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Serum Oxidized LDL Level and Risk of Cognitive Impairment in Older Women

Alain Koyama, MS[a,f], **Katie Stone, PhD**[b], and **Kristine Yaffe, MD**[c,d,e,f]

[a]Northern California Institute For Research and Education, San Francisco, CA, USA

[b]Research Institute, California Pacific Medical Center, San Francisco, CA, USA

[c]Department of Psychiatry, University of California San Francisco, San Francisco, CA, USA

[d]Department of Neurology, University of California San Francisco, San Francisco, CA, USA

[e]Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, USA

[f]San Francisco VA Medical Center, San Francisco, CA, USA

Abstract

We investigated the association between serum level of oxidized low-density lipoprotein (oxLDL) and risk of cognitive impairment (dementia or mild cognitive impairment) among 572 non-demented community-dwelling women from a prospective cohort study of aging. After 5 years of follow-up, 228 (39.9%) developed cognitive impairment; and this did not differ by tertile of baseline oxLDL level (highest compared to lowest tertile 38.2% vs 39.5% OR=0.90; 95% CI: 0.63,1.43). Multivariate adjustment produced similar results (OR: 0.91; 95% CI: 0.60,1.39). These findings suggest that increased levels of serum oxLDL are not associated with a greater risk of incident cognitive impairment in older women.

Keywords

dementia; Alzheimer's disease; oxidized LDL; inflammation; oxidative stress

1. Introduction

Oxidative stress has been hypothesized to lead to or accompany the neurodegenerative processes seen in dementia. Evidence includes post-mortem studies that have suggested oxidative damage occurs early in the pathogenesis of Alzheimer's disease (AD) (Nunomura, et al., 2001) and also may be involved in cell death mediated by amyloid-beta (Bruce-Keller, et al., 2010). Therefore, markers of oxidative stress merit further investigation either as predictive or diagnostic tools or as potential causative agents for dementia. To date, we are

Address for Correspondence/Reprints: Alain Koyama, 4150 Clement St, VAMC 116H, San Francisco, CA 94121, alain.koyama@va.gov, Phone: 415-221-4810 x3076, Fax: 415-379-5624.

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not aware of any prospective cohort studies that have reported on an association between oxLDL level and incident dementia or cognitive decline. We therefore tested the hypothesis that elevated baseline levels of serum oxidized LDL (a common marker of oxidative stress) would be associated with increased risk of dementia or mild cognitive impairment (MCI).

2. Methods

The participants in this study were enrolled in the Study of Osteoporotic Fractures (SOF), a multi-center, prospective, observational study of older women. Briefly, the present study utilized visit 8 (2002-2004) as baseline, and followed 4,727 women 75 years of age and older for 5 years. 1,040 women had oxLDL measured from visit 8 serum samples using a commercial ELISA kit (Alpco Diagnostics) and inter-assay CV was 4.0%. The primary outcomes of interest were dementia and MCI. Dementia was diagnosed based on the DSM-IV criteria and MCI diagnosed using modified Peterson criteria (Petersen, et al., 2001). A total of 572 women had available data on both oxLDL level and followup cognitive status. Further details on participant recruitment, data collection, and dementia adjudication have been published previously (Yaffe, et al., 2011). Logistic regression models were used to test for any association between tertiles of serum oxLDL and incident dementia or MCI.

3. Results

The 572 non-demented women at baseline had a mean age of 82.6 years and a mean education of 12.9 years. None of the baseline characteristics were significantly different by tertile of oxLDL level. After five years of follow-up, 141 women developed MCI and 87 developed dementia for a total of 228 women with cognitive impairment. Compared to women in the lowest tertile of oxLDL, women in the highest tertile did not have greater risk of cognitive impairment (38.2% vs 39.5%, OR= 0.95, 95% CI: 0.63,1.43), nor did women in the middle tertile (41.9%, OR=1.11, 95% CI: 0.73,1.66) . After adjustment for age, race, and education, results remained similar: the OR was 0.91 (95% CI: 0.60,1.39) for women with the highest tertile, and 1.08 (95% CI: 0.71,1.65) for the middle tertile (Table 1). Secondary analyses of oxLDL as a continuous variable or dementia alone as the outcome produced similar results.

4. Discussion

In this longitudinal study of community-dwelling older women, we did not find an association between serum oxLDL level and increased risk of cognitive impairment. Certain characteristics of this study may have prevented us from viewing a true association. First, the study population was relatively homogeneous, comprised of mostly white, all female participants. Second, the mean age of this population was 82.6 years, while previous literature has shown that measures of inflammatory markers at midlife may be a better indicator of cognitive decline compared to those in later life (Schmidt, et al., 2002). Additionally, a single measurement of oxLDL may not be as reliable as multiple measures over time, although oxLDL has been shown to have similar longitudinal stability as total cholesterol or high-sensitivity C-reactive protein (Holvoet, et al., 2006). Lastly, a peripheral marker may not accurately reflect central processes. Indeed, a previous study reported a positive association between CSF antibodies to oxLDL and dementia, but no association between CSF and serum antibodies to oxLDL (Kankaanpaa, et al., 2009). It is also possible that serum oxLDL level is not associated with increased risk of dementia, despite other evidence supporting the oxidative stress hypothesis. As this is the first prospective study to investigate any association between oxLDL and dementia, further studies may be needed to elucidate these findings.

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Table 1

Risk of developing dementia or MCI by level of serum oxidized LDL

	Dementia/MCI		
Serum oxLDL level	**No. of cases/No. at risk**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)***
Tertile 1	75/190	1.0 (ref.)	1.0 (ref.)
Tertile 2	80/191	1.11 (0.73,1.66)	1.08 (0.71,1.65)
Tertile 3	73/191	0.95 (0.63,1.43)	0.91 (0.60,1.39)

* adjusted for age, race, and education