表４　血糖値と生涯医療費の関連

【男性】高血糖

年齢	平均余命		生涯医療費		生涯医療費／平均余命
（歳）	（年）	95%信頼区間	（千円）	95%信頼区間	（千円／年）
40	43.88	(41.51-46.26)	15,589	(13,603-17,575)	355.2
45	38.89	(36.51-41.26)	15,000	(13,092-16,908)	385.8
50	34.73	(32.97-36.49)	14,416	(12,587-16,244)	415.1
55	30.27	(28.82-31.71)	13,889	(12,101-15,677)	458.9
60	25.83	(24.58-27.07)	13,113	(11,362-14,864)	507.7
65	21.38	(20.24-22.53)	11,825	(10,104-13,546)	553.0
70	17.73	(16.69-18.78)	10,678	(8,920-12,437)	602.2
75	13.99	(13.01-14.98)	8,910	(7,074-10,746)	636.7
80	11.24	(10.39-12.08)	7,006	(4,957- 9,056)	623.6
85	8.26	(3.88-12.64)	5,139	(2,144- 8,133)	622.2

正常血糖

年齢	平均余命		生涯医療費		生涯医療費／平均余命
（歳）	（年）	95%信頼区間	（千円）	95%信頼区間	（千円／年）
40	45.95	(45.26-46.64)	14,760	(13,993-15,527)	321.2
45	41.13	(40.53-41.73)	14,409	(13,653-15,165)	350.3
50	36.50	(35.96-37.03)	14,033	(13,284-14,783)	384.5
55	31.91	(31.42-32.40)	13,560	(12,815-14,305)	424.9
60	27.24	(26.78-27.70)	12,844	(12,103-13,585)	471.6
65	22.83	(22.41-23.26)	12,044	(11,299-12,789)	527.5
70	18.61	(18.21-19.01)	10,996	(10,239-11,754)	590.9
75	14.75	(14.37-15.13)	9,509	(8,718-10,299)	644.6
80	11.56	(11.22-11.90)	7,895	(7,020- 8,769)	682.9
85	8.94	(7.12-10.76)	6,353	(4,873- 7,833)	710.5

【女性】高血糖

年齢	平均余命		生涯医療費		生涯医療費／平均余命
（歳）	（年）	95%信頼区間	（千円）	95%信頼区間	（千円／年）
40	58.10	(55.95-60.26)	22,904	(18,722-27,086)	394.2
45	53.10	(50.97-55.24)	22,646	(18,471-26,822)	426.5
50	48.10	(45.97-50.24)	21,853	(17,694-26,013)	454.3
55	43.10	(40.97-45.24)	20,744	(16,612-24,875)	481.3
60	38.10	(35.97-40.24)	19,534	(15,421-23,647)	512.7
65	34.45	(32.58-36.31)	18,920	(14,695-23,144)	549.3
70	30.08	(28.29-31.88)	17,476	(13,201-21,752)	580.9
75	26.46	(24.77-28.15)	16,049	(11,592-20,506)	606.5
80	23.79	(22.41-25.17)	14,481	(9,668-19,294)	608.6
85	20.74	(0.91-40.57)	12,754	(1,240-24,267)	614.9

正常血糖

年齢	平均余命		生涯医療費		生涯医療費／平均余命
（歳）	（年）	95%信頼区間	（千円）	95%信頼区間	（千円／年）
40	57.25	(56.73-57.76)	18,055	(16,806-19,303)	315.4
45	52.25	(51.73-52.76)	17,638	(16,392-18,884)	337.6
50	47.32	(46.82-47.82)	17,124	(15,880-18,367)	361.9
55	42.49	(42.02-42.96)	16,521	(15,276-17,766)	388.8
60	37.80	(37.36-38.25)	15,793	(14,543-17,044)	417.8
65	33.26	(32.85-33.68)	14,908	(13,645-16,172)	448.2
70	28.62	(28.22-29.03)	13,736	(12,461-15,011)	479.9
75	24.39	(24.01-24.77)	12,204	(10,896-13,511)	500.3
80	20.30	(19.96-20.64)	10,479	(9,126-11,832)	516.3
85	16.67	(12.10-21.25)	8,860	(6,293-11,426)	531.3

高血糖：随時血糖140mg/dL以上
正常血糖：随時血糖140mg/dL未満

表５　脂質異常と生涯医療費の関連

【男性】脂質異常

年齢	平均余命		生涯医療費		生涯医療費／平均余命
（歳）	（年）	95%信頼区間	（千円）	95%信頼区間	（千円／年）
40	43.82	(42.54-45.09)	14,740	(13,649-15,831)	336.4
45	39.20	(38.16-40.25)	14,417	(13,360-15,474)	367.8
50	34.89	(33.99-35.80)	13,985	(12,950-15,020)	400.8
55	30.70	(29.92-31.47)	13,539	(12,522-14,557)	441.1
60	26.20	(25.49-26.91)	12,796	(11,788-13,803)	488.4
65	21.93	(21.28-22.57)	11,893	(10,885-12,902)	542.4
70	17.76	(17.15-18.36)	10,681	(9,662-11,699)	601.5
75	13.99	(13.43-14.55)	8,981	(7,929-10,032)	641.9
80	10.74	(10.25-11.23)	6,874	(5,739- 8,010)	640.3
85	7.64	(5.24-10.03)	4,877	(3,159- 6,595)	638.6

脂質正常

年齢	平均余命		生涯医療費		生涯医療費／平均余命
（歳）	（年）	95%信頼区間	（千円）	95%信頼区間	（千円／年）
40	46.56	(45.97-47.16)	14,583	(13,811-15,356)	313.2
45	41.56	(40.97-42.16)	14,211	(13,443-14,979)	341.9
50	36.76	(36.21-37.32)	13,851	(13,087-14,616)	376.8
55	32.12	(31.62-32.63)	13,383	(12,621-14,144)	416.6
60	27.44	(26.97-27.91)	12,681	(11,925-13,437)	462.1
65	22.94	(22.50-23.38)	11,830	(11,073-12,588)	515.7
70	18.78	(18.37-19.19)	10,832	(10,060-11,604)	576.7
75	14.91	(14.52-15.30)	9,397	(8,591-10,203)	630.2
80	11.64	(11.29-11.99)	7,866	(6,978- 8,754)	675.9
85	9.08	(7.19-10.97)	6,394	(4,877- 7,911)	704.0

【女性】脂質異常

年齢	平均余命		生涯医療費		生涯医療費／平均余命
（歳）	（年）	95%信頼区間	（千円）	95%信頼区間	（千円／年）
40	67.43	(66.03-68.83)	24,251	(19,999-28,502)	359.7
45	62.43	(61.03-63.83)	23,910	(19,660-28,160)	383.0
50	57.43	(56.03-58.83)	23,271	(19,026-27,517)	405.2
55	52.71	(51.41-54.01)	22,609	(18,351-26,867)	429.0
60	48.14	(46.93-49.35)	21,862	(17,577-26,147)	454.1
65	44.03	(42.90-45.16)	21,015	(16,653-25,377)	477.3
70	39.43	(38.33-40.54)	19,762	(15,362-24,162)	501.2
75	35.65	(34.61-36.68)	18,342	(13,808-22,877)	514.6
80	32.51	(31.70-33.31)	16,969	(12,198-21,740)	522.0
85	28.69	(6.14-51.25)	15,436	(3,456-27,416)	538.0

