

CEREBROVASCULAR DISEASES IN A FIXED POPULATION
HIROSHIMA AND NAGASAKI

WITH SPECIAL REFERENCE TO RELATIONSHIP BETWEEN TYPE AND RISK FACTORS

広島・長崎の固定集団における
脳血管疾患、各病型とその危険因子との関連

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SUMMARY

A study was made of the incidence of cerebrovascular diseases, their chronological trend, and relationship between the disease types and risk factors on 16,491 subjects of Hiroshima and Nagasaki who underwent medical examination at least once between 1958-74, and who were free of cerebrovascular disease at the initial examination. During the 16-year period, 1,162 cases of cerebrovascular disease developed in this study population with the diagnosis definite in 621, and the annual incidence was 3.2 per 1,000 population. By type, there were 108 cases of cerebral hemorrhage, 469 cases of cerebral infarction, 33 cases of subarachnoid hemorrhage, and 11 cases of other unclassifiable types, with cerebral infarction occurring more frequently than cerebral hemorrhage at the ratio of 4.5:1.

The incidence of cerebrovascular diseases increased with age in both types, but the proportion of younger subjects in cerebral hemorrhage was greater than that in cerebral infarction. A secular trend of declining incidence was noted for both cerebral hemorrhage and cerebral infarction. As a risk factor of cerebral hemorrhage, elevation of systolic and diastolic

要約

広島・長崎において1958年から74年まで最低1回の検診を受け、初診時には脳血管疾患の認められなかった16,491名を対象に脳血管疾患の発生率、その年次の推移、及び病型とその危険因子との関連などについて検討した。本対象者のうち、16年間に脳血管疾患が1,162例発生し、そのうち診断確実例は621名あり、その年間発生率は1,000対3.2である。病型別では脳出血108例、脳梗塞469例、くも膜下出血33例、その他分類不能11例であって、脳出血よりも脳梗塞が多く、その比は1:4.5である。

脳血管疾患の発生率は年齢とともに上昇するが、病型別にみると脳出血は脳梗塞に比べ、比較的若年者の発生が多い。また脳出血、脳梗塞の発生率は共に経年的に減少する傾向がみられる。脳出血の危険因子では、収縮期血圧と拡張期血圧の上昇が発症と最も

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blood pressure was the most closely related to onset, and left ventricular hypertrophy on electrocardiogram (ECG) and proteinuria were also related. However, a tendency was seen for the risk to be somewhat higher the lower the levels of serum cholesterol. In cerebral infarction, aging, like systolic blood pressure, was a most important risk factor. Left ventricular hypertrophy on ECG, proteinuria, and diabetes could also be risk factors. However, the relation to blood pressure, especially diastolic blood pressure, was not so great as in the case of cerebral hemorrhage.

INTRODUCTION

It has been reported that cerebrovascular diseases occur at a higher incidence in Japan than coronary heart diseases, which contrarily occur more frequently in Europe and America.^{1,2} Cerebral arteriosclerosis is considered to be a factor for the high incidence of cerebrovascular diseases in the Japanese, with sclerosis of the small arteries probably playing a major role.³ Rickert et al⁴ reported that sclerotic lesions of the coronary artery were very mild in the Japanese despite comparatively marked atherosclerosis of the aorta and cerebral artery.

According to a recent report,⁵ there occurred in the Japanese during the past 10 or more years a decrease in the incidence and mortality of cerebrovascular diseases, a change in their types and a marked decrease of cerebral hemorrhage, and the cerebral hemorrhage to cerebral infarction ratio tended to decrease yearly. Although there was some difference in the risk factors of cerebrovascular diseases by type, the development of cerebral hemorrhage and cerebral infarction, both had a close correlation to hypertension.⁶ According to a WHO report,⁷ development of cerebrovascular diseases in the Japanese was closely related to hypertension and not too closely related to diabetes, hypercholesteremia, and obesity. Komachi et al⁸ believed, in view of the high incidence of cerebrovascular diseases in the traditional living environment of the Japanese, that the large intake of salt and unbalanced nutrition aggravated hypertension, one of the major causes of cerebrovascular diseases, and westernization of living environment and improved nutrition contributed to the recent decrease of cerebrovascular diseases, especially to the marked decrease of cerebral hemorrhage.

関連が強く、心電図所見左室肥大、蛋白尿などとも関係がある。しかし、血清コレステロールは低値の方がやや危険度が高い傾向が認められる。脳梗塞では、収縮期血圧と同様に加齢も最も重要な危険因子である。また、心電図所見左室肥大、蛋白尿、糖尿病なども危険因子になりうる。しかし血圧、特に拡張期血圧との関連は脳出血の場合に比べて小さい。

緒言

脳血管疾患は日本において冠動脈性心疾患より発生率が高く、欧米ではその逆に冠動脈性心疾患が多い事実は既に指摘されているところである。^{1,2} 日本人に脳血管疾患の発症が高率であることの一つの要因として、脳動脈における動脈硬化症が考えられているが、そのうちでも脳内の小動脈硬化が果たす役割は大きいであろう。³ Rickert ら⁴ は、日本人では大動脈及び脳動脈におけるアテローム性動脈硬化が比較的強度であっても、冠動脈の硬化性病変は極めて軽度であると報告している。

最近の報告⁵によると、この十数年間、日本人の脳血管疾患の発生率と死亡率は減少しており、その病型にも変化がみられ、脳出血の減少は著しく、脳出血と脳梗塞との比率は年々低下の傾向を示している。脳血管疾患の危険因子は病型によりやや異なるが、脳出血と脳梗塞の発症は共に高血圧と強い相関を示す。⁶ WHOの調査⁷によると、日本人の脳血管疾患の発症は高血圧との関係が強く、糖尿病、高コレステロール血症、肥満等との関連は低いと指摘されている。また小町ら⁸は、日本人の在来の生活環境において脳血管疾患が多発している状況から、食塩の多量摂取と栄養素摂取の不均衡が、脳血管疾患発症の大きな原因の一つである高血圧を進展させており、また最近認められている脳血管疾患の減少、特に脳出血の著減には、生活環境の欧米化、栄養向上などが寄与していることを認めている。

Since 1958, RERF in Hiroshima and Nagasaki has made biennial clinical examinations on the members of its Adult Health Study (AHS) and also detailed studies of deaths occurring in the sample. This fixed population provides a unique opportunity for following the natural history of various diseases in the Japanese.

The incidence of cerebrovascular diseases during 1958-64 has already been reported.⁹ The present report extends the follow-up period to 1974 and observes by type of cerebrovascular disease (cerebral hemorrhage, cerebral infarction) the yearly changes in the incidence and the risk factors involved.

MATERIALS AND METHODS

The AHS sample comprised 19,961 subjects when it was established in 1950.¹⁰ Of these, 18,566 were living when Examination Cycle 1 commenced in 1958 and 16,711 were examined at least once during the study period (Table 1). The RERF biennial examination includes clinic history taking, general physical examination, blood pressure test, chest X-ray, 12-lead ECG examination, general blood tests, urinalysis, stool, serum cholesterol, specific anthropometric determinations, and blood sugar test for those with positive urine sugar. The methods have been described in detail previously.¹¹

Periodic examinations are made of study subjects unable to undergo examination at the clinic by visiting them at their homes or where they are hospitalized. As death information is obtained by making periodic koseki (family register) checks on the entire study sample, and death certificates have been obtained for all those who have died, the data concerning deaths are almost 100% complete. Obtaining the consent of bereaved families to perform autopsy on the deceased was difficult because, unlike deaths occurring in hospitals, these occurred in a general local population, but a high autopsy rate of 30% was maintained during the study period.

