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Original Article

Trends and Predictive Factors of Dyslipidemia in the Elderly in Taiwan Based on a 3-Year Longitudinal Study

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SUMMARY

Background: Dyslipidemia is one of the factors that increase the risk of cardiovascular diseases. The prevalence of dyslipidemia is higher in the older population. This study aimed to identify the predictive factors of dyslipidemia in the elderly population in Taiwan.
Methods: This was a longitudinal follow-up study. Data of a total of 1583 adults aged 65 or above who lived in Taipei and participated in a yearly health examination were analyzed. The levels of total cholesterol and triglyceride measured for each subject were used to assess dyslipidemia. The generalized estimating equations method was employed to investigate the predictors of dyslipidemia.
Results: The results showed that the significant predictive factors for hypercholesterolemia, as measured by odds ratios (ORs), were the female gender (1.953), the total cholesterol level in 2008 (1.036), the year 2010 (0.742), no alcohol consumption (0.751), use of cardiovascular medications (0.506), and use of lipid-lowering medications (0.574). The triglyceride measurement in 2008, use of anti-hyperglycemic drugs, and a duration of education greater than 9 years were significant factors relating to hypertriglyceridemia, the odds ratios being 1.021, 1.912, and 0.720, respectively.
Conclusion: The people at high risk of developing hypercholesterolemia in Taiwan were female, aged between 65 and 75, with a high alcohol consumption, a low fruit and vegetable consumption, and no use of lipid-lowering drugs. Future studies are needed to explore the barriers that impede older adults from managing their dyslipidemia and seeking appropriate treatment.

1. Introduction

Cardiovascular disease is the leading cause of death worldwide.[1] Premature coronary heart disease, acute myocardial infarction, and sudden cardiac death are critical health issues in patients with lipid metabolism disorder.[2] With the extension of human life expectancy, the increasing population of older adults is becoming a large issue and a challenge in healthcare globally. The elderly are faced with the possibility of experiencing life-threatening events, which may affect their ability to cope with everyday life. According to the annual statistics published by the Ministry of the Interior, Department of Statisticsin Taiwan, older adults account for 14.0% of the total population currently, leading to higher demands on medical services and greater medical expenditure. Promotion of the health status of older adults is a huge challenge for health professionals.

Dyslipidemia is one of the risk factors for cardiovascular diseases (CVDs).[3] The prevalence of chronic diseases, such as hyperlipidemia, is normally higher in older populations. It is already known that the serum lipid level is an important risk factor related to CVDs;[4] however, the long-term effects of dyslipidemia and hypertriglyceridemia among the elderly are not clear. In order to detect an abnormal blood lipid profile earlier and decrease the risk of development of CVDs, a free annual geriatric health examination is provided for every elderly person in Taiwan. However, data from health examinations have not been analyzed to enable health professionals to draw up better preventive guidelines. This longitudinal study aimed to assess the prevalence and the predictors of dyslipidemia in elderly persons who underwent an annual geriatric health examination.

2. Method

2.1. Study population and ethical approval

The Annual Citizen Health Interview Survey, a basic physical assessment to enable examination of the health status of residents of Taipei, was supported by the National Health Insurance Prevention Program, and the Department of Health, Taipei City Government, was entrusted to administer the survey. A total of 7813 residents aged 65 years or older living in the Wan-Hua district of Taipei participated in the health examination during the 3-year study pe-

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riod. The city government authorized our research group to access the data of a total of 1583 adults aged 65 or over who lived in Taipei and participated in the health examination in 2008, 2009 and 2010 for academic research purposes. All data were fully scrambled and anonymized to avoid any harm caused by the use of data during the research process and to protect the confidentiality and security of personal data. Permission to obtain the Elderly Geriatric Health Examination (GHE) data was released on June 11, 2014, with approval no. TCHB10234865700.

2.2. Inclusion and exclusion criteria of the study population and definition

Elderly residents of Taipei City who used GHE services annually were included in this study. A previous study showed that the utilization rate of health examinations was low. To investigate the longitudinal effects of the health examination on dyslipidemia, only data of 1583 older adults who participated in the health examination in each year of the 3-year study were used for analysis. More than half of individuals who moved out of the area or were not aged 65 or over in the first two years of the study were excluded from the analysis. Information released from the database and used in this study included measurements of cholesterol and triglyceride, age, gender, marital status, duration of education, types of medication, and health-related behaviors such as smoking, alcohol consumption, exercise, and fruit and vegetable consumption.