脂質正常

年齢	平均余命		生涯医療費		生涯医療費／平均余命
（歳）	（年）	95%信頼区間	（千円）	95%信頼区間	（千円／年）
40	55.64	(55.15-56.14)	17,455	(16,345-18,564)	313.7
45	50.64	(50.15-51.14)	17,031	(15,925-18,138)	336.3
50	45.71	(45.23-46.18)	16,506	(15,403-17,608)	361.1
55	40.91	(40.46-41.36)	15,918	(14,814-17,021)	389.1
60	36.17	(35.75-36.60)	15,199	(14,091-16,306)	420.1
65	31.64	(31.24-32.03)	14,340	(13,221-15,459)	453.3
70	27.02	(26.64-27.40)	13,202	(12,072-14,332)	488.6
75	22.77	(22.41-23.13)	11,708	(10,549-12,867)	514.2
80	18.66	(18.34-18.99)	9,967	(8,767-11,168)	534.0
85	15.10	(11.35-18.86)	8,331	(6,128-10,534)	551.7

脂質異常あり：随時中性脂肪200mg/dL以上またはHDLコレステロール40mg/dL未満
脂質異常なし：随時中性脂肪200mg/dL未満かつHDLコレステロール40mg/dL以上

し、女性の高血圧を除けば危険因子のない群で生涯医療費が低いことを示した。しかも男性では、危険因子のない群の方が平均余命は長いのに、生涯医療費は低額であった。

本研究の対象者は、大崎国保コホート対象者でアンケート調査の翌年に基本健康診査を受診した者である。健診受診者は健診非受診者と比較して、①少なくとも翌年の健診を受診できるほどは健康であること、②健診を受診するような者は健康意識が高く、他の生活習慣も健康的であること、③健診を通じた生活習慣の変容や医療介入が行われること、等の理由から平均余命が長くなることが推測された。実際、男性で約6年、女性で約9.5年、40歳の平均余命が長くなった。平均余命1年あたりの医療費は男女とも健診非受診者で健診受診者よりも高かったが、平均余命が長いことを反映して生涯医療費は健診受診者で健診非受診者よりも高かった。

男性では、全ての危険因子で危険因子保有群の方が危険因子非保有群よりも 40 歳の平均余命が長かった。一方、平均余命1年あたりの医療費は危険因子保有群で高かった。結果としての生涯医療費は、危険因子保有群の方で平均余命が短いにも関わらず、むしろ高額になっていた。すなわち高血圧・高血糖・脂質異常の予防及び適切な管理が平均余命の延伸のみならず生涯医療費の低減にも貢献する可能性が示唆された。

女性においても男性と同様、平均余命1年あたりの医療費が危険因子保有群で危険因子非保有群と比べて高かった。しかし血圧については血圧正常群で高血圧群に比べて 40 歳時の平均余命が 12 年以上も長いため、生涯医療費はむしろ血圧が低い群で高額であった。高血糖については平均余命に差がなかったため高血糖者で生涯医療費が高額であった。脂質異常に関しては、むしろ脂質異常のある者で平均余命が長く、生涯医療費も高かった。脂質異常のある者で平均余命が長いということは、死亡のハイリスクである高齢期の脂質低値者が脂質正常群に含まれていることが原因となっているのかもしれない。がんや循環器疾患の既往歴を除外しているため、これらの既往の結果としての低栄養状態を反映している可能性は高くないが、質問紙で捉えられていない消耗性疾患が背景にある可能性も否定はできない。

本研究では危険因子の健診結果のみに依存した危険因子のカテゴリ化を行った。これは、例えば血圧を考えた場合に、正常血圧群を「高齢期に至るまで未治療で正常血圧である者」というかなり特殊で理想的な集団に設定するよりも、降圧薬を用いてでも血圧を十分に管理している人を血圧正常のカテゴリに含んだ方がより現実的で実用的な情報が得られると考えたためである。

わが国においてもこれまでも高血圧や高血糖が期間医療費を増大させるという報告はなされているが、本研究は、生命表を用いることにより、高血圧、高血糖、脂質異常が生涯医療費に与える影響を検討したことが特徴であり、危険因子を管理することが平均余命を伸ばすのみならず生涯医療費をも抑制しうることを示した世界初の研究である。

研究の限界としては、高血圧・高血糖・脂質異常等を重複して持つことがあるが、それらの影響を互いに考慮することが出来なかった点である。同様に、肥満・喫煙など平均余命・医療費に影響を与える要因についても調整を行わなかった点についても限界として考えるべき点であると考える。

E．結　論

女性の高血圧を除いては、危険因子を保有している群で生涯医療費が高くなるという結果が得られた。女性において血圧が低い者ほど生涯医療費が高いことは長い平均余命（12 年以上）が影響していると考えられた。循環器疾患危険因子の予防および適切な管理が対象者の平均余命を伸ばすのみならず、生涯医療費をも

節減しうる可能性が示された。

F．健康危険情報

なし

G．研究発表

1．論文発表

なし

2．学会発表

なし

H．知的財産権の出願・登録状況

なし

Ⅳ．研究成果の刊行に関する一覧

研究成果の刊行に関する一覧

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Original Contribution

Green Tea Consumption and Hematologic Malignancies in Japan

The Ohsaki Study

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Several biologic studies have reported that green tea constituents have antitumor effects on hematologic malignancies. However, the effects in humans are uncertain. The authors used data from the Ohsaki National Health Insurance Cohort Study in Japan to evaluate the association between green tea consumption and the risk of hematologic malignancies. Study participants were 41,761 Japanese adults aged 40–79 years without a history of cancer at baseline who answered a food frequency questionnaire survey in 1994. During 9 years of follow-up beginning in 1995, the authors documented 157 hematologic malignancies, including 119 cases of lymphoid neoplasms and 36 cases of myeloid neoplasms. Hazard ratios were calculated by using the Cox proportional hazards regression model. Risk of hematologic malignancies was inversely associated with green tea consumption. The multivariate-adjusted hazard ratio of hematologic malignancies for 5 cups/day or more compared with less than 1 cup/day of green tea was 0.58 (95% confidence interval: 0.37, 0.89). The corresponding risk estimate was 0.52 (95% confidence interval: 0.31, 0.87) for lymphoid neoplasms and 0.76 (95% confidence interval: 0.32, 1.78) for myeloid neoplasms. This inverse association was consistent across sex and body mass index strata. In conclusion, green tea consumption was associated with a lower risk of hematologic malignancies.

catechin; cohort studies; hematologic neoplasms; Japan; risk; tea

Abbreviations: EGCG, (-)-epigallocatechin-3-gallate; FFQ, food frequency questionnaire; ICD-O-3, *International Classification of Diseases for Oncology*, Third Edition; NHI, National Health Insurance.

Hematologic malignancies are known to have a wide geographic distribution; incidence rates are relatively high in Western countries and low throughout Asia, including Japan and developing countries (1). According to "Global Cancer Statistics, 2002" by Parkin et al. (1), age-standardized incidence rates per 100,000 for non-Hodgkin lymphoma were higher than 10.0 for men and 6.5 for women in North America and in western, northern, and southern Europe, while they were lower than 6.5 for men and 4.0 for women in eastern and southern Asia, including Japan. Similarly, the rates of Hodgkin lymphoma were higher than 2.0 in North and Central America and in Europe and lower than 1.0 in southeastern Asia (1). The reasons for this discrepancy are still unclear. Many epidemiologic studies have explored the risk factors for hematologic malignancies. Cigarette smoking (2–5), high alcohol consumption (5), obesity (6–9), height (6), occupational exposures (10), infection with some viruses, and immunodeficiency (11–13) are thought to induce some types of hematologic malignancies. However, preventive factors for hematologic malignancies are not well known and are a public health concern because the incidence of hematologic malignancies has been increasing worldwide (1).

