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Risk Factors and Triggers of Sudden Death in the Working Generation: An Autopsy Proven Case-Control Study

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Department of Internal Medicine, [1]Preventive Medicine and Public Health, and [2]Legal Medicine, Kitasato University School of Medicine, Sagamihara 228-8555, and [3]Department of Public Health, Niigata University School of Medicine, Niigata 951-8510

Owada, M., Aizawa, Y., Kurihara, K., Tanabe, N., Aizaki, T. and Izumi, T. *Risk Factors and Triggers of Sudden Death in the Working Generation: An Autopsy Proven Case-Control Study.* Tohoku J. Exp. Med., 1999, **189** (4), 245-258 —— In Japan, studies on the risk factors of sudden death in the working generation have been rarely carried out, especially among extremely rare cases of causative disease. Thus, the present study aimed to identify the risk factors and triggers of sudden death in cases whose causes of death were definitely proven by autopsy. We investigated the legal medical records for four years from May 1994 to February 1998. Out of 271 cases, 176 patients 20 to 59 years were enrolled as cases of sudden death in the working generation. Among these, 91 cases, 52%, could be analyzed by telephone interviews from close family members. Only one examiner undertook all phone questions to the case subjects. As control subjects, 1167 persons who consulted us for a health check were employed. Of the sudden death cases, the final diagnosis in 29 cases was coronary artery disease (31.9%), 18, acute cardiac dysfunction (19.8%), 6, other cardiac diseases (6.6%), 4, acute aortic dissection (4.4%), 4, cerebrovascular disease (4.4%) and 30, other diseases (32.9%). Through conditional logistic analysis, the following risk factors emerged as candidates: Long-term stress, history of heart disease, hypertension, chest symptoms, autonomic disturbance, short-term stress and a smoking habit. Short-term stress, autonomic disturbance and a smoking habit increased the risk of sudden death due to coronary artery disease. Long-term stress was associated with an increased risk of sudden death due to acute cardiac dysfunction. It was also demonstrated that autonomic disturbance and stress were closely related to the occurrence of sudden death. Therefore, to prevent sudden death, it would be helpful to identify subjective symptoms to relieve such stress in some way. ———— sudden death; autopsy study; working people; risk factor

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Sudden death is one of the most serious social, economic and medical problems in developed countries. Obviously, sudden death of the members of the working generation is an extremely great loss for their families and also the communities surrounding them. How to protect mankind from sudden death is an essential issue facing sophisticated investigators, and how to detect preventive measures is an urgent task for all mankind.

The incidence of sudden death in developed countries is reported to be 1.5–2.5/1000 person-years (Kannel et al. 1975; Schatzkin et al. 1984). In Japan, sudden death within 24 hours after the onset of acute symptoms in the southern area of Okinawa Prefecture was 0.37/1000 person-years (Tokashiki et al. 1999). According to the cohort study in Hisayama, it was 0.89/1000 person-years and the incidence limited to sudden cardiac death due to coronary artery disease (CAD) within one hour after the onset of acute symptoms was 0.08–0.21/1000 person-years (Hasuo 1987). This incidence is about one tenth of that reported by the Albany-Framingham study based on a similar definition. As to underlying diseases for sudden death, cardiac disease accounted for more than 60% and the risk factors directly reflected those of CAD, namely hypertension, hypercholesterolemia, diabetes mellitus, a smoking habit and familial disposition (Escobedo and Zack 1996; Escobedo and Caspersen 1997). The risk factors and triggers of sudden death were different for each causative disease. The final diagnosis should be made by autopsy. However, in Japan, it has been difficult to gain permission for autopsy from the bereaved families, and thus it has been hard to identify the causative disease underlying sudden death. Mostly these situations are derived either from religious and/or cultural reasons. Accordingly, epidemiological analysis based on the autopsy proven diagnosis has been rarely reported.

The Department of Legal Medicine, Kitasato University School of Medicine examined 893 deaths in Sagamihara City with a population of about 590 000 for 3 years and 9 months. Among these, autopsy studies were carried out in 643 cases. This situation with a high autopsy rate of 72% provided a good opportunity to investigate risk factors and triggers of sudden death. In this study, our interest was directed only to sudden death occurring in the working generation.

