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Brief Communication

Risk of incident coronary artery disease in patients with primary biliary cirrhosis

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Abstract: Background: Patients with primary biliary cirrhosis (PBC) often present hyperlipidemia, which is a risk factor of incident coronary artery disease (CAD). However, few studies have examined CAD in PBC. Methods: We identified 41 patients who developed CAD amongst 2,675 PBC cases across seven years and selected the PBC patients without CAD as controls according to sex and age. Results: Females dominated in these patients with CAD. The median time from the diagnosis of PBC to the onset of CAD was 44 months. The patient group with CAD had higher median levels of low-density lipoprotein cholesterol (4.68 mmol/L *versus* 3.52 mmol/L, *P*=0.036) and higher proportion of cases with hypertension (63.4% *versus* 19.5%, *P*<0.001) compared to that without CAD. In the logistic regression, only hypertension (with *versus* without, *P*<0.001; OR, 1.597; 95% CI, 1.139-2.053) was selected. Conclusion: PBC patients with hypertension should be monitored carefully due to the risk of incident CAD.

Keywords: Coronary artery disease, risk factor, primary biliary cirrhosis

Introduction

Hyperlipidemia is a common finding among patients with primary biliary cirrhosis (PBC), which is a well-known risk factor of incident coronary artery disease (CAD) [1]. Some studies demonstrated that PBC patients usually had impaired cardiovascular functions and particularly, PBC patients with metabolic syndrome should be monitored carefully due to the risk of cardiovascular events [2-4], while in other studies, high serum cholesterol levels were not thought to result in high incidence of cardiovascular events in PBC patients [5-7]. So, considering the existence of controversies and the high mortality of CAD, it is necessary to do studies on the risk of incident CAD in such patients. In the present study, we aim to investigate the risk factors of CAD in PBC patients.

Patients and methods

Study population

We retrospectively identified 41 patients who subsequently developed CAD (myocardial infarction, angina or silent myocardial ischemia) among 2,675 cases who had been diagnosed as PBC between January 2007 and December 2013. The exclusion criteria were: (i) occurrence of CAD prior to the diagnosis of PBC; (ii) hepatic decompensation when PBC was diagnosed; (iii) coexistence or past diagnosis of malignant tumors; (IV) liver transplantation. **Figure 1** shows the patient enrollment.

We selected controls with 1:1 ratio to the cases among the PBC patients without CAD and satisfying the above exclusion criteria. Matching factors were sex and age (±2 years).

The study was approved by the ethics committees of Beijing Anzhen Hospital and Beijing 302 Hospital.

Laboratory parameters

Laboratory profiles, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-c) and high-density lipoprotein cholesterol (HDL-c)

