



## Full length article

# Relationship between betel quid chewing and risks of cardiovascular disease in older adults: A cross-sectional study in Taiwan



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## ARTICLE INFO

## Article history:

Received 28 April 2014

Received in revised form 16 May 2014

Accepted 21 May 2014

Available online 3 June 2014

## Keywords:

Betel quid

Cardiovascular disease

High-sensitivity C-reactive protein

Obesity

## ABSTRACT

**Background:** The association between betel quid (BQ) chewing and oral cancer is well established. However, evidence regarding the relationship between BQ chewing and cardiovascular disease (CVD) is still insufficient.

**Methods:** This cross-sectional study included 2002 men and 1175 women aged 50 and older in a city-level health examination survey of an agricultural and fishing population in 2013. In addition to anthropometric parameters, CVD risks were estimated using high-sensitivity C-reactive protein (hs-CRP), brachial-ankle pulse wave velocity (baPWV) and ankle-brachial index. Age, gender, smoking and alcohol drinking status were all incorporated into the multivariate logistic regression model to delineate the effect of BQ chewing on CVD risks.

**Results:** Two hundred forty-one (12%) males and eight (0.7%) females were ever chewers. BQ chewing was an independent risk factor for general obesity (odds ratio [OR] 1.43, 95% confidence interval [CI] 1.07–1.91,  $p = 0.017$ ), central obesity (OR 2.27, 95% CI 1.53–3.37,  $p < 0.001$ ) and an elevated hs-CRP level (OR 1.38, 95% CI 1.03–1.85,  $p = 0.029$ ). Subjects who chewed more frequently had a higher systolic blood pressure ( $p = 0.025$ ) and baPWV ( $p = 0.006$ ). The waist circumference ( $p = 0.015$ ) and waist-to-height ratio ( $p = 0.022$ ) were greater in current chewers than in former chewers.

**Conclusion:** These findings suggest that BQ chewing is associated with obesity and a higher CVD risk as estimated by hs-CRP. Furthermore, potential beneficial effects of BQ chewing cessation on central obesity were also found.

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## 1. Introduction

Betel quid (BQ) chewing, which is widespread in certain regions of Asia, is a well-known risk factor for the development of oral premalignancy and cancer (Lee et al., 2012; Thomas et al., 2007). Nonetheless, the deleterious effects of BQ chewing are not limited to the oral cavity, and previous studies have demonstrated a systemic hazard affecting numerous parts of the body (Javed et al., 2010). BQ chewers are reported to be at a greater risk of developing metabolic syndrome which implies an increased likelihood of

cardiovascular disease (CVD; Yamada et al., 2013; Yen et al., 2006). Consequently, in recent years new research studies have appeared that tackle the issue of CVD.

Observational cohort studies in Taiwan have examined the relationship between BQ chewing and CVD (Lan et al., 2007; Lin et al., 2008; Wen et al., 2005; Yen et al., 2008). Although discrepancies exist in these studies, most have suggested the association between BQ chewing with CVD (Lan et al., 2007; Lin et al., 2008; Yen et al., 2008) and all-cause mortality (Lan et al., 2007; Lin et al., 2008; Wen et al., 2005). Furthermore, cross-sectional studies have demonstrated an increased rate of hypertension (Heck et al., 2012), self-reported heart disease (Guh et al., 2007) and coronary artery disease (Tsai et al., 2012) among BQ chewers. Despite these findings sufficient evidence is still lacking to show the association of BQ chewing with the development of CVD.

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In addition to conventional risk factors, surrogate markers of inflammation and atherosclerosis have been demonstrated to improve CVD risk prediction (Hirsch et al., 2006; Kawai et al., 2013; Pearson et al., 2003). A recently implemented social welfare program for agricultural and fishing population in northern Taiwan provided an opportunity to assess the effects of BQ chewing using these CVD risk measurements which were non-invasive and suitable for mass screening. The purpose of this study, therefore, was to elucidate the effects of BQ chewing on CVD as measured by these markers.