Currently, there is extensive interest in the health benefits of green tea. Thus, green tea and its major constituent, tea polyphenols, have been widely studied as preventive factors for various diseases, including cancers (14–20). Several biologic studies have reported that green tea constituents, such

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as (-)-epigallocatechin-3-gallate (EGCG), exert antitumor effects against hematologic malignancies by inducing apoptosis and/or suppressing angiogenesis (21–25). However, epidemiologic studies on this topic have been few; to our knowledge, only 3 case-control studies have been conducted (26–28). Two reported that green tea intake was associated with a lower risk of leukemia (26, 28), and another study reported that higher intake of tea flavonoids was inversely associated with the risk of non-Hodgkin lymphoma (27).

This evidence may help explain the low incidence of hematologic malignancies in Asian countries, where consumption of green tea is the highest in the world. However, further evidence from cohort studies or intervention trials is needed to obtain some consensus on this issue. We therefore designed this population-based cohort study to investigate the association between green tea consumption and the risk of hematologic malignancies in a rural area of Japan, where green tea is widely consumed.

MATERIALS AND METHODS

Study cohort

We conducted a population-based cohort study based on data from the Ohsaki National Health Insurance (NHI) Cohort, the details of which have been described previously (29–31). In brief, from October through December 1994, we delivered self-administered questionnaires, including items on dietary intake, to all NHI beneficiaries aged 40–79 years living in the catchment area of the Ohsaki Public Health Center, Miyagi Prefecture, in northeastern Japan. The Ohsaki Public Health Center, a local government agency, provides preventive health services for residents of 14 municipalities in the northern part of Miyagi Prefecture. The study area is a typical rural area of Japan, where the main industry is agriculture.

Of 54,996 eligible individuals, 52,029 returned usable questionnaires; the response rate was 94.6%. We started prospective collection of the NHI withdrawal history files on January 1, 1995, to ascertain the date of and reason for withdrawal from NHI. We excluded 776 participants who had withdrawn from NHI before the baseline questionnaire survey. Thus, 51,253 participants (24,573 men and 26,680 women) were finally entered into the study as our cohort participants. The ethics committee of Tohoku University School of Medicine reviewed and approved the study protocol. We considered the return of self-administered questionnaires signed by the participants to imply their consent to take part in the study.

For the current analysis, we excluded 7 participants (1 man and 6 women) who had incomplete data in the cancer incidence registry, as well as 3,148 participants (1,557 men and 1,591 women) who, as ascertained from self-reports and the cancer registry, had been diagnosed as having cancer before the baseline survey was conducted. We also excluded 6,337 participants (3,266 men and 3,071 women) who had provided incomplete responses regarding frequency of green tea consumption. Consequently, we entered data for 41,761 eligible participants (19,749 men and 22,012 women) into our analysis.

Dietary assessment

We assessed dietary intake of participants at the baseline survey by using the self-administered questionnaire, which included a food frequency questionnaire (FFQ). In this FFQ, we asked participants to report their frequency of recent consumption of 36 food items and 4 beverages, including green tea. The FFQ provided 5 categories of response to describe participants' frequency of green tea consumption: never, occasionally, 1–2 cups/day, 3–4 cups/day, and 5 cups/day or more. The volume of a typical cup of green tea was 100 mL in the study region (19). The questionnaire also consisted of items on personal and family history of disease, physical status, drinking and smoking habits, and occupational and educational status.

We conducted a validation study of the FFQ, as reported previously (32). Spearman's rank coefficient for the correlation between green tea consumption as assessed by the FFQ and four 3-day food records was 0.71 for men and 0.53 for women, and the correlation between consumption measured by 2 FFQs administered 1 year apart was 0.63 for men and 0.64 for women. We examined the total energy intake of each participant from the FFQ responses by converting the selected frequency category for each food to daily intake, using portion sizes based on the median values observed in the validation study (32).

Ascertainment of cases and follow-up

The endpoint of our analysis was the incidence of all hematologic malignancies defined by morphology codes 9590/3–9989/3 in accordance with the *International Classification of Diseases for Oncology*, Third Edition (ICD-O-3) (33). Hematologic malignancies included the following diseases: Hodgkin and non-Hodgkin lymphomas (ICD-O-3 codes 9590/3–9729/3), plasma cell tumors (ICD-O-3 codes 9731/3–9734/3), mast cell tumors (ICD-O-3 codes 9740/1–9742/3), neoplasms of histiocytes and accessory lymphoid cells (ICD-O-3 codes 9750/3–9758/3), immunoproliferative diseases (ICD-O-3 codes 9760/3–9769/1), leukemias (ICD-O-3 codes 9800/3–9948/3), chronic myeloproliferative disorders (ICD-O-3 codes 9950/3–9964/3), other hematologic disorders (ICD-O-3 codes 9970/1 and 9975/1), and myelodysplastic syndromes (ICD-O-3 codes 9980/3–9989/3). Cases were further categorized as follows: lymphoid neoplasms including Hodgkin and non-Hodgkin lymphomas (ICD-O-3 codes 9590/3–9729/3), plasma cell tumors (ICD-O-3 codes 9731/3–9734/3), lymphoid leukemias (ICD-O-3 codes 9820/3–9837/3), hairy cell leukemia (ICD-O-3 codes 9940/3), aggressive NK-cell leukemia (ICD-O-3 codes 9948/3), and lymphoproliferative disorder not otherwise specified (ICD-O-3 codes 9970/1); and myeloid neoplasms including myeloid leukemias (ICD-O-3 codes 9840/3–9931/3), chronic myelomonocytic leukemia not otherwise specified (ICD-O-3 codes 9945/3), juvenile myelomonocytic leukemia (ICD-O-3 codes 9946/3), chronic myeloproliferative disorders (ICD-O-3 codes 9950/3–9964/3), myeloproliferative disease not otherwise specified (ICD-O-3 codes 9975/1), and myelodysplastic syndromes (ICD-O-3 codes 9980/3–9989/3) according to

ICD-O-3 and the *World Health Organization Classification of Tumors* (34).

We ascertained the incidence of cancer through computerized record linkage to the Miyagi Prefecture Cancer Registry, one of the oldest and most accurate population-based cancer registries in Japan (35). Between 1993 and 1997, the percentages registered by death certificates only were, for lymphoma, 23% for men and 21% for women and, for leukemia, 36% for men and 37% for women (35).

We prospectively counted person-years of follow-up for each of the participants from January 1, 1995, until the date of diagnosis of hematologic malignancies, the date of withdrawal from NHI, the date of death, or the end of the follow-up period (December 31, 2003), whichever occurred first. For follow-up, we periodically reviewed the NHI withdrawal history files. When a participant in this study withdrew from the NHI system because of death, emigration, or occupational change, the date of withdrawal and the reason were coded in the files. Follow-up of participants who had withdrawn from the NHI system was discontinued because we were unable to obtain subsequent information on them. During the study period, 5,427 participants (2,147 men and 3,280 women: 13.0% of the total) were lost to follow-up.

