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Is risk-reducing mastectomy in BRCA1/2 mutation carriers with a history of unilateral breast cancer beneficial with respect to distant disease free survival and overall survival?

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Introduction: Risk-reducing mastectomy (RRM) in BRCA1/2 mutation carriers with a history of unilateral breast cancer (BC) significantly reduces the risk of developing contralateral BC (CBC). However, the outcome regarding distant disease free survival (DDFS) and overall survival (OS) is insufficiently known.

Methods: The efficacy of RRM on DDFS and OS was studied in 375 BC patients (283 BRCA1, 92 BRCA2). Characteristics and FU information up to December 31, 2008, were extracted from the medical records. Eventually 111 BRCA1 and 33 BRCA2 mutation carriers underwent RRM. Women contributed person-years of observation (PYO) to the non-RRM group from the date of the first visit at the clinic or primary BC (PBC) diagnosis (whichever came last) to the date of diagnosis of metastatic disease, death, RRM, or last FU. Contribution of PYO to the RRM group started at the date of RRM until similar endpoints as described for the non-RRM group.

Results: Regarding the PBC, no differences in age at diagnosis, hormone-receptor status, and adjuvant systemic treatment were observed between the non-RRM and RRM group. Distribution of TNM stages 0, I, II and III, was 4%, 37%, 46% and 13%, respectively, in the non-RRM group, versus 4%, 51%, 38% and 7% in the RRM group ($p < 0.05$). More women in the RRM group underwent risk-reducing salpingo-oophorectomy (RRSO; 74% versus 46% in the non-RRM group; $p < 0.001$). With a mean FU op 7.4 years, 72 CBC cases were observed in the non-RRM group, while no CBC occurred after RRM. During 1956 PYO, 54 patients in the non-RRM group developed metastatic disease versus 16 patients during 655 PYO in the RRM group, resulting in incidence rates of 0.028 and 0.024, respectively. Concerning the OS, 51 women died during 2092 PYO in the non-RRM group, versus 15 women in the RRM group during 692 PYO, resulting in mortality rates of 0.024 and 0.022, respectively. These data were comparable for BRCA1 and BRCA2 mutation carriers. The effect of RRM on DDFS and OS is being analyzed, taking into account the influence of different variables (e.g. tumor characteristics, mutation status, RRSO), and will be presented at the meeting.

Conclusion: RRM in BRCA1/2 mutation carriers with a history of unilateral BC does not seem to improve DDFS and OS, despite the strong reduction of CBC occurrence. Further research is warranted to identify a set of prognostic factors enabling selection of subgroups of BC patients who possibly may benefit from RRM with respect to DDFS and OS.

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The quality indicator 'tumour positive margin rate after breast conserving surgery': a valid assessment of hospital performance?

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Background: The demand for comparative data of hospital performance and quality of care is growing, but there is solid criticism on the validity of quality indicators and the presentation of the results.

The quality indicator 'tumour positive margin rate after breast conserving surgery for breast neoplasm' is used by two large performance measurement systems in the Netherlands: the Dutch Health Care Inspectorate and the 'Visible Care' program of the Ministry of Health, Welfare and Sport. Both systems use different definitions for 'tumour positive margin'.

Our aim is to determine if the quality indicator 'tumour positive margin rate after breast conserving surgery for breast neoplasm', measures the performance of hospitals consistently and independently of the utilization of different definitions for 'tumour positive margin', differences in casemix, taking statistical random variation into account.

Materials and Methods: We retrieved data of all 762 patients who underwent breast conserving surgery for a breast neoplasm, between July 1 2007 and June 30 2008 in one of the nine affiliated hospitals of the Comprehensive Cancer Centre West (CCCW) in the Netherlands. We compared two indicators for 'tumour positive margin' used by performance measurement systems in the Netherlands, with the reresection rate. We identified riskfactors for tumour margin positivity and reresection with logistic regression. We presented the results of the individual hospitals in a funnelplot, using 95% and 99% confidence limits around the standard.

Results: Depending on the definition, the tumour positive margin rate of the total group varied from 11% to 21% and of individual hospitals varied up to 19%. In situ carcinoma was associated with higher tumour positive margin rates (OR 1.76 [CI 1.06–2.92]). The results of individual hospitals differed significantly ($P < 0.001$). However, the funnelplot showed little variation across the hospitals, except random variation. Moreover, the assessment of hospital performance depended on the used definition and casemix correction. There were discrepancies between the tumour positive margin rates and the reresection rate, indicating differences in interpretation of 'tumour positive margin'.

Conclusions: The demand for comparative data of hospital performance and quality of care is growing, but for a reliable comparison of hospitals clear definitions and adjustment for casemix are needed. The lack of identical definitions for the quality indicator 'tumour positive margin rate' and the lack of casemix correction undermine the validity of the indicator. Clear definitions, standardized reporting and the use of funnelplots can improve healthcare assessment.

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Survival in young women diagnosed with breast cancer. Does pregnancy status make a difference?

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Background: Women diagnosed with gestational breast cancer (i.e. pregnant or within twelve months postpartum) are known to have poor survival when compared to other young women diagnosed with breast cancer. Less is known about how the pregnancy status of women diagnosed breast cancer affects survival. The aim of this cohort study was to determine what affect the pregnancy status of young women at the time they were diagnosed with breast cancer (no associated pregnancy, pregnant or postpartum) had on survival.

Methods: The cohort of women diagnosed with breast cancer in Western Australia when aged less than 45 years between 1 January 1982 and 31 December 2003 was identified. A Cox's proportional hazards regression model was developed which included their age at diagnosis, histological grade, disease stage, lymph node status, pregnancy status (no associated pregnancy, pregnant or postpartum), length of survival and death status. Overall survival was calculated and defined as the time from diagnosis to the date of death or censor date of 31 December 2007.

Results: In the cohort of 2752 women; 182 were diagnosed with GBC (55 when pregnant 127 post partum). In the model, increased histological tumour grade and disease stage and positive lymph node status led to poor survival for all women in the cohort. Gestational breast cancer postpartum cases, however, were found to have a 48% increased risk of death (HR 1.48, 95% CI 1.09, 2.02, $p = 0.012$) compared to non-gestational breast cancer cases. Gestational breast cancer cases who were pregnant at diagnosis, however, had only a 3% increased risk of death (HR 1.03, 95% CI 0.66, 1.61, $p = 0.88$) compared to non-GBC cases.

Conclusion: Women who were diagnosed with GBC postpartum were more likely to die than other young women diagnosed with breast cancer where as women who were pregnant at diagnosis had s a minimal increased risk. This factor suggests that the cumulative effect of pregnancy±breast feeding plays a role in breast cancer prognosis and needs further investigation.

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Is duration of breastfeeding related to risk of different breast cancer subgroups?

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The aim of the present study was to examine duration of breastfeeding in relation to the risk of different subgroups of breast cancer. A prospective cohort, The Malmö Diet and Cancer study, including 17035 women were followed during a mean of 10.2 years and a total of 622 incident breast cancers were diagnosed.