Preventive Medicine Reports 4 (2016) 192–198

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: http://ees.elsevier.com/pmedr

Comparison of serum lipid management between elderly and non-elderly patients with and without coronary heart disease (CHD)

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ARTICLE INFO

Article history:
Received 15 February 2016
Received in revised form 1 June 2016
Accepted 5 June 2016
Available online 08 June 2016

Keywords:
Coronary heart disease (CHD)
Elderly
LDL-cholesterol
Lipid-lowering medication
Non-HDL-cholesterol

ABSTRACT

Serum lipid management in patients aged ≥75 has not been precisely explored. We, therefore, compared the serum lipid management between the two age groups with and without coronary heart disease (CHD).
We, therefore, retrospectively reviewed medical charts of patients who were hospitalized in the departments of internal medicine during a period of 14 months. Serum lipid goal attainment was explored by applying the lipid goals for patients aged <75 to those aged ≥75.
In 1988 enrolled patients, 717 subjects (36.1%) were aged ≥75. Among them, 41.3% and 32.4% of the patients had CHD, 44.2% and 41.0% were primary prevention at high-risk, and 14.5% and 14.6% were primary prevention at moderate-risk in patients aged ≥75 and aged <75, respectively. Serum LDL-C goal achievement rates in CHD were 66.9% and 65.0% in patients aged ≥75 and <75, respectively ($p = 0.334$). In the primary prevention at high-risk, these rates were 73.5% and 63.3%, in patients aged ≥75 and <75, respectively ($p = 0.001$). They were 77.9% and 58.1% in primary prevention at moderate-risk aged ≥75 and <75, respectively ($p < 0.001$). In CHD, lipid-lowering medication subscription rates were significantly lower in patients aged ≥75 (60.1%) than those aged <75 (73.8%, $p < 0.001$).
In conclusion, in CHD, serum lipid goal attainment was comparable between the two age groups although the lipid-lowering drugs were less frequently prescribed in patients aged ≥75. Without CHD, it was significantly better in patients aged ≥75 than those aged <75 although the lipid-lowering drug subscription rates were comparable between the two age groups.

1. Introduction

The incidence and prevalence of atherosclerotic cardiovascular disease (ACVD) increase with age (de Ruijter et al., 2009; Berthold and Gouni-Berthold, 2011; Phan and Bittner, 2014; McDermott, 2007; Petersen et al., 2005; Rosamond et al., 2007), and the majority of ACVD events occur after age 70 years (Stone et al., 2014). In 2009, the annual mortalities from acute myocardial infarction per 100,000 Japanese population were 12.4 and 18.4 in people aged 50 to 54 years and 55 to 59 years, respectively. These rates were 127.8 and 215.0 in the older people aged ≥65 years and ≥75 years, respectively. Thus, more than 10-fold higher ACVD mortality was observed in the elderly (≥75) age group when compared to the middle (50 to 59) age group (Japan Atherosclerosis Society, 2014). Because demographic aging is proceeding at an unprecedented speed in Japan, the incidence for ACVD is also predicted to be increasing. Dyslipidemia, especially the high LDL cholesterol (LDL-C) level, is one of the most important risk factors for ACVD; therefore, management of LDL-C is extremely important for preventing ACVD in the older population. However, the importance of dyslipidemia as an ACVD risk factor in older adults appeared controversial (Ettinger et al., 1992). Several studies have suggested that the association between cholesterol levels and ACVD weakens with age and that there may be little potential benefit from screening and treating older patients with dyslipidemia (Gordon and Rifkind, 1989; Mariotti et al., 1986; Garber et al., 1991). Conversely, some investigators have

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http://dx.doi.org/10.1016/j.pmedr.2016.06.006

shown that cholesterol concentrations retain a significant risk factor for ACVD in the elderly (Benfante and Reed, 1990; Barrett-Connor et al., 1984; Rubin et al., 1990), and lowering serum cholesterol in the elderly may have a greater impact on ACVD than in the middle age people because the absolute attributable risk of ACVD from dyslipidemia is greater in the older age group than in the middle age group, although the relative risk of ACVD derived from dyslipidemia is smaller in the older age group than in the middle age group.

The Japan Atherosclerosis Society guidelines for prevention of atherosclerotic cardiovascular diseases 2012 (JAS2012-GL) suggest the following: Subjects with dyslipidemia whose ages are between 65 and 74 should be treated in the same way as those aged below 65 to achieve their serum lipid goals. In cases of subjects with dyslipidemia whose ages are no less than 75 (≥75), patients with primary prevention for coronary heart disease (CHD) can be treated individually by the specific decision of the attending physician, although dyslipidemic patients with secondary prevention for CHD should be treated equally to those whose ages are below 65 to achieve their serum lipid goals (Japan Atherosclerosis Society, 2014). We, therefore, anticipated that the lipid goal attainment in CHD (secondary prevention) may be similar between patients aged ≥75 and <75 and that it may be better in patients aged <75 than in those aged ≥75 whose serum lipid control may not be mandatory in some cases.

