Sense of Life Worth Living (*Ikigai*) and Mortality in Japan: Ohsaki Study

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Objective: To investigate the association between the sense of "life worth living (*ikigai*)" and the cause-specific mortality risk. The psychological factors play important roles in morbidity and mortality risks. However, the association between the negative psychological factors and the risk of mortality is inconclusive. **Methods:** The Ohsaki Study, a prospective cohort study, was initiated on 43,391 Japanese adults. To assess if the subjects found a sense of *ikigai,* they were asked the question, "*Do you have ikigai in your life*?" We used Cox regression analysis to calculate the hazard ratio of the all-cause and cause-specific mortality according to the sense of *ikigai* categories. **Results:** Over 7 years' follow-up, 3048 of the subjects died. The risk of all-cause mortality was significantly higher among the subjects who did not find a sense of *ikigai* as compared with that in the subjects who found a sense of *ikigai*; the multivariate adjusted hazard ratio (95% confidence interval) was 1.5 (1.3–1.7). As for the cause-specific mortality, subjects who did not find a sense of *ikigai* were significantly associated with an increased risk of cardiovascular disease (1.6; 1.3–2.0) and external cause mortality (1.9; 1.1–3.3), but not of the cancer mortality (1.3; 1.0–1.6). **Conclusions:** In this prospective cohort study, subjects who did not find a sense of *ikigai* were associated with an increased risk of all-cause mortality. The increase in mortality risk was attributable to cardiovascular disease and external causes, but not cancer. **Key words:** sense of life worth living (*ikigai*), Japanese, all-cause mortality, cause-specific mortality.

CVD = cardiovascular disease; **NHI** = National Health Insurance; **PHC** = Public Health Center; **IHD** = ischemic heart disease; **HR** = hazard ratio; **CI** = confidence interval; **BMI** = body mass index.

INTRODUCTION

The psychological factors of people play important roles in the morbidity and mortality risks (1–17). Studies in the US and Europe have reported that the negative psychological factors, as represented by factors such as a low subjective sense of well-being (1), dissatisfaction (2–4), hopelessness (5,6), and self-perception of ill health (7–9), were associated with an increased risk of all-cause mortality. The association between the negative psychological factors and the mortality risk has been reported to be independent of the objective health status, socioeconomic status, or the health-related lifestyle.

In Japanese culture, having a sense of "life worth living (*ikigai*)" is the most commonly used indicator of subjective well-being. The sense of "life worth living (*ikigai*)" does not merely reflect an individual's psychological factors (well-being, hopes) but also an individual's consciousness of the motivation for living, because it has a meaning akin to having a "purpose in life" and "reason for living." The term *ikigai* is commonly used in such phrases as "this hobby is what makes my life worth living (*ikigai*)" or "raising children makes my life worth living (*ikigai*)". In the most authoritative dictionary in Japan, the sense of *ikigai* is described as "joy and a sense of well-being from being alive" and of "realizing the value of being alive" (18). Three earlier studies in Japan have reported that the lack of *ikigai* was significantly associated with an increased risk of all-cause mortality (10–12).

The association between the negative psychological factors and the risk of cause-specific mortality is, however, inconclusive (11,13–16). Some studies have indicated an association with cancer mortality, whereas others have denied any such association (11,13,14). As for cardiovascular disease (CVD) mortality, no agreement has been reached among past studies (11,14–16). A Japanese study reported that the lack of *ikigai* was significantly associated with CVD mortality, but not cancer mortality (11). On the other hand, another study reported that the lack of *ikigai* was associated with an increased risk of breast cancer (17).

Because the causes differ between CVD and cancer, the impact of the psychological factors on mortality risk may also differ between CVD and cancer. Determination of this difference would strengthen our understanding of the mechanism underlying the impact of the psychological factors on physical health and illness. In this study, we attempted to test the hypothesis that the association between *ikigai* and mortality risk is dependent on the specific cause of death. To test this hypothesis, we investigated the association between *ikigai* and the cause-specific mortality in a population-based prospective cohort study in Japan. Among all the studies conducted until now in Japan (10–12), the present study had the largest number of subjects, the largest number of decedents, and the most comprehensive set of covariates for multivariate adjustment.

