Betel nut chewing is associated with increased risk of cardiovascular disease and all-cause mortality in Taiwanese men[1,2]

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ABSTRACT

Background: Betel nut chewing is related to several kinds of cancer, metabolic syndrome, and type 2 diabetes. Whether it is associated with a greater risk of cardiovascular disease (CVD) and all-cause mortality, however, remains unclear.

Objective: We aimed to investigate the association between betel nut chewing and CVD and all-cause mortality.

Design: A baseline cohort of 56 116 male participants ≥20 y old were recruited from 4 nationwide health screening centers in Taiwan in 1998 and 1999. Cox proportional hazards regression analyses were used to estimate the relative risks (RRs) of CVD and all-cause mortality for betel nut chewers during an 8-y follow-up period.

Results: There were 1549 deaths during the follow-up period, 309 of which were due to CVD. After adjustment for age, body mass index, diabetes, hypertension, lipids, smoking, alcohol consumption, physical activity, income, and education level, the RRs (95% CI) of CVD and all-cause mortality among the former betel nut chewers were 1.56 (1.02, 2.38) and 1.40 (1.17, 1.68), respectively, and those among current chewers were 2.02 (1.31, 3.13) and 1.40 (1.16, 1.70), respectively, compared with persons who had never chewed betel quid. Current and former betel nut chewers had a higher risk of CVD mortality (RR: 2.10; $P < 0.05$) than did current and former smokers. Greater frequency of betel nut chewing was associated with greater CVD and all-cause mortality.

Conclusions: Betel nut chewing was independently associated with a greater risk of CVD and all-cause mortality in Taiwanese men. Regular screening for betel nut chewing history may help prevent excess deaths in the future. An anti-betel nut chewing program is urgently warranted for current chewers. *Am J Clin Nutr* 2008; 87:1204–11.

INTRODUCTION

Betel nut (*Areca catechu*) is the fourth most widely used addictive substance in the world. Betel nut chewers now make up ≥10% of the world's population (1, 2). There are many different ways to prepare betel nut. For example, in South Asia, people chew the fresh, dried, or cured betel nuts with slaked lime, betel leaf (*Piper betle* vine), and tobacco leaves (2, 3). In Taiwan, however, people chew betel nuts in combination with *P. betle* (inflorescence or leaf) and lime but without tobacco leaves (3, 4). Four main arecal alkaloids (ie, arecoline, arecaidine, guvacine, and guvacoline) are absorbed during betel nut chewing (1). The arecal alkaloids have been shown to be inhibitors of γ-aminobutyric acid receptor and also to have many physiologic and metabolic effects on the brain, cardiovascular system, lung, gut, and pancreas (1).

Betel nut chewing is linked not only to the development of oral and esophageal caner, hepatocellular carcinoma, and liver cirrhosis (1, 5–10) but also to obesity, type 2 diabetes, hypertension, hyperlipidemia, metabolic syndrome, and chronic kidney disease (11–16). However, it is unclear whether betel nut chewing is associated with cardiovascular disease (CVD), which is one of the leading causes of death worldwide (17). In Taiwan, the prevalence of betel nut chewing is as high as 16.9% (31% in men and 2.4% in women, respectively) (15). Until now, however, there has been no study of the long-term effect of betel nut chewing on CVD and all-cause mortality. Therefore, we investigated the association between betel nut chewing and CVD and all-cause mortality in a large Taiwanese cohort.

SUBJECTS AND METHODS

Subjects and measurements

The data were collected from 4 private nationwide MJ Health Screening Centers in Taiwan in 1998 and 1999. The registered health practitioners in these centers provide a multidisciplinary team approach to the health assessment of their members. Most of the members undergo a health examination every 3–4 y, and ≈30% of them will receive the same health check-up every year. A total of 58 771 male adults ≥20 y old, out of 124 513 subjects, were recruited into the study; female betel nut chewers were excluded because the prevalence of betel nut chewing in women was very low (0.46%). Among the 58 771 male adults, 2655 did not complete the items pertaining to betel nut chewing habits on the questionnaire. Therefore, the baseline cohort analyzed in the study comprised 56 116 participants. The population structure in

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our study was similar to the national data for adult males published by the Taiwanese government (18). Deaths were ascertained by computer linkage to the national death registry by using identification numbers. All deaths that occurred between study entry and December 2005 were included. Deaths with International Classification of Disease, Ninth Revision (ICD-9) codes 390–459 were classified as CVD deaths (19).

