



Cancer Genetics Gazette

A newsletter for specialist clinicians from the Familial Cancer Unit

Nov 2006

Issue 2



Welcome to the second edition of The Cancer Genetics Gazette for 2006. Our feature article is from Dr Graeme Suthers, SA Familial Cancer Unit.

Age-specific cancer risks for counselling women with BRCA1 or BRCA2 mutations.

One of the primary purposes of genetic testing for BRCA mutations in familial breast/ovarian cancer has been to provide accurate advice to at-risk relatives. But the provision of such advice has been hampered by the lack of appropriate penetrance figures. Early studies overestimated the risks of cancer because they were derived from research kindreds with a high prevalence of cancer. Subsequent population-based studies underestimated the penetrance of mutations because many affected carriers did not have a family history of cancer and would not have been referred to a familial cancer clinic.

As a result, carriers have been presented with imprecise estimates of the lifetime risks of developing breast cancer (40-80%) and ovarian cancer (10-30%). The uncertainty generated by these figures was compounded by a lack of information about the short-term risks of cancer. For a 25-year-old carrier, the lifetime risk of cancer does not necessarily help her make decisions in the short term.

Chen et al (2006) recently provided precise and relevant estimates of the relative risks of breast and ovarian cancer in almost 2,000 kindreds with BRCA mutations ascertained through familial cancer clinics across North America. The key outcome of the study was the documentation of the relative risk of breast and ovarian cancer for women of different ages. For carriers of both BRCA1 and BRCA2 mutations, the relative risk of breast cancer was high early in adult life and then declined such that the relative risk in a postmenopausal woman was less than 3-fold. Conversely, the relative risk of ovarian cancer was high in mid-adult life and remained high in the succeeding decades.

The baseline incidence of breast cancer is lower in Australasia than in North America. To correct for this, the relative risks derived from the study have been combined with Australian baseline incidence data to estimate the absolute short- and long-term risks of breast and ovarian cancer for Australasian BRCA carriers of different ages.

For an Australian woman who carries a BRCA1 mutation (see Fig 1), the annual risk of developing breast cancer during her 20s is approximately 0.5%. Between the ages of 30 and 55 years, her annual risk of developing breast cancer is 1-2%. After the age of 60 years, her annual risk drops back to approximately 0.5%. The situation regarding the risk of ovarian cancer is different. For a

woman aged less than 45 years, the annual risk of ovarian cancer is no more than 0.5%. After the age of 45 years, the annual risk gradually rises from 1% to a maximum of 2% by the age of 70.

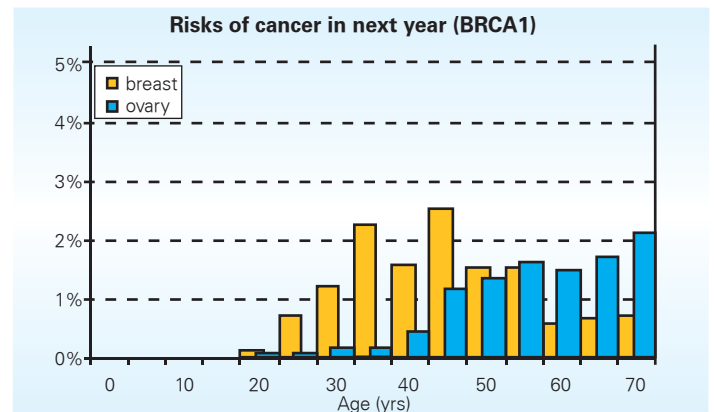


Figure 1: The % risk of a BRCA1 mutation carrier developing breast cancer or ovarian cancer in the next 12 months with increasing carrier age.

For an Australian woman who carries a BRCA2 mutation (see Fig 2), the annual risks of breast cancer are the same as for a BRCA1 carrier. However, the risks of ovarian cancer are lower. For a carrier aged less than 60 years, the annual risk of ovarian cancer is no more than 0.5%. After the age of 60 years, the annual risk gradually rises from 1% to a maximum of 1.5% by the age of 70.

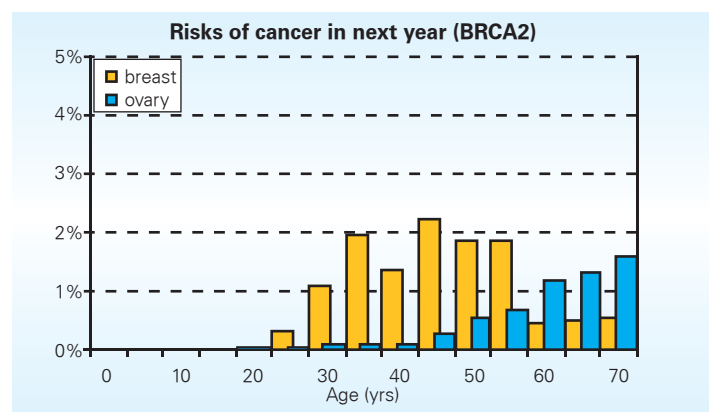


Figure 2: The % risk of a BRCA2 mutation carrier developing breast cancer or ovarian cancer in the next 12 months with increasing carrier age.