METHODS

The present data were derived from the Ohsaki National Health Insurance (NHI) Cohort Study. The study design has been reported previously (19–22). A self-administered questionnaire was distributed between October and December 1994 to all NHI beneficiaries aged 40 to 79 years and living in the catchment areas of the Ohsaki Public Health Center (PHC) (n = 54,996). The Ohsaki PHC, a local governmental agency, provides preventive health services for the residents of 14 municipalities in Miyagi Prefecture in northeastern Japan. The questionnaires were delivered to the subjects' residences by public health officials in each municipality. This procedure yielded a high response rate of 94.6% (n = 52,029). We excluded 811 subjects because they had died or withdrawn from the NHI before January 1, 1995, when we started

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the prospective collection of NHI claim history files, and finally, a total of 51,218 subjects formed the study cohort. This study was approved by the Ethics Committee of Tohoku University School of Medicine. We considered the return of self-administered questionnaires signed by the subjects to imply their consent to participate in the study.

The 93-item questionnaire at the baseline survey consisted of questions related to the following ten factors: past medical history, family history, physical health status, drinking habit, smoking habit, dietary habit, job, marital status, education, and other health-related factors, including *ikigai* (19).

Ikigai was assessed through the subject's response to the question, *"Do you have ikigai in your life?"* The subjects were asked to choose one of three answers: "yes," "uncertain," or "no."

The endpoints were all-cause mortality and cause-specific mortality. To follow up the subjects for mortality and migration, we reviewed the NHI withdrawal history files. When a subject was withdrawn from the NHI system because of death, emigration, or employment, the withdrawal data and its reason were coded on the NHI withdrawal history files. Because we were unable to obtain subsequent information on the subjects who withdrew from the NHI, we discontinued follow-up of the subjects who withdrew from the NHI system because of emigration or employment.

For the decedents, we investigated the cause of death by reviewing the death certificates filed at the Ohsaki PHC. Cause of death was classified according to the International Classification of Diseases, 10th Revision (23). We identified deaths from cancer as codes C00–C97, CVD as codes I00–I99 (including ischemic heart disease (IHD) as codes I20–I25 and stroke as codes I60–I69), pneumonia as codes J10–J18, and external causes as codes V01–V99, W00–W99, X00–X99 (including suicide as codes X60–X84), and Y01–Y34. None of the subjects died of unknown causes. Because the Family Registration Law in Japan requires registration of death, death certificates confirmed all the deaths that occurred in the study area.

Of the 51,218 subjects who participated in the baseline survey, we excluded 2939 subjects who had not indicated any response to the question about *ikigai* and the 4888 subjects who had a history of cancer, myocardial infarction, or stroke. Consequently, our final analysis included the data of 43,391 subjects (20,625 men and 22,766 women).

We counted the person-years of follow-up for each subject from January 1, 1995 until the date of death, date of withdrawal from the NHI, or the end of the study period (December 31, 2001), whichever occurred first. We accrued 269,989 person-years of follow-up. During the follow-up, 3048 (7.0%) subjects died and 5187 (12.0%) subjects were lost to follow-up.

The Kaplan-Meier survival curves were used to obtain estimates of survival at 7 years, and the log-rank test was used to test for significant differences between survival curves for the various response categories for *ikigai*, using the SAS LIFETEST procedure on SAS, version 9.1 (SAS Institute, Cary, North Carolina). Cox proportional hazards regression analysis was used to calculate the hazard ratios (HRs) and 95% confidence intervals (CIs) of all-cause and cause-specific mortality according to the response categories for *ikigai* and to adjust for potential confounders, using the SAS PHREG procedure on SAS, version 9.1. The validity of the proportional hazard assumption was verified by adding a time-dependent variable to each model to confirm that the HR for each covariate did not increase or decrease over time. All p values were two-sided, and differences at $p < .05$ were considered to be statistically significant. Interaction between each variable and *ikigai* was tested by a multiplicative model.