Anthropometric characteristics, blood pressure, and plasma fasting glucose and lipid concentrations were measured and were described in an earlier report (20). In brief, trained staff measured the height (to the nearest 0.1 cm) and weight (to the nearest 0.1 kg) of each participant by using an autoanthropometer (KN-5000A; Nakamura, Tokyo, Japan). Waist circumference was measured (to the nearest 0.1 cm) at the midway point between the inferior margin of the last rib and iliac crest in a horizontal plane by using a nonstretchable tape. Body mass index (BMI; in kg/m^2) was calculated. The blood pressure (BP) was measured in the right arm of a seated participant by using an appropriately sized cuff and a standard mercury sphygmomanometer after participants had ≥5 min of rest. Blood was drawn with minimal trauma from an antecubital vein in the morning after a 12-h overnight fast (20). Diabetes was defined as a fasting glucose concentration ≥ 7.0 mmol/L and a history of diabetes or of taking oral hypoglycemic agents or insulin (or both). Hypertension was defined as systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg (or both) and a history of hypertension or of taking antihypertensive drugs (or both).

All patients provided written informed consent. Approval for patient recruitment and data analyses was obtained from the MJ Research Foundation Review Committee in Taiwan.

Questionnaire

Betel nut chewing, cigarette smoking, alcohol consumption, and physical activity histories were recorded for each subject from a questionnaire. Current, former, and never users were defined as those who reported the current use, any prior use, and

TABLE 1
Baseline characteristics by status of betel nut chewing

	Betel nut chewing			
	Never (n = 44 565)	Former (n = 5568)	Current (n = 5983)	P
Age (y)[2]	43.4 ± 14.3[3]	40.4 ± 12.5	40.1 ± 11.6	<0.001
Height (cm)[2]	168.6 ± 6.3	168.6 ± 6.2	168.5 ± 6.1	0.922
Body weight (kg)[2]	67.3 ± 10.3	68.6 ± 11.3	68.8 ± 11.1	<0.001
BMI (kg/m^2)[2]	23.7 ± 3.2	24.1 ± 3.6	24.2 ± 3.5	<0.001
WC (cm)[2]	81.6 ± 9.7	82.5 ± 10.1	82.8 ± 9.7	<0.001
Systolic BP (mm Hg)[2]	123.3 ± 17.7	122.2 ± 17.4	121.9 ± 17.7	<0.001
Diastolic BP (mm Hg)[2]	75.5 ± 11.3	75.6 ± 11.4	75.8 ± 11.8	0.312
Fasting glucose (mg/dL)[2]	100.2 ± 22.7	101.5 ± 28.9	100.0 ± 24.7	<0.001
TCHOL (mg/dL)[2]	203.1 ± 37.8	203.4 ± 40.2	200.5 ± 40.0	<0.001
Triacylglycerol (mg/dL)[2]	136.6 ± 105.1	160.9 ± 158.9	180.8 ± 187.8	<0.001
HDL-C (mg/dL)[2]	43.5 ± 14.1	41.5 ± 15.0	41.3 ± 16.5	<0.001
Diabetes [n (%)][4]	2225 (5.0)	330 (5.9)	306 (5.1)	0.012
Hypertension [n (%)][4]	9876 (22.2)	1090 (19.6)	1191 (19.9)	<0.001
Alcohol drinking [n (%)][4]				<0.001
Never	30 513 (71.3)	2111 (39.7)	1833 (32.4)	
Former	2054 (4.8)	685 (12.9)	231 (4.1)	
Current	10 238 (23.9)	2522 (47.4)	3587 (63.5)	
Smoking [n (%)][4]				<0.001
Never	24 682 (56.7)	567 (10.5)	573 (10.0)	
Former	5204 (12.0)	1064 (19.7)	376 (6.6)	
Current	13 626 (31.3)	3770 (69.8)	4783 (83.4)	
Physical activity [n (%)][4]				<0.001
None or mild	18 010 (41.8)	2857 (54.8)	3263 (59.6)	
Moderate	17 235 (40.0)	1632 (31.3)	1601 (29.3)	
Vigorous	7805 (18.1)	721 (13.8)	609 (11.1)	
Income [n (%)][4]				<0.001
Low	12 150 (28.3)	1900 (35.8)	1861 (33.0)	
Middle	25 884 (60.3)	3051 (57.6)	3379 (59.9)	
High	4857 (11.4)	350 (6.6)	402 (7.1)	
Education [n (%)][4]				<0.001
Low	6198 (14.1)	1082 (19.8)	1242 (21.3)	
Middle	12 874 (29.3)	2953 (54.2)	3412 (58.5)	
High	24 826 (56.6)	1416 (26.0)	1176 (20.2)	

