Screening and genetic counselling for relatives of patients with breast cancer in a family cancer clinic

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Abstract

Family history is the major risk factor in the aetiology of breast cancer. Breast screening is currently available to women from the age of 50 to 64 through the National Breast Screening Programme. There is, however, an equivalent risk of developing breast cancer below 50 for first degree relatives of women diagnosed with breast cancer premenopausally. We have estimated the risk of breast cancer for relatives of women affected at different ages and used these to establish a family cancer clinic offering breast screening based on individual risk. In three years we have seen 851 patients. Compliance for annual radiology was in excess of 83% over this period and of five cancers detected one had a lump at presentation, two developed interval breast lumps, and two were asymptomatic.

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For women in Britain the lifetime risk of developing breast cancer is approximately 1 in 12 and it is the most common cause of death in women aged between 35 and 55.[1] Although environmental factors and reproductive experience play a role in the aetiology of breast cancer, family history has long been recognised as the most important risk factor.

Epidemiological studies have shown an increase in breast cancer in relatives of patients with breast cancer.[2–7] Family studies have led to the identification of a number of dominantly inherited cancer family syndromes associated with an increased risk of breast cancer,[8,9] including site specific breast cancer, breast ovarian syndrome, the Lynch type II cancer family syndrome, Cowden's syndrome, Muir-Torré syndrome, and Li-Fraumeni syndrome. Furthermore, studies suggest that a dominantly inherited liability to breast cancer may be responsible for around 10% of the total burden of breast cancer and may be responsible for the majority of early onset cases.[10,11]

Recently there has been considerable interest in screening in order to detect breast cancer early in the hope of maximising the potential benefit of treatment.[12] The population risk of breast cancer increases steeply for women over the age of 50 and this underlies the availability of breast screening offered through the National Screening Programme. However, there is an equivalent risk of developing breast cancer below 50 for those first degree relatives of patients diagnosed young.[7] Hence, breast cancer is a concern to a large number of women with close relatives with breast cancer. Using family history there is an opportunity to identify women below the age of 50 in whom screening may be of benefit at an earlier age than is currently available through the National Breast Screening Programme. Our experience in a genetic counselling clinic for those at risk of colorectal cancer[13] led us to recognise the need for a similar service for families with breast cancer and this was established at the Royal Free Hospital in 1988. We report our experience of 851 patients seen in the first three years.

Calculation of risks to first degree relatives

Before the clinic was opened, the risks of breast cancer for first degree relatives were calculated using life tables from 253 consecutive pedigrees taken from patients with breast cancer.[7] When the index patient developed breast cancer under the age of 40 the relative risk for first degree relatives under 50 was 7·35 ($p < 0·05$, 95% confidence limits 0·89 to 26·53), when the index patient was aged less than 50 the relative risk was 3·62 ($p < 0·05$, 95% confidence limits 0·98 to 9·27), and when the index patient was less than 55 the relative risk was 3·72 ($p < 0·05$, 95% confidence limits 1·21 to 8·67). When index patients were older than 55 the relative risk was 1·7 (NS, 95% confidence limits 0·35 to 5·06). These results are similar to previous estimates of relative risk for relatives of patients.[2,5,6]

Screening policy

The risk of breast cancer for each woman attending the clinic was estimated from her family history. The risk was explained and our screening programme discussed. For the first degree relatives of patients diagnosed young, who have a threefold or greater increase in risk, and those families whose pedigrees showed a dominant mode of inheritance of breast or other cancers, annual radiological examination was offered. The risk of breast cancer in these women is similar to that of women aged between 50 and 64 in the general population. Women aged 25 to 39 were offered a baseline mammogram and yearly ultrasound examination of the breasts, women aged 40 to 49 were offered annual mammography, and those over 50 years of age were encouraged to participate

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Source of patients attending the family cancer clinic by region in England and Wales.

in the National Screening Programme. All the women who attended the class were taught breast self examination and were encouraged to join the National Screening Programme at 50 years of age. All ultrasound examinations and mammograms performed at the Royal Free Hospital were reported by one of two consultant radiologists.

Women whose pedigrees were consistent with one of the multiple cancer syndromes, such as the Lynch II cancer family syndrome, were offered additional screening for pelvic and colonic cancers.

Patients and methods

In 1988 a family cancer clinic was opened at the Royal Free Hospital as part of the NE Thames Regional Genetic Service. The clinic was supported by the Imperial Cancer Research Fund and received publicity in the national press. Guidance was given that the family cancer clinic was available for first degree relatives of patients who developed breast cancer premenopausally or who had multiple cancers within their family. We decided to accept self referrals as well as those from medical practitioners.

Results

From March 1988 to September 1990, 851 patients attended the family cancer clinic because of concern about their risk of developing breast cancer. The figure shows the areas of England and Wales from which these patients came. The majority came from areas within or close to London. Table 1 shows the source of referrals to the family cancer clinic. Initially, 91% of patients were self referrals, subsequently an increasing proportion were referred by medical practitioners.

Table 2 shows the age profile of patients attending the clinic; 45% (35 out of 75) of those aged 50 or over were referred by medical practitioners.

Table 3 shows the pattern of risk and syndromes identified in patients attending the clinic. Fifty percent (56 out of 111) of those whose risks were not substantially increased, or whose risks were no more than the population risk, were referred by medical practitioners. Of the cancer family syndromes showing dominant inheritance of cancer, site

Table 1 Sources of referrals to the family cancer clinic.