We considered the following variables as potential confounders; age at baseline (continuous variable), sex (men or women), marital status (married, widowed/divorced, or single), education (junior high school or higher), job (employed or unemployed), self-rated health (bad or poor, fair, or good or excellent), perceived mental stress (high, moderate, or low), bodily pain (severe or moderate, mild or very mild, or none), physical function (limited or unlimited), body mass index (BMI) in kg/m^2 (≤18.4, 18.5–24.9, or ≥25.0), smoking status (never, former, currently smoking 1–19 cigarettes/day, or ≥20 cigarettes/day), alcohol consumption (never, former, current ethanol intake of ≤22.7 g/day, 22.8–45.5 g/day, 45.6–68.3 g/day, or ≥68.4 g/day), time spent walking (<1 hour/day or ≥1 hour/day), sleep duration (≤6 hours/day, 7–8 hours/day, or ≥9 hours/day), and history of hypertension, diabetes mellitus,

TABLE 1. Characteristics of Study Subjects According to *Ikigai* (n = 43,391)

	Ikigai		
	Yes	Uncertain	No
No. of subjects	25,596	15,782	2013
Age at baseline, years (mean ± SD)	60.3 ± 10.2	59.6 ± 10.5	61.4 ± 11.1
Women (%)	50.1	55.6	57.4
Marital status (%)			
Married	84.8	79.2	68.9
Widowed/divorced	12.8	15.0	21.7
Single	2.5	5.7	9.4
Education (%)			
Junior high school	56.9	62.4	67.1
Higher	43.1	37.6	32.9
Job (%)			
Employed	67.3	60.0	47.6
Unemployed	32.7	40.0	52.4
Self-rated health (%)			
Bad or poor	12.3	24.8	46.6
Fair	10.8	20.8	16.9
Good or excellent	76.9	54.5	36.5
Perceived mental stress (%)			
High	12.4	19.2	36.3
Moderate	65.6	70.4	43.2
Low	22.0	10.3	20.5
Bodily pain (%)			
Severe or moderate	13.4	20.0	33.3
Mild or very mild	50.3	54.1	40.9
None	36.3	25.9	25.8
Physical function (%)			
Limited	18.9	29.6	48.6
Unlimited	81.1	70.4	51.4
BMI, kg/m^2 (%)			
≤18.4	3.0	4.0	6.6
18.5–24.9	67.6	67.5	65.1
≥25.0	29.5	28.5	28.4
Smoking status (%)			
Never	53.0	55.0	54.9
Former	14.9	13.1	14.0
Current, 1–19 cigarettes/day	11.8	12.2	12.3
Current, ≥20 cigarettes/day	20.3	19.8	18.9
Alcohol consumption (%)			
Never	42.6	47.0	49.8
Former	6.3	8.3	11.3
Current, ≤22.7 g/day ethanol	21.9	19.2	16.9
Current, 22.8–45.5 g/day ethanol	10.4	8.6	7.6
Current, 45.6–68.3 g/day ethanol	12.5	10.1	7.2
Current, ≥68.4 g/day ethanol	6.3	6.7	7.2
Time spent walking (%)			
<1 hr/day	50.7	57.5	65.0
≥1 hr/day	49.3	42.5	35.0
Sleep duration (%)			
≤6 hrs/day	15.2	16.7	19.5
7–8 hrs/day	69.2	65.9	55.7
≥9 hrs/day	15.6	17.4	24.8

(*Continued*)

TABLE 1. Continued

	Ikigai		
	Yes	Uncertain	No
History of illness (%)			
Hypertension	24.4	26.5	30.0
Diabetes mellitus	5.7	6.1	9.2
Kidney disease	3.5	3.9	5.0
Liver disease	5.1	5.6	6.0
Gastric or duodenal ulcer	14.5	14.2	14.0
Arthritis	8.8	10.0	12.3
Osteoporosis	3.4	4.0	6.0

SD = standard deviation; BMI = body mass index.

kidney disease, liver disease, gastric or duodenal ulcer, arthritis, or osteoporosis (presence or absence).