Statistical analysis

We combined the lower 2 categories of green tea consumption (never, occasionally) into the single category "less than 1 cup/day" for the purpose of this analysis because of the small number of participants and cases in each category. We used the Cox proportional hazards regression model to estimate hazard ratios and 95% confidence intervals for the incidence of hematologic malignancies according to levels of green tea consumption and to adjust for potential confounding variables, using SAS version 9.1 statistical software (SAS Institute, Inc., Cary, North Carolina). We calculated incidence rates of hematologic malignancies by dividing the number of incident cases by the number of person-years in each stratum of green tea consumption. The hazard ratio was computed as the incidence rate among participants in each green tea consumption stratum divided by the rate among participants in the lowest intake stratum (less than 1 cup/day), which was chosen as the reference group. All hazard ratios were calculated as age and sex adjusted and as multivariate adjusted. The P values for the test of linear trends were calculated by scoring the green tea consumption category as an ordinal variable (less than 1 cup/day = 1–5 cups/day or more = 4). All reported P values were 2-sided, and the estimates with $P < 0.05$ were considered statistically significant. We also conducted additional analyses after categorizing hematologic malignancies as lymphoid neoplasms and myeloid neoplasms.

We evaluated and compared the risk across sex and body mass index strata to assess whether any impact of green tea consumption on the risk of hematologic malignancies differed across sex and/or obesity status. To avoid any possible bias resulting from the influence of undiagnosed cancers present at baseline, we repeated the analysis after excluding participants who had been given a diagnosis of cancer within the first 3 years of follow-up and started follow-up from January 1, 1998, 3 years from the baseline date.

We considered the following variables to be potential confounders prior to the analyses: age (continuous variable, years), sex, family history of leukemia (yes or no), history of blood transfusion (yes or no), job status (nonfarmers or farmers, including former farmers), educational level (less than high school, high school, some college or higher), height (≤155, 155–164, ≥165 cm), body mass index (<18.5, 18.5–24.9, ≥25.0 kg/m^2), cigarette smoking (never smoked, former smoker, current smoker of <20 cigarettes/day, current smoker of ≥20 cigarettes/day), alcohol drinking (never drank, former drinker, current drinker of <45.6 g ethanol/day, current drinker of ≥45.6 g ethanol/day), fish consumption (≤2 times/week, 3–4 times/week, every day), soybean products consumption (≤2 times/week, 3–4 times/week, every day), daily miso soup consumption (yes or no), coffee consumption (never, occasionally, ≥1 cup/day), and total caloric intake (continuous variable, kcal/day). To avoid overfitting a model, we included these variables apart from age and sex in our final multivariate-adjusted model as confounders only if each variable met both of the following criteria: 1) it was associated with both green tea consumption and risk of hematologic malignancies (i.e., the probabilities of being exposed and diseased varied more than 5% among the strata of a potential confounder); and 2) after adding the variable into the age- and sex-adjusted model, the hazard ratio point estimate changed more than 1%. In the FFQ, alcohol consumption was classified in terms of "go," a traditional Japanese unit for measuring the amount of alcoholic beverages equal to approximately 180 mL of sake, containing 22.8 g of ethanol.

RESULTS

Participants who consumed more green tea than others tended to be older and were more likely to consume fish and soybean products, the typical sources of protein in the Japanese traditional daily diet (Table 1). Meat consumption was not associated with green tea consumption (data not shown). Men, but not women, who consumed more green tea were less likely to be heavy alcohol drinkers and obese. Furthermore, participants who consumed more green tea were more likely to smoke less, but this association was not obvious when we stratified them by sex.

During 326,012 person-years of follow-up (154,348 person-years for men and 171,664 person-years for women; mean = 7.8, maximum = 9.0 years), we documented 157 hematologic malignancies (in 88 men and 69 women); included were 119 cases of lymphoid neoplasms (66 men and 53 women) and 36 cases of myeloid neoplasms (20 men and 16 women). We found a significant inverse association between green tea consumption and the risk of hematologic malignancies in our participants (Table 2). The multivariate-adjusted hazard ratios for the incidence of hematologic malignancies were 0.88 (95% confidence interval: 0.57, 1.38) for 1–2 cups/day, 0.90 (95% confidence interval: 0.59, 1.39) for 3–4 cups/day, and 0.58 (95% confidence interval: 0.37, 0.89) for 5 cups/day or more (P for trend = 0.02) compared with less than 1 cup/day of green tea consumption. After

Table 1. Characteristics of Subjects (n = 41,761) According to Green Tea Consumption at Baseline, the Ohsaki Cohort, Japan, 1995–2003[a]

Characteristic	Green Tea Consumption, Cups/Day							
	Men (n = 19,749)				Women (n = 22,012)			
	<1 (n = 6,039)	1–2 (n = 4,479)	3–4 (n = 4,008)	≥5 (n = 5,223)	<1 (n = 5,054)	1–2 (n = 4,567)	3–4 (n = 5,046)	≥5 (n = 7,345)
Age in years, mean (SD)	57.9 (10.7)	58.1 (10.8)	60.5 (10.4)	61.9 (9.8)	59.3 (10.9)	60.4 (10.6)	61.8 (9.7)	62.8 (9.2)
Educational level								
Less than high school	62.4	56.9	58.6	61.7	59.4	54.8	54.2	58.3
High school	30.7	34.8	32.4	30.3	33.2	36.5	37.1	33.4
Some college or higher	6.9	8.4	9.0	8.0	7.4	8.7	8.7	8.3
Body mass index, kg/m^2								
<18.5	3.3	3.1	2.7	3.5	4.7	3.6	4.0	3.5
18.5–24.9	69.7	70.9	71.7	71.3	64.0	65.0	65.2	62.9
≥25.0	27.0	26.0	25.6	25.2	31.3	31.4	30.8	33.7
Cigarette smoking, cigarettes/day								
Never	20.7	19.1	19.1	16.8	86.8	90.9	92.2	88.2
Former	24.5	24.1	27.6	27.9	3.0	2.4	2.3	2.7
Current, <20	20.6	21.6	21.0	22.5	6.8	4.7	4.4	6.6
Current, ≥20	34.2	35.2	32.3	32.9	3.3	2.1	1.1	2.5
Alcohol drinking, g of ethanol/day								
Never	16.3	14.6	15.1	18.3	70.8	73.0	75.2	72.3
Former	10.6	9.8	10.3	11.6	5.5	4.0	3.8	4.3
Current, <45.6	59.9	63.2	63.0	59.5	22.7	22.3	20.6	22.9
Current, ≥45.6	13.2	12.4	11.6	10.6	1.0	0.6	0.4	0.6
Fish consumption,[b] times/week								
≤2	31.3	28.3	23.9	19.1	29.1	25.3	20.1	17.0
3–4	34.5	36.1	37.7	35.1	36.7	37.8	40.0	36.7
Every day	34.2	35.6	38.4	45.9	34.2	36.9	39.9	46.3
Soybean products consumption, times/week								
≤2	27.2	21.7	18.3	14.2	21.2	15.1	10.8	10.3
3–4	33.5	33.2	33.5	29.7	30.1	28.2	27.9	24.9
Every day	39.3	45.2	48.3	56.1	48.7	56.7	61.2	64.8

Abbreviation: SD, standard deviation.
[a] All values except those for age are expressed as percentages.
[b] Maximum intake of fresh fish, boiled fish paste, and dried fish.

dividing all hematologic malignancies into lymphoid neoplasms and myeloid neoplasms, we observed similar trends in the former, but not the latter, group.

