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The initiator and timing of referral to breast cancer genetic counselling; an exploration of everyday person-centered practice

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ABSTRACT

Objective: The referral process for genetic counselling in breast cancer patients may be compromised by patient-related factors, like patient's age, referral initiative or cancer history. This study aimed to characterize this referral process in daily clinical practice.

Methods: During genetic counselling a checklist was filled in for each consecutive counselee affected with breast cancer assessing educational level, the initiator for referral and the ethnic background as reported by the counselee. Chi-square tests were used to assess associations between patient-related factors and initiator of referral and timing of genetic counselling.

Results: Included were 96 consecutive breast cancer patients referred to cancer genetic counselling: 52% of them were referred on their own initiative versus 48% on their doctor's initiative. There was no significant relationship between initiator of referral and time since diagnosis, age at time of diagnosis, number of first-degree female relatives and number of first degree relatives affected by any cancer.

Discussion: Patients' interest in genetic testing is not clearly related with time since diagnosis. Family history seems to play a role in the timing for referral.

Conclusion: At one out of two breast cancer patients plays a major role in the referral for genetic counselling. However, we did not establish a relationship between initiative for referral and time since diagnosis.

INTRODUCTION

Not all patients diagnosed with breast cancer are eligible for genetic testing; selection depends on patients' characteristics (e.g. age at diagnosis, personal cancer history) and family cancer history. Specific knowledge concerning hereditary breast cancer and criteria for referrals are not optimal, engendering the risk of suboptimal referral of breast cancer patients [1-5] Underutilization of genetic counselling for hereditary breast cancer of high-risk women is reported recently. [6,7] This may, however, not only result from factors related to the physician, because also the patient plays a role in the referral procedure.

Affected patients with increased susceptibility to hereditary breast cancer appreciate to be informed about genetic testing. [8-10] Rantala and colleagues showed that perceived risk of cancer is not only influenced by the occurrence of breast cancer in family members, but also by a positive family history for any type of cancer. [11] So, having affected first degree relatives can be expected to play a role in initiating referral to genetic counselling by the breast cancer patient herself.

Albada et al found that for the majority of consultations in breast cancer genetic counselling, the initiative for referral is taken by the counselee or by a combined initiative of the counselee and her physician, both in the Netherlands and the UK. [12,13] Women who feel the need for genetic testing at an earlier moment, before her physician discusses referral for genetic counseling, often may have to take initiative for referral themselves.

There is no consensus about the right moment to refer a patient diagnosed with breast cancer. Physicians do not seem to be eager to refer directly after diagnosis as they assume that the patient would not be susceptible for referral in the initial stage after diagnosis and that genetic testing would add too much additional stress. [14] We recently showed that 75% of medical specialists working in Dutch hospitals prefer the follow-up after primary treatment as the most suitable time for genetic testing. [4] This implicates that most breast cancer patients are referred from six months onwards after diagnosis, on their physicians' initiative, when primary treatment is largely completed.

More insight into patients and physicians characteristics influencing the referral process for breast cancer genetic counseling is needed in order to improve the referral process in general, and timing of referral in particular. In the present study, we aim to characterize the referral process for cancer genetic counselling for breast cancer patients in daily clinical practice and determine whether there is a difference in time-point after diagnosis between breast cancer patients who took initiative for referral themselves, when compared to patients in whom the doctor took the initiative. We expected that patients who are enrolled earlier than six months after diagnosis took more often the initiative for referral themselves. We also aimed to assess whether age at diagnosis, cancer history in first degree relatives or number of first degree female relatives play a role in the referral process. We expected that patients who enrolled earlier after diagnosis were younger, had more affected relatives or more first degree female relatives.

METHODS

Participants

The study population consisted of all consecutive patients affected by breast cancer who were referred for breast cancer genetic counselling to the Department of Medical Genetics of the University Medical Centre Utrecht, the Netherlands, from June until December 2007. This study is part of a larger study, which included all consecutive counselees (affected and unaffected) referred for cancer genetic counselling concerning different cancer types. [15]

Procedure

Genetic counselling and DNA testing for hereditary breast cancer consists of at least one consultation with a genetic counsellor or clinical geneticist, in which patient's personal history and family history are explored. When this points to an indication for genetic testing, DNA-testing on a blood sample of an affected patient will be offered to identify a possible mutation in the BRCA1/2 genes. DNA test results are discussed in person with the counselee during a second consultation. If there is no indication for genetic testing, if the counselee is not willing to undergo genetic testing or if no mutation in BRCA1 or BRCA2 is identified, breast cancer risk estimates will be given for the patient's relatives based on family cancer history only. For the present study, clinical geneticists and genetic counsellors filled in a checklist for each counselee concerning their level of education, the initiative for referral and the ethnic background as reported by the counselee. These items are routinely discussed during genetic counselling consultations. Participants were considered to be an immigrant if one or both of their parents were born in another country than the Netherlands. [16] Furthermore, personal and family history regarding cancer were registered as well as the eligibility for BRCA1/2 testing in the counselee.