In addition, we repeated all analyses after excluding the deaths that occurred within the first 2 years of follow-up (644 all-cause deaths), because subjects who died within the first 2 years of follow-up might have been in poor health at baseline. Stratified analyses according to confounders were conducted in relationship to the association between *ikigai* and the mortality risk, because *ikigai* may be associated with the risk of all-cause mortality independent of socioeconomic factors, other psychological factors, physical function, lifestyle habits, or history of illness.

RESULTS

Over the 7 years of follow-up, the total number of deaths was 3048. This number included 1100 deaths from cancer, 971 deaths from CVD (including 207 from IHD and 479 from stroke), 241 deaths from pneumonia, and 186 deaths from external causes (including 90 from suicide).

Among the 43,391 subjects enrolled, 25,596 (59.0%) indicated that they found a sense of *ikigai*, 15,782 (36.4%) indicated they were uncertain, and 2013 (4.6%) indicated they did not find a sense of *ikigai*. As compared with those who found a sense of *ikigai*, those who did not were more likely to be unmarried, unemployed, have a lower educational level, have bad or poor self-rated health, have a high level of perceived mental stress, have severe or moderate bodily pain, have limitation of physical function, and less likely to walk (Table 1).

The Kaplan-Meier curves indicated that those who did not find a sense of *ikigai* were associated with an increased risk of all-cause mortality ($p < .001$) (Figure 1). Table 2 shows the HR (95% CI) of all-cause and cause-specific mortality according to the response categories for *ikigai*. There was a statistically significant association between *ikigai* and the risk of all-cause mortality. As compared with subjects who found a sense of *ikigai*, the multivariate adjusted HR (95% CI) of all-cause mortality was 1.1 (1.0–1.2) for those who were uncertain, and 1.5 (1.3–1.7) for those who did not find a sense of *ikigai*. This finding remained basically unchanged even after excluding the deaths that occurred within the first 2 years of follow-up.

The above-mentioned increase in the all-cause mortality risk was attributable to an increased risk of mortality from CVD, pneumonia, and external causes. However, *ikigai* was not associated with the risk of cancer mortality. As compared with those who found a sense of *ikigai*, the multivariate HR (95% CI) in those who did not find a sense of *ikigai* was 1.6 (1.3–2.0) for CVD, 1.8 (1.2–2.7) for pneumonia, 1.9 (1.1–3.3) for external causes, and 1.3 (1.0–1.6) for cancer.

We further investigated the risk of mortality from IHD and stroke among the CVD mortality. As compared with those who found a sense of *ikigai*, those who did not find a sense of *ikigai* were significantly associated with an increased risk of stroke mortality, but not of IHD mortality. The multivariate HR (95% CI) in those who did not find a sense of *ikigai* was 2.1 (1.6–2.9) for stroke and 0.9 (0.5–1.7) for IHD.

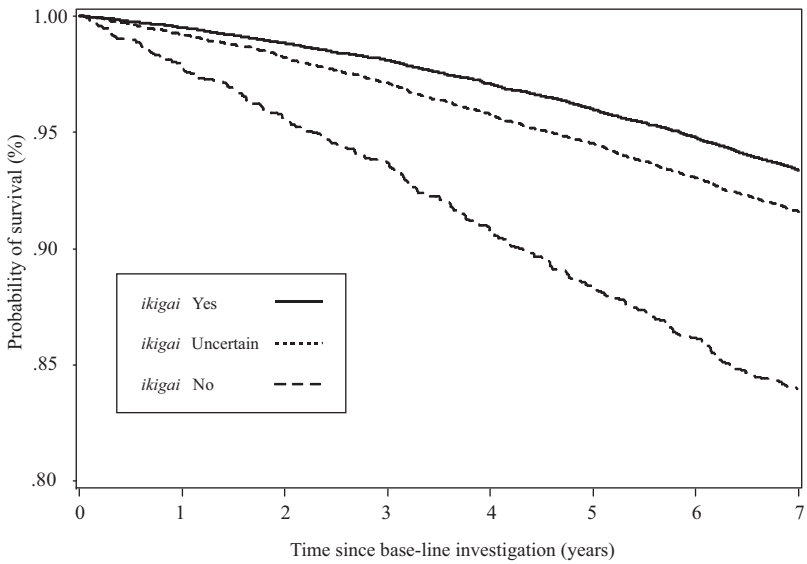

Figure 1. Kaplan-Meier curves of all-cause mortality according to *ikigai* (n = 43,391).