We observed associations similar to those in our primary analysis across the strata of sex and body mass index (Table 3). Furthermore, the likelihood ratio tests between the models with and without interaction were not statistically significant for both sex and body mass index; the P values were 0.80 and 0.99, respectively. Because the numbers of participants and cases in the body mass index stratum of less than 18.5 kg/m^2 were very small, we integrated it and the stratum of 18.5–24.9 kg/m^2 into a new stratum of less than 25.0 kg/m^2 in this stratified analysis.

The risks did not change considerably after we started follow-up 3 years after the baseline date (data not shown).

DISCUSSION

We observed a significant inverse association between green tea consumption and the risk of hematologic

Table 2. Hazard Ratios and 95% Confidence Intervals for the Incidence of Hematologic Malignancies According to Green Tea Consumption, the Ohsaki Cohort, Japan, 1995–2003

	Green Tea Consumption, Cups/Day				*P* for Trend[a]
	<1 (*n* = 11,093)[b]	1–2 (*n* = 9,046)	3–4 (*n* = 9,054)	≥5 (*n* = 12,568)	
All hematologic malignancies					
No. of person-years	85,080	70,127	71,075	99,730	
No. of cases (*n* = 157)	46	34	39	38	
Age- and sex-adjusted hazard ratio	1.00	0.88	0.93	0.62	0.04
95% confidence interval		0.57, 1.38	0.61, 1.43	0.40, 0.95	
Multivariate-adjusted hazard ratio[c]	1.00	0.88	0.90	0.58	0.02
95% confidence interval		0.57, 1.38	0.59, 1.39	0.37, 0.89	
Lymphoid neoplasms					
No. of person-years	85,100	70,143	71,099	99,759	
No. of cases (*n* = 119)	34	29	30	26	
Age- and sex-adjusted hazard ratio	1.00	1.02	0.97	0.57	0.03
95% confidence interval		0.62, 1.67	0.59, 1.58	0.34, 0.96	
Multivariate-adjusted hazard ratio[c]	1.00	1.00	0.92	0.52	0.01
95% confidence interval		0.61, 1.65	0.56, 1.52	0.31, 0.87	
Myeloid neoplasms					
No. of person-years	85,151	70,205	71,180	99,773	
No. of cases (*n* = 36)	11	5	9	11	
Age- and sex-adjusted hazard ratio	1.00	0.54	0.89	0.74	0.67
95% confidence interval		0.19, 1.56	0.37, 2.15	0.32, 1.71	
Multivariate-adjusted hazard ratio[c]	1.00	0.57	0.91	0.76	0.70
95% confidence interval		0.20, 1.64	0.37, 2.23	0.32, 1.78	

[a] *P* values for trend were calculated by treating the green tea consumption categories as an ordinal variable and as 2-sided.

[b] Less than 1 cup/day was chosen as the reference group.

[c] Adjusted for age (continuous variable, years), sex, educational level (<high school, high school, ≥college), cigarette smoking (never smoked, former smoker, current smoker of <20 cigarettes/day, current smoker of ≥20 cigarettes/day), alcohol drinking (never drank, former drinker, current drinker of <45.6 g ethanol/day, current drinker of ≥45.6 g ethanol/day), fish consumption (≤2 times/week, 3–4 times/week, every day), and soybean products consumption (≤2 times/week, 3–4 times/week, every day).

malignancies during 9 years of follow-up in a large population-based cohort of Japanese that included 157 cases of hematologic malignancies. This association was more apparent for lymphoid neoplasms after we categorized hematologic malignancies as lymphoid and myeloid neoplasms. Compared with participants who consumed less than 1 cup/day of green tea, those who consumed 5 cups/day or more had a 42% lower risk of hematologic malignancies and a 48% lower risk of lymphoid neoplasms.

To our knowledge, this population-based cohort study is the first to find an association between green tea consumption and hematologic malignancies; no cohort study and only 3 case-control studies have been known to assess the relation between consumption of green tea or its constituents and hematologic malignancies. In a study from China, longer duration, higher quantity, and frequency of green tea intake were associated with a reduced risk for 107 leukemia cases and 110 controls (26). A study from the United States reported that higher intake of epicatechins, one of the flavonoids present richly in green tea, was associated with lower risk of non-Hodgkin lymphoma in 466 cases and 390 controls (27). The most recent case-control study of 252 leukemia cases and 637 controls from Taiwan reported an inverse association between green tea consumption and the risk of leukemia for individuals aged 16–29 years (28). These results were consistent with those of our study; however, case-control studies are not free from selection bias or recall bias related to retrospective measurement of exposure and other possible confounding factors after a diagnosis of disease.

Table 3. Hazard Ratios and 95% Confidence Intervals for the Incidence of Hematologic Malignancies According to Green Tea Consumption, Stratified by Sex and Body Mass Index, the Ohsaki Cohort, Japan, 1995–2003

	Green Tea Consumption, Cups/Day				*P* for Trend[a]
	<1[b]	1–2	3–4	≥5	
Sex					
Men (n = 19,749)					
No. of person-years	46,846	34,859	31,310	41,333	
No. of cases (n = 88)	30	17	20	21	
Age-adjusted hazard ratio	1.00	0.75	0.85	0.63	0.15
95% confidence interval		0.41, 1.35	0.48, 1.50	0.36, 1.10	
Multivariate-adjusted hazard ratio[c]	1.00	0.75	0.82	0.57	0.07
95% confidence interval		0.41, 1.35	0.47, 1.46	0.32, 1.00	
Women (n = 22,012)					
No. of person-years	38,235	35,267	39,764	58,398	
No. of cases (n = 69)	16	17	19	17	
Age-adjusted hazard ratio	1.00	1.11	1.05	0.62	0.14
95% confidence interval		0.56, 2.19	0.54, 2.03	0.31, 1.22	
Multivariate-adjusted hazard ratio[c]	1.00	1.09	1.01	0.58	0.10
95% confidence interval		0.55, 2.16	0.52, 1.99	0.29, 1.16	
Body mass index, kg/m^2					
<25.0 (n = 28,162)					
No. of person-years	56,667	47,482	48,601	66,647	
No. of cases (n = 101)	30	20	26	25	
Age- and sex-adjusted hazard ratio	1.00	0.78	0.91	0.60	0.10
95% confidence interval		0.45, 1.38	0.54, 1.55	0.35, 1.03	
Multivariate-adjusted hazard ratio[c]	1.00	0.78	0.89	0.56	0.06
95% confidence interval		0.44, 1.38	0.52, 1.51	0.33, 0.97	
≥25.0 (n = 11,586)					
No. of person-years	23,627	19,316	19,553	29,036	
No. of cases (n = 46)	14	10	11	11	
Age- and sex-adjusted hazard ratio	1.00	0.84	0.86	0.57	0.19
95% confidence interval		0.37, 1.89	0.39, 1.90	0.26, 1.27	
Multivariate-adjusted hazard ratio[c]	1.00	0.80	0.79	0.52	0.12
95% confidence interval		0.35, 1.80	0.36, 1.77	0.23, 1.16	

[a] *P* values for trend were calculated by treating the green tea consumption categories as an ordinal variable and as 2-sided.

[b] Less than 1 cup/day was chosen as the reference group.