Measures

Date of diagnosis of breast cancer and date of enrolment at the Department of Medical Genetics were collected from medical records. Age at time of diagnosis was calculated by using date of birth.

Regarding family cancer history, we registered from pedigrees and reports in medical records the number of affected first-degree relatives, both male and female, with any kind of cancer. Affected second-degree relatives were not included.

Statistical analysis

Descriptive statistics were used to describe the referral process and to explore the association between length of time since diagnosis and initiative for referral. All statistical analyses were conducted using SPSS version 15.0.1 software. All *P*-values were two-sided; values less than 0.05 were considered statistically significant.

We defined the following variables: 'time since diagnosis', 'initiative for referral', 'age of the counselee at time of breast cancer diagnosis', 'number of first degree female relatives (= all female first degree relatives, except the mother)' and 'number of first degree relatives affected by cancer (affected mother included)'. The number of first-degree relatives affected with breast cancer was recorded, but the count of this variable was too low to analyse reliably and was therefore not included. Length of time since diagnosis was calculated as follows: starting point was defined as date of breast cancer diagnosis and end point was date of enrolment at the Department of Medical Genetics. Not in all cases date of diagnosis of breast cancer could be precisely determined. In 16 cases only age of the counselee at time of diagnosis was

documented. To minimize calculation errors, we therefore consequently assessed date of birth and year of diagnosis as starting point in each of these cases. When only the month as time of diagnosis was provided, the starting point was defined as the first day of the concerning month.
The variable initiative for referral was dichotomized into 'own initiative' and 'initiative by doctor'. The first includes both initiative from the counselee in person, and initiative from a family member. The second category of initiative by doctor represents not only the medical specialist and the general practitioner, but also the nurse practitioner of the breast cancer clinic.
We subdivided the variable time since diagnosis in three categories, globally based on the different stages of treatment and follow-up, namely 0-6 months after diagnosis, 7 months – 5 years after diagnosis and over 5 years after diagnosis. [17]
Chi-square tests were used to assess associations between the variable initiative for referral versus time since diagnosis, age at time of diagnosis, number of first degree female relatives and number of first degree relatives affected by any cancer. The same method was applied to the variable time since diagnosis versus age at time of diagnosis, number of first-degree female relatives and number of first degree relatives affected by any cancer.

RESULTS

Characteristics of the participants

In the main study, 406 consecutive counselees were included of which 99 (24.3%) were diagnosed with breast cancer and were therefore eligible to participate in the present study. Three women were excluded because they had developed breast cancer in the past, and were now referred for another type of cancer.

[TABLE 1]

Initiator of referral

In nine cases (9.4%), initiative came from both the patient and the doctor. These cases could therefore not be categorized and were consequently excluded from the statistical analysis relating to initiative of referral. Of the remaining 87 patients, 51.7% was referred by their own initiative and 48.3% by their doctor's initiative.

Time since diagnosis

Spread in time since diagnosis was large; mean length of time was 34.0 months (2.8 years; 95% CI 20.5-47.5 months), with a much shorter median of 7.8 months (Table 1). Few were referred in the first month, of these, 71% came by their own initiative.

Patient-related factors, initiator of referral and time since diagnosis

No significant relationship was found between initiative for referral and time since diagnosis, age at time of diagnosis, number of first degree female relatives and number of first degree relatives affected by any cancer (Table 2).

[TABLE 2]

In addition, no significant relationships were found between time since diagnosis and the variables age at time of diagnosis, number of first-degree female relatives and number of first degree relatives affected by any cancer (Table 3). Patients referred between 0-6 months and 7 months-5 years since diagnosis less often had two or more

first degree relatives affected by any cancer (p=0.059), then patients referred >5 years after diagnosis.

[TABLE 3]

DISCUSSION

This study was designed to explore the referral process of breast cancer patients to cancer genetic counselling. We showed that about half of the breast cancer patients is referred on their own initiative, and that the majority is from Dutch Caucasian origin and had an intermediate or high education. Contrary to our expectations, no association was found between time since diagnosis and initiative for referral. Furthermore, also no relationship between initiative for referral with the variables age at time of diagnosis, number of first-degree female relatives and number of first degree relatives affected by any cancer could be established.

