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Chronic Use of Aspirin and Total White Matter Lesion Volume: Results from the Women's Health Initiative Memory Study of Magnetic Resonance Imaging Study

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Objective: To investigate the relationship between aspirin and subclinical cerebrovascular heath, we evaluated the effect of chronic aspirin use on white matter lesions (WML) volume among women. Methods: Chronic aspirin use was assessed in 1365 women who participated in the Women's Health Initiative Memory Study of Magnetic Resonance Imaging. Differences in WML volumes between aspirin users and nonusers were assessed with linear mixed models. A number of secondary analyses were performed, including lobe-specific analyses, subgroup analyses based on participants' overall risk of cerebrovascular disease, and a doseresponse relationship analysis. Results: The mean age of the women at magnetic resonance imaging examination was 77.6 years. Sixty-one percent of participants were chronic aspirin users. After adjusting for demographic variables and comorbidities, chronic aspirin use was nonsignificantly associated with 4.8% (95% CI: -6.8%, 17.9%) larger WML volumes. These null findings were confirmed in secondary and sensitivity analyses, including an active comparator evaluation where aspirin users were compared to users of nonaspirin nonsteroidal anti-inflammatory drugs or acetaminophen. Conclusions: There was a nonsignificant difference in WML volumes between aspirin users and nonusers. Further, our results suggest that chronic aspirin use may not have a clinically significant effect on WML volumes in women. Key Words: Epidemiology-women's health-NSAID-aspirin-white matter lesions—cognition—antiplatelet.

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Introduction

White matter lesions (WMLs) or hyperintensities visible on magnetic resonance imaging (MRI) are thought to represent small-vessel ischemic cerebrovascular disease, and are common among older adults. Larger WML volumes have been linked to cognitive impairment. It has been suggested impairment may be a result of disruption of the networks within the brain leading to decline in processing speeds and cognition. Larger WML volumes have also been linked to higher risks of future dementia, stroke, functional decline, and death. The relationship between aspirin and WMLs has been evaluated in a small number of epidemiologic and laboratory studies. While some studies found a protective effect, findings have not been consistent across studies.

Low-dose aspirin may be effective for prevention of ischemic strokes in women, 14 and has been considered as a possible protective agent against dementia. 15,16 Because of its systemic anti-inflammatory and antiplatelet effects, 17,18 aspirin may protect against subclinical cerebrovascular disease and associated cognitive impairment.¹⁹ However, aspirin is also associated with significant bleeding risks.¹⁸ Clarifying the relationship between aspirin and cerebrovascular health will help quantify the net clinical benefit associated with aspirin use. In this study, we evaluated the relationship between chronic aspirin use and WML volumes among Women's Health Initiative Memory Study of Magnetic Resonance Imaging (WHIMS-MRI) participants. WHIMS participants' medication use was evaluated longitudinally, and a subset of women was assessed with MRI at the end of the WHIMS study. We hypothesized

women who used aspirin would have smaller total WML volumes than nonusers.

Methods

Study Design

WHIMS was an ancillary study to the Women's Health Initiative (WHI) postmenopausal hormone therapy (HT) randomized controlled clinical trials. WHI evaluated the effects of HT on postmenopausal women's risks of cardiovascular disease, cancer, and osteoporosis.20 WHIMS, which included a subset of 7479 women in the WHI HT trials, evaluated the effect of HT on the incidence of dementia and other cognitive outcomes²¹ (see Fig 1). Women were eligible for WHIMS if they were between the ages of 65 and 79 years old and free of dementia at trial enrollment.²² WHIMS-MRI was designed to evaluate structural MRI outcomes among HT trial participants.²² MRI scans were obtained for 1424 women, approximately 8 years post randomization.²³ MRI protocols were developed at the MRI Quality Control Center in the Department of Radiology at the University of Pennsylvania; additional details have been published elsewhere.23 After the exclusion of 59 scans during the MRI image analyses and quality assurance checks, 1365 WHIMS-MRI participants were eligible for the present study (Fig 1).

WML Measurements

Standardized and validated protocols were used for obtaining and processing MRI scans and for measuring volumes.²²⁻²⁵ Series were acquired with field of view = 22 cm

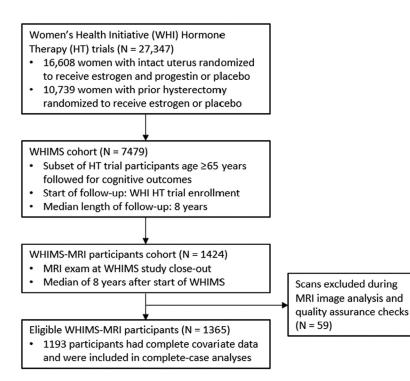


Figure 1. Flow diagram showing participant selection and study eligibility. Abbreviation: WHIMS-MRI, Women's Health Initiative Memory Study of Magnetic Resonance Imaging.

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