## 2. Methods

### 2.1. Study population

This investigation is a hospital-based cross-sectional study. Subjects were retrieved from the database of a city-level health examination survey for agricultural and fishing population in northern Taiwan. All adults aged  $\geq 50$  years that were currently engaged as farmers or fishers were eligible for a government subsidy. From August, 2013 to December, 2013, a total of 3292 subjects (1211 women and 2081 men) who were physically active and apparently healthy voluntarily admitted themselves to the New Taipei City Hospital for a health examination. All subjects with information regarding BQ chewing habit were included for analysis and all information was anonymous. This research designed to examine the public service program was subject to the approval of the Agriculture Department of New Taipei City Government and an exemption of ethical approval was granted. All procedures were performed in accordance with the guidelines of the institutional ethics committee.

### 2.2. Demographics and clinical history

A standardized questionnaire was used by a well-trained nurse to interview all subjects. The questionnaire collected information about the subjects' demographic characteristics and history of using three major substances (cigarette smoking, alcohol consumption, and BQ chewing). A current BQ chewer was defined as a person who had regularly chewed BQ for  $\geq 6$  months and was still chewing in the previous month. A former BQ chewer was defined as a person who had regularly chewed BQ for  $\geq 6$  months, but had not chewed in the previous month. Self-reported diseases including diabetes mellitus, hypertension, heart disease, lung disease, renal disease, cerebral stroke and malignancy were also recorded. Every subject had the discretion regarding whether to answer any of these questionnaire items.

### 2.3. Anthropometric measurements

Anthropometric measurement of each subject was performed by trained nurses in the morning. Body height was recorded to the nearest 0.1 cm and body weight to the nearest 0.1 kg. Body mass index (BMI) was defined as body weight (kg) divided by the square of body height (m). Waist circumference was measured in the horizontal plane midway between lowest rib and the iliac crest of a normal expiration. The waist-to-height ratio ( $W/Ht$ ) was computed as waist circumference (cm) divided by height (cm).

### 2.4. CVD risk measurements

Blood pressure (BP) was taken after at least 5 min of rest while seated, with appropriately sized cuffs positioned at heart level and both arms supported. The ankle-brachial index (ABI) was measured by an oscillometric BP monitor (Microlife WatchBP Office) which was thought to be comparable with the standard Doppler measurement (Kollias et al., 2011). The lower measurement of left and right ABI was used for analysis. Brachial-ankle pulse wave velocity (baPWV), an indicator of arterial stiffness and the development of atherosclerotic disease, was measured using an automated device (form PWV/ABI; Colin, Co., Ltd., Komaki, Japan) (Yamashina et al., 2002). The average measurement of left and right baPWV was used for analysis. Plasma high-sensitivity C-reactive protein (hs-CRP) levels were measured by automatic analyzers (UniCel Dx C 600i Synchron Access Clinical Systems; Beckman Coulter, Inc., US).

### 2.5. Definitions

Optimal cut-off values of tests were determined for CVD risk measurements on the basis of published literature. A high BP was defined as a systolic BP of  $\geq 140$  mmHg and/or a diastolic BP of  $\geq 90$  mmHg (Chobanian et al., 2003). General obesity was defined if a BMI was  $\geq 25$  kg/m<sup>2</sup>; increased waist circumference was defined if an abdominal circumference was  $\geq 90$  cm in men and  $\geq 80$  cm in women according to the Asian-adapted definitions (Nestel et al., 2007). Central obesity was defined as a waist-to-height ratio ( $W/Ht$ )  $\geq 0.5$  in both genders (Hsieh and Muto, 2005). By the hs-CRP value, CVD risk status could be stratified as low ( $<1.0$  mg/L), intermediate ( $1.0$ – $3.0$  mg/L) or high ( $>3.0$  mg/L) (Pearson et al., 2003); therefore, an elevated hs-CRP level was defined as  $1.0$  mg/L or more. An ABI between  $0.41$  and  $0.9$  was

interpreted as mild to moderate peripheral artery disease (PAD) and an ABI of  $\leq 0.4$  as severe PAD (Hirsch et al., 2006); we defined an ABI as abnormal if the ABI was  $<0.9$  in at least one leg. A baPWV higher than  $1750$  cm/s is an independent risk factor of CVD and stroke (Kawai et al., 2013); an abnormal baPWV was defined if the average value of the right and left legs was  $\geq 1750$  cm/s.