Time since diagnosis as a variable with respect to referral for breast cancer genetic counselling has been studied earlier. However, these studies were in a population of patients who were recruited especially for the study and show that in general, patients are satisfied with referral soon after diagnosis. [18-20] Since these patients were actively approached, they could not play an active role in the referral. In one study, eligibility for genetic testing was assessed in 36 breast cancer patients at different time points after diagnosis. [18] For eligible patients, a relationship between visiting the genetics department and time since diagnosis or treatment stage could not be established. To our knowledge, our study is the first to investigate the association between initiative for referral and time since diagnosis in daily clinical practice. In a large patient population, we found no significant difference between the two groups of initiators of referral and time since diagnosis. We expected that patients who came for cancer genetic counselling within six months after diagnosis more often had taken initiative for referral themselves, since the preference of medical specialists is to refer the patient during the follow-up stage. [4] The majority of all patients who were referred by their GP or medical specialist stated that the referral was made after they raised concerns of risk of hereditary breast cancer in their family themselves, which we would consider as mainly own initiative. [21,22] So, a possible disruptive factor is that even if one person is the initiator (physician or patient), both can have played an important role in the actual referral process. In this study, we asked the patient who, in her opinion, has taken the first step for referral. This approach might have caused some bias in the results and might deviate from the perspective of the physician.

Interestingly, five of the seven patients who were enrolled in the first month after diagnosis were referred by their own initiative. Thus, it appears there are cases in which early DNA testing is requested by patients themselves. Although studies show that a large part of the patients is satisfied with referral soon after diagnosis, decliners of referral indicated that they might be willing to be referred at a later time point. [19,20] So, determining the optimal time for referral is complex and must be explored for each counselee.

Brown et al found that patients with breast cancer at age younger than 45 years, who did not discuss genetic testing at some time point during the treatment or follow-up phase, put forward as most frequent reason that their physician had not brought up the option of genetic testing. [1] This suggests that patients might take initiative of

referral themselves after a period of time in which their expectation that their physician would bring up the subject has not been fulfilled. It is therefore understandable that it will take more time before the patient enrols at the Department of Medical Genetics. On the other hand, one should keep in mind that not only the patient, but also the physician can take a responsibility in assuming an active attitude in the referral process. Part of the physicians fall short in being aware of all criteria of referral for cancer genetic counselling, among which young age at diagnosis, as observed in other studies. [1,3,4,23]

In a survey among 551 women diagnosed with breast cancer before age 45 years, Brown et al observed that the rate of referrals was positively correlated with the strength of family history, but not with younger age at diagnosis. [1] This study is in agreement with our results since they also found no statistically significant difference in the rate of referrals between women diagnosed at different ages or women diagnosed at different time-points (less than one year ago versus 1 to 3 years ago versus 3 to 5 years ago). Women diagnosed more than 5 years ago were least likely to have been referred. [1] Age might play a role in a different respect: age at time of referral appears to be positively correlated with age of diagnosis in a family member, both for breast cancer as for any cancer. [21,22] Unfortunately, due to our design we cannot examine this relationship for our counselees.

Breast cancer patients at risk for a mutation in the BRCA genes have a wide variety in reasons for attending the Department of Medical Genetics. To find out about the risk to their children, especially daughters, is more often cited as reason for attending by affected counselees, [21] followed by risk implications for female siblings and other female relatives. [8,10,24] Hence, patients are very concerned about the risk for their children and female relatives. We expected, therefore, that patients who took initiative themselves had more female first-degree relatives than patients who are referred by their doctor. Although this seems to be the case, the difference did not reach statistical significance. It would be useful to examine this in a larger group of patients referred for breast cancer genetic counselling.

A family history of breast cancer is another reason to opt for genetic testing among patients. Due to small numbers, it was not possible to draw conclusions about this from our data. Patients with a positive family history were more likely to discuss referral with their physician than those without a family history of breast cancer. [1] It might be plausible to suppose that patients witnessing favourable disease courses in relatives affected by any cancer are less concerned about genetic testing, since a higher frequency of observing lethal outcomes is associated with an overestimation of the risk of developing cancer. [25] On the other hand, it is legitimate to wish not to confront oneself with the knowledge of being a carrier of a BRCA1/2 mutation with all its impact. Yet, explanations are unlikely to be simple. Prior studies, focussing on a family history of breast cancer, also reported contradictory results. [1,26] Schlich-Bakker et al reported more psychological distress among affected patients with no breast cancer in the family, when compared to patients with affected first and/or second degree relatives. [27] It has also been shown that risk perceived by women with a positive family history for breast cancer does not correlate with the strength of the family history. [6] Possibly, positive experiences concerning treatment course may overweigh the negative experiences of (hereditary) breast cancer in the family. Family members and (cancer) events in family history enlarge risk awareness and can stimulate the conscientious breast cancer patient to seek genetic counselling,