TABLE 2. Hazard Ratios (HRs) of Mortality According to *Ikigai* (n = 43,391)

	Ikigai		
	Yes	Uncertain	No
Person-years of follow-up	160,910	97,232	11,847
All-cause			
No. of cases	1547	1206	295
Age and sex adjusted HR (95% CI)	1.0 (reference)	1.4 (1.3–1.5)	2.5 (2.2–2.9)
p-values	—	<.001	<.001
Multivariate HR1 (95% CI)	1.0 (reference)	1.1 (1.0–1.2)	1.5 (1.3–1.7)
p-values	—	.006	<.001
Multivariate HR2 (95% CI)	1.0 (reference)	1.1 (1.0–1.2)	1.4 (1.2–1.6)
p-values	—	.082	<.001
Cancer			
No. of cases	653	374	73
Age and sex adjusted HR (95% CI)	1.0 (reference)	1.1 (0.9–1.2)	1.5 (1.2–2.0)
p-values	—	.45	<.001
Multivariate HR1 (95% CI)	1.0 (reference)	0.9 (0.8–1.1)	1.3 (1.0–1.6)
p-values	—	.36	.061
Multivariate HR2 (95% CI)	1.0 (reference)	0.9 (0.8–1.1)	1.2 (0.9–1.6)
p-values	—	.41	.22
Cardiovascular disease			
No. of cases	460	399	112
Age and sex adjusted HR (95% CI)	1.0 (reference)	1.5 (1.4–1.8)	3.0 (2.5–3.7)
p-values	—	<.001	<.001
Multivariate HR1 (95% CI)	1.0 (reference)	1.2 (1.0–1.4)	1.6 (1.3–2.0)
p-values	—	.014	<.001
Multivariate HR2 (95% CI)	1.0 (reference)	1.1 (0.9–1.3)	1.6 (1.2–2.0)
p-values	—	.24	<.001
Ischemic heart disease			
No. of cases	96	97	14
Age and sex adjusted HR (95% CI)	1.0 (reference)	1.8 (1.4–2.4)	1.9 (1.1–3.3)
p-values	—	<.001	.029
Multivariate HR1 (95% CI)	1.0 (reference)	1.4 (1.0–1.8)	0.9 (0.5–1.7)
p-values	—	.048	.81
Multivariate HR2 (95% CI)	1.0 (reference)	1.4 (1.0–2.1)	0.9 (0.4–1.9)
p-values	—	.048	.73
Stroke			
No. of cases	222	192	65
Age and sex adjusted HR (95% CI)	1.0 (reference)	1.5 (1.3–1.9)	3.6 (2.7–4.8)
p-values	—	<.001	<.001
Multivariate HR1 (95% CI)	1.0 (reference)	1.2 (1.0–1.5)	2.1 (1.6–2.9)
p-values	—	.035	<.001
Multivariate HR2 (95% CI)	1.0 (reference)	1.1 (0.9–1.4)	1.9 (1.3–2.7)
p-values	—	.37	<.001
Pneumonia			
No. of cases	102	105	34
Age and sex adjusted HR (95% CI)	1.0 (reference)	1.9 (1.5–2.5)	4.0 (2.7–5.9)
p-values	—	<.001	<.001
Multivariate HR1 (95% CI)	1.0 (reference)	1.3 (1.0–1.7)	1.8 (1.2–2.7)
p-values	—	.091	.008
Multivariate HR2 (95% CI)	1.0 (reference)	1.3 (0.9–1.7)	1.3 (0.8–2.2)
p-values	—	.13	.30
External cause			
No. of cases	91	76	19
Age and sex adjusted HR (95% CI)	1.0 (reference)	1.5 (1.1–2.0)	3.0 (1.8–4.9)
p-values	—	.011	<.001
Multivariate HR1 (95% CI)	1.0 (reference)	1.3 (0.9–1.7)	1.9 (1.1–3.3)
p-values	—	.15	.018
Multivariate HR2 (95% CI)	1.0 (reference)	1.2 (0.8–1.8)	2.4 (1.3–4.4)
p-values	—	.27	.003

