

Letter

Is there a positive association between mammographic density and bone mineral density?Gillian S Dite¹, John D Wark², Graham G Giles³, Dallas R English^{3,4}, Margaret RE McCredie⁵ and John L Hopper¹¹Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, The University of Melbourne, Australia²Department of Medicine, The University of Melbourne, Royal Melbourne Hospital, Melbourne, Australia³Cancer Epidemiology Centre, Cancer Council Victoria, Australia⁴School of Population Health, The University of Melbourne, Australia⁵Department of Preventive and Social Medicine, University of Otago, New ZealandCorresponding author: John L Hopper, j.hopper@unimelb.edu.au

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In a recent issue of this journal, Crandall and colleagues [1] reported a positive association between percent mammographic density and bone mineral density at the hip and lumbar spine in postmenopausal women. These associations were only observed after excluding women who were "recent" users of hormone replacement therapy and even then were of marginal, and not independent, significance ($p = 0.04$ and $p = 0.08$, respectively). The previously reported null findings from the larger studies by Kerlikowske and colleagues [2] and Buist and colleagues [3] were discounted by Crandall and colleagues [1] for not having stratified by hormone replacement therapy use. In a recent publication

from our twin study we found no overlap between the genetic determinants of variation in percent mammographic density and bone mineral density [4].

We have now analysed our data on 268 pre- and postmenopausal female twins following the approach of Crandall and colleagues [1]. We fitted linear regression models with robust standard errors that took into account the clustering within twin pairs. Percent mammographic density was the outcome variable and bone mineral density measures (g/cm^2) were the key exposure variables. As in Crandall and colleagues [1], we adjusted for age, body mass index (weight

Table 1**Regression coefficients for the effect of bone mineral density measures on percent mammographic density, adjusting for age, body mass index and smoking**

	Estimate	Standard error	p-value
Total hip bone mineral density			
All	-0.09	0.11	0.41
Past or never HRT	-0.23	0.12	0.06
Postmenopausal: past or never HRT	0.05	0.18	0.78
Postmenopausal: current or recent HRT	-0.07	0.24	0.79
Lumbar spine bone mineral density			
All	-0.02	0.08	0.79
Past or never HRT	-0.10	0.10	0.33
Postmenopausal: past or never HRT	0.02	0.09	0.85
Postmenopausal: current or recent HRT	0.24	0.18	0.19

HRT, hormone replacement therapy; past HRT, HRT use >1 year ago; recent HRT, HRT use ≤1 year ago.

kg/height m²) and smoking (ever/never), even though there was no evidence in our data that smoking was associated with percent mammographic density.

We found no evidence of a positive association with bone mineral density at the hip or lumbar spine either overall or for women who were not current or recent users of hormone replacement therapy (Table 1) and no tests of interaction between hormone replacement therapy use and bone mineral density were significant. After restricting analyses to postmenopausal women and stratification by use of hormone replacement therapy, to replicate the analyses of Crandall and colleagues [1], the lack of an association persisted both for women who were past or never users and for women who were current or recent users. Similar results were obtained for analyses of bone mineral density at the forearm and femoral neck and total body bone mineral content (data not shown). There was also no evidence that “recent hormone use has residual effects that may obscure the [putative positive] association between mammographic density and bone mineral density” [1].

Consequently, Crandall and colleagues' [1] claims of a positive association between mammographic density and bone mineral density and for a “unifying biological mechanism behind bone mineral density, mammographic density and breast cancer risk” may be overstated. Their apparent finding may be an artefact of having conducted multiple analyses, having been misled by outliers or influential points, chance or by assuming effect modification without having tested for it. It may also reflect a true association but, given others' null findings [2,3], may be weaker than reported. As we have discussed [5], the absence of a strong association between mammographic density and bone mineral density may be an important observation; hormonal factors may explain little of the large variation across the population in mammographic density.

Competing interests

The authors declare that they have no competing interests.

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