Subjects and Methods

Subjects

We defined sudden death as "the natural death occurring within at least 24 hours after the onset of acute symptoms," a definition proposed by the sudden death project team of the Ministry of Health and Welfare in Japan (Konishi 1993). Among the 893 cases of sudden death, who were examined in the Department of Legal Medicine from May 1994 to February 1998, 271 cases belonged to patients 20–59 years of age. An autopsy was performed in 232 cases, 85.6%. Out of these, we selected 176 cases whose data prior to death was obtainable. Finally,

among these 176 cases, 91 persons, 51.7%, could be investigated, because the close family members collaborated with our proposal and gave permission for a phone interview.

As to the control group, 1167 persons who consulted us for a health check organization in Niigata City from April 1995 to March 1996, were employed. Among these, we selected 958 healthy people 20–59 years of age.

Method of investigation

For the sudden death group, we mailed questionnaires to the closest family members of each case, and the selected collaborators were interviewed by telephone. Only one examiner undertook all phone questions to the case subjects. The reply rate reached up to 51.7%. The respondents consisted of husbands or wives, 46.1%, parents or children, 35.2%, grandparents, brothers or sisters, 16.5%, nieces or nephews, 1.1% and others/fathers-in-law, 1.1%. For the control group, we obtained the consent of subjects when they had a health check, and later after that we phoned them for an interview. In order to prevent the inquiry from being biased, two-trained interviewers under our guidance administered the questionnaire. We referred to previous study to prepare the format of questionnaire (Tanabe et al. 1996).

Statistical analysis

Analysis was performed using SAS analytical application, utilizing conditional logistic regression analysis. For sex and age, we adjusted the analysis stratifying the subjects into age groups in increments of 10 years. For comparison between groups, we used a χ^2 or t-test. If any significant difference was observed in the χ^2-test, we performed Pearson residual analysis to calculate a Pearson-R value for each item.

Determination of the causes of death

The main causes of death were identified only by pathologic findings. We examined the legal medical records provided by the Department of Legal Medicine, which issued the death certificate, and we adopted the description of direct causes of death according to International Classification of Diseases (ICD) 10th version of WHO. If such direct causes of death did not indicate causative diseases, we adopted those in the following list. From the results of autopsy, we classified the diagnosis into the following 7 categories. (1) CAD, which was divided into 2 subcategories. One was acute myocardial infarction having obvious thrombus in a coronary artery or grossly obvious acute infarcted focus in the cardiac muscle tissue. Another was heart failure due to CAD, which was accompanied by obvious coronary arteriosclerosis (with 75% or larger stenosis in the cross section of the stricture's area of at least two branches) or by an old myocardial infarction with pulmonary congestion. (2) Acute cardiac dysfunc-

tion, classified as other sudden death of an unknown cause (R96) by ICD 10th, was diagnosed when no obvious organic lesions contributed to death in whole organs including the heart even after the autopsy. (3) Other cardiac diseases including cardiomyopathy, myocarditis, valvular disease and cardiovascular anomaly, etc. (4) Acute aortic dissection. (5) Cerebrovascular disease, which was divided into cerebral hemorrhage and subarachnoid hemorrhage. (6) Other diseases including gastrointestinal disease, respiratory disease, hepatic disease and others.

Definition of variables

We defined autonomic disturbance as dizziness, habitual diarrhea or constipation, abnormal sweating or flushing. A history of heart disease, diabetes mellitus or hypercholesterolemia was inquired into. We defined chest symptoms as any subjective symptoms of chest pain, chest oppression or chest discomfort within one month before onset. Stress was categorized into two groups according to their duration. Short-term stress was defined as subjective stress like mental fatigue or deep trouble within one week before onset. Long-term stress was defined as chronic and continuous stress occurring more than one week previous to onset. Occasional stress or no subjective stress was classified as negative. We classified smoking habit into two groups: A group of regular smokers and the other group being occasional, former or non-smokers. For drinking, we classified into a group of regular drinkers and that of light, social, or non-drinkers.

