New studies on surgical options in inherited breast cancer show drastic treatment is not always best

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Two studies to be presented at the seventh European Breast Cancer Conference (EBCC7) in Barcelona today (Friday) and tomorrow (Saturday), shed light on the treatment options facing women carrying the BRCA1 and BRCA2 genetic mutations which predispose them to breast cancer. In the first, Ms Annette Heemskerk-Gerritsen, a PhD student in the Department of Medical Oncology, Erasmus Medical Centre, Rotterdam, The Netherlands, will tell the conference this afternoon (Friday) that prophylactic mastectomy (where women who have been treated for breast cancer in one breast have the remaining breast tissue removed as a risk-reducing measure) does not improve disease-free or overall survival in this group of patients.

In the second, to be presented to the conference tomorrow (Saturday) Professor Lori Pierce, Professor of Radiation Oncology at the University of Michigan, Ann Arbor, USA, will report the findings of an international study of treatment outcomes after either breast conserving therapy (BCT) or mastectomy in 655 BRCA1 and BRCA2 carriers. The study found more recurrences in the breast with BCT compared to recurrences at the chest wall following mastectomy, but similar rates of recurrence when BCT patients also received chemotherapy.

Women who carry a mutated BRCA1 or BRCA2 gene have a risk of between 55% and 85% of developing cancer in their lifetime, and those who do develop it have to make difficult decisions about their treatment,

often opting for the most radical therapy in the belief that they will have a better chance of overcoming their disease. Until now there has been little data on the longer-term effects of such treatments on these patients.

Ms Heemskerk-Gerritsen and her team looked at the efficacy of risk-reducing mastectomy (RRM) on disease-free and overall survival in 390 patients who carried the BRCA1/2 mutation and who had already had cancer in one breast. Of these, 138 patients underwent RRM, while the others continued regular surveillance. There were no differences in age at diagnosis, hormone-receptor status, and adjuvant hormonal treatment between the RRM and non-RRM groups. The numbers of women receiving adjuvant chemotherapy as well as numbers of women undergoing risk-reducing salpingo-oophorectomy (removal of the fallopian tubes and ovaries) were higher in the RRM group.

During 2033 person years observation (PYO - the total sum of the number of years that each member of the study population has been under observation), 54 patients in the non-RRM group developed metastatic disease as opposed to 18 patients during 642 PYO in the RRM group, incidence rates of 0.027 and 0.028 respectively. As for overall survival, 56 women in the non-RRM group died during 2164 PYO, and 16 in the RRM group during 682 PYO, mortality rates of 0.026 and 0.023, respectively.

"While RRM obviously reduces the incidence of breast cancer in the other breast to zero, as opposed to 66 cases in the non-RRM group, we found that there was very little difference in disease-free and overall survival between the two groups," says Ms Heemskerk-Gerritsen. "We intend to follow up this study by identifying a set of prognostic factors related to survival in breast cancer patients with a BRCA1 or BRCA2 mutation. In this way, we hope to be able to identify a subgroup of patients who may benefit from RRM. In the meantime, we hope that our findings will provide additional information to improve the counselling

of breast cancer patients considering risk-reducing mastectomy, by emphasising that the gain that may be obtained by this radical surgery is mainly in respect of reducing the risk of contralateral breast cancer. As yet we have found no benefits with respect to disease-free and overall survival."

In the second study, Professor Pierce and her collaborators from the USA, Australia, Spain, and Israel found that patients treated with BCT had significantly higher rates of cancer recurring in the breast (23.5%) than did patients who had mastectomy (5.5%) at 15 years. But when they looked at patients who had received chemotherapy as well as BCT, they found that the risk of recurrence was much reduced and the overall risk with this treatment was not significantly different from the mastectomy group (11.9%). And despite the higher rates of local recurrence in the BCT group, other risks - metastasis, breast cancer-specific survival, and overall survival - were similar.

When they compared rates of developing cancer in the unaffected breast, which exceeded 40% in both groups, the researchers found that the use of radiotherapy after surgery did not increase risk in comparison with those women who did not receive radiation treatment.

Although there have been many trials comparing breast conserving surgery and radiotherapy with mastectomy in women with non-hereditary cancer, data on those women with the inherited form of the disease are limited and this has made it difficult for patients and doctors alike to know how best to proceed. Ideally, the researchers say, such studies should be randomised, but because treatments for patients who carry the BRCA1/2 mutation are so individualised and the decision-making so complex, a randomised trial is unlikely.

"To the best of my knowledge, ours is the first multi-institutional systematic comparison of BCT versus mastectomy in BRCA1/2

carriers," Professor Pierce will tell the conference. "It will provide important data to patients trying to decide what will be the best treatment for their hereditary breast cancer, as well as to the doctors advising them.

"If a woman with BRCA1/2-associated breast cancer is considering breast conserving surgery and radiotherapy, our findings show that she will have fewer recurrences in the breast if chemotherapy is also used. And our conclusion that 15-year outcomes of BCT and mastectomy are similar should reassure recently diagnosed women who may find the thought of an immediate mastectomy overwhelming. We strongly encourage patients to discuss local therapy options with their doctors before starting treatment."

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