even at a much later time point after diagnosis. Health care professionals have to realize that women's interest in genetic testing is not clearly related with time since diagnosis. [28] Continuous attention for the need of referral is therefore essential.
Our study has several limitations. A limitation is the subjective interpretation of the initiatorship of the referral which is only based upon the perception of the patient. Interviewed retrospectively, the patient may value her role in the referral process in a different way than when compared to direct observations of the conversation with the physician. [21] To minimalize the effect of recall bias, it is recommended in further studies to audiotape or videotape consultations in which genetic counselling is discussed between the patient and her physician. In that way, it can be determined who first raises concerns about family history, risks and advices for family members and therefore starts the discussion leading to referral for cancer genetic counseling.
Another limitation is that we did not assess motives of attending the Department of Medical Genetics. Therefore, as we contemplate the variable number of first-degree female relatives, we should not lean solely on this quantitative value in looking for an association with initiative for referral and length of time since diagnosis.
Lastly, the homogeneity of the study population with respect to ethnicity limits the generalizability of the results to a more ethnically diverse population. Nonetheless, the sample reflects the normal population of patients of a Dutch Department of Medical Genetics, referred on a regular basis and hereby limit selection bias.

CONCLUSION

The results of our study show that at least one out of two breast cancer patients plays a major role in the referral for genetic counselling. However, we did not establish a relationship between initiative for referral and time since diagnosis. Further research is needed to determine if patient behaviour is of influence in taking initiative for referral. Do patients feel confident enough to discuss referral with their physician? And also, in what way do both patients and physicians express their thoughts and beliefs towards each other?
To fulfil the needs of the patients as optimal as possible, knowledge of hereditary cancer and awareness with cancer genetic counselling in both patients and physicians is important, just as optimal circumstances for the referral process. Because only then one can be sure that the patient and physician take the step to breast cancer genetic counselling at the appropriate time for an individual patient.

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The authors declare that they have no conflicts of interest and that they did not receive financial support. Data were retrieved from patients' medical files and relevant items were routinely discussed during genetic counselling consultations. According to the Dutch law, no further approval from the medical ethical committee was needed.

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TABLES

Table 1. Sociodemographic and family characteristics of participants (n=96) diagnosed with breast cancer referred for cancer genetic counselling

		N (%)	Mean	SD	95% CI	Median	Range
Gender	female	90 (93.8)					
	male	6 (6.2)					
Origin[1]	Dutch native	87 (90.6)					
	immigrant	9 (9.4)					
Education[2]	low	1 (1.1)					
	intermediate-1	30 (31.6)					
	intermediate-2	31 (32.6)					
	high	33 (34.7)					
Age at time of diagnosis (years)			48.5	11.6	46.1-50.8	47.0	27-83
Age at enrolment (years)			51.0	12.2	48.5-53.5	49.5	28-83
Time since diagnosis (months)			34.0	66.6	20.5-47.5	7.8	0-453[5]
Number of first degree female relatives[3]			2.8	1.8	2.5-3.2	3.0	0-8
Number of first degree relatives affected by any cancer[4]			1.1	1.2	0.9-1.4	1.0	0-7

SD = Standard Deviation
CI = 95% confidence interval
[1] Dutch native = counselee of who both parents are born in The Netherlands; immigrant = counselee of who at least one of the parents is not born in The Netherlands
[2] n=95, data from one counselee missing. Low = (pre-)primary education or first stage of basis education; Intermediate-1 = lower secondary or second stage of basis education; Intermediate-2 = (upper) secondary education; High = tertiary education.
[3] Exclusion of mother.
[4] Inclusion of mother.
[5] One value of 453 months. Without this counselee, the range is 0-244 months.

Table 2. Chi-square analysis of patient-related factors versus initiative for referral.

		Initiative for referral			
		Initiative taken by counselee	Initiative taken by physician	χ^2	P-value (2-sided)
Time since diagnosis	0-6 months	18	19	0.395	0.821
	7 months – 5 years	19	15		
	>5 years	8	8		
Age at time of diagnosis	≤50 years	27	26	0.033	0.856
	>50 years	18	16		
Number of first degree female relatives[1]	0-1	8	14	2.782	0.095
	≥2	37	28		
Number of first degree relatives affected by any cancer[2]	0-1	32	29	0.044	0.834
	≥2	13	13		

[1]= Exclusion of mother
[2]= Inclusion of mother

Table 3. Chi-square analysis of patient-related factors versus time since diagnosis.

		Time since diagnosis				
		0-6 months	7 months – 5 years	>5 years	χ^2	P-value (2-sided)
Age at time of diagnosis	≤50 years	23	27	10	2.903	0.234
	>50 years	19	10	7		
Number of first degree female relatives[1]	0-1	10	8	5	0.389	0.823
	≥2	32	29	12		
Number of first degree relatives affected by any cancer[2]	0-1	32	28	8	5.654	0.059
	≥2	10	9	9		

[1]= Exclusion of mother
[2]= Inclusion of mother