	1988		1989		1990	
Source of referral	No	%	No	%	No	%
Self referral	361	91	135	58	127	58
By general practitioner	29	7	90	38	88	40
By hospital practitioner	7	2	9	4	5	2

Table 2 Age profile of patients attending the family cancer clinic.

<25	66	8
25–39	500	59
40–49	210	25
50+	75	9

Table 3 Pattern of risks and syndromes identified.

Pattern of risks	No	%
Less than 1·7	111	13
Greater than 3·5	740	87
Specific syndromes identified		
Site specific breast cancer	179	21
Breast ovarian cancer	20	2
Lynch type II cancer family syndrome	108	13
Li-Fraumeni syndrome	4	0·5
Cowden's syndrome	2	0·2
Muir-Torré syndrome	5	0·6

specific breast cancer and the Lynch type II cancer family syndromes were most frequently encountered, accounting for 39% of all those at increased risk.

Of the women who were estimated to be at a high risk of developing breast cancer, 595 accepted screening at the Royal Free Hospital and it is the experience of these women that is reported, not those who chose to be screened at other centres. Table 4 shows the results of radiological screening and compliance rates for those patients offered screening at the Royal Free Hospital. Compliance rates in both age groups were in excess of 83% throughout the period of the study. All women with suspicious abnormalities on radiological examination were referred to breast surgeons. Altogether 1028 radiological breast examinations were carried out at the Royal Free Hospital and five cancers were detected. Three cancers were detected by screening, one was felt at presentation, and two were detected by radiology, one by ultrasound examination and one by mammography (table 4). Two interval breast cancers occurred in women who had in each case had two preceding negative screens; one in a woman aged 49 by two annual mammograms and one in a 38 year old by mammogram followed by ultrasound. Both were found by self examination. The false positive rate was 1%.

Discussion

A large proportion of women in the general population are aware that having a close relative with breast cancer places them at increased risk.[14] Those who are under 50 years of age whose relatives have been diagnosed at an early age cannot be reassured through the National Screening Programme though their risk may be the same as that of women who are eligible for screening between the ages of 50 and 64.

Compliance is a major factor influencing the potential benefit of screening for breast cancer. While it is generally acknowledged that a reduction in mortality from breast screening of around 25 to 30% is possible through breast screening of women over the age of 50,[15] high rates of compliance have proved difficult to achieve in the general population. In the United Kingdom the uptake of breast screening through the National Screening Programme is about 66% and is even lower in the North-East Thames region, and there is little to suggest that offering screening to women aged 40 to 49 in the general population would achieve an increased rate of compliance. Probably the most important factor in achieving a high rate of compliance for breast screening is a belief in a personal susceptibility to breast cancer and this may account for the high rates of compliance in the family cancer clinic.[16,17] Our experience in a family cancer clinic suggests that if family history is used as a criterion for offering screening to women under the age of 50, a high rate of compliance can be achieved.

The efficacy of radiological screening for young women is acknowledged to be less than for postmenopausal women.[18] This must in part be because of the expected incidence of breast disease in the younger age group which is approximately threefold less than in the postmenopausal age group. However, for the first degree relatives of patients diagnosed young the expected incidence of breast cancer is the same as that of women who are currently being offered breast screening. Despite the small number of patients in this study, our results suggest that screening a high risk group of young women would achieve a similar pick up rate to that of the National Breast Screening Programme for women over 50 years.

As well as concern over the efficacy of breast screening, there is controversy over possible psychological morbidity associated with breast screening programmes.[19–21] We were therefore aware that anxieties might be raised by discussing actual risks during counselling and that false expectations regarding screening could develop. Both these problems were discussed freely with our patients; however, there is a need to evaluate systematically the psychological effect of such counselling and of participating in our screening programme. There is a great variation in people's requirements for reassurance about their family risk of cancer and the high proportion of self referrals to the family cancer clinic who were found to be at high risk suggest that women are very adept at self selection for this type of screening programme.

At present family history is a useful criterion for selection of patients for screening, but in the future molecular genetic analysis will refine this process further. The first gene responsible for early onset breast cancer has been localised to the long arm of chromosome 17[22] and it is very likely that gene markers

Table 4 Compliance rates and results of breast screening. Values are numbers (percentages).

		Years of screening					
		1		2		3	
Women aged 25–39							
Compliance		96%		84%		89%	
Results	Normal	388	(92)	217	(95)	70	(95)
	Benign lesions	21	(5)	11	(4)	4	(5)
	Suspicious lesions	12	(3)	1	(1)		
	Biopsy confirmed breast cancer	1					
Women aged 40–49							
Compliance		93%		89%		97%	
Results	Normal	132	(91)	97	(95)	51	(89)
	Benign lesions	10	(7)	4	(4)	5	(9)
	Suspicious lesions	3	(2)	1	(1)	1	(2)
	Biopsy confirmed breast cancer			1		1	
Compliance overall		95%		89%		97%	

useful for diagnosis will soon become available. Germline point mutations of the tumour suppressor gene p53 are reported to be responsible for at least a proportion of cases of the Li-Fraumeni syndrome.[23 24] The screening programme used in this study detected only three out of five breast cancers in 566 young women at risk. Those at risk will soon be identified with more certainty but the best protocol for screening younger women still needs to be defined. This will probably only be determined by long term follow up of large multicentre studies.

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