The authors reviewed the clinical records, autopsy protocols, and death certificates of 1,162 study subjects diagnosed as cerebrovascular disease (No. 430-438, International Statistical Classification of Diseases and Causes of Death, 8th Revision). Further, four grades of certainty of diagnosis were established according to the diagnostic standard shown in Table 2 to make it

広島及び長崎放影研では、1958年以來、成人健康調査対象者に対し2年間隔で臨床検査を行い、また、その死亡に関する詳細な調査も行っている。この固定集団は、日本人の各種疾患についての自然経過を観察する絶好の機会を提供している。

1958-64年間における脳血管疾患の発生率に関しては、既に報告されている。⁹ 本報告は、観察期間を更に1974年まで延長し、かつ、脳血管疾患を病型別(脳出血、脳梗塞)に分け、その発生率の年次的推移及び関連ある危険因子について観察を行った。

対象及び方法

成人健康調査の対象者は1950年の設定時には19,961名であったが、¹⁰ 1958年の第1回診察開始時に生存していた者は18,566名で、調査期間中少なくとも1回以上の検診を受けた者は16,711名であった(表1)。放影研の外来では、2年ごとに各対象者に対し病歴聴取、一般理学的検査、血圧測定、胸部X線検査、12誘導心電図検査、一般血液検査、検尿、検便、血清コレステロール、特定の身体計測及び尿糖陽性者に血糖検査などを行っている。その検査方法は既に他の報告に詳しく記載されている。¹¹

なお、外来に受診できない者については家庭又は入院先を訪れて定期検診を実施している。死亡情報は、調査対象者全員の戸籍照合を定期的に行うことによつて得られる。全死亡者についての死亡診断書を入手しているので、死亡に関する資料はほとんど100%完全に求められる。死亡者の剖検は、病院内死亡とは異なり一般地域集団内の死亡なので、遺族の承諾が困難なこともあったが、調査期間中の剖検率は30%の高率を維持している。

著者らは、脳血管疾患(第8回修正国際疾病及び死因統計分類、番号430-438)と診断された調査対象者1,162名について、その臨床記録、剖検記録及び死亡診断書を検討した。更に表2に示した診断基準により、

TABLE 1 CLASSIFICATION OF STUDY SAMPLE ACCORDING TO EXAMINATION STATUS

表1 検診状態による調査対象者の分類

Examination status	Total	Male	Female
Alive at 1st examination	18566	7216	11350
Never examined during study period	1855	782	1073
Died during study period	299	136	163
Alive in 1975	1556	646	910
Examined at least once during study period	16711	6434	10277
Prevalence case	220	128	92
Subjects at risk	16491	6306	10185
Died during study period	2666	1340	1326
Examined only once	404	203	201
Examined more than once	2262	1137	1125
Alive in 1975	13825	4966	8859
Examined only once	768	320	448
Examined more than once	13057	4646	8411

possible on the one hand to distinguish on the basis of reliable data the group with the highest possibility of having cerebrovascular disease and, on the other hand, to gather as many cases as possible with even the slightest sign of the disease by taking up all individuals who present any findings indicating cerebrovascular disease. This diagnostic standard was prepared with reference to the standard described in the Committee Report of the National Institute of Neurological Diseases and Blindness.¹² Cases reported as cerebrovascular disease on the death certificate, but without support of autopsy or clinical records, were judged to be cases of "possible" diagnosis. As a result, 621 cases were obtained who came under "probable" or higher certainty of diagnosis. Of this number, 317 came to autopsy. For classification by type, 304 cases, excluding autopsy cases, were classified as cerebral hemorrhage and cerebral infarction according to the standards for differential diagnosis of the Japan Apoplexy Research Team,¹³ and the International Classification of WHO.¹⁴ In the present analysis of risk factors, study was made of the relation between such examination findings as systolic blood pressure, diastolic blood pressure, serum cholesterol values, relative body weight, ECG findings, and incidence of cerebral hemorrhage and cerebral infarction. The degree of relation was indicated using age-adjusted morbidity, and statistical evaluation of the relation was made by Mantel-Haenszel's χ^2 -test.¹¹ Multiple regression analysis was made to study the relation of various risk factors.

診断の確実度について四つの段階を設け、一方では確実な資料に基づいて脳血管疾患の可能性が最も高い集団の区別ができるようにするとともに、他方では、脳血管疾患を示すいかなる所見を呈した者も取り上げることにより、本症の徴候を少しでも示す症例をできるだけ多数集められるようにした。この診断基準は、米国神経疾患及び盲目研究所の委員会報告¹²の基準を参考にして作成した。なお、脳血管疾患と死亡診断書に記載されている症例で、剖検あるいは臨床記録による裏付けのない症例は"診断不確実"例と判断した。その結果、"診断ほぼ確実"以上に該当する者621例を得た。そのうち剖検例は317例であった。更に、病型を分類するには剖検例を除く304例について、日本脳卒中研究班¹³及びWHO国際分類¹⁴の鑑別診断基準に従い、脳出血と脳梗塞として分類した。今回の危険因子についての解析では収縮期血圧、拡張期血圧、血清コレステロール値、比体重、心電図所見などの検査と脳出血及び脳梗塞の発症との関係を検討した。年齢訂正罹患率を用いて関連の度合いを示したが、その統計的評価はMantel-Haenszelの χ^2 検定によった。¹¹また、各危険因子の関係を検討するため多重回帰解析も行った。

TABLE 2 DIAGNOSTIC CRITERIA FOR CEREBROVASCULAR DISEASES

表2 脳血管疾患の診断基準

DEFINITE 診断確定

AUTOPSY 剖検

Cerebral hemorrhage, subarachnoid hemorrhage, or cerebral infarction verified macroscopically or microscopically with clinical symptoms. Blood diseases and trauma are omitted.

脳出血、くも膜下出血、脳梗塞が肉眼的又は顕微鏡的に証明され、その臨床症状があるもの。ただし外傷、血液疾患等によるものを除く。

DEATH CERTIFICATE AND CLINICAL DATA 死亡診断書と臨床資料

Cases entered as “cerebrovascular diseases” in the Death Certificates.

死亡診断書に「脳血管疾患」の記載があるもの。

1. Cerebral hemorrhage and cerebral infarctions accompanied by history of hemiplegia or definite unilateral symptoms.

脳出血、脳梗塞については片麻痺などの病歴及び一側性徴候が明確なもの。

2. Subarachnoid hemorrhage which has been proven by history and lumbar puncture, operation, or arterial encephalography.

くも膜下出血については病歴と腰椎穿刺、手術、脳動脈造影で証明されたもの。

CLINICAL DATA 臨床資料

1. Cerebral hemorrhage or cerebral infarction with sudden onset of hemiplegia accompanied by unilateral signs and symptoms persisting for at least 1 week after which there was improvement.

脳出血、脳梗塞については一側性の徴候を伴う片麻痺が突然起こり、少なくとも1週間持続した後に症状の改善があったもの。

2. Subarachnoid hemorrhage proven by lumbar puncture, operation, or arterial encephalography.

くも膜下出血については腰椎穿刺、手術、脳動脈造影で証明されたもの。

PROBABLE 診断ほぼ確定

DEATH CERTIFICATE AND CLINICAL DATA 死亡診断書と臨床資料

Cases entered as “cerebrovascular diseases (suspected cases included)” in Death Certificates and also clinical findings of hemiplegia, etc., are mentioned as clinical data.

死亡診断書に「脳血管疾患(疑いを含む)」の記載があり、かつ片麻痺などの臨床所見の記載が臨床資料に認められたもの。

CLINICAL DATA 臨床資料

1. Cases with history of hemiplegia persisting for over 1 month, but without unilateral symptoms.

片麻痺が1か月以上持続した病歴はあるが一側性徴候の記載がないもの。

2. Cases with sudden onset of clouding of consciousness accompanied by elevation of blood pressure, but not by fever, who expired within 7 days after onset.

血圧上昇を伴う意識障害が突然起こったもので発熱はなく、その死亡が発病後7日間以内のもの。

POSSIBLE 診断不確定

DEATH CERTIFICATE AND CLINICAL DATA 死亡診断書と臨床資料

Entered as “cerebrovascular disease” in Death Certificate, but without supporting data or evidence.

死亡診断書に「脳血管疾患」の記載はあるが、それを裏付ける資料のないもの。

CLINICAL DATA 臨床資料

1. Cases in whom clouding of consciousness, speech disorder, or disorientation persisted for at least 1 week, and in whom diseases other than cerebral vascular disease cannot be considered.

