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Breast Cancer in the Elderly

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Increasing age is the greater risk factor for breast cancer. Almost half of all breast cancers occur in patients aged 65 years and older, and the number of cases of breast cancer is on the rise due to aging of the population. Despite breast cancer in the elderly representing a public health problem, its treatment is largely based on limited retrospective subgroup analyses and on extrapolation of results from clinical trials in younger patients. Such extrapolation may not be valid, not in the least part because breast cancer biology differs in older patients.

Particular treatment challenges in older women are: Competing causes of mortality: many older patients with operable breast cancer die of non-cancer related causes. The benefit of cancer therapy in individuals likely to die at an early stage from non-cancer related causes is questionable. However, it is difficult for clinicians to identify these individuals. Assessment of co-morbidity and the need for assistance in activities of daily living (ADLs) and Instrumental Activities of Daily Living (IADLs) predict the likelihood of early death from non-breast cancer causes.

Presence of co-morbid conditions: co-morbidities increase with age, with the potential implications of reduced fitness for standard treatment, short life expectancy, poly-pharmacy and drug-drug interactions, and treatment tolerance. Co-morbidities may affect choice of treatment (e.g. trastuzumab in patients with cardiomyopathy) and treatment tolerability (e.g. aromatase inhibitor therapy in patients with pre-existing arthralgia / myalgia).

Avoidance of under-treatment: despite competing causes of death, breast cancer is the cause of death in a substantial number of older patients. In women $\geqslant$80 years at diagnosis, up to 40% die from breast cancer. Underestimation of life expectancy and fitness for therapy may result in age-related under-treatment, itself a risk factor for breast cancer recurrence and death.

Quality of life: maintenance of quality of life is a priority for elderly patients, who are less willing than younger patients to compromise quality of life for potential treatment benefits. General health and functional independence are key components of quality of life which should be key considerations in management decisions.

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Local Treatment

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Adjuvant radiotherapy (RT) is required by over 70% of patients with operable invasive breast cancer (IBC). However the evidence base for its effectiveness differs markedly between younger and older patients with a much stronger level 1 evidence base among younger patients, largely reflecting the historical exclusion of patients over the age of 70 from randomised trials.

Among younger women the desire to reduce the risks of loco-regional recurrence has to be balanced against impaired cosmesis after breast conserving surgery and compromise of breast reconstruction after mastectomy. For older women there are mental and physical comorbidities that the limit the technical feasibility of delivering RT.

Among younger patients treated by mastectomy, surgeons commonly avoid immediate reconstruction because of concerns that adjuvant RT may compromise graft viability and cosmesis. However the evidence base for the impact of adjuvant RT on reconstruction is weak. The MRC/EORTC SUPREMO trial evaluating adjuvant chest wall RT in 'intermediate risk' breast cancer identifies type of reconstruction (1). There is no group of 'low risk' older patients after BCS from whom breast RT can be omitted. In the CALGB trial (2) evaluating postoperative WBRT after BCS in TI,NO,MO HR+ breast cancer in women $\geqslant$70, the 5 year difference in local failure favoured RT (1% vs 4%). However at 10 years of follow up the gap is widening (2% vs 9%) (3) reflecting the cumulative risk of local recurrence with time. The role of partial breast irradiation remains investigational.

Shorter hypofractionated courses of radiotherapy (HFR) are attractive irrespective of age. However, the interpretation of the RCTs evaluating hypofractionation in IBC differs internationally. ASTRO guidelines (4) confine breast HFR to women >50, not receiving adjuvant chemotherapy or peripheral lymphatic RT. In the UK HFR has been adopted for most patients treated by BCS or candidates for chest wall RT.

For women <50, the EORTC boost trial shows a significant advantage in local control from the addition of 16 Gy boost after BCS and 50 Gy RT. At 5 years of follow up this was not statistically significant in women >50 (5). However follow up at 10 years shows a small but statistically significant reduction in local recurrence from a boost in women >60 (6). This argues that all patients irrespective of age should be considered for a boost.

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21 Proffered paper oral

Pregnancy Following Estrogen Receptor-Positive Breast Cancer is Safe − Results From a Large Multi-center Case-control Study

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Background: We recently reported a meta-analysis showing that pregnancy after breast cancer (BC) could be protective; an observation that is likely confounded by selection bias of the cases, known as 'Healthy mother effect' *(Azim et al; EJC 2011)*. In addition, none of the included studies in this analysis addressed the effect of pregnancy on outcome in estrogen receptor-positive (ER+) BC patients.

Materials and Methods: This is a multi-center (n = 7) case-control study, in which patients who became pregnant anytime following BC diagnosis were matched to BC patients with similar ER status, pN, age, year of diagnosis ($\pm$5 years) and systemic adjuvant therapy. To adjust for selection bias, BC controls had to have a disease-free interval as long as the time lapsing between BC diagnosis and date of conception of the matched case. Using these criteria, we tried to obtain 3 controls for each case. To allow adequate follow-up, only patients diagnosed with BC until 31/12/2005 were included in this study. The 1^{ry} endpoint was disease-free survival (DFS) for patients with ER+ tumors. DFS was calculated from the date of conception, or in the control group, from date of diagnosis + the time between diagnosis and conception of the matched case. DFS in estrogen receptor-negative (ER−) patients was a 2^{ry} endpoint. With a 2-sided 5% significance level and power of 80%, a total of 329 events were required to detect a difference in DFS corresponding to a hazard ratio (HR) of 0.70. Assuming a 30% event rate in the whole population, 1110 patients were required. A unified case report form (CRF) was used for data collection from all sites. Data cleaning and analysis were done in the Institut Jules Bordet. The study was approved by the ethics committees of all the participating centers.

Results: A total of 1183 patients (328 pregnant and 855 controls) were enrolled. The mean age was 34 years (range: 21−48). 57% and 44% of patients were ER+ and node+ respectively. At a median follow-up of 4.7 years from conception, the overall event rate was 30%. No differences were observed in DFS for either ER+ (HR: 0.91[0.66–1.24]) or ER− (HR: 0.76[0.52–1.11]) cohorts comparing the pregnant and control groups. In a predefined subgroup analysis, patients who became pregnant within 2 years following BC diagnosis had better DFS compared to their matched controls (HR: 0.64[0.46–0.89], p = 0.008), with a HR = 0.72 in ER+ and 0.58 in ER−. Breastfeeding and abortion did not have an effect on BC outcome.

Conclusions: This is the 1^{st} study to address the safety of pregnancy in ER+ BC patients adjusted for 'selection bias'. Interestingly, pregnancy within 2 years after BC diagnosis appeared to have a protective effect. The study is statistically powered to confirm that pregnancy is safe and should not be discouraged following BC diagnosis irrespective of ER status.