Original Article

Intake of Tea Decreased the Incidence of Cardiovascular Disease in Taiwan

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Purpose: The pathogenesis of diabetic cardiovascular disease is affected by many lifestyle factors, including diet, physical activity and healthful behavior. This research was to assess the effect of tea in patients with type 2 diabetes mellitus on prevention of cardiovascular disease.

Methods: This was a cohort study on demographic data, lifestyle factors and clinical characteristics of stratified selected clients in Taiwan from 2004/01/01 to 2005/12/31. During the two year study period, 435 diabetic subjects with non- cardiovascular disease were included in this study. Applicable analysis weights, Stata 11.0, were applied, to adjust the design variables for clustering and stratification.

Results: A univariate cox proportional hazards evaluation model showed the beneficial effect of dietary factors (including vegetables, fruits, and tea). The results of a multivariate cox proportional hazards evaluation model were similar to those of a univariate cox proportional hazards evaluation model. Older age and presence of hypertension both influence the progression of cardiovascular disease in diabetic subjects. Consumption of vegetables and tea can delay the progression of diabetic cardiovascular disease. Moreover, tea consumption showed a beneficial effect on the progression of diabetic cardiovascular disease in a dose-dependent manner.

Conclusions: In this study, the consumption of tea slowed the progression of cardiovascular disease in diabetic patients.

Key words: Cohort study, DM, Cardiovascular disease, Tea, Stratification

Introduction

The International Diabetes Federation (IDF) has estimated that the global diabetic population was 151 million in 2000, and 366 million in 2011. This population is expected to be 552 million by 2030[1]. In Taiwan, the number of diabetic patients also increased rapidly during these years. According to the database from the Taiwan National Health Insurance (NHI) program, the age-standardized prevalence of diabetes in Taiwan increased from 4.7% to 6.5% for men and from 5.3% to 6.6% for women between 1999 and 2004[2]. Diabetes, hypertension and dsylipidemia are risk factors that contribute to the increased incidence of cardiovascular disease. Besides, macrovascular

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Table 1. ***Demographic data of study population (n=435)***

		Unweighted sample	*Weighted prcentage n (%)*
Age, mean±SD			55.54±13.51
Sex			
	Female	200	45.3
	Male	235	54.7
BMI			
	< 18.5	11	1.7
	18.5-23.9	153	37
	≧ 24	271	61.3
Education			
	≦ Elementary school	221	45.1
	Junior school	65	15.6
	High school	84	22.4
	≧ College	65	16.9
Marital status			
	No	96	19.8
	Yes	339	80.2
Household monthly income			
	< $30,000	156	32.4
	$30,000~$49,999	99	21.2
	$50,000~$69,999	63	16
	≧ $70,000	117	30.4
Physical activity			
	No	185	40.9
	Yes	250	59.1
Drinking			
	No	304	68.1
	Yes	131	31.9
Smoking			
	No	303	69.1
	Yes	132	30.9
CCI†			
	0	264	62.4
	1	137	31.1
	≧ 2	34	6.6
Dyslipidemia drug			
	No	357	81.4
	Yes	78	18.6
Hypertension drug			
	No	194	46.7
	Yes	241	53.3
Diet¶ (mean±SD)			
	Meat/livestock		4±2.1
	Seafood		5.4±2. 8
	Egg		2.5±2
	Milk		2±2.4
	Soybean		1.9±1.8
	Vegetables		5.8±0.9
	Fruit		4.7±1.9
	Coffee		0. 9±1.7
	Tea		3±2.6

†Charlson comorbidity index
¶average number of weekly diet and standard deviation

complications of cardiovascular disease (CVD) are the leading cause of morbidity and mortality in patients with diabetes.

For decades, lifestyle modifications were not only the primary way to prevent diabetes, but also suppressed the course of diabetes and its complications. Pathogenesis of diabetic cardiovascular disease was affected by many lifestyle factors, including dietary factors, physical activity, and healthful behaviors. Among lifestyle modifications, physical activity is an optimal lifestyle factor for the treatment of type 2 diabetes, and current guidelines for physical activity are available[3].