[1] WC, waist circumference; BP, blood pressure; TCHOL, total cholesterol; HDL-C, HDL cholesterol.
[2] ANOVA was used for comparing mean values of continuous variables between groups.
[3] $\bar{x}$ ± SD (all such values).
[4] Pearson chi-square test was used for categorical data.

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TABLE 2
Baseline characteristics by survival status and causes of death[1]

	Survivors (n = 54 567)	CVD deaths (n = 309)	All-cause deaths (n = 1549)
Age (y)[2]	42.2 ± 13.6[3]	64.5 ± 12.3[4]	62.0 ± 13.4[4]
Height (cm)[2]	168.7 ± 6.2	164.7 ± 6.1[4]	165.1 ± 6.1[4]
Body weight (kg)[2]	67.7 ± 10.4	65.4 ± 10.7[4]	64.1 ± 10.9[4]
BMI (kg/m^2)[2]	23.8 ± 3.3	24.1 ± 3.4	23.5 ± 3.4[4]
WC (cm)[2]	81.7 ± 9.7	86.5 ± 9.8[4]	84.2 ± 10.7[4]
Systolic BP (mm Hg)[2]	122.7 ± 17.3	142.3 ± 24.6[4]	135.6 ± 23.8[4]
Diastolic BP (mm Hg)[2]	75.5 ± 11.3	81.6 ± 13.6[4]	78.5 ± 13.0[4]
Fasting glucose (mg/dL)[2]	99.9 ± 22.6	117.3 ± 43.9[4]	113.8 ± 45.5[4]
TCHOL (mg/dL)[2]	202.8 ± 38.1	215.2 ± 43.4[4]	204.6 ± 45.1
Triacylglycerol (mg/dL)[2]	143.5 ± 122.9	164.9 ± 149.8[5]	152.0 ± 144.5[6]
HDL-C (mg/dL)[2]	43.0 ± 14.4	42.5 ± 16.9	43.1 ± 16.8
Betel nut chewing [n (%)][7]			
Never	43 345 (79.4)	246 (79.6)	1220 (78.8)
Former	5402 (9.9)	31 (10.0)	166 (10.7)
Current	5820 (10.7)	32 (10.4)	163 (10.5)
Smoking [n (%)][7]			
Never	25 275 (47.6)	112 (37.7)[4]	547 (36.4)[4]
Former	6356 (12.0)	64 (21.5)	288 (19.2)
Current	21 512 (40.5)	121 (40.7)	667 (44.4)

[1] WC, waist circumference; BP, blood pressure; TCHOL, total cholesterol; HDL-C, HDL cholesterol; CVD, cardiovascular disease. Statistical analysis was performed to compare variables between survivors and CVD deaths and between survivors and all-cause deaths.
[2] Student's t test was used to compare continuous variables.
[3] $\bar{x}$ ± SD (all such values).
[4] $P < 0.001$.
[5] $P < 0.01$.
[6] $P < 0.05$.
[7] Pearson's chi-square test was used to compare categorical data.

no use of betel nuts, respectively, at baseline survey. Furthermore, current betel nut chewers were divided into 2 groups according to the frequency of use: those who reported chewing betel nut 1–6 times/wk and those who reported chewing it ≥7 times/wk. Current, former, and never smokers were defined as those who reported current use, prior use, and no use of cigarette smoking, respectively. Current, former, and never drinkers of alcohol were defined as those who reported current use, prior use, and no use of alcohol, respectively. Physical activity was divided into 3 levels: none to mild (exercised <1 h/wk), moderate (exercised 1–4 h/wk), and vigorous (exercised >5 h/wk) physical activity. Income was divided into 3 levels: low (<$12 500/y; US$1 = 32 New Taiwan dollars), middle ($12 500–$37 500/y), and high (>$37 500/y). Education was also divided into 3 levels: low (elementary school and below), middle (junior and senior high school), and high (college or university and above).