[c] Adjusted for age (continuous variable, years), sex, educational level (<high school, high school, ≥college), cigarette smoking (never smoked, former smoker, current smoker of <20 cigarettes/day, current smoker of ≥20 cigarettes/day), alcohol drinking (never drank, former drinker, current drinker of <45.6 g ethanol/day, current drinker of ≥45.6 g ethanol/day), fish consumption (≤2 times/week, 3–4 times/week, every day), and soybean products consumption (≤2 times/week, 3–4 times/week, every day). The model stratified by sex did not include the variable for sex.

Recent animal and in vitro studies have reported that green tea and some of its constituents, especially EGCG, have antitumor activities against several types of hematologic malignancies. For instance, green tea inhibited angiogenesis and induced apoptosis in animal models of human non-Hodgkin lymphoma (21); EGCG suppressed vascular endothelial growth factor production and induced apoptosis in chronic lymphocytic leukemia B cells (22); EGCG induced apoptotic cell death in malignant B cells in vitro (23); EGCG induced apoptotic cell death in human

lymphoblastoid B cells through several pathways, such as production of intracellular reactive oxygen species (24); and EGCG and some of the other green tea catechins inhibited matrix metalloproteinase-9 secretion, thus affecting myeloid cell differentiation and angiogenesis (25). Furthermore, a clinical case report documented antitumor effects of oral green tea extracts in 4 patients with low-grade B-cell malignancies (36). This evidence supports our results and might explain the mechanisms of the observed association of green tea with a reduced incidence of hematologic malignancies.

Our present results indicate that the preventive effect of green tea consumption against hematologic malignancies seems to have a threshold effect rather than a dose-response effect. The lower risks of hematologic malignancies were obvious only in the group consuming 5 cups or more of green tea daily (Tables 2 and 3). This result is inconsistent with recent biologic studies indicating a dose-dependent manner of green tea constituents against hematologic tumor cells (22–25). These discrepancies between animal experiments and our epidemiologic observations might be due to differences in species, metabolism of green tea constituents, accuracy of exposure measurement, degree of confounding and/or bias, and essential differences in study design. Moreover, although we observed that green tea consumption was inversely associated with the incidence of all hematologic malignancies as a whole and lymphoid neoplasms, we were unable to find any significant association with myeloid neoplasms alone. Because the number of cases of myeloid neoplasm in this study was very small, we were unable to conclude whether this lack of association was due to insufficient statistical power or to pathogenetic differences between malignant lymphoid and myeloid cells, such as differences in sensitivity to green tea constituents or in the mechanisms of development, proliferation, and/or differentiation.

Infection with human immunodeficiency virus, human T-cell leukemia virus type-1, and Epstein-Barr virus is an established risk factor for hematologic malignancies (11–13). Although we were unable to acquire any information about such viral infections in our participants, infection with human immunodeficiency virus and human T-cell leukemia virus type-1 is very rare in this region (37, 38); Japan is known to have a relatively high rate of human T-cell leukemia virus type-1 infection, but the endemic area is southern Japan, far from our study area. Epstein-Barr virus is widespread throughout the world, and most adults in any country are seropositive against Epstein-Barr virus antigen (38). We thus considered that our inability to assess infection with such viruses would not substantially distort our result.

Our study had some limitations. First, 13% of all participants were lost to follow-up. Nevertheless, this proportion did not vary across the 4 green tea consumption categories: the proportions of participants lost to follow-up at the lowest to highest green tea consumption levels were 14%, 14%, 13%, and 12%.

Second, the number of cases of hematologic malignancies among our participants was modest in comparison with the Western population. Therefore, we were unable to evaluate the association between green tea consumption and risk of each subtype of hematologic malignancy (e.g., Hodgkin lymphomas, non-Hodgkin lymphomas, lymphoid leukemias, or myeloid leukemias), even though the risk factors probably vary according to subtype.

Third, the quality and completeness of the Miyagi Cancer Registry were not high enough regarding hematologic malignancies: the level of death-certificate-only diagnosed lymphoma and leukemia was higher than 20%. Such a fairly high proportion of death-certificate-only cases might have led to failure to ascertain some individuals who had hematologic malignancies but did not die during the study period.

Fourth, we were unable to obtain enough information related to occupational exposures, ionizing radiation, benzene, and so forth, which may affect the risk of hematologic malignancies (10). Even though we added a variety of potential confounders to our analysis, there were a considerable number of unmeasured confounders.

Finally, we excluded 6,337 participants from our analysis because they provided incomplete answers for, or did not answer the question on, green tea consumption. In this excluded group, 31 cases of hematologic malignancies were diagnosed. Because the distribution of baseline characteristics among those participants was similar to that among participants in the lowest green tea consumption stratum (data not shown), we assumed that they were likely to consume no or less green tea. Using this assumption, we conducted a sensitivity analysis after including those participants in the lowest stratum of green tea consumption. The result of this analysis did not differ from that of our primary analysis: the multivariate-adjusted hazard ratios were 0.86 (95% confidence interval: 0.57, 1.30), 0.90 (95% confidence interval: 0.61, 1.34), and 0.58 (95% confidence interval: 0.39, 0.87) for 1–2, 3–4, and 5 cups/day or more, respectively, compared with less than 1 cup/day.

We previously reported that green tea consumption was not associated with risk of gastric cancer (39, 40), breast cancer (41), colorectal cancer (42), prostate cancer (43), and lung cancer (44). Hematologic malignancies are the first and only malignant tumors for which we have derived a significant inverse association with green tea consumption. The differences in evidence between our previous studies and the present one indicate that hematologic malignancies may have specific characteristics that result in a response to certain green tea components.

We concluded that green tea consumption was inversely associated with the risk of hematologic malignancies in the general rural population of Japan. Our results have implications for not only primary prevention of hematologic malignancies but also treatment and/or recurrence prevention. Further biologic studies and clinical trials are necessary to confirm the role of green tea in prevention and treatment of hematologic malignancies.

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Original Article

Factors Associated With Psychological Distress in a Community-Dwelling Japanese Population: The Ohsaki Cohort 2006 Study

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ABSTRACT

Background: In Asia, there has been no population-based epidemiological study using the K6, a 6-item instrument that assesses nonspecific psychological distress.

Methods: Using cross-sectional data from 2006, we studied 43 716 (20 168 men and 23 548 women) community-dwelling people aged 40 years or older living in Japan. We examined the association between psychological distress and demographic, medical, lifestyle, and social factors by using the K6, with psychological distress defined as 13 or more points out of a total of 24 points.

Results: The following variables were significantly associated with psychological distress among the population: female sex, young and old age, a history of serious disease (hypertension, diabetes mellitus, stroke, myocardial infarction, or cancer), current smoking, former alcohol drinking, low body mass index, shorter daily walking time, lack of social support (4 of 5 components), and lack of participation in community activities (4 of 5 components). Among men aged 40 to 64 years, only "lack of social support for consultation when in trouble" and a history of diabetes mellitus remained significant on multivariate analysis. Among men aged 65 years or older, age was not significantly associated with psychological distress, and the significant association with current smoking disappeared on multivariate analysis. Among women aged 40 to 64 years, a history of stroke was not associated with psychological distress. Among women aged 65 years or older, the significant association with current smoking disappeared on multivariate analysis.

Conclusions: A number of factors were significantly associated with psychological distress, as assessed by the K6. These factors differed between men and women, and also between middle-aged and elderly people.