Other lifestyle modifications including dietary factors, such as vegetables, fruits, tea and coffee, have been associated with diabetic cardiovascular disease[4]. According to the suggestions in dietary guidelines, the healthful diet is rich in fruits and vegetables which have a lot of soluble and non-soluble fiber, phytochemicals, antioxidants, and many other important nutrients[5,6]. Furthermore, tea leaves and coffee beans are also a rich source of phytochemicals. Tea consumption, which has been a cultural tradition of Asians for 4000 years, is positively associated with lower incidences of cardiovascular disease[7]. Flavonoids including catechin, epicatechin (EC), epigallocatechin (EGC), epicatechin gallate (ECG), and epigallocatechin gallate (EGCG) are the major polyphenol compounds in tea, accounting for around 30 % of the chemical content of tea leaves[8,9]. In contrast, many cohort studies have shown controversial relationship between coffee consumption and risk of CVD[10,11]. The major compounds in coffee beans are caffeine, alkaloids, phenolic compounds, and diterpenes[12]. Although there are many benefits in coffee, and caffeine could increase risk of CVD due to increased blood pressure and homocysteine[11]. The objective of this cohort study was to investigate the influence of dietary factors in patients with type 2 diabetes mellitus on prevention of diabetic cardiovascular disease.

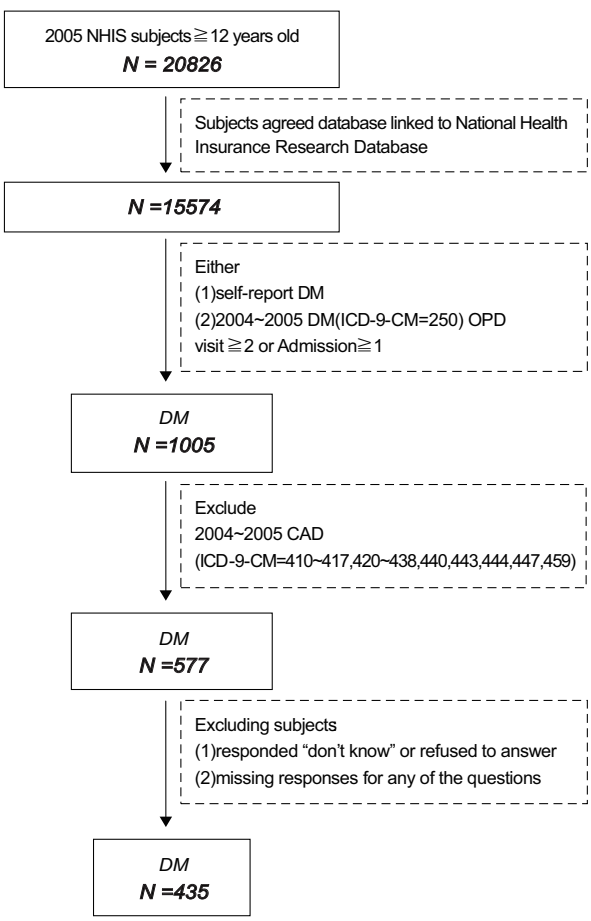

Fig. 1 Identification process for the study population

Material and Methods

Study population

The demographic data, clinical characteristics and lifestyle factors of stratified selected subjects were obtained for this Taiwan cohort study (2004/01/01 to 2005/12/31). All subjects had completed the questionnaire and agreed to link their survey data in the Taiwan National Health Insurance Research Database[13]. Based on the questionnaire, each subject's age, sex, BMI, education, physical activity, drinking and smoking habits, past medical records and questionnaire survey, and simple food frequency were used to describe the demographic properties of the group. 24-hour dietary recall, food frequency, dietary habits, and dietary supplements were provided by the dietary questionnaires of Nutrition and Health Survey in Taiwan (NAHSIT)[14]. A dietary frequency questionnaire contained 21 items of food identified in the Nutrition and Health Survey in Taiwan (NAHSIT). After link the Taiwan National

Health Insurance Research Database, we identified all subjects with a diagnosis of diabetes (including ICD-9-CM=250 for OPD visits more than twice or admission more than once during the study period from 2004 to 2005) and non-cardiovascular disease (excluded were ICD-9-CM=410~417, 420~438, 440, 443, 444, 447, and 459 during the study period from 2004 to 2005) in the ICD-9-CM coding system during the study period, from 2006/01/01 through 2007/12/31 (Figure 1). Hypertension and dyslipidemia medication were also included as parameters of subjects. This study has been approved by Institutional Review Board of Chung Shan Medical University Hospital (CS13068).

