Research paper

The association between low level of high-density lipoprotein cholesterol and mood disorder using time-dependent analysis

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ARTICLE INFO

ABSTRACT

Background: Although many studies have identified factors associated with mood disorder, the association between high-density lipoprotein cholesterol (HDL-C) and mood disorder is still controversial. The aim of our study was to evaluate the association between low HDL-C and onset of mood disorder in Korea based on different cut-off levels.

Methods: We used National Health Examinations Service cohort data from 2009 to 2013. We used time-dependent Cox regression analysis to evaluate the association between low level of HDL-C and onset of mood disorder. Hazard ratios (HRs) for onset of mood disorder were estimated for 1- to 2-year time intervals, starting at the first health examination and accounting for the duration until the next health examination.

Results: A total of 400,803 participants (male: 220,573; female: 180,230) were included in our study. A total of 4576 (2.07%) males and 7598 (4.22%) females developed mood disorder. Based on dyslipidemia (< 40 mg/dL), low level of HDL-C was associated with the risk of mood disorder in both male and female, however, only females showed statistically significant (HR: 1.097, 95% CI: 1.012–1.189). Based on quartile-based approach, females with low levels of HDL-C (< 47 mg/dL) and males with high levels of HDL-C (≥ 59 mg/dL) were associated with subsequent risk of mood disorder.

Conclusions: Our findings suggest that level of HDL-C is associated with potential risk factors in mood disorder. However, a flexible threshold value in HDL-C level would be needed to evaluate the subsequent risk of mood disorder. Thus, further studies are needed to help improve the mental health in susceptible individuals.

1. Introduction

A low level of high-density lipoprotein cholesterol (HDL-C) is considered an important risk factor for cardiovascular disease in both women and men (Barter et al., 2007; Cooney et al., 2009; Rader and Hovingh, 2014). Many epidemiological studies suggest links between a low serum cholesterol level, coronary heart disease, and death from cardiovascular causes (Briel et al., 2009; Langsted et al., 2011; Morrison and Hokanson, 2009). Furthermore, it has been suggested that HDL-C level is also associated with mental problems such as depression and suicide (Almeida et al., 2014; Lehto et al., 2010; Tedders et al., 2011; Zhang et al., 2005). These studies show that a low level of HDL-C is linked to mood disorder. Possible mechanisms of these phenomena may involve vascular abnormalities and poor uptake of serotonin (Barter

et al., 2007; Kim et al., 2011; Martinowich and Lu, 2008). However, other studies report a lack of correlational evidence for HDL-C and mental health (da da Graça Cantarelli et al., 2015; Hildrum et al., 2009). Therefore, although an association between level of HDL-C and somatic morbidity has been suggested, the link between mental problems and HDL-C is still controversial.

In Korea, mental health problems are major concerns to policy-makers and have contributed to many other social and economic problems (Chang et al., 2012; Cho et al., 2012; Kim and Yoon, 2013). According to the Organization for Economic Co-operation and Development (OECD), in 2013, Korea had the highest suicide rate with nearly 30 deaths per 100,000 people (average in OECD countries: 12 deaths per 100,000 people) (OECD, 2015). Suicide is a major leading cause of death in Korea, and this has not changed since 2004 (5th and 4th

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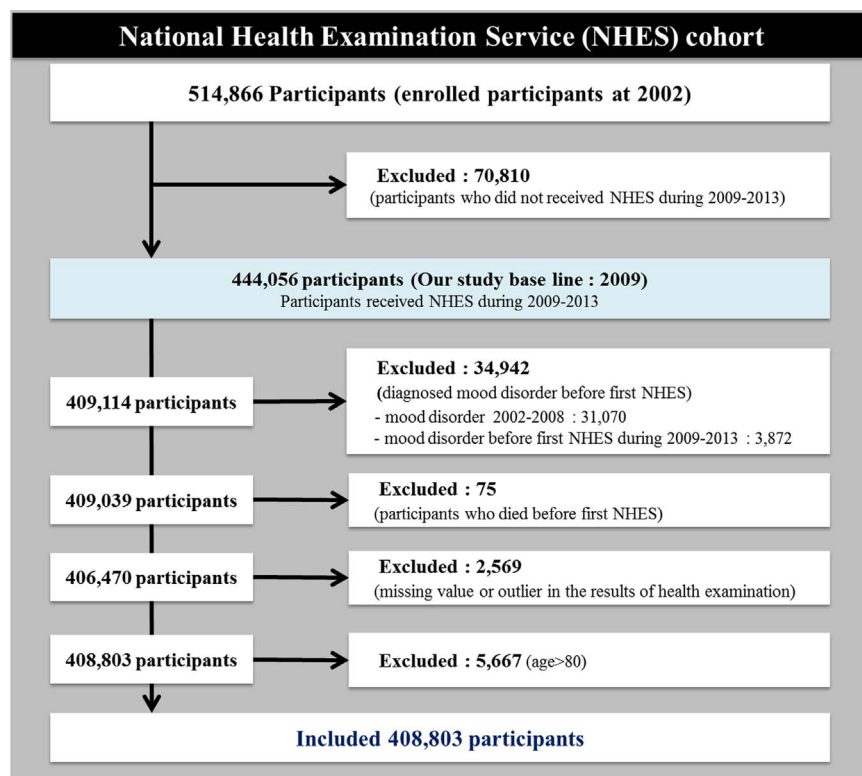
Fig. 1. Flow diagram of the study population.