(*Continued*)

TABLE 2. Continued

	Ikigai		
	Yes	Uncertain	No
Suicide			
No. of cases	44	38	8
Age and sex adjusted HR (95% CI)	1.0 (reference)	1.5 (1.0–2.3)	2.7 (1.3–5.7)
p-values	—	.067	.011
Multivariate HR1 (95% CI)	1.0 (reference)	1.4 (0.9–2.2)	2.0 (0.9–4.4)
p-values	—	.15	.11
Multivariate HR2 (95% CI)	1.0 (reference)	1.4 (0.8–2.5)	2.5 (0.9–6.7)
p-values	—	.21	.079

HR1 denotes the HR with death from all-causes included in the model.
HR2 denotes the HR with death from all-causes in the first two years of follow-up (644 deaths) excluded from analysis in the model.
Multivariate HR are adjusted for age (continuous variable), sex (men or women), marital status (married, widowed/divorced, or single), education (junior high school or higher), job (employed or unemployed), self-rated health (bad or poor, fair, or good or excellent), perceived mental stress (high, moderate, or low), bodily pain (severe or moderate, mild or very mild, or none), physical function (limited or unlimited), body mass index in kg/m^2 ($\leq$18.4, 18.5–24.9, or $\geq$25.0), smoking status (never, former, currently smoking 1–19 cigarettes/day, or $\geq$20 cigarettes/day), alcohol consumption (never, former, current ethanol intake of $\leq$22.7 g/day, 22.8–45.5 g/day, 45.6–68.3 g/day, or $\geq$68.4 g/day), time spent walking ($<$1 hour/day or $\leq$1 hour/day), sleep duration ($\geq$6 hours/day, 7–8 hours/day, or $\geq$9 hours/day), and history of hypertension, diabetes mellitus, kidney disease, liver disease, gastric or duodenal ulcer, arthritis, or osteoporosis (presence or absence).
Numbers in parentheses are 95% confidence intervals (CIs).
CI = confidence interval.

Regarding the external causes of death (186 deaths), suicide (90 deaths) was the most commonly encountered cause. The risk of suicide mortality was associated with the sense of *ikigai* at an almost significant level. As compared with those who found a sense of *ikigai*, the multivariate HR (95% CI) in those who did not find a sense of *ikigai* was 2.0 (0.9–4.4) for suicide.

The association between *ikigai* and pneumonia mortality disappeared after excluding the deaths that occurred within the first 2 years of follow-up. As compared with those who found a sense of *ikigai*, the multivariate HR (95% CI) in those who did not find a sense of *ikigai* was 1.3 (0.8–2.2) for pneumonia. The risk of other cause-specific mortality remained basically unchanged after excluding the deaths that occurred within the first 2 years of follow-up. The results obtained after excluding the deaths that occurred within 3 to 4 years of follow-up also showed an increase in the all-cause mortality risk among the subjects lacking a sense of *ikigai*.

We found that those who did not find a sense of *ikigai* were associated with an increased risk of all-cause mortality, independent of socioeconomic factors, other psychological factors, physical function, lifestyle habits, and history of illness. As shown in Table 1, the lack of *ikigai* was associated with poorer psychosocial status and poorer physical health status. We conducted stratified analyses to examine whether the association between the *ikigai* and mortality was dependent on the variables listed in Table 1. As shown in Table 3, there were no differences across age strata (p for interaction = .80). Likewise, no significant effect modification of other confounding variables was shown either (p for interaction = $>$.05). The lack of *ikigai* was associated with an increased risk of all-cause mortality, independent of the sex, marital status, educational level, employment, self-rated health, perceived mental stress, bodily pain, and physical function. We also attempted to conduct stratified analyses according to lifestyle variables and history of illness. The lack of *ikigai* was associated with an increased risk of all-cause mortality, independent of the BMI, smoking status, alcohol consumption, time spent walking, sleep duration, and a history of illness (data not shown).