意識障害、言語障害、見当識障害が少なくとも1週間続き、脳血管疾患以外の疾病が考えられないもの。

2. Cases with abnormal neurological findings consistent with cerebrovascular disease, but without definite unilateral symptoms.

脳血管疾患と一致する神経学的異常所見があるが、一側性徴候が明確でないもの。

INDEFINITE 診断不明

DEATH CERTIFICATE AND CLINICAL DATA 死亡診断書と臨床資料

Entered as "cerebrovascular diseases suspected" in Death Certificate, but without supporting clinical data or evidence.

死亡診断書に「脳血管疾患の疑い」の記載はあるが、それを裏付ける臨床資料がないもの。

CLINICAL DATA 臨床資料

Cases with hemiplegia or unilateral symptoms, but considered as caused by diseases of the central nervous system and not by cerebrovascular disease.

片麻痺、一側性の徴候はあるが、脳血管疾患以外の中枢神経系疾患と考えられるもの。

RESULTS

Incidence of Cerebrovascular Diseases

By Sex and Age. The number of cases of definite (including probable cases) and possible cerebrovascular disease (including indefinite cases) occurring during the 16-year period from Examination Cycle 1 to 31 December 1974 was 1,162 (603 males, 559 females) (Table 3). Of this number, 621 were definite cases. By sex and age, the incidence was marked from the age of 45 in males, and increase was noted from the age of 55, 10 years later, in females, and although incidence was increased with age in both sexes, it was highest in males. By type, of the 621 definite cases 108 (17.4%) were cerebral hemorrhage, 469 (75.5%) cerebral infarction, 33 (5.3%) subarachnoid hemorrhage, and 11 unclassifiable. The incidence increased with age in both types, but the proportion of younger persons who developed cerebral hemorrhage was greater than that for cerebral infarction. Therefore, although the ratio of cerebral hemorrhage to cerebral infarction was 1:4.5 for all ages, it was 1:1.5 in the 35-44 age group, 1:2.2 in the 45-54 age group, 1:3.0 in the 55-64 age group, 1:7.8 in the 65-74 age group, and 1:5.4 in the 75-or-more age group.

Secular Trend. The secular trend of cerebrovascular disease incidence is shown in Figure 1. The incidence tended to decrease with time in both sexes and in all age groups, but the tendency was especially drastic in Nagasaki. Not only the incidence of cerebral hemorrhage but also the incidence of cerebral infarction decreased with time.

結果

脳血管疾患の発生率

性・年齢別. 第1回診察以後1974年12月31日までの16年間に発生した脳血管疾患の診断確実(ほぼ確実を含む)及び不確実(不明を含む)例は1,162(男603,女559)であった(表3)。そのうち診断確実例は621であった。性及び年齢別の発生率では、男性は45歳からの発症が著しく、女性は10年遅れて55歳からの発症の増加が認められ、両者共年齢とともに増加しているが、特に男性の発生率は最も高い。次に、診断確実の621例について病型別にみると、脳出血は108例(17.4%)、脳梗塞は469例(75.5%)、くも膜下出血は33例(5.3%)、その他分類不能は11例であった。脳出血、脳梗塞共に年齢とともに発生率は上昇するが、脳出血の方が脳梗塞よりも若年での発生率が多くなっている。したがって脳出血と脳梗塞との比率は、全年齢では1:4.5であるが、これは35-44歳の群では1:1.5、45-54歳の群では1:2.2、55-64歳の群では1:3.0、65-74歳の群では1:7.8、75歳以上の群では1:5.4となっている。

年次的推移. 脳血管疾患発生率の年齢別推移は図1のとおり男女、各年齢群共経年的に減少傾向がみられたが、特にこの傾向は長崎の方が急激である。また脳出血のみならず脳梗塞の発生率も経年的に減少している。

TABLE 3 INCIDENCE OF CEREBROVASCULAR DISEASE BY AGE, SEX, AND SUBTYPE

表3 脳血管疾患の発生率；年齢，性，病型別

Certainty of Diagnosis	Subtype		Age							Total
			<25	25-34	35-44	45-54	55-64	65-74	75+	
	Male	Person years	3699	11811	16633	12296	14250	9605	2495	70792
Definite + Probable	CH*	No.	-	-	4	8	21	13	5	51
		Rate ($\times 10^3$)			0.24	0.65	1.5	1.4	2.0	0.72
	CI	No.	-	-	1	25	67	120	61	274
		Rate			0.06	2.0	4.7	12.5	24.4	3.9
	SAH	No.	-	1	3	3	8	3	-	18
		Rate		0.09	0.18	0.24	0.56	0.31		0.25
	Unk	No.	-	-	-	-	3	1	1	5
		Rate					0.21	0.10	0.40	0.07
	Total	No.	-	1	8	36	99	137	67	348
		Rate		0.09	0.48	2.9	7.0	14.3	26.9	4.9
Possible + Indefinite	No.	-	3	5	8	64	97	78	255	
	Rate		0.25	0.30	0.65	4.5	10.1	31.3	3.6	
Total	No.	-	4	13	44	163	234	145	603	
	Rate		0.34	0.78	3.6	11.4	24.4	58.1	8.5	
	Female	Person years	4561	16758	34176	25277	22130	13834	3973	120708
Definite + Probable	CH	No.	1	1	2	9	15	12	17	57
		Rate ($\times 10^3$)	0.22	0.06	0.06	0.36	0.68	0.88	4.3	0.47
	CI	No.	-	-	8	13	42	74	58	195
		Rate			0.23	0.51	1.9	5.3	14.6	1.6
	SAH	No.	-	-	-	4	4	3	4	15
		Rate				0.16	0.18	0.22	1.0	0.12
	Unk	No.	-	-	-	-	2	1	3	6
		Rate					0.09	0.07	0.76	0.05
	Total	No.	1	1	10	26	63	90	82	273
		Rate	0.22	0.06	0.29	1.0	2.8	6.5	20.6	2.3
Possible + Indefinite	No.	1	1	6	23	64	97	94	286	
	Rate	0.22	0.06	0.18	0.91	2.9	7.0	23.7	2.4	
Total	No.	2	2	16	49	127	187	176	559	
	Rate	0.44	0.12	0.47	1.9	5.7	13.5	44.3	4.6	

*CH: Cerebral hemorrhage; CI: Cerebral infarction; SAH: Subarachnoid hemorrhage

CH: 脳出血；CI: 脳梗塞；SAH: くも膜下出血

Risk Factors

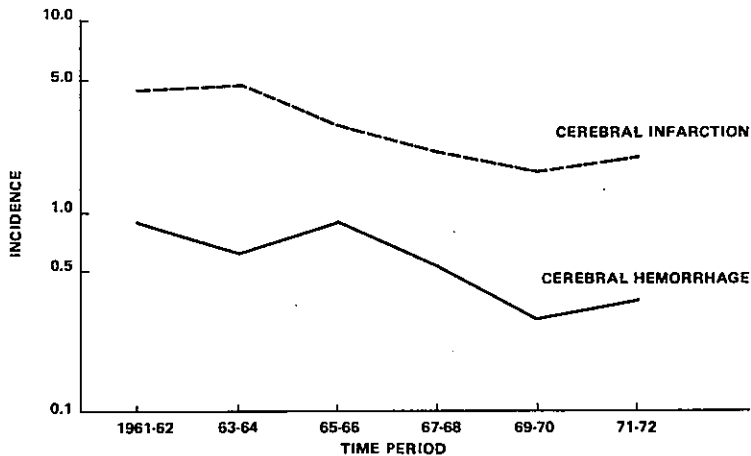
The systolic and diastolic blood pressure, serum cholesterol, relative body weight, left ventricular hypertrophy on ECG, diabetes, hematocrit volume and protein urine, at initial examination, smoking and drinking history, triglyceride value, and hemoglobin level, were considered as risk factors in the present analysis. However, smoking and drinking history, triglyceride value, and hemoglobin level were excluded from the

危険因子

今回の解析では、危険因子として初診時における収縮期及び拡張期血圧値、血清コレステロール値、比体重、心電図所見左室肥大、糖尿病、ヘマトクリット値、蛋白尿及び喫煙、飲酒歴、トリグリセライド値、ヘモグロビン値などを検討した。しかし喫煙、飲酒歴、トリグリセライド値、ヘモグロビン値は

FIGURE 1 SECULAR TRENDS IN THE INCIDENCE OF CEREBRAL HEMORRHAGE
& CEREBRAL INFARCTION

図1 脳出血及び脳梗塞の発生率における年度別推移



present study, because no statistically significant differences were found on analysis.