Statistical analysis

The data are presented as the means and SDs for continuous variables. The Kolmogorov-Smirnov test was assessed before further analyses, and log transformation was used for variables with significant deviation from normal distribution. Student's t

TABLE 3
Relative risks (and 95% CIs) of betel nut chewing for cardiovascular disease (CVD) and all-cause mortality in several different models using Cox proportional hazards regression analyses adjusted for some potential confounders

Betel nut chewing	Mortality	Model 1[1]	Model 2[2]	Model 3[3]
Never	CVD	1.00 (reference)	1.00 (reference)	1.00 (reference)
Former	CVD	1.79 (1.23, 2.62)[4]	1.62 (1.06, 2.47)[5]	1.56 (1.02, 2.38)[5]
Current	CVD	2.02 (1.39, 2.95)[6]	2.01 (1.30, 3.10)[4]	2.02 (1.31, 3.13)[4]
Never	All-cause	1.00 (reference)	1.00 (reference)	1.00 (reference)
Former	All-cause	1.78 (1.51, 2.10)[6]	1.22 (1.30, 1.75)[6]	1.40 (1.17, 1.68)[6]
Current	All-cause	1.85 (1.57, 2.19)[6]	1.21 (1.28, 1.78)[6]	1.40 (1.16, 1.70)[4]

[1] Adjusted for age and BMI.
[2] Adjusted for age, BMI, alcohol consumption, smoking, physical activity status, income, and education level.
[3] Adjusted for age, BMI, diabetes, hypertension, total cholesterol, HDL cholesterol, triacylglycerol, alcohol consumption, smoking, physical activity status, income, and education level.
[4] $P < 0.01$.
[5] $P < 0.05$.
[6] $P < 0.001$.

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test for unpaired data was used to compare mean values between 2 groups. Proportions and categorical variables were tested by the chi-square test and by the 2-tailed Fisher's exact method when appropriate. Cox proportional hazards regression analyses adjusted for possible confounders were used to estimate the relative risks (RRs) for CVD and all-cause mortality. Survival curves adjusted for other covariates were drawn for current and never betel nut chewers, never smokers, and never betel nut chewers, respectively (21, 22). These statistical analyses were performed by using SPSS statistical software (version 13.0; SPSS Inc, Chicago, IL).

RESULTS

There were 1549 deaths over 8 y of follow-up; of these deaths, 309 were due to CVD. At the baseline survey, there were 44 565 (79.4%) never chewers, 5568 (9.9%) former chewers, and 5983 (10.7%) current betel nut chewers. The current betel nut chewers were younger and had higher BMI, waist circumference, and triacylglycerol than did never chewers, as is shown in **Table 1**. There was a higher proportion of smoking and alcohol consumption among current and former betel nut chewers than among never chewers. As shown in **Table 2**, participants who died of CVD were older and had greater waist circumference, higher systolic and diastolic BP, and fasting glucose, total cholesterol, and triacylglycerol concentrations than did survivors. Participants who died of any cause also were older and had greater waist circumference, higher systolic and diastolic BP, and higher fasting glucose and triacylglycerol concentrations than did survivors.

Using Cox proportional hazards regression analyses with adjustment for potential confounders, the RRs for CVD and all-cause mortality were higher among current and former betel nut chewers than among never chewers (**Table 3**). Among the 3 models, there was no interaction ($P > 0.05$) between betel nut chewing and smoking status for predicting the risk of CVD and all-cause mortality. The adjusted RRs for CVD and all-cause mortality were 1.56 (95% CI: 1.02, 2.38) and 1.40 (1.17, 1.68) in former users and 2.02 (1.31, 3.13) and 1.40 (1.16, 1.70) in current users, respectively (model 3 in Table 3).

Among the current and never chewers, increased frequency of betel nut chewing was associated with greater CVD and all-cause mortality. The adjusted RRs for CVD and all-cause mortality were higher among those who currently chewed betel nut ≥7 times/wk than among those who currently chewed betel nut <7 times/wk and the never chewers (**Figure 1**). The adjusted RRs for CVD and all-cause mortality among the current chewers who chewed ≥7 times/wk were 2.37 (1.07, 5.23) and 2.18 (1.53, 3.10), respectively, compared with those who chewed <7 times/wk. Similarly, among the never smokers, the adjusted RRs for CVD and all-cause mortality were also higher among those who currently chewed betel nut ≥7 times/wk than among those who currently chewed betel nut <7 times/wk and never chewers (**Figure 2**). Among the never chewers, the adjusted RRs for CVD and all-cause mortality in the current smokers were higher than that among the never smokers (**Figure 3**).

