR[a]	1.00	1.58 (0.29–8.49)	2.62 (0.45–15.1)	1.86 (0.40–8.72)	0.73	1.36 (0.75–2.48)
Coronary heart disease						
No. of cases	17	20	28	48		
No. of controls	27	28	29	29		
Age and community-matched OR	1.00	1.20 (0.52–2.78)	1.73 (0.71–2.78)	2.99 (1.30–6.91)	0.003	1.60 (1.20–2.13)
Multivariable OR[a]	1.00	1.69 (0.48–6.02)	2.50 (0.63–9.99)	3.68 (1.02–13.3)	0.04	1.67 (1.08–2.57)
Total cardiovascular disease						
No. of cases	86	94	118	186		
No. of controls	120	121	122	121		
Age and community-matched OR	1.00	1.20 (0.75–1.67)	1.39 (0.93–2.08)	2.25 (1.54–3.30)	<0.001	1.37 (1.20–1.56)
Multivariable OR[a]	1.00	1.13 (0.72–1.75)	1.26 (0.79–1.99)	2.31 (1.49–3.59)	<0.001	1.36 (1.17–1.58)
Women						
Serum hs-CRP						
Median (mg/L)	0.16	0.30	0.58	1.77		
Range (mg/L)	0.04–0.18	0.19–0.40	0.41–0.92	0.93–37.5		
Total stroke						
No. of cases	75	68	52	62		
No. of controls	70	63	58	66		
Age and community-matched OR	1.00	0.99 (0.62–1.56)	0.82 (0.49–1.39)	0.86 (0.52–1.41)	0.57	0.96 (0.80–1.14)
Multivariable OR[a]	1.00	1.38 (0.78–2.42)	0.94 (0.50–1.77)	1.07 (0.58–1.97)	0.48	0.99 (0.81–1.22)
Ischemic stroke						
No. of cases	37	30	20	34		
No. of controls	38	22	26	35		
Age and community-matched OR	1.00	1.34 (0.68–2.64)	0.72 (0.32–1.62)	0.94 (0.47–1.90)	0.77	0.91 (0.71–1.16)
Multivariable OR[a]	1.00	2.14 (0.85–5.36)	0.74 (0.23–2.33)	1.00 (0.39–2.61)	0.54	0.89 (0.65–1.22)
Hemorrhagic stroke						
No. of cases	35	35	29	26		
No. of controls	29	41	27	28		
Age and community-matched OR	1.00	0.73 (0.38–1.40)	0.87 (0.41–1.81)	0.77 (0.41–1.61)	0.74	1.02 (0.85–1.22)
Multivariable OR[a]	1.00	0.88 (0.35–2.20)	1.14 (0.42–3.14)	1.78 (0.61–5.22)	0.78	1.50 (0.99–2.28)
Coronary heart disease						
No. of cases	11	20	26	39		
No. of controls	22	25	24	25		
Age and community-matched OR	1.00	1.78 (0.63–5.05)	2.18 (0.82–5.77)	3.40 (1.29–8.97)	0.02	1.54 (1.13–2.10)
Multivariable OR[a]	1.00	3.67 (0.74–18.2)	3.09 (0.76–12.6)	3.74 (0.91–15.3)	0.20	1.49 (0.94–2.36)
Total cardiovascular disease						
No. of cases	99	112	113	131		
No. of controls	114	114	112	115		
Age and community-matched OR	1.00	1.14 (0.78–1.66)	1.18 (0.80–1.74)	1.35 (0.92–1.99)	0.18	1.14 (1.00–1.30)
Multivariable OR[a]	1.00	1.63 (1.07–2.51)	1.42 (0.91–2.23)	1.69 (1.06–2.68)	0.47	1.17 (1.00–1.36)

[a] Adjusted for body mass index (quartiles), serum total and HDL-cholesterol (mmol/L), current smoking (yes vs. no), ethanol intake (never, ex- and current), n-3polyunsaturated fat intake (quartiles), walking (rarely, 30, 30–59, ≥ 60 min/day), sports (rarely, 1–2, 3–4, ≥ 5 h/week), and history of hypertension and diabetes (yes vs. no) as well as matching for age and community.