For a young carrier of either a BRCA1 or BRCA2 mutation, these annual risks translate into a 50% risk of developing breast cancer by the age of 70 years. In the case of BRCA1, the equivalent risk of developing ovarian cancer is 40%. In the case BRCA2, the equivalent risk of developing ovarian cancer is 25%.

It is important to note that these long-term risks are substantially modified for an older woman who has already lived into mid-adult

life without developing breast or ovarian cancer. For a 60-year-old carrier (of either gene) who is cancer-free, the risk of developing ovarian cancer in the next decade is substantially greater than the risk of developing breast cancer.

These observations have important implications for genetic counselling and decisions regarding prophylactic surgery:

1. Decisions regarding prophylactic surgery do not need to be made in haste. The annual risk of breast or ovarian cancer is sufficiently low that a woman has time to make a considered decision.
2. The lifetime risk of developing breast cancer is substantially lower than previous studies had suggested.
3. By the age of 50-60 years, the major cancer threat for a woman carrying a BRCA mutation is ovarian cancer, not breast cancer.

This information has been developed as a leaflet to provide women who carry one of these mutations with information to assist in their decision-making. The leaflets are available from the Familial Cancer Unit on request.

Reference

Chen et al. Characterization of BRCA1 and BRCA2 mutations in a large United States sample. *J Clin Oncol* 2006; 24:863-871. A copy of this paper is available on request (print or email) from Carolyn Harrington at The Cancer Council South Australia.

Invitation to contribute articles to The Cancer Genetics Gazette

We invite contributions to the 2007 editions of The Cancer Genetics Gazette. Contributions must be relevant to the area of cancer genetics and may include:

- Websites of interest/review
- Research project snapshots/updates
- Letters to the Editor
- Conference reports
- New discussion documents / papers released
- New national initiatives
- Relevant journal article for discussion
- Grants/funding opportunities
- Collaborations, clinical trials

For further details contact the editor, Carolyn Harrington at charrington@cancersa.org.au or on 08 8291 4269. Submissions can be emailed directly. Word limit is 700 words for feature articles. Deadline for Issue 1 is 10 March, 2007 and Issue 2 is 17 September, 2007. All articles should include the author's contact details, including phone and email.

Web watch

www.ncbi.nlm.nih.gov/entrez/query/static/clinical.shtml#medgen
PubMed Clinical Queries provides the following specialized PubMed searches for clinicians: (1) search by clinical study category, (2) find systemic reviews, and (3) medical genetics searches.

The Cancer Council Australia www.cancer.org.au now hosts The Cancer Genetics Resource Directory www.cancergenetics.org.au. This national resource directory provides the Australian general public and health professional community with accurate and updated details of a variety of cancer genetics resources.

www.cdc.gov/genomics/hugenet/

Human Genome Epidemiology Network from the National Office of Public Health Genomics is a global collaboration for assessment of the impact of human genome variation on population health and how genetic information can be used to improve health and prevent disease. This site has fact sheets, peer reviewed articles and information about family history for the general public and professionals interested in preventing disease and promoting health.

www.cdc.gov/genomics/update/current.htm

A weekly update from the Centre for Disease Control that provides information about the impact of human genetic discoveries on health care, disease prevention and population health.

www.nchpeg.org/

Link to "Genetic Applications In Practice" newsletter containing up-to-date, topical, well delivered articles and case studies around genetic testing.

www.nbcc.org.au/resources/clinicalupdate

Clinical Update - Breast Cancer is a newsletter from the National Breast Cancer Centre (NBCC) for health professionals. It provides timely expert comment on relevant journal articles in context for the Australian healthcare system. Subscription to e-alerts available.

www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME

The Cochrane Library provides high-quality, independent evidence to inform healthcare decision-making, including reliable evidence from Cochrane and other systematic reviews, clinical trials and more. Cochrane reviews are recognised as the gold standard in evidence-based health care.

Family Health History Can Matter:

The Centre for Genetics Education has a section for health professionals about the Family Health History Campaign (launched in NSW July 2006) at www.genetics.com.au/fhh/fhhhp.htm with a printable family health history form for patients www.genetics.com.au/publications/fhtcons.htm and information pamphlet www.genetics.com.au/fhh/pdf/fhh2006record.pdf

If you wish to receive The Gene Pool or other cancer genetics newsletters:

Cancer Genetics Gazette (for specialist clinicians)
Gene Trek newsletter (for Familial Cancer Unit clients)
in hard copy or electronically please contact Carolyn Harrington at charrington@cancersa.org.au

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