Key words: cross-sectional; K6; population-based; psychological distress

INTRODUCTION

Mental health is an important component of overall well-being. About 14% of the global disease burden has been attributed to mental illness, mostly due to the chronically disabling nature of depression and other common mental disorders.[1,2] Although numerous studies have produced systematic evidence regarding the risk factors for physical health, the understanding of factors related to mental health, particularly in Asian countries, is still limited.[2]

In 2002, in an attempt to devise a method to easily assess mental health in general population surveys, Kessler and colleagues developed a scale of nonspecific psychological distress—the K6—that comprises only 6 questions.[3] The K6 was originally developed to identify persons with a high likelihood of developing mental conditions, such as depression and mood or anxiety disorders.[4] However, the K6 and the K10 (the K6 plus 4 additional questions related to symptoms of distress) have also been used to estimate the prevalence of nonspecific psychological distress in general population surveys,[5] and as part of the World Health Organization's World Mental Health Surveys.[6] Although it is brief enough to be added to lengthy general health questionnaires, a major limitation of the K6 is that it does not

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provide information on the particular psychiatric diagnosis or diagnoses a respondent may have. Nevertheless, researchers have begun to use the K6 for studies in clinical settings,[7] as well as in epidemiological studies[8,9] and large, nationally representative surveys. Despite the frequent use of the K6, no population-based epidemiological study has used this scale to clarify the factors associated with mental health in Asian countries.

The objective of the present study was to use the K6 to identify factors associated with psychological distress in a community-dwelling Japanese population. We also briefly describe the overall design of the study, as this is the first report from a new prospective cohort study, the Ohsaki Cohort 2006 Study.

METHODS

Study design, setting, and participants

The Ohsaki Cohort 2006 Study is a prospective cohort study, from which we analyzed cross-sectional data from a baseline survey. The source population for the baseline survey comprised community-dwelling individuals aged 40 years or older who were included in the Residential Registry for Ohsaki City, Miyagi Prefecture, northeastern Japan, as of December 1, 2006. The Residential Registry identified 78 101 persons (36 397 men; 41 704 women) living in the area.

The baseline survey was conducted from December 1 to December 15, 2006. A questionnaire was distributed by the heads of individual administrative districts to individual households, and returned by mail. Of the 78 101 persons, 866 were ineligible due to death, move-out, or hospitalization, yielding an eligible population of 77 235. The baseline questionnaires (described below) were collected from 50 210 persons, and valid responses were received from 49 855 (22 547 men and 27 308 women), who ultimately formed the study population of cohort participants. Among the study population, 26 512 persons (53.2%) were aged 40 to 64 years, and 23 343 (46.8%) were aged 65 years or older. The response rate was calculated by dividing the study population by the total eligible population, yielding 64.5%. The corresponding response rates, with respect to sex and age categories, were 54.9% and 60.4% among men and women aged 40 to 64 years, respectively, and 77.1% and 73.2% among men and women aged 65 years or older, respectively.

When analyzing the prevalence of psychological distress and its associations with demographic, medical, lifestyle, and social factors, we excluded participants for whom K6 data were missing ($n = 6139$). Consequently, the analyzed population comprised 43 716 participants (20 168 men and 23 548 women; 56.6% of the eligible population).

Baseline survey

The baseline questionnaires for persons aged 40 to 64 years consisted of the following details in sequence: (1) history of diseases, (2) family history of diseases, (3) health status during the preceding year, (4) smoking status, (5) alcohol drinking status, (6) dietary habits,[10] (7) job status and educational status, (8) present and past body weight and height, (9) health status in general, (10) sports and exercise,[11,12] (11) psychological distress (K6),[3,4] (12) social support,[13] (13) participation in community activities, (14) dental status, and (15) reproductive factors (among women).

The baseline questionnaires for persons aged 65 years or older consisted of the following details in sequence: (1) a frailty checklist (the Kihon checklist),[14] (2) history of diseases, (3) health status during the preceding year, (4) smoking status, (5) alcohol drinking status, (6) dietary habits,[10] (7) past body weight and height, (8) health status in general, (9) pain, (10) daily activities, (11) sports and exercise,[11,12] (12) psychological distress (K6),[3,4] (13) social support,[13] (14) participation in community activities, and (15) dental status.

Questionnaire items for persons aged 65 years or older were identical to those for persons aged 40 to 64 years, except that the former excluded family history of diseases, job status and educational status, present and past body weight and height, and reproductive factors in women, and included the frailty checklist, past body weight and height, pain, and daily activities.

Measurement of psychological distress

The K6 was used as an indicator of psychological distress.[3,4] The 6 questions were as follows: "Over the last month, how often did you feel: (1) nervous, (2) hopeless, (3) restless or fidgety, (4) so sad that nothing could cheer you up, (5) that everything was an effort, (6) worthless?" Participants were asked to respond by choosing "all of the time" (4 points), "most of the time" (3 points), "some of the time" (2 points), "a little of the time" (1 point), and "none of the time" (0 points). Total point score therefore ranged from 0 to 24. The K6 has been developed using modern psychometric theory and has been shown to be superior to some existing scales in brevity and psychometric properties.[3,4,15] The Japanese version of the K6 has been recently developed, using the standard back-translation method, and has been validated.[16] As suggested by Kessler and colleagues,[15] we classified participants with scores of 13 points or more as having psychological distress.

Measurement of other variables

The degree of social support available to each person was assessed by asking the following questions[13]: (1) Do you have someone with whom you can consult when you are in trouble?, (2) Do you have someone with whom you can consult when your physical condition is bad?, (3) Do you have someone who can help you with your daily housework?, (4) Do you have someone who can take you to a hospital when you do not feel well?, and (5) Do you have someone

who can take care of you when you are ill in bed? This social support questionnaire consisted of 5 questions, each requiring an answer of yes or no. This questionnaire was only available in Japanese, and its validity and reliability were not evaluated.

The frailty checklist is a tool developed by the Japanese Ministry of Health, Labour, and Welfare to screen for frail persons and is designed to measure actual task performance.[14] Researchers have also begun to use this tool in epidemiological surveys.[14]

Ethical issues

The return of questionnaires completed by the participants was regarded as consent to participate in the study, which involved cross-sectional analysis of the baseline survey data and the longitudinal study of subsequent mortality and immigration. The study protocol was reviewed and approved by the Ethics Committee of Tohoku University Graduate School of Medicine.

Statistical analysis

We used univariate and multivariate logistic regression analysis to calculate the odds ratios (ORs) for psychological distress (a K6 total score of ≥13 points) relative to demographic, medical, lifestyle, and social factors. In these analyses, we investigated the following factors: sex, age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, ≥85 years), history of hypertension (yes, no), history of diabetes mellitus (yes, no), history of stroke (yes, no), history of myocardial infarction (yes, no), history of cancer (yes, no), smoking status (never, former, current), alcohol drinking (never, former, current), body mass index (kg/m^2) calculated with self-reported weight and height; <18.5, 18.5–24.9, ≥25.0), daily walking time (<30 min/day, 30 min–1 hour/day, ≥1 hour/day), social support (yes, none), participation in community activities (yes, none). In the multivariate models, the above variables were all adjusted for each other. Analyses were repeated by stratifying the population by sex and age categories (40–64 years, 65 years or older). When analyzing the data for men and women aged 40 to 64 years, we further added current employment status (yes, no) and duration of education (≤12 years, >12 years) as covariates. All statistical analyses were performed with SAS version 9.1 (SAS Inc., Cary, NC, USA), and all statistical tests were 2-sided. A P value less than 0.05 was considered to indicate statistical significance.

