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Serum vitamin E concentrations among highly functioning hip fracture patients are higher than in nonfracture controls

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Abstract

Malnutrition after hip fracture is common and associated with poor outcomes and protracted recovery. Low concentrations of vitamin E have been associated with incident decline in physical function among older adults and may, therefore, be particularly important to functionally compromised patients hip fracture patients. Serum concentrations of α-tocopherol and γ-tocopherol, the 2 major forms of vitamin E, were assessed in 148 female hip fracture patients 65 years or older from the Baltimore Hip Studies cohort 4 around the time of fracture (baseline) and at 2, 6, and 12 month postfracture follow-up visits (recovery). It was hypothesized that mean concentrations of both forms of vitamin E among these hip fracture patients would be lowest at the baseline visit and increase at each study visit during the year after fracture. Linear regression and generalized estimating equations were used to assess changes in vitamin E concentrations after adjustment for covariates and to determine predictors of vitamin E concentrations at baseline and throughout recovery. It was also hypothesized that vitamin E concentrations shortly after hip fracture would be lower than those in nonfracture controls after adjustment for covariates. To evaluate this hypothesis, linear regression was used to perform adjusted comparisons of baseline vitamin E concentrations among Baltimore Hip Studies cohort 4 participants to 1076 older women without history of hip fracture from the Women's Health and Aging Study I, Invecchiare in Chianti Study, and the National Health and Nutrition Examination Surveys. Mean α-tocopherol was lowest at baseline, and time from fracture to blood draw was positively associated with baseline α-tocopherol ($P = .005$). Mean γ-tocopherol did not change appreciably throughout the year after fracture, although it fluctuated widely within individuals. Serum concentrations of α-tocopherol and γ-tocopherol were highest among the hip fracture population after adjustment ($P < .0001$). In general, highly cognitively and physically functioning hip fracture patients demonstrated higher vitamin E concentrations.

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Thus, the relatively high degree of function among this cohort of hip fracture patients may explain their higher-than-expected vitamin E concentrations.

Keywords: Vitamin E; Tocopherols; Antioxidants; Micronutrients; Hip fracture; Older women

Abbreviations: BHS4, Baltimore Hip Studies cohort 4; BMI, body mass index; GDS, Geriatric Depression Scale; GEE, generalized estimating equations; IADLs, instrumental activities of daily living; InCHIANTI, Invecchiare in Chianti Study; LPADLs, lower extremity physical activities of daily living; MMSE, mini–mental state examination; NHANES, National Health and Nutrition Examination Survey; SFPF, Short Form 36 Physical Functioning Domain; WHAS, Women's Health and Aging Study I; YPAS, Yale Physical Activity Survey.

1. Introduction

Hip fracture is a problem of increasing public health concern. Each year, there are 1.6 million hip fractures worldwide [1]; and the annual incidence is projected to more than double by the year 2050 [2], due in large part to the continuing growth of the population of older adults in whom this injury is most common. The consequences of hip fracture are severe. Between 16% and 32% of patients with hip fracture die within a year after the injury [3-5], and survivors are typically burdened with considerable physical, cognitive, and social impairments [6]. Thus, the identification of modifiable factors associated with improved recovery from hip fracture is of critical importance.

Nutritional status is one such factor with substantial implications for hip fracture recovery. Postfracture malnutrition has been associated with a wide variety of adverse outcomes, including increased risk of mortality [7], longer hospital stays [8], and impaired recovery of physical function [9]. Between 50% and 68% of hip fracture patients suffer from some form of postfracture malnutrition [8,10,11], with the most consistently identified areas of malnutrition being insufficient protein and total energy intakes. Consequently, postfracture nutritional interventions have focused almost exclusively on increasing protein and total energy intakes. These studies have shown mixed results in reducing mortality and improving recovery [10,12,13], and more comprehensive nutritional interventions may be necessary to improve hip fracture outcomes. Inclusion of key micronutrients may confer additional benefits, as the intake of calcium, selenium, iron, and other micronutrients has been shown to be inadequate after hip fracture [8]. However, concentrations of many other important micronutrients remain unexplored after hip fracture, including vitamin E.

Vitamin E is the collective name for the tocopherols and tocotrienols, 8 structurally related compounds with antioxidant properties [14]. α-Tocopherol is the most biologically active and abundant form of vitamin E in the body [15]. As a potent lipid-soluble antioxidant, α-tocopherol protects cell membranes from lipid peroxidation, a process in which free radicals damage the cell membrane and compromise cellular function and communication [15]. This antioxidant activity is one mechanism that has been proposed for the associations noted between both high intake and serum concentrations of α-tocopherol and lower risk of cardiovascular disease [16], cancer [17], Alzheimer's disease [18], and other chronic illnesses [19]. Although not yet studied as extensively as α-tocopherol, an increasing amount of research has focused on the γ-tocopherol form of vitamin E. In recent observational studies, high concentrations of γ-tocopherol were more strongly associated with reduced risk of colorectal and prostate cancers than α-tocopherol [20,21]. Higher concentrations of γ-tocopherol have also been associated with lower risk of cardiovascular disease [22]. These associations may be due to the powerful anti-inflammatory effects of γ-tocopherol, which has been shown to inhibit tumor necrosis factor α, nitrogen oxides, and the cyclooxygenase 2 enzyme [23].

These strong antioxidant and anti-inflammatory properties suggest that vitamin E may play a particularly important role in hip fracture recovery. The persistent generation of reactive oxygen species [24] and inflammatory cytokines [25] shown to occur after bone fractures may be ameliorated by the presence of vitamin E. Both high intake and serum concentrations of α-tocopherol have been shown to be associated with reduced risk of many common sequelae of hip fracture, including decreased physical function [26], incident frailty [27], sarcopenia [28], bone loss [29], and cognitive decline [30]. High serum concentrations of γ-tocopherol have also been associated with lower risk of muscle weakness among older adults [31]. High serum vitamin E concentrations appear to offer protection against many of the sequelae of the hip fracture injury that contribute to protracted recovery and lasting impairments. Furthermore, hip fracture might deplete serum vitamin E even in the absence of the deleterious dietary changes shown to occur after fracture. Serum concentrations of α-tocopherol have been found to be nearly completely depleted after instances of bodily trauma [32] and major surgical procedures [33]. Hip fracture is a traumatic injury that is most often surgically repaired, and all participants in Baltimore Hip Studies cohort 4 (BHS4) had the hip fracture surgically repaired before baseline vitamin E assessment. Thus, it is postulated that vitamin E levels are likely to be depleted in hip fracture patients.

In light of the previous findings about vitamin E among older adults and the possibility of its depletion after fracture, the primary aim of this study was to examine how serum α-tocopherol and γ-tocopherol concentrations change throughout the year after hip fracture. We hypothesized