Systolic Blood Pressure. The risk of cerebral hemorrhage was relatively higher the higher the systolic blood pressure. The incidence of cerebral hemorrhage was, in males, 4-fold higher in the 140-179 mmHg group and 8-fold higher in the 180 mmHg-or-more group than in the normotensive (110-139 mmHg) group. Although the degree of association was less striking, the risk of cerebral infarction also increased with elevation of systolic blood pressure. Compared with the normotensive group, the incidence of cerebral infarction was 2-fold higher in the 140-179 mmHg group, and as much as 4-fold higher in the 180 mmHg-or-more group (Figure 2). This finding was the same for both males and females.

Diastolic Blood Pressure. As with systolic blood pressure, incidence of cerebral hemorrhage increased markedly with elevation of diastolic blood pressure (Figure 3). Compared with the diastolic normotensive (70-89 mmHg) group, it was 4-fold higher in males and 3.5-fold higher in females in the 90-109 mmHg group, and 9-fold higher in males and 16-fold higher in females in

解析の結果、統計的に有意の差が認められなかったので、今回検討の対象としなかった。

収縮期血圧。 脳出血の発症の危険度は、収縮期血圧が高いほど相対的に上昇した。脳出血の発症は、男性では正常血圧(110-139mmHg)群に対し、140-179mmHgの群では4倍、180mmHg以上の群では8倍の発生率となっている。関連の度合いは小さいが、脳梗塞の危険度は血圧の上昇とともに高くなる。脳梗塞の発症は血圧正常群に対し、140-179mmHgの群では2倍、180mmHg以上の群では4倍も高い発生率となっている(図2)。この結果は女性も同様であった。

拡張期血圧。 収縮期血圧と同様に、拡張期血圧が上昇するに従い脳出血の発症が著増し(図3)、拡張期血圧正常群(70-89mmHg)に対し、90-109mmHgの群では男性で4倍、女性で3.5倍、110mmHg以上の群では男性で9倍、女性で16倍も高い発生率となっ

FIGURE 2 INITIAL LEVELS OF SYSTOLIC BLOOD PRESSURE -- RELATIVE RISK FOR MALE

図2 初診時の収縮期血圧値—男性の相対的危険度

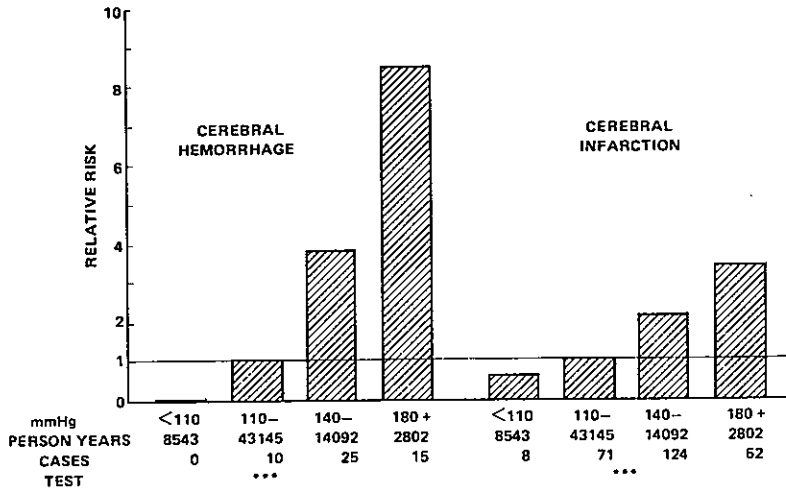


FIGURE 3 INITIAL LEVELS OF DIASTOLIC BLOOD PRESSURE -- RELATIVE RISK FOR MALE

図3 初診時の拡張期血圧値—男性の相対的危険度

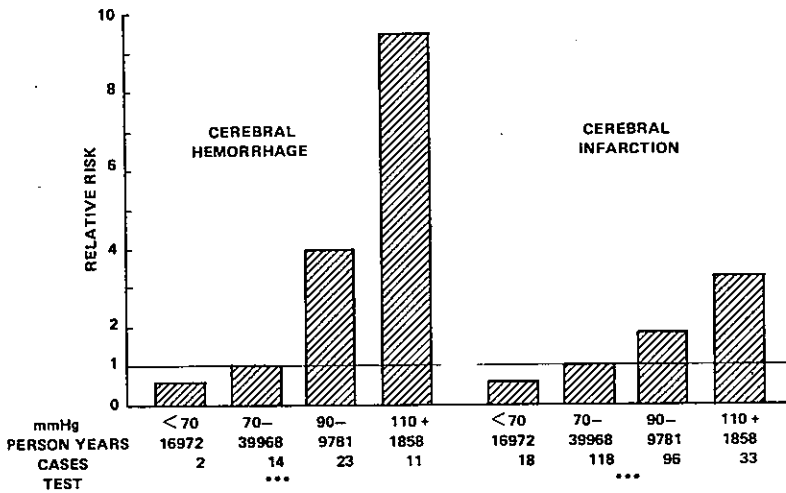
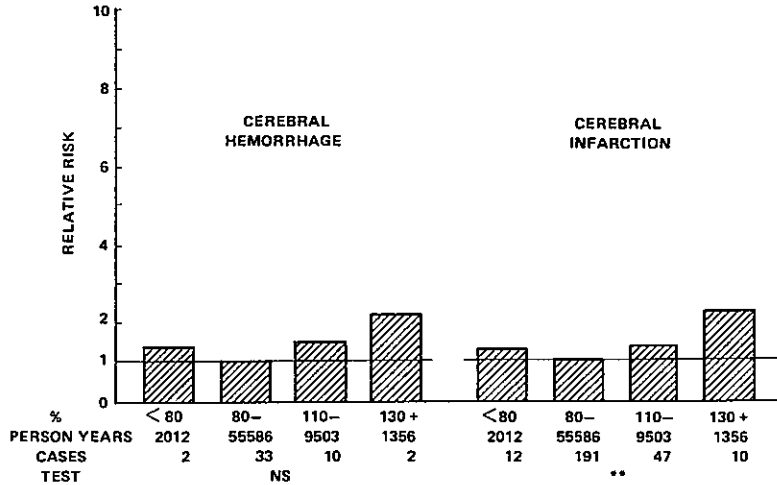


FIGURE 4 INITIAL LEVELS OF RELATIVE BODY WEIGHT – RELATIVE RISK FOR MALE

図4 初診時の比体重値—男性の相対的危険度



the 110 mmHg-or-more group. Incidence of cerebral infarction also increased with elevation of diastolic blood pressure, but the relative risk was smaller compared with cerebral hemorrhage.

Relative Body Weight. Relative body weight was used as an index of obesity.¹⁵ As Figure 4 shows, the risk of cerebral hemorrhage showed the so-called U shape, tending to be high in the lowest and the highest relative body weight groups. This tendency was markedly evident especially in males. The risk of cerebral infarction also appeared to show the U shape as same as the risk of cerebral hemorrhage.