2.3. Definition of dyslipidemia

Dyslipidemia is defined as elevated levels of cholesterol, triglyceride, or both. According to the Ministry of Health and Welfare in Taiwan and the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report,[5] the following definitions were used in this study: hypercholesterolemia was defined as cholesterol $\geq$ 200 mg/dl; hypertriglyceridemia was defined as triglyceride $\geq$ 150 mg/dl.

2.4. Statistical analysis

In this longitudinal study, dyslipidemia was assessed according to the values of total cholesterol and triglyceride measured for each subject in 2009 and repeated in 2010. Thus, the dependent variables analyzed were (1) high total cholesterol = 1 if total cholesterol $\geq$ 200 mg/dl, otherwise 0; and (2) high triglyceride = 1 if triglyceride $\geq$ 150 mg/dl, otherwise 0. Variables were evaluated as independent predictors, including the levels of total cholesterol and triglyceride measured in 2008, year (2010 vs. 2009), age, gender, marital status, duration of education, types of medication, smoking, alcohol consumption, exercise, and fruit and vegetable consumption. Descriptive analysis was performed using IBM SPSS Statistics 20.0 software (IBM Corporation, Somers, NY, USA). Logistic regression models with the generalized estimating equations (GEE) method were employed to analyze the repeated measures data using R 3.0.2 software (R Foundation for Statistical Computing, Vienna, Austria). The GEE method was used to account for the correlations between repeated measurements for each subject.[6,7] A first-order autocorrelation structure (i.e., AR(1)) was assumed between the repeatedly measured observations. Computationally, the GEEGLM function (with the default robust estimator of standard error) of the GEEPACK package was used to fit GEE logistic regression models of correlated binary responses in R.[8,9] In statistical testing, a two-sided p value ≤ 0.05 was considered statistically significant. To ensure the quality of the analysis results, basic model-fitting techniques for (1) variable selection, (2) goodness-of-fit (GOF) assessment, and (3) regression diagnostics were applied to our regression analyses.

Specifically, the stepwise variable selection procedure (with iterations between the forward and backward steps) was applied to obtain the best candidate final GEE logistic regression model. All the available independent variables and some of their interactions were put on the variable list to be selected. The significance levels of entry (SLE) and stay (SLS) were set to 0.15 (or larger), being conservative. Then, with the aid of substantive knowledge, the best candidate final GEE logistic regression model was identified manually by dropping the covariates with a p value > 0.05 one at a time until all regression coefficients were significantly different from 0. GOF measures, including the estimated area under the receiver operating characteristic (ROC) curve (also called the c statistic) and the adjusted generalized R^2, and the Hosmer-Lemeshow GOF test were examined to assess the GOF of the fitted GEE logistic regression model. In practice, the value of the c statistic ($0 \leq c \leq 1$) ≥ 0.7 suggested an acceptable level of discrimination power, yet the values of the adjusted generalized R^2 ($0 \leq R^2 \leq 1$). Larger p values of the Hosmer-Lemeshow GOF test indicated better fit of the logistic regression model. Simple and multiple generalized additive models (GAMs) were fitted to detect nonlinear effects of continuous covariates and identify appropriate cut-off point(s), if necessary, during the stepwise variable selection procedure. Computationally, the VGAM function (with the default values of smoothing parameters) of the VGAM package was used to fit GAMs for binary responses in R.[8,9] Finally, the statistical tools of regression diagnostics for residual analysis, detection of influential cases, and check for multicollinearity were applied to identify any model or data problems. A value of the variance inflating factor (VIF) $\geq$ 10 in continuous covariates or VIF $\geq$ 2.5 in categorical covariates indicated the occurrence of the multicollinearity problem among some of the covariates in the fitted GEE logistic regression model.

3. Results

The study population was predominantly male, aged from 65 to 98 years, married, with a duration of education shorter than 10 years. Over the 3 years, there was an increasing trend in the use of long-term medications (74.9%, 79.7%, 80.7%, respectively). Antihypertension medications were the most used medications in this elderly population, followed by heart disease medications (Table 1). With respect to health behaviors, there were decreasing trends in smoking, alcohol consumption, and a sedentary lifestyle, and an increasing trend in eating two fruit servings and three vegetable servings per day (Table 2). It appears that the health behaviors of this elderly population improved over the years of study.

Table 3 shows data obtained in the three years of study, including average cholesterol measurements of 196.96 (SD = 34.54), 196.35 (SD = 35.76), and 192.21 (SD = 33.53) mg/dl, respectively. The rate of hypercholesterolemia was 43.5%, 44.5%, and 39.5%, respectively, and the average triglyceride measurement was 124.86 (SD = 72.08), 122.19 (SD = 66.56), and 121.35 (SD = 73.21) mg/dl, respectively. The rate of hypertriglyceridemia was 25.5%, 25.8%, and 23.3%, respectively, over the three years of study (Table 3).