The adjusted RRs for CVD and all-cause mortality among various combinations of smoking and betel nut chewing status are shown in **Table 4**. Current and former betel nut chewers had higher risks of CVD (RR: 2.10; $P = 0.05$) and all-cause (RR: 1.19; $P = 0.354$) mortality than did current and former smokers.

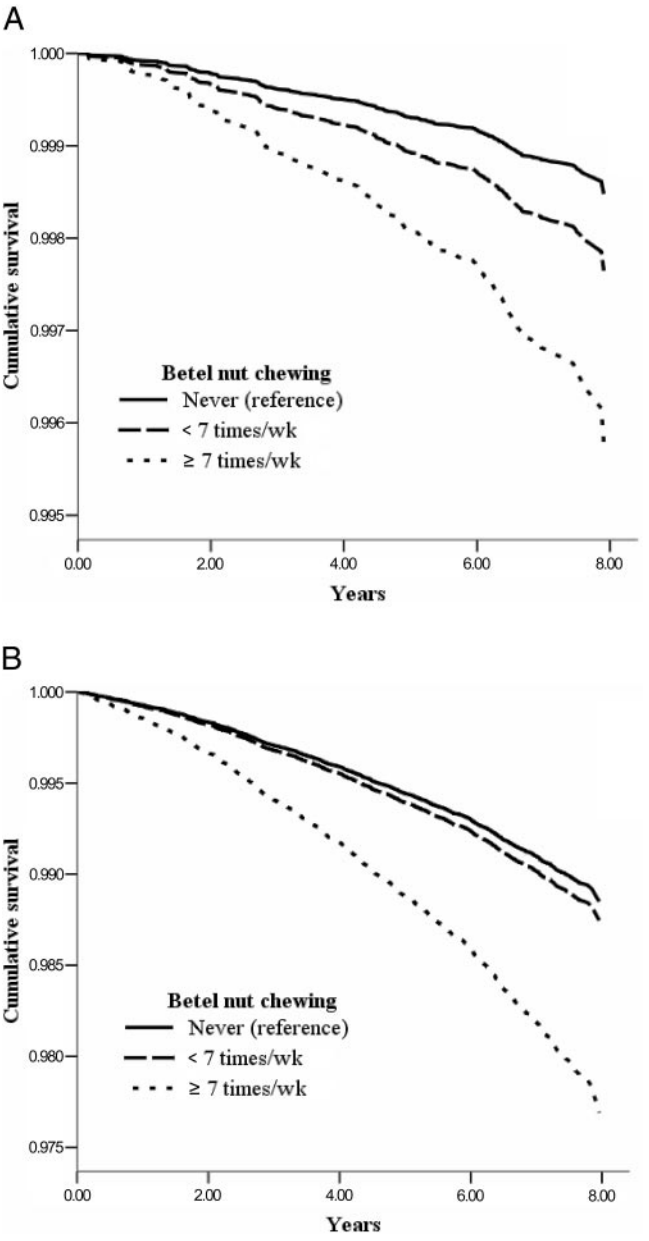

FIGURE 1. Survival curves for current and never chewers ($n = 50\,548$) after adjustment for other covariates. Cox proportional hazards regression analyses were adjusted for age, BMI, diabetes, hypertension, total cholesterol, HDL cholesterol, triacylglycerol, alcohol consumption, smoking, physical activity status, income, and education level. A: The adjusted relative risk (RR) (and 95% CIs) for CVD mortality among subjects who currently chewed betel nut ≥7 times/wk and <7 times/wk was 2.77 (1.58, 4.88) and 1.55 (0.86, 2.80), respectively, compared with those who never chewed. B: The adjusted RR for all-cause mortality among subjects who currently chewed betel nut ≥7 times/wk and <7 times/wk was 2.02 (1.57, 2.60) and 1.09 (0.84, 1.42), respectively, compared with those who never chewed.