Serum Cholesterol Level. The serum cholesterol level was determined as a part of each Cycle examination by the method of Abell et al¹⁶ during 1958-64, and subsequently by auto-analyzer. The relative risk of cerebral hemorrhage in males indicated the U shape, it being high in the groups with high and low levels of serum cholesterol at initial examination (Figure 5). This was not evident for females. On the other hand, hardly any significant relation was observed between the two for both sexes in regard to cerebral infarction. However, as blood pressure tends to be high in the high cholesterol

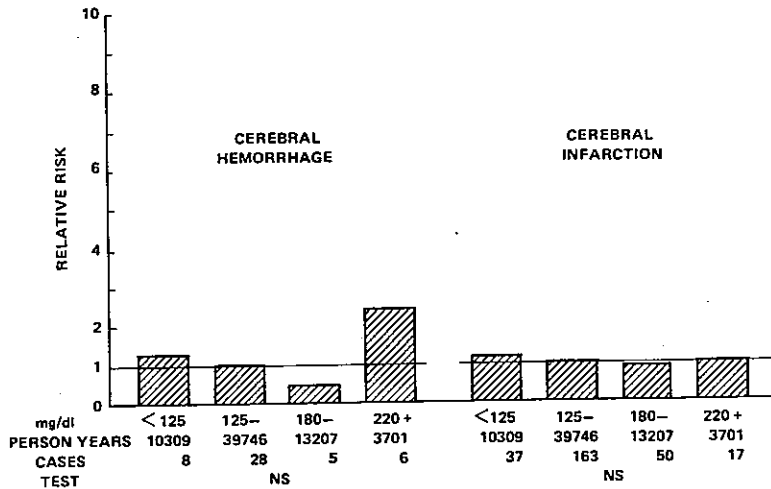
ている。脳梗塞の発症も拡張期血圧が上昇するにつれて高くなるが、脳出血に比べて相対的危険度は小さい。

比体重。肥満の指標として比体重を用いた。¹⁵ 脳出血の発症は図4に示すように比体重の最も低い群及び最も高い群に危険度が高い傾向がうかがわれ、いわゆるU型を示している。特にこの傾向は男性に著しく認められた。脳梗塞も脳出血と同様にU型を示しているようである。

血清コレステロール値。血清コレステロール値は検査の一部として1958-64年はAbellの方法で、その後は自動分析装置で毎回測定された。¹⁶ 男性における脳出血の相対的危険度はU型を示し、初診時の低及び高血清コレステロール群に危険度が高い(図5)。女性では、この関係はみられなかった。一方脳梗塞については、男女共両者の間にほとんど有意な関係を認めなかった。しかし、高コレステロール群は血圧も高い傾向があるので、収縮期血圧値を140mmHg未

FIGURE 5 INITIAL LEVELS OF SERUM CHOLESTEROL - RELATIVE RISK FOR MALE

図5 初診時の血清コレステロール値-男性の相対的危険度



group, the relation to serum cholesterol was observed by blood pressure level, dividing the subjects by systolic blood pressure into two groups, less than 140 mmHg and 140 mmHg or more (Figure 6). The relative risk of cerebral hemorrhage tended to be the higher the lower the serum cholesterol level in both the low and high blood pressure groups, and this tendency was especially marked in males. Though not as marked as cerebral hemorrhage, cerebral infarction also presented in males a tendency for the relative risk to be the higher the lower the cholesterol level. However, this tendency was not evident in females.

Left Ventricular Hypertrophy on ECG. The condition was evaluated as left ventricular hypertrophy when it included 3-1, 4-1, 4-2 or 4-3, 5-1, and 5-2 or 5-3 of the Minnesota Code. The relative risks of cerebral hemorrhage and cerebral infarction were each 2-3 fold higher in the group with the finding of left ventricular hypertrophy on ECG at initial examination than in those who presented no such findings (Figure 7).

Diabetes. The condition was evaluated as diabetes when a diabetic blood sugar curve was

滴とそれ以上の二群に分け、血圧値別に血清コレステロールとの関係を観察した(図6)。脳出血では、血圧の低い群、高い群共に、血清コレステロール値が低い程相対的危険度が高い傾向がみられ、この傾向は、男性で特に顕著である。脳梗塞でも男性では、脳出血ほど著明ではないが、コレステロール値が低い程相対的危険度が高くなる傾向がみられる。しかし女性ではこの傾向はみられない。

心電図所見左室肥大。Minnesota Code 3-1, 4-1, 4-2又は4-3, 5-1, 及び5-2, 又は5-3を加えたものを左室肥大と判別した。初診時に左室肥大の心電図所見があった群では、脳出血及び脳梗塞の発症の相対的危険度は共に左室肥大所見のないものに比較して2-3倍高い発生率となっている(図7)。