The GEE method was used to investigate the predictors of hypercholesterolemia. The results showed that significant predictive factors for hypercholesterolemia, reported with odds ratios (ORs), were the female gender (1.953), total cholesterol level in 2008 (1.036), the year 2010 (0.742), no alcohol consumption (0.751), use

of cardiovascular medications (0.506), and use of lipid-lowering medications (0.574). The ROC was 0.806 (Table 4).

The triglyceride measurement in 2008, use of anti-hyperglycemic drugs, and a duration of education longer than 9 years were significant factors related to hypertriglyceridemia, with odds ratios of 1.021, 1.912, and 0.720, respectively. The ROC was 0.852 (Table 5). Observations with missing values were dropped in the original GEE regression analyses. To be comprehensive, we applied the formal multiple imputation method to deal with the missing values in the statistical software R.[10,11] We attempted to perform GEE analysis on each of the 10 imputed full data sets and report the weighted averaged result, but the combined results of the imputed data were quite similar to the original models. Therefore, we used the results of the original models as our main results.

Table 1
Demographic characteristics and health status of the study sample (n = 1583).

Variable	2008 n (%)	2009 n (%)	2010 n (%)
Gender			
Male		905 (57.2)	
Female		678 (42.8)	
Age (years)			
65–74	909 (57.4)	831 (52.5)	752 (47.5)
≥ 75	674 (42.6)	752 (47.5)	831 (52.5)
Range	65–96	66–97	67–98
Mean ± SD	74.63 ± 6.29	75.63 ± 6.29	76.63 ± 6.29
Duration of education			
≤ 9 years		1051 (66.4)	
> 9 years		509 (32.2)	
Missing		23 (1.5)	
Marital status			
Married		1258 (79.5)	
Other		325 (20.5)	
Long-term medications			
No	397 (25.1)	322 (20.3)	306 (19.3)
Yes	1186 (74.9)	1261 (79.7)	1277 (80.7)
Types of medication[1]			
Hypertension	702 (44.3)	758 (47.9)	794 (50.2)
Heart disease	140 (8.8)	127 (8.0)	132 (8.3)
Diabetes	203 (12.8)	213 (13.5)	211 (13.3)
Dyslipidemia	257 (16.2)	276 (17.4)	314 (19.8)
Cardiovascular	38 (2.4)	72 (4.5)	37 (2.3)
Stroke	15 (0.9)	34 (2.1)	22 (1.4)
Number of medications[1]			
0	618 (39.0)	570 (36.0)	546 (34.5)
1	649 (41.0)	647 (40.9)	667 (42.1)
2	248 (15.7)	273 (17.2)	277 (17.5)
3	62 (3.9)	86 (5.4)	84 (5.3)
≥ 4	6 (0.4)	7 (0.4)	9 (0.6)

[1] Medications only included the cardiovascular disease-related drugs listed in the table.

4. Discussion

The prevalence rate of dyslipidemia continues to rise, although the mechanism and clinical guidelines of disease treatment were well established.[12–14] We analyzed data from the geriatric health examination and investigated the trends and predictive factors of dyslipidemia in a longitudinal follow-up study. We hope that the Asian evidences in Taiwan can make a contribution and clinical implication to deal with this worldwide public health challenge. Compared with another survey,[15] the average cholesterol measurement in this study was lower (196.96 ± 34.54–192.21 ± 33.53 vs. 199.0 ± 36.7 mg/dl). Similar results were obtained for the triglyceride level (124.86 ± 72.08–121.35 ± 73.21 vs. 126.8 ± 85.0 mg/dl). As compared with a study conducted in Turkey,[16,17] the prevalence of hypercholesterolemia and hypertriglyceridemia in the elderly were 51.8% and 30.5% respectively, which were higher than in this study (44.5–39.5% and 25.8–23.3% respectively). Another study[18] conducted in Changsha (eastern central China) found that the prevalence rate of dyslipidemia in the elderly was 43.72%, similar to the result of this study. Generally, the prevalence rate of hypercholesterolemia was 12.6% for men and 24.4% for women.[17] Aged younger elders between 65 and 75 and unhealthy lifestyles

Table 2
Health behaviors of the study sample (n = 1583).