Thus, to examine whether patients with dyslipidemia aged ≥75 (the elderly group) are treated differently from those aged <75 (the non-elderly group), serum lipid goal achievement rates were compared by applying the lipid goal for the patients aged <75 to those aged ≥75 by use of the JAS-GL2012. In addition, those rates were further compared between the two age groups in different risk category subgroups, such as high-risk and moderate-risk patients with primary prevention for CHD and those with secondary prevention for CHD. Furthermore, contents of lipid-lowering medication were compared between the elderly and non-elderly groups.

2. Methods

2.1. Study population

Medical charts of all the patients who were hospitalized in the Departments of Nephrology, Diabetes, Neurology, Respiratory Medicine and Cardiology, at Kobe City Medical Center General Hospital, Kobe, Japan, from April 1st, 2012 to May 31st, 2013 were retrospectively reviewed. This hospital has 700 beds, which comprises approximately 4.6% of the total number of the hospital beds (15,367) in Kobe City, whose population is 1,535,037. Subjects who underwent regular dialysis because of chronic renal failure or without serum lipid data were excluded. Chronic kidney disease (CKD) at the stage III or higher, according to the guideline from the Japanese Society of Nephrology, was regarded as a high risk for ACVD. Diabetes mellitus (DM) was diagnosed according to the guideline from the Japan Diabetes Society. CHD was defined as myocardial infarction, angina pectoris, or history of percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery which was described in the medical chart. We have assessed their medical conditions by reading the medical chart one by one, and confirmed them by, at least, two different investigators. LDL-C levels were calculated by Friedewald's formula. When serum TG levels were above 200 mg/dL, measured values of LDL-C by a direct LDL-C measurement kit from Sekisui Medical Co. Ltd. were utilized. Direct measurement of LDL-C was performed in the clinical laboratory at the hospital as a part of clinical practice. When lipid levels were evaluated more than once, their steady state levels after admission were utilized. In this study, CKD group (CKD-G) did not include CKD with CHD or DM, and DM group (DM-G) did not contain DM with CHD, because of the risk stratification under the JAS-GL. This study protocol has been approved by the ethical committees in Kobe City Medical Center General Hospital and Kobe Gakuin University.

2.2. Statistical analysis

Continuous variables are presented as mean ± standard error of mean (SEM), and categorical variables are shown as percentages and numbers. Continuous variables were compared using the Student's *t*-test and Welch's *t*-test, if the Levene test showed the equal and unequal variance, respectively. The significance in the differences for categorical variables was determined by the χ^2 test. Moreover, supplementary residual analysis was performed for comparisons of more than two categories. All statistical analyses were carried out using IBM SPSS Statistics 23 (SPSS Inc.). *P* values below 0.05 ($p < 0.05$) were considered as statistically significant.

3. Results

3.1. Patient enrollment

Medical charts of all the 3785 patients who were hospitalized in the Departments of Nephrology, Diabetes, Neurology, Respiratory Medicine and Cardiology at Kobe City Medical Center General Hospital, from April 1st, 2012 to May, 31st, 2013 were retrospectively reviewed. Sixteen hundred and sixty (1660) subjects without lipid data, as well as 137 patients who underwent regular dialysis because of chronic renal failure, were excluded. As a result, a total of 1988 patients were enrolled. The numbers of patients who were enrolled from Departments of Nephrology, Diabetes, Neurology, Respiratory Medicine and Cardiology were 180, 176, 41, 277 and 1314, respectively.

3.2. Patient characteristics

Characteristics of enrolled patients are summarized in Table 1. There was a significant difference in the proportion of patients aged ≥75 (overall: $p < 0.001$), due to the higher prevalence of patients aged ≥75 in Department of Respiratory Medicine ($p < 0.01$) and the lower prevalence of those in Departments of Nephrology ($p < 0.05$) and Diabetes ($p < 0.01$). BMI ($p < 0.001$), all lipid levels ($p < 0.001$) and eGFR ($p < 0.001$) were significantly lower in patients aged ≥75 than those aged <75. In addition, the prevalence of female ($p < 0.001$), HT ($p = 0.001$), CKD ($p < 0.001$) and CHD ($p < 0.001$) was significantly higher in patients aged ≥75 than those aged <75.

3.3. Comparison of LDL-C and non-HDL-C levels and their target level achievement rates between male and female

To explore whether the gender imbalance between patients aged ≥75 and <75 can be the cause for the differences in lipid levels between the two age groups, lipid profiles were compared between male and female. As shown in Table 2, LDL-C ($p < 0.001$), HDL-C ($p < 0.001$) non-HDL-C ($p < 0.001$) levels were significantly higher in female than in male. However, TG ($p < 0.001$) level was significantly lower in female than in male. LDL-C target level achievement rates were 68.4% and 66.8%, in male and in female, respectively ($p = 0.255$). These rates for non-HDL-C were 70.8% and 70.3%, respectively ($p = 0.427$). Thus, lipid target level achievement rates were comparable between male and female, although there were significant differences in lipid levels.

3.4. Comparison of risk stratification profiles between the elderly and the non-elderly age groups

Prevalence of CHD was 41.3% and 32.4% in patients aged ≥75 and <75, respectively, (Fig. 1). In addition, none of the patients in patients aged ≥75 was stratified into low-risk, even though 12.0% of the patients were stratified into low-risk in patients aged <75 (Fig. 1). Prevalence of