DISCUSSION

In this population-based prospective study, we showed that betel nut chewing was associated with greater CVD and all-cause mortality in Taiwanese men. Similarly, Lan et al (4) showed that areca nut chewing is associated with greater CVD and all-cause mortality in the Taiwanese elderly. In addition, we also found

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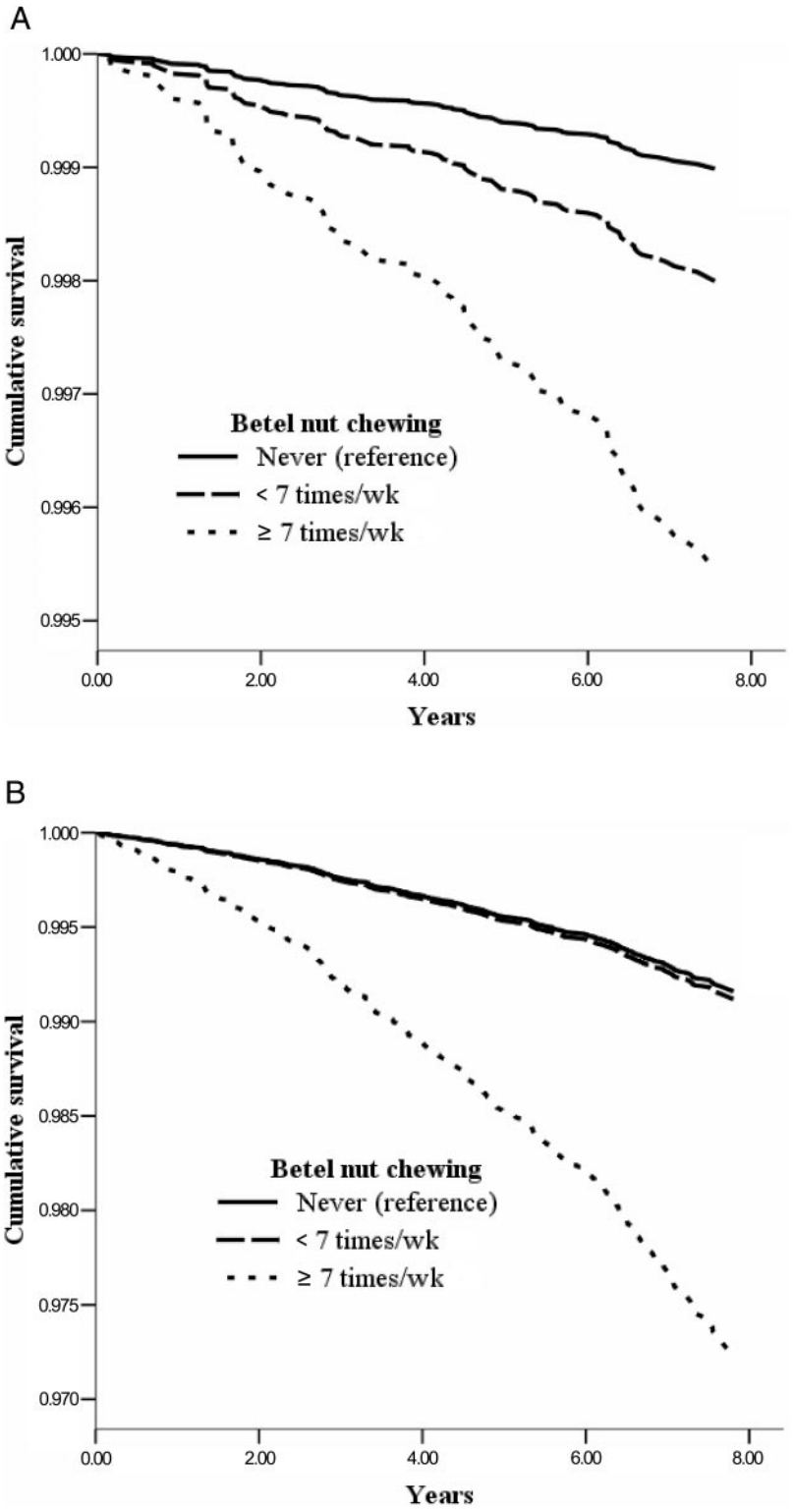

FIGURE 2. Survival curves for never smokers (n = 25 822) after adjustment for other covariates. Cox proportional hazards regression analyses were adjusted for age, BMI, diabetes, hypertension, total cholesterol, HDL cholesterol, triacylglycerol, alcohol consumption, physical activity status, income, and education level. A: The adjusted relative risk (RR) (and 95% CIs) for CVD mortality among subjects who currently chewed betel nut ≥7 times/wk and <7 times/wk was 4.49 (1.04, 19.5) and 1.98 (0.47, 8.36), respectively, compared with those who never chewed. B: The adjusted RR for all-cause mortality among subjects who currently chewed betel nut ≥7 times/wk and <7 times/wk was 3.34 (1.63, 6.84) and 1.05 (0.46, 2.38), respectively, compared with those who never chewed.

