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Editorial

It's not for me... It's for my daughter

Hereditary breast cancer is a tough clinical issue not only for medical reasons, but also because it deals with familial transmission of a dreadful disease affecting a symbolic organ. The first words of a new patient are very meaningful. In my experience as a consultant in a hereditary cancer clinic, it's not uncommon that a woman starts by denying any individual concern ('It's not for me') but rather focus on the familial utility of the consultation ('... It's for my daughter'). We have to comply with the demands of these women¹ and keep in mind their willingness to 'protect' their relatives; but affected women and oncologists should be aware that BRCA breast cancer (BC) differs from other BC and that therapeutic options should therefore be different. The review by Liebens et al. in this issue of the journal,² definitively shows that management of BRCA1/2 -BC is an individual and clinical issue, as much as a familial one.

Clinical management of BRCA-BC is an important and growing concern.

Important since high-impact-wide audience journals often publish contributions on that topic and growing since, according to references included in this review, a 400% increase in the number of publications is observed between the 1995–96 and the 2005–06 periods. Moreover, almost 70% of the references quoted have been published in oncology journals.

The review by Liebens et al.² focused on three main endpoints: the risk of ipsilateral recurrence, the risk of contralateral BC, and survival.

Among the many therapeutic options women and physicians face, the kind of surgery, mastectomy versus breast conserving treatment, is again at stake.

For women with a known, or highly probable, mutation of BRCA 1 or 2, the question is whether breast conserving therapy (BCT) is a reasonable option or not. In an editorial comment in this journal³ published in 2004, the answer was yes. Currently, the answer is still yes, as according to the table 3.2 in the review by Liebens et al.,² in which 12 out of the 17 studies did not report an increase of local recurrence. We have to underline, however, that only in four out of eight studies in which patients were exclusively treated by BCT, was information on histological margins available.

However despite the absence of evidence for an increase risk of local recurrence, knowing a positive BRCA1/2 status at the time of surgical decision may lead clinicians/women to favour mastectomy. In my opinion it's the risk perception

rather than the factual risk that lead to this decision.⁴ Increasing knowledge is not enough, increasing the quality of counselling is also required to achieve a well-informed decision.

If, at present, local management of BRCA-BC follows the same guidelines as so-called sporadic BC, the question of mastectomy still remains, not to reach a local control (therapeutic mastectomy) but to protect from a second BC (prophylactic mastectomy).

The two main criteria for any preventive intervention are:

- The life expectancy without the intervention.
- The impact of the intervention on the incidence of the disease, not only the risk reduction rate. A decrease of 80% is meaningless in a disease with an incidence below 1/10000 (i.e. one case avoided for 12,500 persons treated) but is a dramatic improvement for a disease with an incidence above 25/100 (i.e. one case avoided for five persons treated).

Decision about prophylactic surgery might follow a four step process:

1. Is life expectancy high enough to consider the intervention as relevant?
2. Is the incidence of the disease high enough to consider the benefit of the intervention?
3. Is the benefit of the prophylactic surgery high enough to balance the negative side-effects?
4. Do the woman's values, risk perception, benefit perception, specific risk-aversion lead to an arbitration which favours prophylactic mastectomy?

Some advocates of autonomy-based decision could argue that only the step 4 deserves attention regardless of the first three ones. However, women should be informed of the global risk/benefit assessment and therefore should be disclosed all worthy information at each step. With regard to this process, this review gave us updated information about the first two points.

For the first step, there is no significant trend to support higher aggressiveness of BRCA-BC. Contrasted reports do exist, but it can be expected that the difference, if any, should not be huge (it would otherwise have been already and easily demonstrated).

The second point in this review deals with the incidence of a second BC. Publications about contralateral and ipsilateral BC incidence have been analysed.

Even if it appears that the rate of contralateral BC is high enough to consider and discuss contralateral prophylactic mastectomy, this analytical option is, however, enshrined in a global risk management which contains the risk/side-effects/utility of many options among which the efficacy of MRI screening and the impact of prophylactic oophorectomy on both ovarian cancer and second breast cancer have to be considered. In this global approach, consultations should be aimed at the management of woman's breasts as an entity. In my experience contralateral mastectomy for a woman with a first BRCA-BC treated with a mastectomy is more acceptable than a contralateral mastectomy for a woman who benefited from breast conserving surgery. To treat more aggressively the healthy breast than the affected one is an offence to common sense.

Currently a few things could be said to a woman affected with a BRCA-BC which has not been treated by mastectomy. According to this review,² local control may be achieved with the same rate of local recurrence than sporadic-BC. However, I would be more skeptical. Indeed looking at the graphics published in the articles analysed by Liebens et al., comparing the risk of ipsilateral events in the follow up of sporadic-BC and BRCA-BC, there is no difference in the first 7–10 years afterwards. However, the results might be different for longer follow up (10–15 years).

Bearing in mind that almost 50% of BRCA1 gene mutation carriers who will develop BC will be affected before the age of 50, the long term survival is relatively high; risk management has to deal with long term issues and obviously long term data are needed.

We indeed have to give information on efficacy and risks of prophylactic mastectomy, impact of prophylactic oophorectomy and value of screening. But, above all, we have to listen to our patients; that was my first point and will be my last one. It is important to understand the reasons why a woman prefers prophylactic surgery. It's not unusual that at the end of my 'explanations' and description of the risk

of being affected with a second cancer, women tell me 'I'm not really afraid of being affected with breast cancer again, but I do not want to undergo a new chemotherapy'. This is a strong argument for these women against screening, and reinforces the value of prophylactic surgery and... chemoprevention.

Conflict of interest statement

None declared.

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