糖尿病。日本糖尿病学会が勧告した基準¹⁷に基づ

FIGURE 6 SYSTOLIC BLOOD PRESSURE AND SERUM CHOLESTEROL - RELATIVE RISK FOR MALE

図6 収縮期血圧と血清コレステロール—男性の相対的危険度

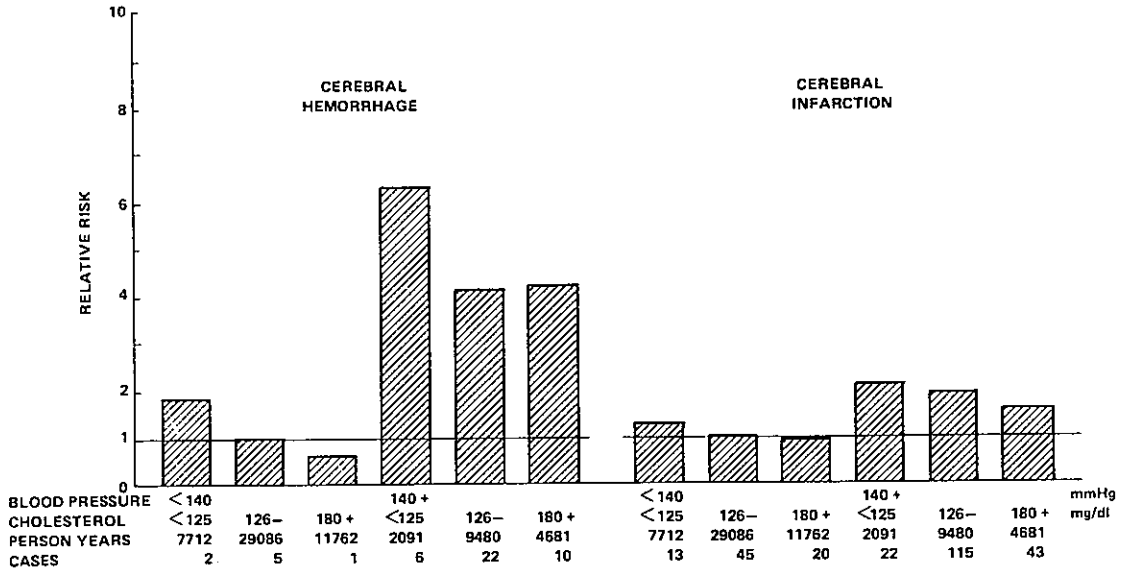


FIGURE 7 INITIAL LEVELS OF ECG (LVH, LVS) - RELATIVE RISK FOR MALE

図7 初診時の心電図所見 (LVH, LVS) —男性の相対的危険度

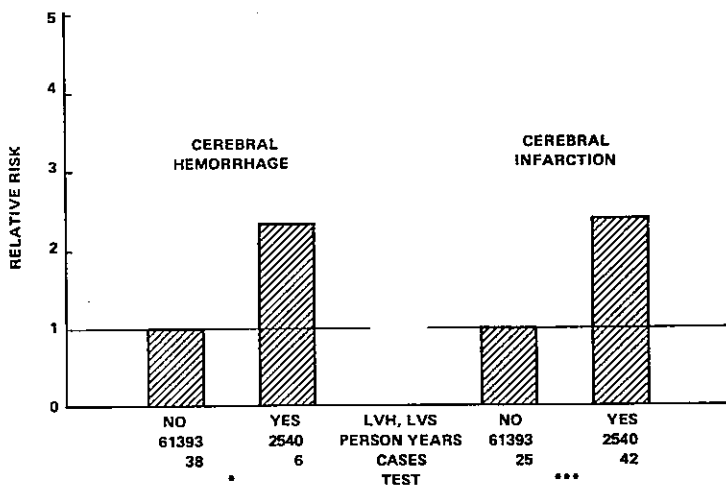
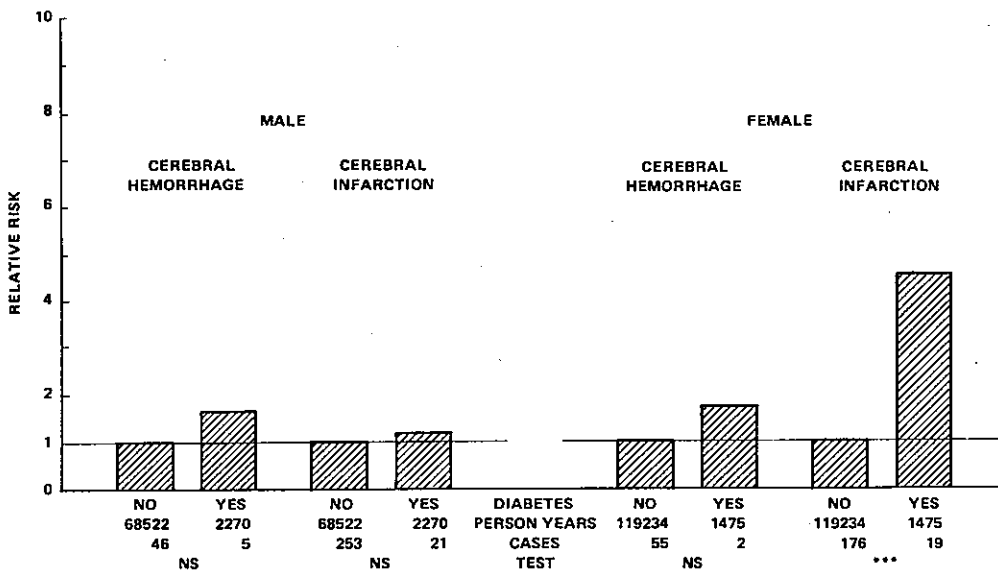


FIGURE 8 INITIAL LEVELS OF DIABETES - RELATIVE RISK FOR MALE AND FEMALE

図 8 初診時糖尿病状態—男性及び女性の相対的危険度



observed in 50 or 100g glucose tolerance tests, based on the criteria recommended by the Japan Diabetes Society.¹⁷ Accordingly, the relative risk of cerebral hemorrhage tended to be high in diabetics, but the difference was not statistically significant (Figure 8). The risk of cerebral infarction was significantly high in females only.

Combination of Hypertension and Other Factors. The effect on cerebrovascular disease was studied for hypertension alone and in combination with other risk factors (Figure 9). Proteinuria, diabetes, and electrocardiographic abnormality were used as risk factors other than hypertension. Cerebral hemorrhage and cerebral infarction both showed a high relative risk with hypertension alone, but the relative risk rose drastically when it was combined with other risk factors. This tendency was strong in cerebral hemorrhage. Groups with only factors other than hypertension showed no great relative risk.

Multivariate Analysis. Since some of the risk factors under consideration are interrelated, multiple regression analysis was made to ascertain the individual effect of the factors with consideration of their interrelation. Nine

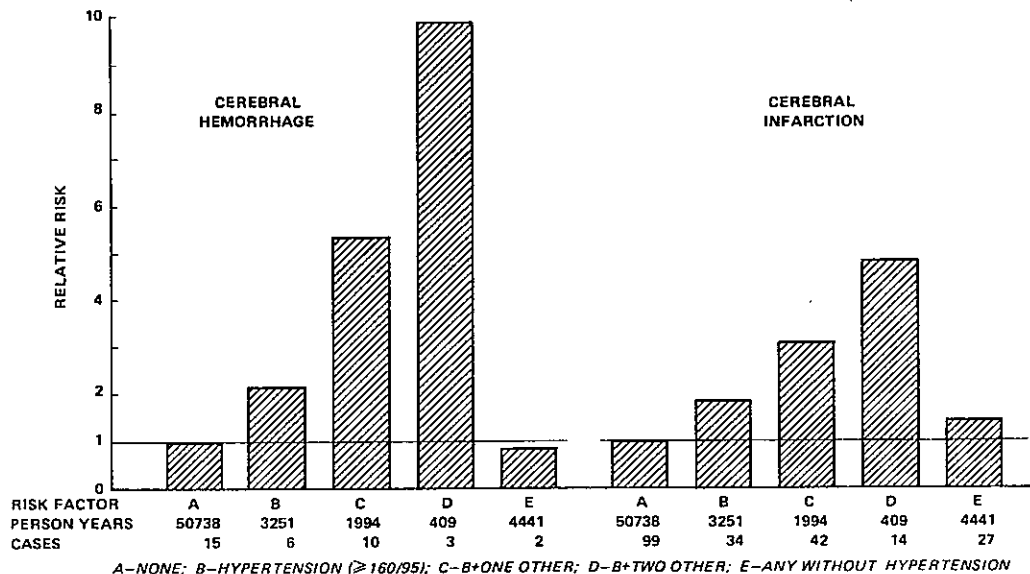
き、50gあるいは100gブドウ糖負荷試験で糖尿病型血糖曲線を示したものを糖尿病とした。それによると脳出血発症の相対的危険度は糖尿病に高い傾向は認められるが、統計的には有意でない(図8)。脳梗塞の危険度は、女性だけに有意に高かった。

高血圧とその他の因子の組み合わせ。高血圧単独の場合と、高血圧に他の危険因子を合併する場合の脳血管疾患に及ぼす影響を観察した(図9)。高血圧以外の危険因子としては、蛋白尿、糖尿病、心電図異常を用いた。脳出血、脳梗塞共に、高血圧単独においても高い相対的危険度を示すが、高血圧に他の危険因子を併合した場合には、その相対的危険度は急激に上昇した。この傾向は脳出血に大である。高血圧以外の因子のみを有する群は、大きな相対的危険度を示さなかった。

多変量解析。考慮の対象となっている危険因子の幾つかは相関があるので、各因子間の関係を考慮して、各因子単独の影響をみるために多重回帰解析を

FIGURE 9 COMBINATION OF HYPERTENSION AND OTHER RISK FACTORS
(PROTEINURIA, DIABETES, ECG) - RELATIVE RISK FOR MALE

図9 高血圧とその他の因子の組み合わせ
(蛋白尿, 糖尿病, 心電図異常) - 男性の相対的危険度



variables were used, namely, systolic blood pressure, diastolic blood pressure, serum cholesterol level, relative body weight, hematocrit volume, proteinuria, diabetes, left ventricular hypertrophy on ECG, and age. Table 4 shows the standardized regression coefficients, by type of cerebrovascular disease, and sex.

Among the various factors, systolic blood pressure had the greatest effect in cerebral hemorrhage and this was followed by diastolic blood pressure, proteinuria, left ventricular hypertrophy, and age in the order given. In cerebral infarction, the factors having significant positive effect were, in the order of the magnitude of their effect, systolic blood pressure, age, left ventricular hypertrophy, proteinuria, diabetes, and hematocrit volume, and the factor with significant negative effect was cholesterol level. The significant negative association of diastolic pressure with the risk of cerebral infarction is an artifact due to a high correlation between systolic pressure and diastolic pressure. Systolic blood pressure was a factor with the greatest effect in both cerebral hemorrhage and cerebral infarction, but diastolic blood pressure presented significant effect only in cerebral hemorrhage. Though not a factor with too

行った。変数としては収縮期血圧, 拡張期血圧, 血清コレステロール値, 比体重, ヘマトクリット値, 蛋白尿, 糖尿病, 心電図所見左室肥大, 年齢の9変数を使用した。表4に標準化回帰係数を脳血管疾患の病型, 性別に示した。

