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Do mutations in *BRCA1*/*BRCA2* confer a higher risk of skin cancer?

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BRCA1 and *BRCA2* are human genes that encode tumour suppressor proteins. In women, mutations in these genes lead to a well-known increased risk of developing breast cancer or ovarian cancer. Men with these mutations also have a higher risk of breast cancer.[1] Previous studies have also revealed potential links between mutations in *BRCA1*/*BRCA2* and an increased risk of other human cancers, including prostate and pancreatic cancer.[2,3] Interestingly, an increased risk of skin cancer, including melanoma and nonmelanoma skin cancer, has also been associated with these mutations, raising concern about the excessive incidence of skin cancer among carriers of the mutations.

In this issue of the *BJD*, in order to aid clinical decision making regarding skin cancer screening, Gumaste *et al.* provide an overview of the current literature on the risk of melanoma and nonmelanoma skin cancers associated with *BRCA1*/*BRCA2* mutations.[4] After a systemic investigation, the authors found limited evidence to support an elevated risk of melanoma among *BRCA2* mutation carriers, and no evidence for a statistically significant risk of melanoma in *BRCA1* mutation carriers. Specifically, studies on this topic have several major limitations, including selection bias of study participants, the absence of genetic confirmation for '*BRCA1*/*BRCA2* carrier' and self-report of melanoma cases without pathological confirmation, all of which may have distorted the true association between mutation status and melanoma risk. With respect to nonmelanoma skin cancers, limited studies have yielded conflicting results. The authors concluded that, in the absence of standard risk factors (e.g. sun exposure), the present medical knowledge is not sufficient to warrant increased skin cancer surveillance of patients with a confirmed *BRCA1*/*BRCA2* mutation or a family history of a *BRCA1*/*BRCA2* mutation.

This review may help relieve the concern about a potential excessive skin cancer risk among *BRCA1*/*BRCA2* mutation carriers. However, it may be too early to reach a final conclusion based on the present literature. Most of the available studies on *BRCA1*/*BRCA2* mutations and skin cancer risk are cross-sectional and only have small numbers of skin cancer cases (for studies among *BRCA1*/*BRCA2* mutation carriers) or detected *BRCA1*/*BRCA2* mutations (for studies among skin cancer cases), therefore precluding definitive inference of the association. It is noteworthy that a series of cancer registry-based studies have reported an increased risk of skin cancer among patients with breast cancer and vice versa,[5–9] and an increased risk of breast cancer has been reported among familial *CDKN2A* (a high-risk gene for melanoma) mutation carriers.[10] These findings, together with the inconclusive evidence for a higher risk of skin cancer among *BRCA1*/*BRCA2* mutation carriers, may suggest shared genetic susceptibility between skin cancer and breast cancer. However, whether the higher skin cancer risk among patients with breast cancer can be attributed to *BRCA1*/*BRCA2* mutations is unknown. Therefore, further large, prospective studies with well-framed research strategies are needed in order to uncover the potential genetic link between skin cancer and breast cancer. Nevertheless, suspected *BRCA1*/*BRCA2* mutation carriers should still be counselled about the risks of skin cancer and may benefit from annual full skin examinations in clinical practice, as pointed out by Gumaste *et al.*[4]

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Conflicts of interest

None declared.

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