Variable	2008 n (%)	2009 n (%)	2010 n (%)
Smoking			
No	1452 (91.7)	1455 (91.9)	1484 (93.7)
Occasionally	39 (2.5)	41 (2.6)	27 (1.7)
< 1 pack/day	81 (5.1)	69 (4.4)	64 (4.0)
≥ 1 pack/day	8 (0.5)	10 (0.6)	7 (0.4)
Missing	3 (0.2)	8 (0.5)	1 (0.1)
Alcohol consumption			
No	1238 (78.2)	1245 (78.6)	1288 (81.4)
Occasionally	302 (19.1)	285 (18.0)	269 (17.0)
Heavy	38 (2.4)	46 (2.9)	25 (1.6)
Missing	5 (0.3)	7 (0.4)	1 (0.1)
Exercise			
No	215 (13.6)	197 (12.4)	187 (11.8)
Occasionally	459 (29.0)	389 (24.6)	399 (25.2)
3–5 times/week	896 (56.6)	907 (57.3)	683 (43.1)
Missing	13 (0.8)	90 (5.7)	314 (19.8)
Consumption of 2 fruit and 3 vegetables per day			
Yes	1187 (75.0)	1162 (73.4)	1182 (74.7)
No	386 (24.4)	411 (26.0)	392 (24.8)
Missing	10 (0.6)	10 (0.6)	9 (0.6)

Table 3
Prevalence of dyslipidemia in the study sample (n = 1583).

Variable	2008		2009		2010	
	n (%)	Valid percent	n (%)	Valid percent	n (%)	Valid percent
Cholesterol						
Mean ± SD	196.96 ± 34.54		196.35 ± 35.76		192.21 ± 33.53	
≥ 200 mg/dl	670 (42.3)	43.5	691 (43.7)	44.5	619 (39.1)	39.5
< 200 mg/dl	870 (55.0)	56.5	862 (54.5)	55.5	948 (59.9)	60.5
Missing	43 (2.7)		30 (1.9)		16 (1.0)	
Triglyceride						
Mean ± SD	124.86 ± 72.08		122.19 ± 66.56		121.35 ± 73.21	
≥ 150 mg/dl	393 (24.8)	25.5	401 (25.3)	25.8	365 (23.1)	23.3
< 150 mg/dl	1147 (72.5)	74.5	1152 (72.8)	74.2	1202 (75.9)	76.7
Missing	43 (2.7)		30 (1.9)		16 (1.0)	

Table 4
Predictors of dyslipidemia (total cholesterol ≥ 200 mg/dL) identified by fitting the logistic regression model with the generalized estimating equations (GEE) method.

Covariate	Estimate	SE	Odds ratio	95% CI of odds ratio		VIF
				Lower	Upper	
Female	0.665	0.113	1.953	1.558	2.404	1.171
Level of cholesterol in 2008	0.035	0.002	1.036	1.031	1.041	1.036
Year 2010	-0.299	0.081	0.742	0.633	0.869	1.013
No alcohol consumption	-0.287	0.127	0.751	0.586	0.963	1.119
Use of cardiovascular medications	-0.680	0.260	0.506	0.304	0.844	1.013
Use of lipid-lowering medications	-0.556	0.208	0.574	0.381	0.863	1.142
2 fruit servings and 3 vegetable servings per day	-0.185	0.104	0.831	0.678	1.018	1.009
Use of lipid-lowering medications in 2008	0.397	0.205	1.487	0.996	2.221	1.128
Age ≥ 75 years	-0.194	0.105	0.824	0.670	1.012	1.057
Intercept	-6.402	0.483	–	–	–	–

CI, confidence interval. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; area under the ROC curve = 0.806; [1] $p = 0.074$ for 2 fruit servings and 3 vegetable servings per day, [2] p in the var. of use of lipid-lowering medications in 2008, and [3] p for aged above 75 yrs were borderline. The significance levels for entry (SLE) and for stay (SLS) were set to 0.15, being conservative.

Table 5
Predictors of hypertriglyceridemia (triglyceride ≥ 150 mg/dL) identified by fitting the logistic regression model with the generalized estimating equations (GEE) method.

Covariate	Estimate	SE	Odds ratio	95% CI of odds ratio		VIF
				Lower	Upper	
Level of triglyceride in 2008	0.021	0.001	1.021	1.018	1.024	1.002
Use of anti-hyperglycemic drugs	0.648	0.154	1.912	1.414	2.585	1.001
Education > 9 years	-0.329	0.130	0.720	0.558	0.929	1.001
Intercept	-3.943	0.194	–	–	–	–

CI, confidence interval. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; area under the ROC curve = 0.852.

were new findings of independent risk factors. We conclude we should educate highrisk people to notice risk factors. Taiwan is economically vibrant with highly urbanized areas, and the mean cholesterol and triglyceride values decreased yearly in this study, in line with the trends of developed countries. A necessity of comprehensive education approaches or programs to promote the level of public awareness of dyslipidemia by early detection; the risk factors are modifiable by early modification of lifestyle to the public.