Results

Causes of deaths

The causes of sudden deaths included 29 cases of coronary artery disease (31.9%), 18 of acute cardiac dysfunction (19.8%), 6 of other cardiac diseases (6.6%), 4 of acute aortic dissection (4.4%), 4 of cerebrovascular disease (4.4%) and 30 other diseases (32.9%). Among 29 cases of CAD, there were 13 cases of acute myocardial infarction, being 14.3% of the total. The remaining 16 cases died from heart failure due to CAD. The cases of cerebrovascular disease included 2 cases of cerebral hemorrhage and 2 of subarachnoid hemorrhage. Other diseases included liver failure or esophageal varix rupture due to liver cirrhosis, upper gastrointestinal hemorrhage, aspiration pneumonia, bronchial asthma, acute pancreatitis and others. There was no obvious sex difference in causes of death (Table 1).

Sex and age

For all cases of sudden death, the ratio of male to female was 77/14 (5.5). The average $\pm$ S.D. of age at onset was 45 ± 11 years for male and 40 ± 14 years for female, without significant difference. Age and sex distribution of sudden death and the control group is shown in Table 2. For all sudden death cases, including nonautopsied cases, Table 3 shows age and sex distribution.

TABLE 1. *Causes of death by sex*

Diagnosis	Subcategory	Male (%)	Female (%)	Total (%)
Coronary artery disease	Acute myocardial infarction	13 (16.9)	0 (0.0)	13 (14.3)
	Heart failure	13 (16.9)	3 (21.4)	16 (17.6)
Acute cardiac dysfunction		15 (19.5)	3 (21.4)	18 (19.8)
Other cardiac diseases		5 (6.5)	1 (7.1)	6 (6.6)
Acute aortic dissection		3 (3.9)	1 (7.1)	4 (4.4)
Cerebrovascular disease	Cerebral hemorrhage	2 (2.6)	0 (0.0)	2 (2.2)
	Subarachnoid hemorrhage	1 (1.3)	1 (7.1)	2 (2.2)
Other diseases		25 (32.4)	5 (35.9)	30 (32.9)
Total		77 (100.0)	14 (100.0)	91 (100.0)

TABLE 2. *Age and sex distribution of sudden death group compared with control subjects*

Age group (years)	Sudden death group			Control group		
	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)
20–29	6 (7.8)	5 (35.7)	11 (12.1)	27 (5.0)	34 (5.0)	61 (6.4)
30–39	16 (20.8)	1 (7.2)	17 (18.7)	58 (10.7)	85 (20.5)	143 (14.9)
40–49	24 (31.2)	3 (21.4)	27 (29.7)	196 (36.1)	146 (35.2)	342 (35.7)
50–59	31 (40.2)	5 (35.7)	36 (39.5)	262 (48.2)	150 (36.1)	412 (43.0)
Total	77 (100.0)	14 (100.0)	91 (100.0)	543 (100.0)	415 (100.0)	958 (100.0)

The subjects were only autopsied cases and control subjects aged from 20 to 59.

TABLE 3. *Age and sex distribution of all sudden death cases including non-autopsied case*

Age groups (years)	Male (%)	Female (%)	Total (%)
0–9	21 (3.6)	14 (4.5)	35 (3.9)
10–19	5 (0.9)	3 (1.0)	8 (0.9)
20–29	10 (1.7)	12 (3.8)	22 (2.5)
30–39	35 (6.1)	5 (1.6)	40 (4.5)
40–49	52 (9.0)	16 (5.1)	68 (7.6)
50–59	117 (20.3)	24 (7.6)	141 (15.8)
60–69	140 (24.3)	55 (17.5)	195 (21.9)
70–79	122 (21.1)	82 (26.1)	204 (23.0)
80–89	69 (12.0)	89 (28.4)	158 (17.7)
90–99	6 (1.0)	13 (4.1)	19 (2.1)
100–	0 (0.0)	1 (0.3)	1 (0.1)
Total	577 (100.0)	314 (100.0)	891 (100.0)

The subjects were the total of sudden death cases from May, 1994 to February, 1998, including non-autopsied cases.