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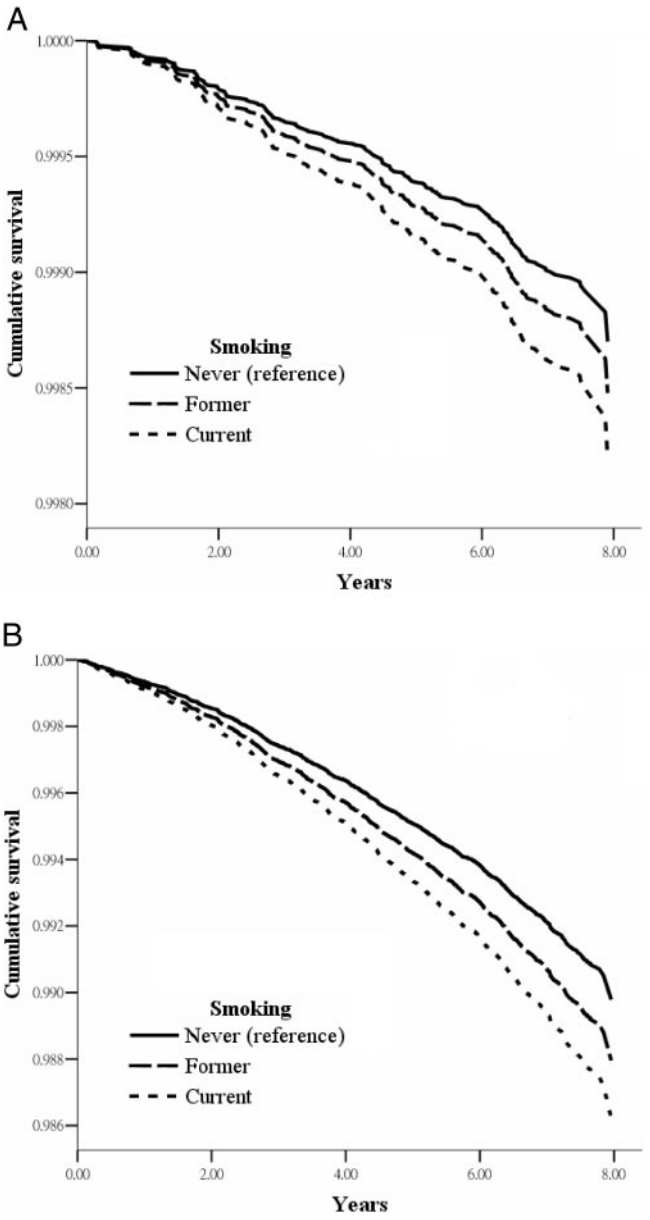

FIGURE 3. Survival curves for never chewers of betel nut (n = 44 565) after adjustment for other covariates. Cox proportional hazards regression analyses were adjusted for age, BMI, diabetes, hypertension, total cholesterol, HDL cholesterol, triacylglycerol, alcohol consumption, physical activity status, income, and education level. A: The adjusted relative risk (RR) (and 95% CIs) for CVD mortality among subjects who were current and former smokers was 1.39 (1.01, 1.91) and 1.17 (0.82, 1.68), respectively, compared with those who never smoked. B: The adjusted RR for all-cause mortality among subjects who were current and former smokers was 1.35 (1.17, 1.56) and 1.18 (1.00, 1.39), respectively, compared with those who never smoked.

that the RRs for CVD and all-cause mortality increased with the frequency of betel nut chewing. Furthermore, betel nut chewing was associated with a higher risk of CVD and all-cause mortality than was smoking. Betel nut chewing, therefore, has become a big challenge to public health in Taiwan as well as in other areas with high prevalence of betel nut chewing.

Although most of the world's betel nut chewers are in Asia (2), the growing number of immigrants from Asia to Europe and North America means that betel nut chewing is becoming a global problem. The number of betel nut chewers has been estimated at up to 600 million worldwide (3). Previous studies have clearly shown arecal alkaloids to be carcinogens, which increase the risk of various cancers of the oral cavity, esophagus, and liver (3, 8, 9, 23, 24). In addition, betel nut chewing has been found to be associated with obesity, metabolic syndrome, diabetes, and chronic kidney disease (13, 14, 16, 25). Although these diseases are closely related to the development of CVD, the relation between betel nut chewing and CVD remains unclear.