脳出血においては, 各因子の影響の度合いは収縮期血圧が最も強く, 次いで拡張期血圧, 蛋白尿, 左室肥大, 年齢の順であった。脳梗塞においては, 正に働く有意な因子の影響の度合いの大きさの順は, 収縮期血圧, 年齢, 左室肥大, 蛋白尿, 糖尿病, ヘマトクリット値であり, コレステロール値は負に働く有意な因子であった。脳梗塞の危険度と拡張期血圧との間にみられた負に働く有意な関係は, 収縮期血圧と拡張期血圧間の強い相関に起因するものである。収縮期血圧は脳出血, 脳梗塞の両方に最も影響が大きい因子であるが, 拡張期血圧は脳出血のみに有意な影響を示した。また年齢は, 脳出血ではあま

TABLE 4 STANDARDIZED MULTIPLE REGRESSION COEFFICIENTS
表 4 標準化多変数回帰係数

Risk factor	Disease category						
	Cerebral hemorrhage			Cerebral infarction			
	Male	Female	Total	Male	Female	Total	
Blood pressure	Systolic	0.098*	0.050*	0.072*	0.17*	0.14*	0.15*
	Diastolic	0.030	0.046*	0.039*	-0.023*	-0.058*	-0.041*
Cholesterol		-0.0028	-0.015	-0.011	-0.013	-0.0028	-0.023*
Relative body weight		0.011	-0.018	-0.0086	-0.015	-0.0089	-0.015
ECG		-0.012	0.070*	0.034*	0.041*	0.044*	0.043*
Hematocrit		-0.020	0.0053	-0.0033	-0.0032	0.015	0.033*
Proteinuria		0.033*	0.038*	0.036*	0.037*	0.049*	0.041*
Diabetes		0.0091	-0.0069	0.0013	0.0040	0.064*	0.035*
Age		0.0071	0.028*	0.020*	0.17*	0.11*	0.14*
R ² %		1.9	2.3	1.9	8.3	5.3	6.6
Number of subjects		5428	8646	14074	5428	8646	14074

*Significant (P<.05)

strong an effect in cerebral hemorrhage, age was a factor equally as important as systolic blood pressure in cerebral infarction.

DISCUSSION

The incidence, mortality, and risk factors of cerebrovascular diseases have been described previously in a report of a 6-year period of surveillance during 1958-64 in Hiroshima.⁹ The annual incidence of cerebrovascular diseases in the population of the present study is slightly lower than that described in the previous report.⁹ This is a reflection of the secular trend of declining incidence of cerebrovascular diseases.

In the present study a secular trend of declining incidence was noted for both cerebral hemorrhage and cerebral infarction. The mortality statistics for all Japan, however, show a decreased incidence for cerebral apoplexy as a whole; by type it is decreased for cerebral hemorrhage, but contrarily increased for cerebral infarction. These being statistics of causes of death based on death certificates, the accuracy of the causes when divided by type is questionable. Probable causes of this decrease in the incidence of cerebral hemorrhage and cerebral infarction with time are chronologically decreased systolic blood pressure,¹⁸ and decreased risk due to chronologically elevated serum cholesterol level. The

り影響の強い因子でないが、脳梗塞では収縮期血圧と並ぶ重要な因子となっている。

考 察

脳血管疾患の発生率、死亡率及び危険因子については、広島における1958年から64年までの6年間の調査報告において既に記述した。⁹ 今回の調査集団における脳血管疾患の年間発生率は前回の報告⁹より少し低い。これは脳血管疾患の発生率が経年的に減少する傾向を反映している。

今回の調査で脳出血、脳梗塞共に発生率が経年的に減少していることが分かった。しかし日本全国の死亡統計では、脳卒中全体では減少しているが、病型別にみると脳出血は減少し、脳梗塞は逆に増加している。これは死亡診断書に基づく死因統計であるので、病型別に分けた場合の死因の正確性に問題がある。この脳出血、脳梗塞発生率の経年的減少の原因としては、年次的に収縮期血圧が低下していること¹⁸と血清コレステロール値の年次的上昇による危険度の減少が考えられる。脳血管疾患の発生率及び死亡率

incidence and mortality of cerebrovascular diseases is remarkably different between various countries in the world.¹⁹ Within Japan also, regional differences are marked due to difference of environmental factors such as mode of living.²⁰ In a comparison between cities, the incidence of cerebrovascular diseases in Nagasaki is higher than in Hiroshima and this probably is because the mode of living in Nagasaki is more Japanese than in Hiroshima,²¹ but the difference in incidence needs to be studied in further detail.

In a follow-up study made in Hisayama-cho²² the risk of cerebral hemorrhage was highest in the hypertensive group 40-59 years of age and cerebral infarction occurred at a significantly higher frequency at age 60 or more in both sexes. On the other hand, the Framingham Study reported that the frequency of nonembolic cerebral infarction increased with age in both sexes. Nearly the same results were obtained in the present study population. The incidence of cerebral infarction in particular increased with age and was highest in the 75-years-or-more group. In multivariate analysis also, the regression coefficients of age were lower than those of other factors in cerebral hemorrhage, but, as for systolic blood pressure, they were highest in cerebral infarction, suggesting that age is important as a risk factor of cerebral infarction. It is accepted in numerous study reports that hypertension is the most important as a risk factor of cerebrovascular diseases.²³⁻²⁵

In the present study the risk of cerebral hemorrhage increased markedly with elevation of both the systolic and the diastolic blood pressure. The results of multivariate analysis also demonstrated that systolic blood pressure was the most important risk factor, followed by diastolic blood pressure. The relative risk levels of systolic and diastolic blood pressure were lower, and the effect of blood pressure smaller, in cerebral infarction than in cerebral hemorrhage.

By multivariate analysis, systolic blood pressure was the most important factor, but diastolic blood pressure was not a significant risk factor. The follow-up study of Hisayama-cho²⁶ showed that the risk of cerebral hemorrhage was greater the higher the blood pressure (especially the level of diastolic blood pressure) and the longer it persisted, and the risk of cerebral infarction was greater the higher the level of both the systolic and diastolic blood pressure.

は各国間で著しく差異がある。¹⁹ 日本国内でも、生活様式などの環境因子の差異によって地域差が著しい。²⁰ 広島と長崎を比較してみると、長崎の脳血管疾患の発生率は広島の発生率より高い。これは長崎の生活様式が広島より日本的であるためであろうが、²¹ この発生率における差については更に詳細な調査検討が必要である。

久山町における追跡調査²²によれば、脳出血は40-59歳の高血圧群に最も危険度が高く、脳梗塞は男女共60歳以上の者に有意に多発すると報告している。一方、Framingham Study²も男女共加齢とともに非塞栓性脳梗塞の発症頻度が高くなることを報告している。この調査集団でもほぼ同様の結果が得られている。特に脳梗塞の発生率は年齢とともに増加し、75歳以上の群に最も発生率が高い。更に多変量解析においても、年齢の回帰係数は脳出血では他の因子と比較して低いが、脳梗塞では収縮期血圧が最も高く、年齢は脳梗塞の危険因子として重要であることを示唆している。脳血管疾患の危険因子として、高血圧が最も重要であることは多くの調査報告で認められている。²³⁻²⁵

本調査では脳出血は収縮期血圧、拡張期血圧共に、その上昇に伴って危険度が著しく上昇している。また多変量解析の結果からも収縮期血圧値、次いで拡張期血圧が最も重要な危険因子であることが明らかにされた。脳梗塞では脳出血に比べて収縮期血圧、拡張期血圧共に相対的危険度の値が小さく、血圧の影響はより小さい。

多変量解析では収縮期血圧は最も重要な因子であったが、拡張期血圧は有意な危険因子ではなかった。久山町の追跡調査²⁶でも高血圧(特に拡張期血圧のレベル)が高い程、またその持続が長い程出血の危険度が大きく、収縮期血圧及び拡張期血圧共に高い程、脳梗塞の危険度も大きいと報告している。

As regards the relation between relative body weight and cerebrovascular disease, the risk tended rather to be higher the smaller the relative body weight, but this was not so pronounced as in the case of serum cholesterol whereby the incidence of cerebrovascular disease decreased with serum cholesterol value.