TABLE 4. *Characteristics of sudden death cases compared with control subjects*

Category	Sudden death group Mean ± S.D.	Control group Mean ± S.D.	p-value
Body mass index male	22.4±4.43 (n=65)	23.2±2.79 (n=662)	n.s.
female	20.6±2.23 (n=12)	22.1±2.87 (n=504)	n.s.
Smoking consumption[a,b]	22.4±11.4 (n=56)	23.7±12.20 (n=365)	n.s.
Alcohol consumption[a,c]	2.96±2.18 (n=38)	1.59±0.91 (n=502)	$p<0.001$

n.s., not significant. [a]male and female combined. [b]cigarretes/day. [c]unit of 180 ml of sake (Japanese wine); parenthesis represents number of subjects.

Characteristics of the two groups

Comparing averages between the sudden death and control groups, there was no significant difference in body mass index in either male or female as shown in Table 4. The number of cigarettes for regular smokers of two groups was not significantly different. However, comparing the average daily total alcohol consumption depicted as amount of 180 ml of sake for regular drinkers, drinking quantity in the sudden death group was significantly greater than that in the control group ($p<0.001$).

Occupations

As shown in Table 5, there was a significant difference in composition of occupations between sudden death and control groups ($p<0.001$). Pearson residual analysis indicated that the proportion of office workers in the sudden death group was less than that of the controls, while those of workers in manufacture, construction, transportation and tele communication industries, manual workers, unemployed people and housewives were higher than the controls.

Background factors

Twenty-two percent of the sudden death group was living alone, while only 6.3% of the control group was ($p<0.001$). Regarding condition of usual life, 8.8% of the sudden death group cases were "sometimes ill in bed," while everyone in the control group spent a normal life ($p<0.001$). Eighty-four percent of the control group regularly had a health check, compared to 52% of the sudden death group ($p<0.001$). As to consultation with medical doctors within one year, 70.3% of the sudden death group cases had consulted with them compared with 54.6% of the control group ($p<0.001$). There were no hospitalized nor bedridden cases in either group (Table 6).

TABLE 5. *Type of occupation*

Category	Sudden death group (%)	Control group (%)	Total
Office work	9(10.7)	230(24.0)	239
Agriculture, forestry and marine products industry	1(1.2)	22(2.3)	23
Manufacture and construction industry and manual work	23(27.3)	116(12.1)	139
Transportation and telecommunication industry	6(7.1)	23(2.4)	29
Sales	5(6.0)	107(11.2)	112
Service industry	10(12.0)	97(10.1)	107
Professional occupation or engineering	4(4.8)	102(10.7)	106
Police	2(2.4)	24(2.5)	26
Administration	7(8.3)	146(15.2)	153
Unemployed or housewives	17(20.2)	91(9.5)	108
Total	84(100.0)	958(100.0)	1042

TABLE 6. *Characteristics of background factors in sudden death compared with control subjects*

Variables	Categories	Sudden death group (%)	Control group (%)	p-value
Living alone	Yes	20(22.0)	65(6.3)	
	No	71(78.0)	893(93.6)	$p<0.001$
Condition of life	Normal	83(91.2)	958(100.0)	
	Sometimes ill in bed	8(8.8)	0(0)	$p<0.001$
Health check	Regular	47(51.6)	809(84.4)	
	Others	38(41.8)	146(15.3)	$p<0.001$
	Unknown	6(6.6)	3(0.3)	
Visit to physician within 1 year	Yes	64(70.3)	523(54.6)	
	No	25(27.5)	430(44.9)	$p<0.001$
	Unknown	2(2.2)	5(0.5)	