National Health Examination Service (NHES) cohort

514,866 Participants (enrolled participants at 2002)

Excluded : 70,810
(participants who did not received NHES during 2009-2013)

444,056 participants (Our study base line : 2009)
Participants received NHES during 2009-2013

409,114 participants

Excluded : 34,942
(diagnosed mood disorder before first NHES)
- mood disorder 2002-2008 : 31,070
- mood disorder before first NHES during 2009-2013 : 3,872

409,039 participants

Excluded : 75
(participants who died before first NHES)

406,470 participants

Excluded : 2,569
(missing value or outlier in the results of health examination)

408,803 participants

Excluded : 5,667 (age>80)

Included 408,803 participants

ranking cause of death in 2004 and 2012, respectively) (Shin et al., 2016b). One of the factors contributing to a high suicide rate is an increased prevalence of mood disorder, including depressive disorder (Cho et al., 2015; Park et al., 2013; Tondo et al., 2015). The lifetime prevalence of mood disorder in Korea is estimated to be 4.8% for men and 10.1% for women, which are higher rates than those for other mental disorders (Cho et al., 2015). In addition, the age distribution for mood disorder differs from that of other countries. According to previous studies, 30 years was the median age of lifetime risk for mood disorder, and the distribution of mood disorder was increase from the youngest (18–29 years) to older age groups (30–44 years); it is lowest in the oldest age group (≥ 60 years) (Kessler et al., 2005). However, the prevalence of depressive symptoms in Korea has been reported to increase with older age in both male and female groups (Oh et al., 2013). Particularly, older adults (older than 70 years of age) have been shown to be more likely to have depressive symptoms than younger subjects (19–29 years).

Late-life time onset of mood disorder is considered a major problem in Korea, with a higher occurrence rate reported in the country compared to other Asian nations as well as Western countries. Such difference in distribution of mood disorder may result from the rapid socioeconomic change in Korea. Over the past decades, Korea underwent tremendous changes in social, economic, and political sectors, all of which were enough to induce a segmented family structure as well as a lack of social and emotional support in the overall population (Park et al., 2012, 2010). These changes were some of the reasons for the apparent increase of mood disorder in Korea's elderly population. In addition, low rate of health care utilization by those with mental disorders also contributed to the late-life time onset of mood disorder. In general, Koreans tends to avoid visiting health care center to treat mental disorder. As a result, patients had long duration of untreated psychosis. Means that patients had a long time gap between manifestation of the first psychotic symptom and the utilization of healthcare facility for initial treatment (Lee et al., 2012; Marshall et al., 2005). Therefore, early detection of psychiatric problems is considered important for improving patient care and reducing the high suicide rate in

Korea. Many previous studies suggest that individual risk factors, such as socioeconomic status and chronic medical disorders, contribute to mood disorder (Douglas et al., 2010; Strine et al., 2015; Yohannes et al., 2010). In addition, an association between vascular risk factors, including dyslipidemia and depression, has been suggested (Fiedorowicz et al., 2011; Taylor et al., 2013). However, evidence of an association between low level of HDL-C and mood disorder is lacking in Korea. Considering the remarkably high rates of suicide over the last decade, it is important to investigate whether low level of HDL-C is related to the onset of mood disorder in Korea.

The aim of our study was to evaluate the association between HDL-C level and the onset of mood disorder in Korea. In order to achieve this, we first considered low level of HDL based on 40 mg/dL that was considered as dyslipidemia; accordingly, we used this value to evaluate whether similar results also existed in Korea. Second, we hypothesized an association between abnormal level of HDL-C and mood disorder, and then conducted an explanatory test based on quartile to investigate such association.

2. Methods

2.1. Data collection

We performed an observational study using NHES cohort data from 2008 to 2013 to investigate the association between level of HDL-C and onset of mood disorder. The NHES is based on National Health Insurance Act. All people over 40 years of age in Korea biennially undergo a clinical examination, anthropometric measurements, and blood sampling, and also receive a questionnaire; blue-collar workers receive these evaluations annually. The practice, which is designated as a health examination site by the Ministry of Health and Welfare, provided the examination services. In addition, to maintain quality of care in health examination, evaluation for practice was performed annually based on the Framework Act on Health Examination in Korea. Eligible participants were insured by the National Health Insurance Services (NHIS), and approximately 10% of participants, from ages 40–79 years,