RESULTS

Prevalence proportion, and univariate and multivariate analysis of psychological distress among the total population

The crude prevalence proportion of psychological distress in the analyzed population was 6.7% (2921/43 716; 95% confidence interval [CI], 6.5 to 6.9). Univariate analysis showed that the following were significantly associated with a higher prevalence of psychological distress: female sex, young and old age, a history of serious disease, a current smoking habit, a former alcohol drinking habit, low BMI, shorter daily walking time, lack of social support, and lack of participation in community activities.

After mutual adjustment for the variables shown in Table 1, women had approximately 1.6 times the odds of psychological distress, relative to men. There was a U-shaped association between age category (5-year categories from 40–44 to ≥85 years) and the prevalence of psychological distress, with a nadir for those aged 65 to 69 years.

History of hypertension, diabetes mellitus, stroke, myocardial infarction, or cancer were all associated with a significantly higher prevalence of psychological distress in the multivariate models (Table 1). Among these diseases, a history of stroke was most strongly associated with psychological distress, and had more than 2 times the odds of psychological distress, relative to those who had no history of stroke.

A current smoking habit (vs never smoker), former smoking habit (vs never smoker), former alcohol drinking habit (vs never drinker), low BMI (vs normal BMI), and less daily walking time (vs time spent walking ≥1 hr) were associated with a higher odds for psychological distress, even in multivariate analysis (Table 1). In contrast, a moderate daily walking time (vs time spent walking ≥1 hr) was associated with a significantly lower odds.

Among the variables studied, lack of social support for consultation when in trouble was most strongly associated with a high prevalence of psychological distress in the multivariate models, although the association between other components of lack of social support and psychological distress was substantially attenuated in multivariate analysis (Table 1). The multivariate-adjusted OR (95% CI) for psychological distress associated with lack of social support for consultation when in trouble was 2.24 (1.97 to 2.56). The association of lack of participation in community activities with psychological distress was also attenuated, but lack of participation in neighborhood association activities, sports or exercise, volunteering, and community social gatherings were all associated with a higher prevalence of psychological distress, even in multivariate analysis.

Stratified analysis by sex and age categories (40 to 64 years, 65 years or older)

Stratified analysis by sex and age categories (40 to 64 years, 65 years or older) yielded results similar to those for the participants as a whole (Table 1), but the statistically significant associations that had been observed between several factors and psychological distress disappeared in each stratum.

Table 1. Univariate and multivariate analysis of the associations between psychological distress and demographic, medical, lifestyle, and social factors among the total study population[a]

Variables	No. of persons with psychological distress /No. of participants	Univariate OR (95% CI)	Multivariate OR (95% CI)[b]
Sex			
Male	1146/20 168	1.00 (referent)	1.00 (referent)
Female	1775/23 548	1.35 (1.25–1.46)	1.58 (1.41–1.76)
Age group (years)			
40–44	316/3702	1.00 (referent)	1.00 (referent)
45–49	380/4739	0.93 (0.80–1.09)	0.93 (0.79–1.09)
50–54	390/5712	0.79 (0.67–0.92)	0.79 (0.67–0.93)
55–59	398/6734	0.67 (0.58–0.79)	0.65 (0.56–0.77)
60–64	226/4461	0.57 (0.48–0.68)	0.54 (0.45–0.65)
65–69	240/5091	0.53 (0.45–0.63)	0.52 (0.43–0.63)
70–74	296/5242	0.64 (0.54–0.76)	0.57 (0.47–0.68)
75–79	281/4167	0.78 (0.66–0.92)	0.60 (0.50–0.72)
80–84	214/2347	1.08 (0.90–1.29)	0.74 (0.60–0.91)
≥85	180/1521	1.44 (1.19–1.75)	0.87 (0.69–1.08)
History of diseases			
Hypertension	907/12 658	1.11 (1.03–1.21)	1.17 (1.07–1.28)
Diabetes mellitus	319/3819	1.31 (1.16–1.48)	1.26 (1.11–1.44)
Stroke	156/1012	2.63 (2.21–3.14)	2.12 (1.76–2.57)
Myocardial infarction	122/1147	1.69 (1.40–2.05)	1.51 (1.23–1.86)
Cancer	225/2432	1.46 (1.27–1.68)	1.48 (1.28–1.73)
Smoking status			
Never	1443/22 219	1.00 (referent)	1.00 (referent)
Former	553/9030	0.94 (0.85–1.04)	1.15 (1.01–1.31)
Current	701/9699	1.12 (1.02–1.23)	1.32 (1.17–1.49)
Alcohol drinking status			
Never	1187/17 041	1.00 (referent)	1.00 (referent)
Former	407/3633	1.69 (1.50–1.90)	1.49 (1.31–1.70)
Current	1156/20 840	0.78 (0.72–0.85)	0.94 (0.84–1.04)
Body-mass index			
<18.5 kg/m^2	226/1803	2.12 (1.82–2.45)	1.59 (1.36–1.86)
18.5–24.9 kg/m^2	1689/26 610	1.00 (referent)	1.00 (referent)
≥25.0 kg/m^2	752/12 231	0.97 (0.89–1.06)	0.96 (0.87–1.05)
Time spent walking per day			
<30 min	1426/16 476	1.64 (1.49–1.80)	1.26 (1.14–1.40)
30 min–1 hr	710/14 190	0.91 (0.82–1.02)	0.89 (0.79–0.99)
≥1 hr	658/12 024	1.00 (referent)	1.00 (referent)
Lack of social support:			
(i) to consult when you are in trouble	873/5354	3.46 (3.18–3.77)	2.24 (1.97–2.56)
(ii) to consult when you are in bad physical condition	698/4167	3.39 (3.09–3.72)	1.24 (1.08–1.44)
(iii) to help with your daily housework	852/6701	2.47 (2.27–2.69)	1.12 (0.99–1.27)
(iv) to take you to a hospital	579/3834	2.86 (2.60–3.16)	1.27 (1.10–1.46)
(v) to take care of you	769/5563	2.71 (2.48–2.96)	1.42 (1.25–1.61)
No participation in community activities			
(i) Activities of neighborhood association	1952/22 109	2.26 (2.08–2.46)	1.27 (1.15–1.41)
(ii) Sports or exercise	2090/23 258	2.70 (2.47–2.95)	1.63 (1.47–1.81)
(iii) Volunteering	2307/28 871	2.48 (2.23–2.75)	1.17 (1.03–1.32)
(iv) Social gatherings	2016/22 568	2.48 (2.27–2.71)	1.31 (1.18–1.46)

Abbreviations: OR, odds ratio; CI, confidence interval.
[a]The K6 was used as an indicator of psychological distress,[3,4] with a cut-off point of ≥13 out of 24 points.[15]
[b]In the multivariate models, all variables shown in Table 1 were adjusted for each other.

The statistically significant association between history of hypertension and psychological distress disappeared in all strata. Among men aged 40 to 64 years, there was loss of significant associations with a history of myocardial infarction, history of cancer, being a former smoker, spending less than 30 min per day walking, lacking social support for consultation when in a bad physical condition, lacking social support for transport to a hospital, lacking social support for receiving care, lack of participation in community activities in a neighborhood association, and lack of participation in