Risk factors and triggers

Conditional logistic analysis adjusted by sex, age and multiple factors revealed that, long-term stress (odds ratio, 95% confidence interval; 3.02, 1.55-5.88), history of heart disease (2.71, 1.39-5.28), hypertension (2.40, 1.30-4.45), chest symptoms within one month (2.17, 1.14-4.14), autonomic disturbance (2.12, 1.18-3.79), short-term stress (1.90, 1.03-3.52) and a smoking habit (1.90, 1.06-3.41) were positively associated with an increased risk of sudden death of all causes (Table 7). Further, adjusted for profession, a similar trend was observed and

TABLE 7. *Risk factor for the sudden deaths compared with control subjects*

Variable	Odds ratio (95%CI)[a]	Odds ratio (95%CI)[b]
Hypertension	2.40 (1.30–4.45) **	1.80 (0.89–3.65)
Diabetes mellitus	1.65 (0.63–4.36)	1.20 (0.37–3.87)
Hypercholesterolemia	0.55 (0.25–1.20)	0.70 (0.30–1.64)
Heart disease	2.71 (1.39–5.28) **	2.25 (1.04–4.85) *
Chest symptoms	2.17 (1.14–4.14) *	2.33 (1.16–4.71) *
Autonomic disturbance	2.12 (1.18–3.79) *	2.12 (1.13–3.99) *
Short-term stress	1.90 (1.03–3.52) *	1.78 (0.90–3.50)
Smoking	1.90 (1.06–3.41) *	1.91 (1.02–3.59) *
Drinking	0.81 (0.46–1.44)	0.70 (0.37–1.30)
Long-term stress	3.02 (1.55–5.88) **	2.63 (1.30–5.35) **

CI, confidential interval; $n=60$, for sudden death; $n=913$, for controls.

[a]Multivariate adjusted for age, sex, and the above risk factors using the conditional logistic regression model.

[b]Multivariate adjusted for age, sex, the above risk factors and occupation using the conditional logistic regression model.

$^{*}p<0.05$. $^{**}p<0.01$.

TABLE 8. *Odds ratio for coronary artery disease and acute cardiac dysfunction*

Variable	Coronary artery disease		Acute cardiac dysfunction	
	Odds Ratio (95%CI)[a]	Odds Ratio (95%CI)[b]	Odds Ratio (95%CI)[a]	Odds Ratio (95%CI)[b]
Long-term stress	0.44 (0.06– 3.45)	0.64 (0.08– 5.15)	6.42 (1.00–41.20)	8.68 (0.55–135.94)
Smoking habit	3.52 (1.17 10.57) *	4.64 (1.44–14.96) *	1.26 (0.29– 5.54)	1.13 (0.14– 9.16)
Short-term stress	5.97 (2.41–14.76) ***	5.20 (2.00–13.54) ***	0.27 (0.03– 2.66)	0.37 (0.03– 5.20)
Autonomic disturbance	3.57 (1.43– 8.94) **	3.99 (1.49–10.68) **	2.34 (0.60– 9.19)	3.76 (0.56– 25.33)

CI, confidential interval.

[a]odds ratio adjusted for age, sex and the above risk factors.

[b]odds ratio adjusted for age, sex, occupation and the above risk factors.

$^{*}p<0.05$. $^{**}p<0.01$. $^{***}p<0.001$.

strong association of sudden death with long-term stress, history of heart disease, chest symptoms, autonomic disturbance and a smoking habit was found. However these odds ratios were slightly lower than the former.

We selected significant risk factors including long and short-term stress, a

smoking habit and autonomic disturbance, and made another model for CAD and acute cardiac dysfunction (Table 8). Short-term stress (odds ratio, 95% confidence interval; 5.97, 2.41-14.76), autonomic disturbance (3.57, 1.43-8.94) and a smoking habit (3.52, 1.17-10.53) increased the risk of sudden death due to CAD. Further adjustment for occupation in this trend did not change the significance, and the influence of a smoking habit was augmented. Long-term stress tended to increase the risk of sudden death due to acute cardiac dysfunction (6.42, 1.10-41.20). Even after job adjustment, association with long-term stress appeared strong, though not significant.