Statistical analyzes

All data were expressed as the mean ± S.D. Applicable analysis weights were applied and the design variables were used to adjust for clustering and stratification (Stata 11.0). The Cox proportional hazards model was used to identify the influence of baseline characteristics on diabetic subjects. The results of all tests with $p<0.05$ were considered to be statistically significant.

Results

CIn this study, 435 diabetic subjects with non-cardiovascular diseases were included during a two year study period. Figure 1 is the flowchart of the identification process.

The demographic data, clinical characteristics and lifestyle factors of 435 diabetic subjects without cardiovascular disease are shown in Table 1. The duration of follow-up is 1.93±0.29 year, and there were 26 diabetic subjects had cardiovascular disease. The average of age of diabetic subjects without cardiovascular disease was 55.54±13.51 years. 61.32 % of subjects had a BMI greater than 24. 40.89 % of diabetic subjects without cardiovascular disease reported no physical activity. Frequency of consumed vegetables, fruits, coffee and tea were 5.76±0.87, 4.74±1.91, 0.89±1.72, and 2.97±2.64 per week, respectively.

As shown in Table 2, the univariate and multivariate cox proportional hazards models of 435 diabetic subjects were adjusted for cardiovascular disease and all variables, respectively. The results of the univariate cox proportional hazards model showed a significant effect of age, use of hypertension drugs and dietary factors (vegetables, fruits, and tea). Older subjects used higher doses of medication for hypertension. There was also an increase in the risk of diabetic cardiovascular disease (HR: 1.04 and 2.66, respectively). Among dietary factors, the intake of more vegetables, fruits, and tea were associated with a decrease in the risk of diabetic cardiovascular disease (HR: 0.73, 0.84 and 0.82, respectively). The results of the multivariate cox proportional hazards model showed a significant association with age, use of hypertension drugs and dietary factors (vegetables and tea). All results were similar to the univariate cox proportional hazards model, but there was no significant association with the intake of more fruits. The hazard ratios of age and medication for hypertension were 1.06 and 3.85, respectively. Among dietary factors, the intake of more vegetables and tea were associated with a decrease in the risk of diabetic cardiovascular disease (HR: 0.63 and 0.80, respectively).

Finally, the effect of tea consumption is shown in Figure 2. Tea consumption was not only beneficial for the outcome of and diabetic cardiovascular disease but was also beneficial in a dose-dependent manner.

Discussion

Cardiovascular disease is the major macrovascular complication and leading cause of death in diabetic patients around the world. Hypertension is a main risk factor contributing to an increased incidence of sudden death, stroke, coronary artery disease, heart failure, and kidney disease[12,15,16,17]. More than 50% of elderly people in Taiwan are hypertensive[18]. In our study, we found that diabetic subjects using hypertension medications could enhance the progression of cardiovascular disease. Table 2 showed that the results of both the univariate and multivariate cox proportional hazards models of 435 diabetic

Table 2. ***Variables and hazard ratio (HR) of cardiovascular disease in diabetic clients***