In the present study, we found that current and former betel nut chewers had greater CVD mortality than did never chewers. Furthermore, betel nut chewing and smoking were independently associated with CVD mortality. We also found that current and former betel nut chewers had a higher risk of CVD mortality (RR: 2.10; $P < 0.05$) than did current and former smokers. Moreover, the RRs for CVD and all-cause mortality increased with the frequency of betel nut chewing. Therefore, betel nut chewing should be treated as a major risk factor for CVD. Developing a cessation program should be considered as an intervention strategy for CVD among betel nut chewers.

Several possible mechanisms may explain the relation between betel nut chewing and greater CVD mortality. First, betel nut chewing appears to activate the sympathetic nervous system, thereby inducing the secretion of adrenal catecholamines (1, 26). Second, arecal alkaloids act as inhibitors of γ-aminobutyric acid receptor. The blockade of the inhibitory effects of γ-aminobutyric acid on glucagon and somatotrophin may result in the secretion of glucagon and subsequently in the development of diabetes. Greater appetite and glucose intolerance due to γ-aminobutyric acid inhibition and diabetogenic arecal nitrosamines may also play an important role in the development of diabetes (1, 11, 13, 14, 25, 27, 28). Third, betel nut chewing enhances oxidative stress, which increases the risk of CVD (29, 30). Fourth, betel nut chewing may induce periodontal disease, which is a chronic inflammatory disease with T cell activation and production of inflammatory mediators (31). Among these factors, interleukin-6 and tumor necrosis factor-α are proinflammatory cytokines related to the development of CVD (32–34). It is interesting that, in a meta-analysis of 9 cohort studies, Janket et al (35) showed that persons with periodontal disease have a greater incidence of CVD than do those without periodontal disease. Therefore, the complex pathogenesis of CVD related to betel nut chewing deserves further study.

Although we have shown that betel nut chewing is associated with a greater risk of CVD and all-cause mortality, the present study has some limitations. First, the questionnaires were lacking in details about betel use, such as the numbers of quids used per day, the duration of the habit, and the preparation used. Therefore, the exact duration and cumulative exposure of betel nut could not be quantified in the present study. Similar limitations were noted for smoking status. Second, our study population was drawn from generally healthy volunteers who attended health screening centers rather than from nationally representative subjects. External validation is necessary in future studies. Third, the fact that only baseline data for these participants were available may have led to possible misclassifications of betel nut chewing status during follow-up.

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TABLE 4
Relative risks (and 95% CIs) among the various combinations of smoking and betel nut chewing status for cardiovascular disease (CVD) and all-cause mortality using Cox proportional hazards regression analyses[1]

	CVD	All-cause
Never smoking and never betel nut chewing (n = 24 682)	1.00 (Reference)	1.00 (Reference)
Former smoking and never betel nut chewing (n = 5204)	1.17 (0.81, 1.67)	1.17 (0.99, 1.38)
Current smoking and never betel nut chewing (n = 13 626)	1.27 (0.92, 1.74)	1.30 (1.13, 1.49)[2]
Current or former betel nut chewing and never smoking (n = 1140)	2.91 (1.43, 5.93)[3]	1.61 (1.11, 2.34)[4]
Current or former betel nut chewing and current or former smoking (n = 9993)	2.03 (1.38, 3.00)[2]	1.80 (1.52, 2.12)[2]

[1] Model adjusted for age, BMI, diabetes, hypertension, total cholesterol, HDL cholesterol, triacylglycerol, alcohol consumption, physical activity status, income, and education level. There was no interaction between betel nut chewing and smoking status for predicting the risk of CVD (P = 0.192) or all-cause (P = 0.087) mortality.
[2] $P < 0.001$.
[3] $P < 0.01$.
[4] $P < 0.05$.

In conclusion, we have shown betel nut chewing to be independently associated with greater CVD and all-cause mortality after control for possible confounders in Taiwanese men. The RRs for CVD and all-cause mortality increased with the frequency of betel nut chewing. Furthermore, betel nut chewing had a greater risk of CVD mortality than did smoking. At the national level, it is crucial to develop a special program to help betel nut chewers quit their habit. For physicians and other health workers, it is important to screen people for betel nut chewing in their clinical practices. Furthermore, the detailed relation between betel nut chewing and CVD requires further investigation.

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