Published in final edited form as:

Cancer Res. 2010 February 15; 70(4): 1743. doi:10.1158/0008-5472.CAN-09-3311.

Comment re: Pre-menopausal mammographic density and hormone levels

Dr. Kate Walker and Dr. Isabel dos Santos Silva

Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London WC1E 7HT, UK

Keywords

Breast cancer; mammographic density; steroid hormones and receptors; growth factors and receptors; prolactin

Dear Editor,

We thank Ligiou and colleagues for their insightful letter in which they discuss indirect evidence in support of a possible negative association between circulating levels of IGF-II and breast cancer risk. There is insufficient direct evidence to determine whether or not IGF-II levels influence the risk of breast cancer. To our knowledge only two small prospective studies have examined the role of IGF-II levels on breast cancer risk with inconsistent results¹⁻². Similarly, few studies have examined the role of IGF-II on mammographic density. Ligiou et al. discussed our finding of an unexpected negative association between IGF-II levels and density in pre-menopausal women but, as we highlighted in our paper, this finding should be interpreted with caution as the association disappeared upon adjustment for body mass index (BMI). Moreover, no association between IGF-II levels and density was found in another study of pre-menopausal women³ although findings from studies conducted among post-menopausal women are more consistent with a possible inverse association³⁻⁴.

Ligiou et al. reported higher levels of umbilical cord blood IGF-II in Asians compared to Caucasians. Interestingly, cross-sectional studies suggest that such ethnic gradients may not persist into adulthood, with young adult Asians having significantly lower circulating levels of this growth factor than Caucasians⁵, perhaps reflecting ethnic differences in body composition and other lifestyle variables. Similarly, Afro-Caribbean post-menopausal women, known to have a lower breast cancer risk than Caucasians, have been shown to have lower levels of IGF-II⁶. In fact, ethnic difference in circulating levels of IGF-II, as well as in levels of IGF-I, IGFBP3 and sex steroid hormones, explained little of the ethnic gradient in mammographic density which, as expected, was higher among Caucasian than Afro-Caribbean women⁶. Unfortunately, no similar comparisons have been carried out among pre-menopausal women.

We agree with Ligiou et al. that the associations between IGF-II, mammographic density and breast cancer risk have so far been vastly overlooked, and based on the findings of studies of IGF-I and IGFBP3, they should be investigated separately in pre- and post-menopausal women.

References

1. Gronbaek H, Flyvbjerg A, Mellekjær L, et al. Serum insulin-like growth factors, insulin-like growth factor binding proteins, and breast cancer risk in postmenopausal women. *Cancer Epidemiol Biomarkers Prev.* 2004; 13:1759–64. [PubMed: 15533904]
2. Allen NE, Roddam AW, Allen DS, et al. A prospective study of serum insulin-like growth factor-I (IGF-I), IGF-II, IGF-binding protein-3 and breast cancer risk. *Br J Cancer.* 2005; 92:1283–7. [PubMed: 15756268]
3. dos Santos Silva I, Johnson N, De Stavola B, et al. The insulin-like growth factor system and mammographic features in premenopausal and postmenopausal women. *Cancer Epidemiol Biomarkers Prev.* 2006; 15:449–55. [PubMed: 16537700]
4. McCormack VA, Dowsett M, Folkerd E, et al. Sex steroids, growth factors and mammographic density: a cross-sectional study of UK postmenopausal Caucasian and Afro-Caribbean women. *Breast Cancer Res.* 2009; 11:R38. [PubMed: 19545414]
5. Hopkins KD, Lehmann ED, Jones RL, et al. Ethnicity affects IGFBP-3 and IGF-II in normal healthy young adult subjects. *Clin Endocrinol (Oxf).* 1996; 45:327–31. [PubMed: 8949571]
6. McCormack VA, Dowsett M, Folkerd E, et al. Sex steroids, growth factors and mammographic density: a cross-sectional study of UK post-menopausal Caucasian and Afro-Caribbean women. *Breast Cancer Res.* 2009; 11:R38. [PubMed: 19545414]