DISCUSSION

In this population-based prospective cohort study in Japan, those who did not find a sense of *ikigai* were significantly associated with an increased risk of all-cause mortality. The increase in mortality risk was attributed to an increase in the mortality from CVD (mainly stroke) and external causes, but not to the morality risk from cancer. In our study subjects, those who did not find a sense of *ikigai* were likely to have a poorer socioeconomic status and poorer objective health status. However, the mortality risk in those who did not find a sense of *ikigai* was consistently increased, irrespective of socioeconomic factors, other psychological factors, physical function, lifestyle habits, and a history of illness.

Although many studies have reported an association between the psychological factors and all-cause mortality risk (1–12), the association between the negative psychological factors and the risk of cause-specific mortality remains inconsistent. In Japan, only one study has investigated the association between *ikigai* and the risk of cause-specific mortality (11). The lack of *ikigai* was associated an increased risk of CVD mortality, but not of cancer mortality. Our findings were consistent with this previous report. In addition, we have shown new evidence indicating that the lack of *ikigai* may also be associated with an increased risk of mortality from external causes, but not from pneumonia.

TABLE 3. Multivariate Hazard Ratios (HRs) of All-Cause Mortality According to *Ikigai* Stratified by Socioeconomic Factors, Other Psychological Factors, or Physical Function

	No. of Subjects	No. of Cases	*Ikigai*			*p* for Interaction*
			Yes	Uncertain	No	
Age, yr						
≤64	28,002	959	1.0 (reference)	1.1 (0.9–1.2)	1.1 (0.8–1.4)	.80
≥65	15,389	2089	1.0 (reference)	1.1 (1.0–1.2)	1.6 (1.4–1.9)	
Sex						
Men	20,625	1874	1.0 (reference)	1.1 (1.0–1.2)	1.4 (1.2–1.7)	.20
Women	22,766	1174	1.0 (reference)	1.1 (1.0–1.3)	1.6 (1.3–2.0)	
Marital status						
Married	32,089	2043	1.0 (reference)	1.1 (1.0–1.2)	1.6 (1.3–1.9)	.47
Widowed/divorced or single	7003	632	1.0 (reference)	1.2 (1.0–1.4)	1.5 (1.1–1.9)	
Education						
Junior high school	24,621	1971	1.0 (reference)	1.1 (1.0–1.2)	1.5 (1.2–1.7)	.24
Higher	16,893	858	1.0 (reference)	1.2 (1.0–1.4)	1.6 (1.2–2.2)	
Job						
Employed	20,372	995	1.0 (reference)	1.2 (1.1–1.4)	1.8 (1.4–2.4)	.43
Unemployed	11,566	1163	1.0 (reference)	1.1 (1.0–1.3)	1.5 (1.2–1.8)	
Self-rated health						
Good or excellent	28,893	1496	1.0 (reference)	1.2 (1.1–1.3)	1.6 (1.3–2.1)	.71
Bad to fair	14,312	1524	1.0 (reference)	1.1 (0.9–1.2)	1.5 (1.3–1.7)	
Perceived mental stress						
Low	7600	593	1.0 (reference)	1.1 (0.9–1.3)	1.7 (1.3–2.2)	.32
High or moderate	35,342	2380	1.0 (reference)	1.1 (1.0–1.2)	1.4 (1.2–1.7)	
Bodily pain						
None	12,983	795	1.0 (reference)	1.1 (1.0–1.3)	1.3 (1.0–1.8)	1.00
Severe to very mild	27,487	1997	1.0 (reference)	1.1 (1.0–1.3)	1.6 (1.4–1.9)	
Physical function						
Unlimited	32,161	1584	1.0 (reference)	1.1 (1.0–1.3)	1.3 (1.0–1.6)	.10
Limited	10,245	1348	1.0 (reference)	1.1 (1.0–1.3)	1.6 (1.3–1.9)	

