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Ethical principles of autonomy and beneficence in genetic screening for breast cancer

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For a patient with breast cancer and for her adult relative, genetic counselling will usually increase their autonomy and may be beneficial. No benefit for autonomy and markedly negative influence regarding beneficence may be attributed to genetic screening in a young relative who is not yet in the age group at risk for developing breast cancer. For a woman without family history of breast cancer, we may expect an insignificant benefit with respect to her autonomy and beneficence, and potential cost from her false perception of a low risk for breast cancer. These considerations lead to a conclusion that at the present state of knowledge, genetic screening for breast cancer should be restricted to relatives of patients with breast cancer who are already in the age group at risk for developing the disease.

Key words: breast neoplasms-genetics; genetic screening, ethics medical

Introduction

For many decades, familial predisposition towards breast cancer has been recognised as one of the risk factors. Recent research has linked this predisposition to mutation of particular genes, thus allowing us to understand and much more precisely estimate the risk.

We start this paper with a brief summary of current understanding about genetic predisposition towards breast cancer. Then the ethical issues are presented and discussed. We conclude by proposing some practically-oriented ethical guidelines for genetic screening of breast cancer.

Genetic predisposition towards breast cancer

The familial breast cancer syndromes include the site-specific breast cancer, breast cancer with extremely early onset, the breast-ovarian cancer syndrome, the Li-Fraumeni syndrome and some other cancers and rare hereditary conditions which are associated with an increased incidence of breast cancer.[1] About 5 % of all cases of breast cancer and 25 % of those occurring under 35 years of age are due to inheritance of mutations in dominant susceptibility genes which confer a high lifetime risk of the disease.[2]

A number of molecular abnormalities with a loss of heterozygosity have been described in familial and also in sporadic breast cancer.[1] A mutation of BRCA 1 gene on chromosome 17, normally serving as a negative regulator of mammary epithelial cell growth, is at present considered as the most important cause for a genetic predisposition to breast cancer.[3-5] Mutation of this gene has been found in most families with multiple cases of breast and ovarian cancers, and in about half of the families with the early-onset breast cancer.[6] BRCA 2 gene on chromosome 13 has also been implicated in the etiology of some familial breast cancers,[7] and other mutated genes, linked to development or progression of breast cancer, have been recently described.[8]

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Ethical issues in genetic testing and screening

In order to give structure to our discussion of the ethical issues we will use the method of ethical analysis[9] with a simple framework in two dimensions.[10] The first dimension specifies the persons affected, i.e. the patient with breast cancer, her adult relative (who is already in the age group at risk for developing breast cancer), her minor relative, and an adult woman without a family history of breast cancer. The second dimension specifies the relevant value-premises. We will use the two principles of autonomy and beneficence. The first principle states the moral obligation to respect the right to self determination, while the second one states the moral obligation to benefit others, especially not to harm them. Issues of justice are at the present state of knowledge less relevant.

1. A patient with breast cancer

Should the physician offer genetic testing to a patient with breast cancer? Gene diagnostics offers additional information on prognosis and on probability for contralateral disease, and may benefit the patient and help her reach a rational decision regarding follow-up and eventual preventive measures.[5] It therefore seems reasonable to assume that she would like the physician to inform her about the possibility of testing.

However, a patient who has been informed about her genetic predisposition has hardly any choice but to forget about the privacy of her disease and feel a strong responsibility for other women among her relatives. She might feel guilty because of the implications for her daughters, and would feel obliged to inform and perhaps even advise them. But we doubt that she, in this situation, would be the best advisor for her relatives concerning genetic screening or preventive measures.

To sum up: genetic testing offered to a patient with breast cancer would principally be to her advantage, both from the point of view of the principle of autonomy and the principle of beneficence. However, a positive result of screening may also imply ethical costs such as guilt and a loss of privacy (Table 1, first row).

2. Adult female relative of a patient with breast cancer

A woman who is in the age group at risk for developing breast cancer and who has a close relative with the disease is nowadays often aware of the familial predisposition towards the disease. Testing for genetic predisposition will allow her either to dismiss her fears, or to reach a rational approach towards future preventive or screening activities.

A positive result of screening for genetic predisposition may also have adverse effects. The permanent threat of breast cancer may be an unbearable burden and a source of extreme concern. Probable involvement of psychological factors in the multifactorial etiology of breast cancer[11,12] is explained by studies of molecular mechanisms for stress-induced alterations in susceptibility to cancer:[13] we may therefore speculate that genetic screening, with its possible negative effect on the woman's emotional stability could in fact increase the chances that the woman will actually develop the disease.

To sum up: to offer testing to the adult relative would provide her with an opportunity for more rational decisions about screening and eventual preventive measures, but a positive result would almost certainly adversely affect the quality of her life (Table 1, second row).