Based on analysis of the results of this study, the people at higher risk of hypercholesterolemia were female, of an older age, with a high alcohol consumption, a low fruit and vegetables consumption, and did not use lipid-lowering drugs. Consistent with other reports, older females are more likely to have dyslipidemia and cardiovascular diseases because their sex hormones decrease after the menopause.[19,20] Other results of the study showed that maintaining a healthy lifestyle, such as abstaining from alcohol intake and having a diet rich in vegetables, could help to prevent metabolic syndrome, cardiovascular diseases, and their risk factors, such as hypertension, hyperglycemia and hyperlipidemia.[16,20–22] Consistent with previous reports, alcohol consumption and insufficient fruit and vegetables consumption were confirmed as risk factors for hypercholesterolemia in this study. Furthermore, elderly persons aged younger than 75 years were a group at high risk of hypercholesterolemia in this study. Possible explanations could be that people in this age group, with better mobility, have more opportunities to eat diverse foods. Adversely, the older elderly may gradually reduce their food consumption, with decreased function of the GI system and a reduced liver synthetic ability.

A notable finding in this study was that the elderly with hypercholesterolemia who used lipid-lowering drugs but in whom the condition was not controlled well in 2008 tended to suffer from hypercholesterolemia in 2009 and 2010, while participants in the same situation in 2008 but who used lipid-lowering drugs in 2009 or 2010 could reduce their level of cholesterol back to normal. This may suggest that lipid-lowering drugs are effective in these elderly subjects. However, approximately two-thirds of high-risk primary care patients are not taking adequate medications for dyslipidemia. Poor patient adherence, typically below 50%, adds further difficulty to controlling the levels of cholesterol and triglyceride.[23,24] More referrals and management strategies should be provided for the elderly with dyslipidemia, and the benefits of adherence to medications should be stressed. Future studies should also explore the barriers that impede older adults from being appropriately treated or managing their dyslipidemia. The development of a national policy for dyslipidemia prevention is also needed in Taiwan.

According to the national standardized prevalence rate in Taiwan (reported in 2025 White Paper of Ministry of Health and Welfare, MOHW; based on the national nutrition survey 2013–2014), in Taiwan, the prevalence rate of hypertension, hyperglycemia, and dyslipidemia are 19.7%, 10.3%, and 20.4%, respectively, among community-dwelling Taiwanese above 18 years of age. It shows that the prevalence rate of dyslipidemia in the elderly was higher than that of general population in Taiwan.[14,17,25] We should pay more attention to populations with comorbidities[12] and with lower levels of education and design suitable preventive strategies for a better health outcome.

The policy of offering elderly annual health examination attempts to improve the rate of case finding and promote the concept of self-management. For example, annual health examination helps the patients' awareness of blood glucose levels, and therefore to improve the control rate of dyslipidemia. Approximately 80% of diabetic patients in the world suffer from dyslipidemia in which hypertriglyceridemia is the most popular type of diabetic dyslipidemia. Additionally, diabetic dyslipidemia is one of the major causes associated with CVD. Antihyperglycemic drugs can assist to regulate free fatty acid and glucose metabolism, enhance insulin

sensitivity, and lower the serum levels of triglyceride. Interestingly, we observed that the elderly patients who received anti-hyperglycemic drugs were high risk group of hypertriglyceridemia. The potential reason was that these mentioned patients were also with a low educational level that might negatively impact the adherence of drugs. Compared to patients with a lower educational level, patients with a higher educational level may get more health resources, have a healthier life-style, and a better adherence to drugs. Based on the findings in the present study, we provided a valuable clinical implication that promotion of health education program may be positively associated with an effective prevention for dyslipidemia.[14,25]

The strengths of this study included its use of a longitudinal method to explore the trends and predictive factors of dyslipidemia. However, this study had some limitations. First, errors and missing values existed in the annual geriatric health examination data. Second, the results might be biased by the participants, who were all voluntary and tended to be healthier. The cohort investigated in this study consisted of older adults who underwent health examinations in each of the three years of study; these participants were volunteers with a strong motivation towards disease prevention.

5. Conclusion and suggestions

Reducing alcohol consumption, encouraging fruit and vegetable consumption, and treating dyslipidemia with lipid-lowering medications at the appropriate time are prevention strategies. Future studies are needed to explore the barriers that impede older adults from appropriately treating or managing their dyslipidemia.

Declarations of interest

None.

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