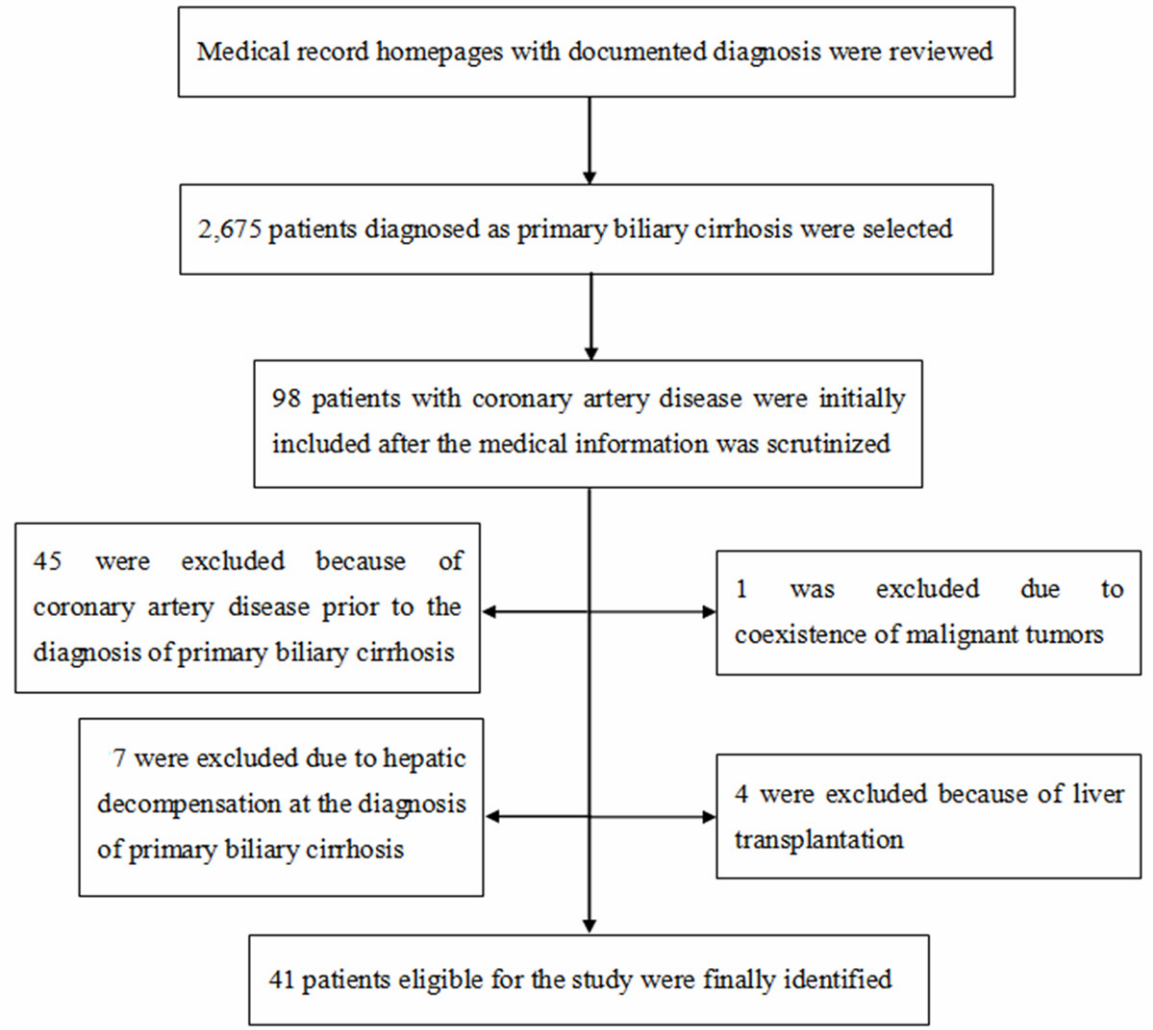

Figure 1. Patient enrollment in the study.

were measured using standard laboratory procedure. The normalized levels of ALT, AST, TC, TG, LDL and HDL were respectively <40U/L, <40U/L, 2.8-5.2 mmol/L, 0.5-1.7 mmol/L, 2.1-3.1 mmol/L and 1.1-1.9 mmol/L.

Statistical analysis

Data analyses were performed using SAS 9.2 software (SAS Institute Inc., Cary, NC, USA). Continuous data were expressed as median (inter-quartile range) or mean ± standard deviation. Categorical data were expressed as the number of subjects or percentages. Group comparisons were performed using the Wilcoxon rank sum test or t test for continuous variables. Logistic regression was used for selecting the risk factors of incident CAD. A probability (*P*) value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics at the diagnosis of PBC

According to the matching ratio and factors, another 41 patients who did not develop CAD as controls were selected. The sex distribution between the case group (patients with CAD) and control group (patients without CAD) were same. Comparison of the parameters at the diagnosis of PBC is listed in **Table 1**. Patients with CAD had higher median levels of low-den-

Table 1. Clinical characteristics at the diagnosis of primary biliary cirrhosis

Parameters	Case group	Control group	*P* value
Sex (female/male)	36/5	36/5	1.000
Age (years)	59 (19)	59 (17)	0.996
Body mass index (kg/m^2)	25.3 (27.2)	24.4 (31.8)	0.441
Resting heart rate	81 (10)	77 (6)	0.220
Alanine aminotransferase (U/L)	67±54	80±66	0.102
Aspartate aminotransferase (U/L)	91±88	82±79	0.115
Total cholesterol (mmol/L)	5.82 (5.98)	5.59 (6.43)	0.376
Triglyceride (mmol/L)	1.75 (1.82)	1.72 (2.01)	0.455
Low-density lipoprotein cholesterol (mmol/L)	4.68 (10.27)	3.52 (7.85)	0.036
High-density lipoprotein cholesterol (mmol/L)	1.92 (2.39)	1.96 (2.57)	0.339
Family history of cardiovascular diseases (yes/no)	13/28	9/32	0.319
Hypertension (with/without)	26/15	8/33	<0.001
Diabetes (with/without)	5/36	4/37	0.670

Case group: patients with coronary artery disease (n=41). Control group: patients without coronary artery disease (n=41).

sity lipoprotein cholesterol compared to those without CAD (4.68 mmol/L *versus* 3.52 mmol/L, *P*=0.036), and the proportion of patients with hypertension in the case group was much higher than that in the control group (63.4% *versus* 19.5%, *P*<0.001). No statistical difference could be detected with respect to the other variables, including body mass index, resting heart rate, ALT, AST, TC, TG and HDL-c.

Risk factors associated with incident CAD

In the multivariate analysis, all the above parameters both in the case group and the control group were included. Finally, only hypertension (with *versus* without, *P*<0.001; odds ratio, 1.597; 95% confidence interval, 1.139-2.053) was selected through the logistic regression.

The median time from the diagnosis of PBC to the onset of CAD was 44 months and its 95% confidence interval was 12-106 months.

Discussion

CAD and chronic liver diseases are increasingly recognized as major public health problems worldwide. Studies in the field have profound social and economic significance. Beijing 302 Hospital is the largest hospital specializing in hepatology and Beijing Anzhen Hospital is one of the largest cardiovascular disease hospitals in China. Therefore, such an investigation in the two hospitals possesses certain representativeness. To ensure accurate findings, any factors which might influence the results were strictly controlled. For example, we excluded the patients with hepatic decompensation at the diagnosis of PBC as it could have a significant impact on the metabolism [8, 9], and additionally, we excluded the patients who had developed CAD prior to the diagnosis of PBC.

Serum cholesterol levels were elevated in most of the patients with PBC. In the present study, irrespective of patients with CAD or patients without CAD, the median levels of serum TC, TG, LDL-c and HDL-c were higher than the normal upper limits. For the particular population with both hepatic and coronary diseases, whether lipid lowering treatment was appropriate remained controversial [10]. Our study showed that hypertension was a risk factor of incident CAD. So, we suggested that, in the real-world clinical practice, it would better use lipid lowering drugs in these PBC patients with hypertension for the physicians. Additionally, larger scale, prospective studies were required to determine the necessity of lipid treatment in this patient group.

The limitation of this study was that the number of subjects was not large enough; therefore, a more extensive investigation should be further performed.

In conclusion, PBC patients with hypertension should be monitored carefully due to the risk of incident CAD. Whether hyperlipidemia requires therapeutic interventions in such patients deserves formal studying within clinical trials.

Disclosure of conflict of interest

None.

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