### 2.6. Statistical analysis

The Kolmogorov–Smirnov test was used to verify the normality of the data and all continuous variables were found to be nonparametric. The data were presented as number (percentage), number/total number (percentage) or median (interquartile range [IQR]). Chi-square or Fischer's exact tests were used to compare categorical variables where appropriate, and the Mann–Whitney  $U$  test was used to compare continuous variables. Univariate logistic regression analysis was carried out to analyze the effect of BQ chewing on CVD risks and any variable with a  $p$  value of  $<0.1$  in univariate analysis was incorporated into multivariate models. Univariate logistic regression analysis was also used to analyze the association between obesity and systemic inflammation. Statistical significance was set at  $p < 0.05$ . All analyses were performed using the SPSS version 12.0 (SPSS, IBM Inc., Chicago, IL, USA).

## 3. Results

### 3.1. Description of study population

Information about BQ chewing was available in a total of 3177 subjects, including 2002 men (63%) and 1175 women (37%). The median age of the total study population was 63 years (IQR 57–71). Overall, 249 (7.8%) subjects were ever chewers, including 241 (12%) of males and 8 (0.7%) of females. In the chewer group, 126 (50.6%) were former chewers. Among the 123 current chewers, 30 (24.4%) were daily BQ chewers. Table 1 compares the characteristics of the chewers and non-chewers. Individuals of the chewer group were more likely to be male and younger than those of the non-chewer group. In addition, an association between BQ chewing and obesity, drinking and smoking was observed.

### 3.2. Association of BQ chewing and CVD risks

Using univariate logistic regression, the relationships between BQ chewing and parameters which are accompanied by an increased risk of CVD were demonstrated (Table 2). BQ chewing is significantly associated with five of these parameters, including general obesity ( $BMI \geq 25$  kg/m<sup>2</sup>), central obesity ( $W/Ht \geq 0.5$ ), diastolic hypertension (diastolic BP  $\geq 90$  mmHg), an elevated hs-CRP level ( $\geq 1.0$  mg/L) and an abnormal baPWV ( $\geq 1750$  cm/s).

All five significant parameters in the univariate analysis were further analyzed in the multivariate logistic regression adjusted for smoking, drinking, age and gender (Table 3). BQ chewing is an independent factor for general obesity (OR 1.43, 95% CI 1.07–1.91,  $p = 0.017$ ), central obesity (OR 2.27, 95% CI 1.53–3.37,  $p < 0.001$ ) and an elevated hs-CRP level (OR 1.38, 95% CI 1.03–1.85,  $p = 0.029$ ).

### 3.3. Effects of BQ chewing frequency and cessation

Comparison between daily and non-daily current BQ users is shown in Table 4. Among the current chewers, subjects who chewed daily had a higher systolic BP ( $p = 0.025$ ) and baPWV ( $p = 0.006$ ). A comparison between current and former BQ users is shown in Table 5. Although more former chewers had also smoked when compared with current chewers, cessation of BQ chewing was associated with a decreased waist circumference ( $p = 0.015$ ) and  $W/Ht$  ( $p = 0.022$ ).

### 3.4. Association between obesity and hs-CRP

As a whole, both central obesity (OR 2.75, 95% CI 2.32–3.25,  $p < 0.001$ ) and general obesity (OR 1.97, 95% CI 1.71–2.27,  $p < 0.001$ ) are associated with hs-CRP elevation. Among ever chewers, significance in central obesity (OR 2.07, 95% CI 1.01–4.23,  $p = 0.047$ )

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