Discussion

In the developed countries in Europe and North America, cardiac death accounts for 60-80% of all sudden death (Reichenbach et al. 1977; El Fawal et al. 1987; Fornes et al. 1993). In the Hisayama study, the most frequent cause of sudden death was cerebrovascular disease, about 51.1% of total and second was cardiac disease about 37.8% (Hasuo 1987). In the present study, sudden cardiac death was 58.3% of the total causes of sudden death, as shown in Table 1, which was higher than any previous reports from Japan and similar to those of the developed countries. In our study, we excluded patients who were older than 60 years old, and our autopsy rate was extremely high. These were reasons for the increased rate of cardiac death.

It is well known that risk factors of CAD are most common to those of sudden death. Particularly, a smoking habit, hypertension, hypercholesterolemia and a history of ischemic heart disease were stated to also be predictive for sudden death by representative prospective works (Cupples et al. 1992; Wannamethee et al. 1995; Jouven et al. 1999). The present study also indicated high odds ratios for the following factors: A history of heart disease, hypertension and a smoking habit. This was because cardiac disease reached up to 60% of the total causes of sudden death, and therefore the risk factors of cardiac disease had a strong influence on those of all sudden death.

A smoking habit provided a significantly high odds ratio for sudden death of all causes and also CAD. This finding indicates a smoking habit provokes sudden death. As an acute effect, nicotine, one of 4000 or more toxic components in smoke, accelerates the release of catecholamine from the sympathetic nerve endings. The release enhances blood pressure and heart rate (Folts et al. 1990). Nicotine also has a chronic effect on lipid metabolism in accelerating arteriosclerosis (Winniford 1990). This acceleration may also induce ventricular arrhythmia leading to cardiac arrest (Hallstrom et al. 1986). Burke et al. (1997, 1998) emphasized that, among sudden death cases, cigarette smoking was predisposed to acute thrombosis. Abnormal serum cholesterol concentrations, particularly elevated ratios of total cholesterol to high density lipoprotein cholesterol, led to rupture of vulnerable plaque. In addition, a smoking habit reduces blood flow

within gastric mucosa, and caused gastric ulceration. Therefore, a smoking habit was nominated as a representative risk factor of sudden death not only in cardiac diseases but also in other underlying illnesses.

On the other hand, no obvious difference could be detected for a habit of drinking in this study. The group who regularly drink seemed to be protected from sudden death in comparison with the group who occasionally drink. However, the amount of daily alcohol consumption in the sudden death group tended to exceed that of the control. This finding may support that moderate alcohol intake is probably associated with risk reduction of sudden death, while heavy intake accelerates it. Recently, it has been emphasized that moderate alcohol intake has a protective effect for ischemic heart diseases and cerebrovascular diseases (Kitamura et al. 1998; Muntwyler et al. 1998). Hypothetically, moderate intake increases coronary blood flow due to vasodilatation, and decreases systemic vascular resistance. Therefore, it is understood that moderate alcohol intake can contribute to reducing the risk of sudden death. Besides, drinking is apt to bring about mental relaxation. This effect also seems to decrease negative loading on the subjects, and to result in protection against sudden death.

The present study showed that the effects of stress and autonomic disturbance might lead to sudden death. Middlekauff et al. (1997) tested stress loading on patients with advanced heart failure compared with healthy persons. In their report, acute mental stress significantly increased muscle sympathetic nerve activity, heart rate and blood pressure. Especially, patients with advanced heart failure showed high sympathetic activity even in the resting state. They had higher activity during mental stress testing than in healthy persons, although the responses of muscle sympathetic nerve activity tended to be blunted in patients with heart failure. Under chronic sleep deprivation, healthy male volunteers showed a significant decrease of erythrocyte magnesium as well as an increase of both thromboxane B2 and thromboxane B2/6-keto-prostaglandin F1α ratios, as described by Tanabe et al. (1997). These findings support the hypothesis that acute coronary syndrome derived from arterial vasospasm may occur in chronic sleep deprivation. Whether acute or chronic, stress loading on subjects seems to have a great influence on hemodynamics either through the autonomic nervous system and/or vasoactive substances. In this study, long-term and short-term stress increased the risk of the sudden death. Especially, long-term stress was stronger than short-term, taking into account such factors as hypertension and a previous history of heart disease. In cases of acute cardiac dysfunction, the odds ratio of long-term stress was markedly high, while, in coronary artery disease, autonomic disturbance, a smoking habit and short-term stress showed a close association with sudden death. These results showed that, for acute cardiac dysfunction, long-term stress might accelerate sympathetic nerve activity. These conditions can develop the substrate, which facilitates induced lethal arrhythmia. For coronary artery disease, short-term stress as a trigger can increase enough

blood pressure and heart rate to provoke abrupt rupture of coronary artery plaque.