It has been reported recently with regard to serum cholesterol level and development of cerebral hemorrhage that the incidence of cerebral hemorrhage was high in the group with the lowest serum cholesterol level.²⁷ In the present study, the risk was high in males in the high and low cholesterol groups and presented a U shape. Okada et al²⁵ reported similar results. However, on observation by systolic blood pressure level, because blood pressure also tended to be high in the high cholesterol group, a tendency was found for the risk to be higher the lower the cholesterol level in both the low and high blood pressure groups. In multivariate analysis also, serum cholesterol presented a minus regression coefficient and its effect on development of cerebral hemorrhage was greater the lower its level. On the other hand, many studies have not found a significant relation between cerebral infarction and serum cholesterol level.^{25,28} In the present study also, no significant correlation was found for any serum cholesterol level in males or females regarding its relation to development of cerebral infarction, but on observation by blood pressure level the risk in males tended to be higher the lower the cholesterol level though this was not so marked as in the case of cerebral hemorrhage. The most notable characteristic in the development of cerebral infarction in the Japanese is the limited involvement of serum cholesterol, as Kuller and Reisler²⁹ have reported. Kieffer et al³⁰ in a Japan-U.S. collaborative study on cerebrovascular disease reported that whereas intracranial vascular lesions were more frequent in the Japanese, extracranial vascular lesions were more frequent in American whites. Kameyama and Yamanouchi³¹ reported that infarction of extracranial artery was rare in autopsy confirmed cases of cerebral infarction in the Japanese and atherosclerosis was severer in the intracranial artery. Konishi³ reported that development of cerebral infarction was much affected by arteriosclerosis in the cerebral parenchyma in addition to atherosclerosis of the basilar artery, and hypertension was more involved in its formation than abnormality of lipid metabolism. Recently

比体重と脳血管疾患の関連は、比体重が小さい方が危険度がむしろ高い傾向を示しているが、血清コレステロールの場合程著明ではない。すなわち、脳血管疾患の発症が血清コレステロール値の上昇とともに減少した。

血清コレステロール値と脳出血の発症について、血清コレステロール値の最も低い群に脳出血の発生率が高いとの最近の報告がある。²⁷ 本調査では男性において、低コレステロール群と高コレステロール群に危険度が高くU型を示している。岡田²⁵も同様な結果を報告している。しかし高コレステロール群は血圧も高い傾向があるので、収縮期血圧値別に観察すると、血圧の低い群、高い群共に、コレステロール値が低い程危険度が高い傾向がみられる。更に多変量解析においても、血清コレステロールは負の回帰係数を示しており、血清コレステロールが低値を示す程、脳出血の発症に強い影響を及ぼしている。一方、脳梗塞と血清コレステロール値については、多くの研究であまり有意な関連を認めていない。^{25,28} 本調査でも男女共、脳梗塞の発症と血清コレステロール値について検討した結果、いずれの値においても有意な相関を認めなかったが、血圧値別の観察では男では脳出血程著明ではないが、コレステロール値が低い程危険性が高くなる傾向がみられる。KullerとReisler²⁹が報告したとおり、日本人の脳梗塞の発症における最も顕著な特徴は、血清コレステロールの関与がとりわけ少ないことである。またKiefferら³⁰は、脳血管疾患に関する日米共同研究において、日本人は頭蓋内血管病変が多いのに対し米国白人は頭蓋外血管病変が多いことを指摘している。亀山及び山内³¹も、剖検で確かめた日本人の脳梗塞例では頭蓋外動脈の閉塞は少なく、アテローム性動脈硬化の程度も頭蓋内動脈の方が強いと報告している。更に小西³は、脳梗塞の発症には脳底部動脈のアテローム性動脈硬化のほか、脳実質内小動脈硬化の影響が大きく、その生成には脂質代謝の異常よりも高血圧の関与が大きいと指摘している。最近加藤³²と三山ら³³

Kato³² and Mitsuyama et al³³ made similar reports in the Ni-Hon-San Study.

Many reports show a high frequency of cerebrovascular diseases in hospitalized diabetics, but there is as yet no established theory concerning their decreased glucose tolerance level.³⁴ In the Framingham Study a 5-fold higher incidence of cerebrovascular diseases was found in the 120mg/100ml or more blood sugar level group as measured by blood sugar determination, and a significant risk of cerebrovascular diseases was found in also the 110-119mg/100ml group, especially in females. In the Hisayama-cho Study also, cerebral thrombosis occurred at a high frequency in diabetics, and a significant correlation was noted between diabetic glucose tolerance abnormality and cerebral infarction in autopsy cases also.³⁵ In the present study both cerebral hemorrhage and cerebral infarction tended to be frequent in cases of diabetes.

Many studies have found a significant correlation between ECG abnormalities and development of cerebrovascular diseases.^{6,9,26} A follow-up of the Framingham Study showed that the risk of ischemic cerebral disease was 3-fold greater in those who presented QRS high voltage on ECG and the risk of cerebral infarction was as much as 9-fold higher in the group with left ventricular hypertrophy.² The Hisayama-cho Study also found a high incidence of cerebral infarction among study subjects applicable to any one or more of the Minnesota codes I, III, IV 1-3.⁶ In the present study the risk of cerebral hemorrhage and cerebral infarction was high in the group with left ventricular hypertrophy (QRS high voltage + ST depression).

The decreased incidence of cerebrovascular diseases, especially the remarkable decrease of cerebral hemorrhage, is not to be interpreted merely as the result of hypertension control by the widespread use of hypotensors, for there is, of course, also the effect of improvement of the living environment.⁸ In any case, although many risk factors of cerebrovascular diseases are closely interrelated, almost all of them except aging, namely, high blood pressure, left ventricular hypertrophy on ECG, diabetes, serum cholesterol, and obesity are controllable, so that incidence and mortality of cerebrovascular diseases can be expected to decrease further as the risk factors of cerebrovascular diseases are controlled by improvement of living environment factors such

も Ni-Hon-San Study で同様の報告をしている。

病院例において糖尿病患者に脳血管疾患の多発についての報告は多いが、脳血管疾患患者の耐糖能低下についてはまだ定説がない。³⁴ Framingham Study では、血糖測定で血糖値 120mg/100ml 以上の群で 5 倍の脳血管疾患の発症を認め、特に女性においては 110—119mg/100ml の群においても、有意に脳血管疾患の発症の危険性を認めている。久山町の研究においても、糖尿病患者に脳血栓の発症が多く、剖検例でも糖尿病型耐糖能異常と脳梗塞との間に有意の相関を認めている。³⁵ 本調査では脳出血、脳梗塞共に糖尿病症例に多い傾向を認めた。

心電図異常と脳血管疾患の発症には有意な相関があることが、多くの調査で認められている。^{6,9,26} Framingham Study の追跡調査の結果において、心電図 QRS 高電位を呈したものに虚血性脳疾患発生の危険度が 3 倍、左室肥大を有する群では脳梗塞発生の危険度が 9 倍に達していることを報告している。² 久山町の研究でも、Minnesota Code I, III, IV 1—3 のいずれか一つまたはそれ以上に該当する者から脳梗塞が多発している。⁶ 本調査では左室肥大 (QRS 高電位 + ST 低下) のあった群に、脳出血及び脳梗塞の危険度が高くなっている。

脳血管疾患の発生率の減少、特に脳出血の顕著な減少は、単に降圧剤の使用普及による高血圧の抑制だけで理解されるものでなく、もちろんその他の生活環境の改善もこれに影響を及ぼしているようである。⁸ いずれにしても、脳血管疾患の各危険因子は相互に関連性の深いものが多いが、加齢を除き、高血圧、心電図所見左室肥大、糖尿病、血清コレステロール、肥満などはほとんど抑制が可能であるので、高血圧の抑制は無論のこと、栄養摂取の不均衡など生活環境因子の改善、糖尿病の治療など、脳血管疾患の危険因子の抑制が実施されるにつれ、脳

as balanced nutrition, treatment of diabetes, etc.,
not to mention control of high blood pressure.

血管疾患の発生率、死亡率も一層低下することが
期待される。

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