		Model 1			*Model 2*		
			95% CI			*95% CI*	
		HR	*Lower*	*Upper*	*HR*	*Lower*	*Upper*
Age		1.04 *	1.00	1.08	1.06 **	1.02	1.11
Sex							
	Female	1			1		
	Male	1.41	0.64	3.10	1.94	0.58	6.53
BMI							
	< 18.5	1			1		
	18.5-23.9	0.80	0.97	6.52	2.35	0.09	59.89
	≧ 24	0.68	0.84	5.43	1.20	0.05	26.95
Education							
	≦ Elementary school	1			1		
	Junior school	0.93	0.19	4.50	1.84	0.48	6.96
	High school	1.33	0.47	3.74	3.16 *	1.25	8.01
	≧ College	1.17	0.33	4.13	2.54	0.38	17.21
Marital status							
	No	1			1		
	Yes	0.65	0.24	1.77	0.79	0.24	2.57
Household income							
	< $30,000	1			1		
	$30,000~$49,999	0.26	0.06	1.14	0.30	0.07	1.17
	$50,000~$69,999	0.85	0.33	2.16	1.00	0.30	3.29
	≧ $70,000	0.43	0.88	2.07	0.32	0.05	1.88
Physical activity							
	No	1			1		
	Yes	0.76	0.35	1.65	0.40	0.12	1.41
Drinking							
	No	1			1		
	Yes	0.73	0.24	2.19	0.73	0.16	3.27
Smoking							
	No	1			1		
	Yes	1.11	0.57	2.17	1.14	0.48	2.71
CCI†							
	0	1			1		
	1	0.33	0.11	1.03	0.23 *	0.07	0.80
	≧ 2	0.89	0.18	4.50	0.33	0.03	3.41
Dyslipidemia drug							
	No	1			1		
	Yes	1.20	0.47	3.10	1.30	0.38	4.50
Hypertension drug							
	No	1			1		
	Yes	2.66 *	1.04	6.78	3.85 **	1.62	9.15
Diet¶ (mean±SD)							
	Meat/livestock	1.06	0.85	1.33	1.20	0.90	1.59
	Seafood	1.00	0.88	1.15	1.01	0.88	1.16
	Egg	0.94	0.75	1.17	0.96	0.70	1.31
	Milk	1.06	0.89	1.26	1.10	0.91	1.32
	Soybean	1.04	0.73	1.48	1.22	0.89	1.68
	Vegetables	0.73 *	0.54	0.97	0.63 *	0.44	0.89
	Fruit	0.84 *	0.72	0.97	0.90	0.66	1.24
	Coffee	0.97	0.71	1.30	0.91	0.72	1.14
	Tea	0.82 *	0.69	0.98	0.80 **	0.69	0.92

Model 1: The univariate adjustment was made for cardiovascular disease.
Model 2: The multivariate adjustment was made for age, sex , BMI, education, marital status, household monthly income, physical activity, drinking, smoking, CCI, dyslipidemia drug, hypertension drug, and diet.
Note: Cox proportional hazards model was weighted in estimation.
†Charlson comorbidity index
p<0.05,p<0.01*

subjects using medications for hypertension had increased risk of diabetic cardiovascular disease (HR: 2.66 and 3.85, respectively). Among diabetics with hypertension, especially for those cogently treated with hypertension drugs, the risk of suffering from cardiovascular disease was higher than if there was no history of hypertension in diabetic patients. Thus, hypertension was a risk factor for cardiovascular disease.

Lifestyle factors, such as dietary factors and physical activity, are the cornerstone in diabetes management. The World Health Organization (WHO) has indicated that regular, moderate intensity physical activity can decrease the risk of cardiovascular diseases, diabetes, colon and breast cancer, and depression. Regular, moderate intensity physical activity, such as walking, cycling, or participating in sports, has many beneficial effects in healthy and diabetic subjects, especially to improve all parameters associated with the microvascular and macrovascular diabetic complications such as blood pressure and serum lipid levels[19,20,21]. In this study, we had only proved that physical activity has beneficial effects in diabetic cardiovascular disease, but there were no significant differences by two cox proportional hazards models (shown in Table 2, HR: 0.76 vs. 0.40, respectively). However, our study was limited by only two years of follow-up. We still need longer clinical studies to clarify the impact of physical activity on CVD.