There have been few reports which have stressed the close link between autonomic disturbance and sudden death. In a case-control study performed by Tanabe et al. (1996), there were significantly high rates of autonomic disturbances within one week before the onset of sudden death. The authors concluded that these manifestations are predictive factors of prodrome symptoms of sudden death. The Autonomic Tone and Reflexes After Myocardial Infarction study was a multicenter international prospective study on prognostic factors following acute myocardial infarction. They reported that both low values of heart rate variability and baroreflex sensitivity as autonomic markers are independent predictive factors of cardiac death. These proposals indicate a close link between autonomic imbalance and cardiac death (La Rovere et al. 1998). How autonomic imbalance emerges as a subjective symptom has not yet been resolved. However, it is certain that several symptoms including subjective complaints precede sudden death. Therefore it seems necessary to identify such prodrome symptoms in order to prevent sudden death.

In this investigation, diabetes mellitus and hypercholesterolemia did not show significant odds ratios for sudden death. No definite relationship between these diseases and sudden death has been discovered.

There was an obvious difference in job distribution between sudden death and the control group. Karasek (Karasek et al. 1988; Karasek 1989) proposed the psychosocial job strain model for evaluation of stress due to occupation. This model assumes that a higher psychological demand of work and lower decision latitude creates higher job strains. In this model, assemblers, freight handlers and waiters were regarded as higher strain jobs. LaCroix (1984) found that men and women exhibited 1.5 and 1.4 times the risk of coronary heart disease respectively, when employed in high strain jobs compared to low strain jobs. In our investigation, the rates of workers in manufacture, construction, transportation and telecommunication industries and manual workers in the sudden death group were higher than those of the control group. These workers were regarded as high strain workers. High job strain may produce mental stress as well as a higher consumption of tobacco. In the sudden death group, the proportion of unemployed people and housewives were also high. In order to conclude the association between profession and sudden death, environmental factors and other risk factors should be thoroughly investigated and it seems necessary to further investigate this problem by using appropriate control subjects.

The sudden death group consulted for a health check less frequently than the control group in this study. The sudden death group paid less attention to their health in their daily lives. The living-alone rate of sudden death group was 22%, higher than that of the control group of 6%, suggesting their irregular daily lives including meals. Concern about such a lifestyle in daily life as well as control over one's own health may influence the occurrence of sudden death. The rate of

consulting with medical institutes within one year was 55% for the control group, while that for the sudden death group was 70%, being significantly higher. In the sudden death group, many people may have complained of some physical disorders within one year. Therefore, careful treatment seems to be necessary for potential sudden death cases of higher risk as well as other risk factors.

Finally, we would like to discuss some of the limitations of this study. In this investigation, certain examinees for health check lived in Niigata City were employed as the control group. Niigata City is an urban city having a similar population to Sagamihara City. Because of its location, the climate and lifestyle are different from that in Sagamihara area where the sudden death cases were obtained. They may be more conscious of health, have a reserve of economic power and possibly good health. Interviews were directly performed on the control subjects, while there was a time lapse in contacting family members in the sudden death group. Thus, a recall bias may exist between them.

Sudden death may occur by intricate combinations of various factors. In our study, intrinsic factors such as underlying diseases as well as personality and extrinsic factors including workplace, long-term stress and lifestyle consolidated the foundation of sudden death. Sudden death may occur when short-term stress as a trigger is added to these conditions. Therefore, to prevent sudden death it is necessary to identify the subjective symptoms which lead to such stress.

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