Pregnancy in women with a history of breast cancer

The effect of pregnancy on survival and the best time to conceive are uncertain, so consideration of individual priorities is essential

Young women diagnosed with breast cancer before completing their families face difficult decisions about future childbearing. Effective treatment tends to reduce fertility, and uncertainties remain regarding the effect of future pregnancy on survival. For women who decide that they do want to become pregnant, the optimal timing of conception is not known.

A population based study by Ives and colleagues in this week’s BMJ assesses the effect of becoming pregnant on survival after breast cancer.1 The study used the Western Australian data linkage system to identify 123 women aged 15-44 who became pregnant after being diagnosed with breast cancer. During a median of 10.7 years of follow-up, 39% experienced recurrent breast cancer and 15% died.1

The study shows that pregnancy is uncommon after breast cancer; only 4.8% of women aged 15-44 diagnosed with breast cancer became pregnant during the study period and 2.6% had a live birth.1 The study adds to the limited body of evidence showing that women with breast cancer who become pregnant or have a live birth seem to have comparable or better survival than those who do not.1,2,3 This evidence is difficult to interpret; women who become pregnant after breast cancer are a highly selected group, and they differ from those who do not become pregnant in ways that affect future survival, including prognostic factors.1 Women with a worse prognosis are also more likely to receive chemotherapy, which reduces fertility. Furthermore, for reasons that are unclear, women who are pregnant at the time of diagnosis or have given birth during the five years before diagnosis have lower survival rates than other women.4,5

Such women might be less likely to conceive after diagnosis because they already have children.

Because the relative risk of death after diagnosis can differ more than 30-fold between extreme categories of prognostic variables,6 even a small amount of residual confounding between prognosis and the decision to get pregnant could generate a spurious protective effect. Many studies adjust for basic prognostic factors, such as tumour size and disease stage. However, it is not possible to account fully for all factors that might influence both survival and whether women get pregnant after breast cancer—including tumour grade, number of positive lymph nodes, treatment, and reproductive history.1,3 Therefore, we cannot reliably assess the effect that pregnancy after breast cancer has on survival.

Nor can we exclude an adverse effect of pregnancy after breast cancer on survival. Consider this example; observational studies show consistently improved disease-free survival and overall survival in women with breast cancer who use hormonal therapy for the menopause after diagnosis, compared with women who do not (summary relative risk of recurrence 0.64, 95% confidence interval 0.50 to 0.82).4 The apparent advantage in survival persists after adjustment for disease stage.9 However, randomised controlled trials show that hormonal therapy for the menopause significantly increases the recurrence of breast cancer (3.41, 1.59 to 7.33).4 For obvious reasons, randomised data on the effect of pregnancy after breast cancer on survival are not available.

Given these uncertainties and the small number of events in the studies of pregnancy after breast cancer (19 deaths among exposed women in the current study9),

This has resulted in the formation of organisations such as the UK Clinical Research Collaboration (www.ukcrc.org). However, in the two years since implementation of the regulations, recruitment to clinical trials in unconscious patients in emergency situations has been slow in the UK.8 The evidence base for trauma care was already seriously lacking,9 and the regulations did not help. Unconscious patients in emergency situations should have the right to benefit from medical research, but the 2004 regulations put this right in jeopardy.

The amendment to the clinical trials regulations will be welcomed by emergency doctors. NHS research and development departments urgently need to develop guidance on how to implement this amendment. In the meantime, emergency doctors can be reassured that the new guidance allows patients to be enrolled without prior written consent if approved by the ethics committee, and that clinical trials once again have the potential to provide the evidence needed to improve emergency care.

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Mechanical circulatory support in the UK
It is time to do a trial of left ventricular assist devices for lifetime use

In June the National Institute for Health and Clinical Excellence (NICE) published welcome but bewildering guidelines for short term circulatory support with left ventricular assist devices (LVADs) as a bridge to cardiac transplantation or recovery.1 Welcome because the guidelines will support funding of these devices but bewildering because few, if any, guidelines for use were actually provided. The limited evidence was derived from the USA and Europe, where LVADs have been used for 20 years, and the guidelines are silent on a third potential use for these devices—their longer term use as a lifetime treatment.

First generation LVADs were designed to replace the failing left ventricle by providing stroke volume and pulsatile blood flow. Blood is taken from the ventricle and pumped in a pulsatile manner into the aorta at a rate of 4-10 litres per minute. These devices provide symptomatic relief, reverse multorgan dysfunction, and reduce the cytokine and humoral responses to heart failure.2 Transplant survival is improved following the use of a device.3 Resting the heart and increasing coronary flow with an LVAD has marked effects on the diseased myocardium. Reduced wall tension and stroke work contribute by decreasing myocyte hypertrophy, apoptosis, myocytolysis, and fibrosis.4 Myocyte genetic expression and metabolism change towards normal. As a result LVADs can occasionally be removed after function improves in the native heart (bridge to recovery).5 This occurs more...