Multivariate HR are adjusted for age (continuous variable), sex (men or women), marital status (married, widowed/divorced, or single), education (junior high school or higher), job (employed or unemployed), self-rated health (bad or poor, fair, or good or excellent), perceived mental stress (high, moderate, or low), bodily pain (severe or moderate, mild or very mild, or none), physical function (limited or unlimited), body mass index in kg/m^2 (≤18.4, 18.5–24.9, or ≥25.0), smoking status (never, former, currently smoking 1–19 cigarettes/day, or ≥20 cigarettes/day), alcohol consumption (never, former, current ethanol intake of ≤22.7 g/day, 22.8–45.5 g/day, 45.6–68.3 g/day, or ≥68.4 g/day), time spent walking (<1 hr/day or ≥ 1 hr/day), sleep duration (≤6 hr /day, 7–8 hr/day, or ≥9 hr/day), and history of hypertension, diabetes mellitus, kidney disease, liver disease, gastric or duodenal ulcer, arthritis, or osteoporosis (presence or absence). Numbers in parentheses are 95% confidence intervals (CIs).

* In calculating *p* for interaction, we treated age as continuous variable and others as dichotomous variable.

The present study had several methodological advantages as compared with previous studies on the association between *ikigai* and mortality. First, we investigated a variety of causes of death (all-cause; cancer; CVD including IHD or stroke; pneumonia and external causes including suicide). Second, we controlled extensively for potential confounders, including socioeconomic factors, other psychological factors, physical function, lifestyle habits, and a history of illness. We repeated all the analyses after excluding the deaths that occurred within the first 2 years of follow-up, and we attempted to conduct stratified analyses by confounders. In addition, the subjects with a history of cancer, myocardial infarction, and stroke were more likely to answer the lack of *ikigai*. If we included these subjects, the association between *ikigai* and the mortality risk would have been overestimated because of confounding. Thus, we excluded from our analysis the subjects with a history of cancer, myocardial infarction, and stroke. Based on our findings after taking the above details into consideration, we concluded that the association between the negative psychological factors and the mortality risk was independent of socioeconomic factors, other psychological factors, physical function, lifestyle habits, and a history of illness.

On the other hand, the present study also had some limitations. First, we had no information on the prevalence of mental illnesses, such as depression. Second, the sense of *ikigai* among our study subjects may have been altered positively or negatively during the follow-up period. However, we had no information on such changes. Third, we excluded those who failed to respond to the question on whether or not the subjects found a sense of *ikigai*. As compared with the characteristics of those who were included in this study (43,391 subjects), those who did not indicate their response to the question on *ikigai* (2939 subjects) tended to be older (mean age in years: 60.1 versus 65.1) and were more likely to have bad or poor self-rated health (18.4% versus 30.1%), severe or moderate bodily pain (16.7% versus 22.0%), and limitation of physical function (24.2% versus 49.1%). Thus, the association between

ikigai and mortality could have been underestimated, assuming that the missing respondents were in poor health with more pain, limited physical function, and/or older in age.

The increased risk of all-cause mortality among those who did not find a sense of *ikigai* was mainly attributable to an increased risk of mortality from CVD. There have been no reports on the reasons for the increase in the mortality from CVD in subjects lacking a sense of *ikigai* for the time being. However, a previous study reported that subjects with hopelessness tended to have abnormal platelet functions and reduced heart rate variability (6). The negative psychological factors in relationship to *ikigai* was associated with increased serum levels of C-reactive protein and inflammatory cytokines, and decreased serum levels of high-density lipoprotein (24–26)—all of which are known risk markers for CVD mortality.

In conclusion, this population-based prospective, cohort study in Japan demonstrated that the lack of *ikigai* was associated with an increased risk of all-cause mortality. This increase was mainly attributable to an increased mortality from CVD (mainly stroke) and that from external causes.

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