3. Minor female relative of a patient with breast cancer

At present, we can offer no practical advice to a child or a woman younger than the age group at risk for developing breast cancer. Whether she undergoes screening or not and regardless the result of the test, no activity seems advisable.

There are two possible outcomes. If the tests turn to be negative, the young relative will be relieved of her fears. But a positive result of testing starts a life-long and increasing anxiety. One may speculate that the relief of fears is insignificant when compared to potential harmful effects of the news about a positive genetic predisposition: while a teenager tends to accept positive news as granted, she will probably show extreme concern about even minor negative aspects of her body image, or of predictions about future life.

It is natural to share our secret fears with those whom we love. Unfortunately, however, a young woman who has told this news to her boyfriend may soon realise how weak and full of prejudices is the human nature: the news may spread and adversely affect her social life.

To sum up: testing a young woman for genetic predisposition will result in information which has,

at present, no practical implications. If the test is negative she will experience relief, but a positive test would almost certainly have a serious negative impact on her emotional stability and social life (Table 1, third row).

4. Adult woman without a family history of breast cancer

The likelihood of detecting a mutation of BRCA1 or of another gene predisposing to breast cancer among women without a family history is very low: less than one among 500 will be positive.[2] On the other hand, breast cancer is a frequent disease, affecting close to 1 in 10 women in Western Europe and North America.

In the rare instance when the test is positive, the benefits and costs to such a woman will be the same as discussed under the category of an adult relative of a patient with breast cancer. If the result is negative, however, it will be very difficult not to leave the woman with a feeling that her risk of developing breast cancer is small – when, in fact all what a negative test says is that she is not among those very few women who, in spite of a negative family history, develop breast cancer as a result of their genetic predisposition. Such a false feeling of safety might affect the compliance to the established, cost-effective and life-saving programmes of self-examination and mammographic screening.

To sum up: testing a woman without family history of breast cancer will most probably yield a negative result, implying an insignificant ethical benefit with respect to the woman's autonomy and beneficence. At the same time, potential serious cost may arise from her false perception of a low risk for breast cancer (Table 1, last row).

Discussion and conclusions

Many women, and especially relatives of patients with breast cancer, are now aware of a high incidence of breast cancer and of the possibility that the risk is genetically determined, and the demand for genetic counselling and the related screening and prevention strategies is increasing.[14-16] A survey among first-degree relatives of ovarian cancer patients revealed that 75 % would definitively want to be tested for a mutation of BRCA1 gene.[17] Still, in spite of the efforts to convey an objective information, the perception of the true risk for developing the disease is often very unprecise;[18] compliance with the recommended programmes for early diagnosis is poor;[19] and psychological distress is often so severe that professional counselling is needed.[20, 21]

It seems that for a patient and for her adult relatives, the advantages of testing often outweigh the potential disadvantages. This opinion is in concordance with a high level of interest for genetic screening among adult members of families with an elevated risk for breast or ovarian cancer.[17, 22] On the other hand, few advantages and severe negative effects shift the balance to the opposite side in a young woman. The potential harm induced by genetic screening in this age group far outweighs the benefits. Until something can be done to remove the genetic defect, we believe that genetic screening should not be done to persons younger than the earliest age when the disease may be detected. We also see few advantages, and possible costs in testing women without a family history of breast cancer: there may be no public health benefit in screening the general population for genetic susceptibility to common, multifactorial disorders.[23]

According to a Statement of The American Society of Human Genetics,[24] genetic testing for breast

Table 1. Ethical costs and benefits of testing for genetic predisposition for breast cancer. As a base-line, no such testing is assumed.

	AUTONOMY	BENEFICENCE
A patient with breast cancer	Benefits and possible costs	Benefits and possible costs
An adult female relative	Benefits	Benefits and possible costs
A minor female relative	Neither benefits nor costs	Minor benefits or severe costs
Adult woman without a family history of breast cancer	Insignificant benefits	Insignificant benefits and potential serious costs

cancer predisposition is not a routine, and it is premature to offer population screening. A clear indication for testing can be found only in families with a mean age at diagnosis of less than 45 years, and controlled studies are urgently needed to assess the value of the recommended screening protocols.[25,26] An important issue in testing for a genetic predisposition is the psychological harm caused by an embarrassing information which is accompanied by an unprecise practical advice.[20, 21] While we share this concern, the aim of this report is to show that neither of the two extreme positions regarding genetic screening may be generally acceptable. Careful weighting of the ethical costs and benefits in applying these procedures may identify groups of women for whom the procedure seems advisable, and others in whom the ethical cost is prohibitive. This clearly applies to the present state of knowledge: if removal of the genetic defect becomes possible or if targeted methods of prevention become available, ethical evaluation will lead to a different conclusion.

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