The effect of dietary factors, especially vegetables, fruits, coffee and tea, were associated with diabetic cardiovascular disease[4]. Daily Dietary Guidelines for Taiwan, 2011, recommend to consume 5-9 servings of vegetables and fruits depending on energy needs per day to lower the risk of chronic diseases and cancer. In Table 1, the results showed that the average consumption frequency of vegetables and fruits were 5.76 and 4.74 per week, respectively. An observational epidemiological study showed that consumption of vegetables and fruits could lower the risk of cardiovascular disease[22]. In our study, the results from a univariate cox proportional hazards model also proved that consumption of vegetables and fruits could reduce the pathogenesis of diabetic cardiovascular disease (Table 2). But the consumption of fruits was not statistically different in a multivariate cox proportional hazards model (Table 2). In 2008, Villegas indicated that fruit intake was not associated with lower risk of development of diabetes, due to the fact that high levels of fructose could counteract the positive effects of the antioxidants, fiber, and other components of fruits[23]. Therefore, higher consumption of vegetables was better than fruits consumption in diabetic patients with cardiovascular disease. On the other hand, both coffee and tea are common beverages in Asian and Western countries. This Taiwan cohort study showed that consumption of tea was more popular than that of coffee (Table 1: 2.97 vs 0.89). Furthermore, consumption of tea had a favorable effect in diabetic cardiovascular disease in univariate and multivariate cox proportional hazards models (HR: 0.82 and 0.80, respectively), but coffee consumption was not associated with a significant difference (HR: 0.97 and 0.91, respectively). Tea is manufactured from the leaves of Camellia sinensis and classified into three types based on the level of fermentation. These three kinds of tea are black tea (fermented), oolong tea (partially fermented) and green tea (unfermented), respectively. The consumption of black tea is most common in Europe, North America, and North Africa; green tea and oolong tea are most common in Asia[24,25]. About 80-90% catechins and 10% of the total flavonoids were present in green tea while 50-60% theaflavins and 20-30% catechins of the total flavonoids were found in black tea[9,26]. Previous studies demonstrated that the total polyphenol content of different types of tea were determined during the manufacturing process [9]. In an animal model, Vinson et al. found that green tea and black tea were both equally effective in decreasing the development of atherosclerosis in hamster[27]. There is recent evidence reporting inverse association between tea consumption and cardiovascular disease in humans[28]. Habitual tea

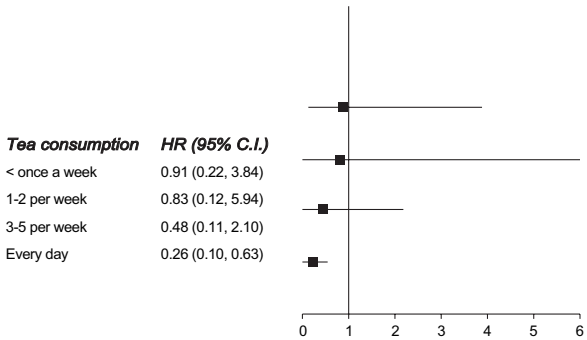

Fig. 2 Hazard ratio (HR) for incident cardiovascular disease in different frequency of tea consumption. The reference category for each group was never drinkers. The multivariate adjustment was made for age, sex, BMI, education, marital status, household monthly income, physical activity, drinking, smoking, CCI, dyslipidemia drug, hypertension drug, and diet. Horizontal bars, 95% confidence interval (CI).

consumption has antiatherosclerotic properties, including impaired foam cell formation, lowering LDL cholesterol, total cholesterol, and fibrinogen levels[27]. It can decrease oxidative stress and enhance nitric oxide (NO) radicals[29]. Besides, Figure 2 showed that tea consumption had a dose-dependent effect in diabetic cardiovascular disease. The hazard ratio of everyday tea consumption was 0.26. Results of this study should be considered in light of some limitations. In this two year follow-up cohort study of subjects in Taiwan, our study demonstrated that tea consumption is an important dietary factor for management of diabetic cardiovascular disease and could delay the progression of cardiovascular disease in diabetic patients.

However, there are some limitations in this Taiwan cohort study. First of all, the questionnaire on dietary frequency only focused on the frequency of intake for all kinds of foods (such as type of tea), instead of real quantities. Second, the strength, period, and type of physical activity for the individuals were not matched across the group. Third, the influence of tea consumption in individuals on laboratory data cannot be obtained in the current study. In future research, we should investigate the effect of the quantity and type of tea consumption with diabetic patients in order to find the relative benefits of various teas for prevention and treatment of diabetic cardiovascular disease.

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