Impact of family history risk assessment on surgical decisions and imaging surveillance at breast cancer diagnosis

S Jones, P Turton, R Achuthan

Leeds Teaching Hospital NHS Trust, UK

ABSTRACT

INTRODUCTION In June 2013, the National Institute for Health and Care Excellence (NICE) published guidance on the management of women with a family history (FH) of breast cancer (BC) and a personal diagnosis of BC. When diagnosed with BC, pressure of timely treatment takes priority and there is potential for a significant FH to be overlooked. This can affect treatment options and follow-up imaging (FUI) surveillance.

METHODS The practice in our breast unit was compared with the NICE guidance with regard to arranging appropriate FUI and referral to the genetics team for women diagnosed with BC with a FH of BC. Data were obtained retrospectively on 200 women with BC, identified from the breast multidisciplinary team meetings from January to March 2014. Initial audit showed poor compliance with recording of FH. A standardised history taking proforma was produced for clinic use. A re-audit was conducted on a further 200 women between May and July 2016.

RESULTS In the initial audit, FH was taken in 151 women (76%) compared with 174 women (87%) in the re-audit. Thirty-seven women (25%) were thought to be of moderate risk (MR) or high risk (HR) based on FH in the first audit. Re-audit identified 35 women (20%) with MR or HR FH. Under half (43%) of the women of HR were referred to the genetics team initially; this increased to 70% in the second audit. While almost half (46%) of the women with MR or HR had inappropriate FUI in the initial audit, this fell to 11% in the re-audit.

CONCLUSIONS A proportion of women diagnosed with BC would fall into the MR or HR categories as defined in the NICE FH guidance. Inadequate recording of FH could result in inadequate FUI surveillance and in some cases missing the opportunity for a genetic referral to assess suitability for gene testing.

KEYWORDS

Breast cancer – Family history – Risk assessment – Imaging surveillance – Genetics

Accepted 11 February 2020

CORRESPONDENCE TO

Stacey Jones, E: staceyjessica.jones@nhs.net

Introduction

Breast cancer (BC) continues to be a major global problem affecting around 55,000 women in the UK per year.¹ Although there has been a steady reduction over the years in the mortality rates from BC in many Western countries, the incidence of BC continues to rise. The population lifetime risk of being diagnosed with BC in the UK is less than 17%.² In addition to this population risk of BC, other risk factors such as family history (FH), lifestyle factors, reproductive history and use of synthetic hormones can significantly modify women's risk. Apart from age, a significant FH is an important risk factor for BC.³

In up to 10% of BC diagnoses, this is a consequence of mutations in cancer susceptibility genes including *BRCA1*, *BRCA2*, *TP53*, *PTEN*, *STK11* and *CDH1*,² the most common

being *BRCA1* and *BRCA2*,^{4,5} resulting in a 56–87% lifetime risk of developing BC and a risk of up to 45% of developing ovarian cancer.⁶ Developments in genetics have made it possible to identify women who are at increased risk of BC owing to the existence of cancer predisposing genes or mutations.⁷ However, the majority of women with a diagnosis of BC and a FH of BC do not have mutations in the abovementioned genes. At present, one can only risk stratify this group,⁸ and the National Institute for Health and Care Excellence (NICE) guidance from 2013 (updated 2019) helps clinicians to do this.²

FH risk stratification can be used for unaffected at-risk women as well as women diagnosed with BC who additionally have a FH of BC or ovarian cancer. NICE guidelines for risk stratification classify women into three

BC risk categories: those with a lifetime BC risk of less than 17% are classified as near population risk, those with a risk of greater than 17% but less than 30% are classified as MR and those with a risk of 30% or greater are classified HR.²

Women of near population risk are offered lifestyle modification advice and mammography surveillance as part of the national breast screening programme (NBSP) from the age of 50 to 70 years. Women with a MR should be offered annual mammography surveillance from 40 to 59 years of age, after which they would enter the NBSP. Chemoprevention using tamoxifen or anastrozole depending on a woman's menopausal status can be offered for a period of five years.²

Women categorised as HR should be offered a referral for a genetics consultation to assess whether they are eligible for gene mutation testing. Additionally, they can be offered imaging surveillance annually from age 40 to 59 years (or until 69 years if deemed very high risk [ie *BRCA* mutation carrier]).² Algorithms such as BOADICEA, BRCAPRO, IBIS and the Manchester scoring system can help to calculate the probability of carrying specific mutations in an individual.⁹ Women confirmed to be *BRCA1*, *BRCA2* or *TP53* mutation carriers can be offered risk reducing surgery that can reduce the risk of BC by approximately 90%.⁶

Women diagnosed with BC have many choices regarding treatments including surgery. Breast conserving surgery followed by radiotherapy has comparable overall survival and local control rates with mastectomy.¹⁰ A woman classified as HR because of her FH or because she is identified as carrying a gene mutation such as *BRCA1* or *BRCA2* may decide on a mastectomy rather than breast conserving surgery for initial surgical management of her BC.¹¹ Consequently, FH risk assessment of BC in women diagnosed with BC is essential to facilitate appropriate surgical planning discussions and genetic referral if needed. Following their cancer treatment, women would be offered follow-up imaging (FUI) surveillance. The duration of FUI surveillance can be influenced by their FH risk stratification, which may extend the surveillance duration significantly.

Despite the importance of FH in cancer risk assessment, it is well known that such data are not routinely or meticulously obtained^{12–14} owing to time restraints, interpretation of FH data,¹⁵ and the inconsistency of the risk assessment criteria used among institutions and individual clinicians. These difficulties could be largely overcome through the use of a proforma to collect relevant personal history and FH in a structured format to provide input to overall risk assessment. Failing to identify these women may have significant health consequences for the patient and her family.¹⁵ The purpose of the current study was to assess FH documentation and the use of this information to risk stratify women diagnosed with BC with a FH of BC in order to arrange appropriate FUI and genetic referral when indicated.

Methods

The practice in our breast unit was compared with the NICE standards² with regard to FUI surveillance and referral to the genetics team for women diagnosed with BC with a FH of BC or ovarian cancer. Data were obtained retrospectively on 200 consecutive women with BC, identified from the breast multidisciplinary team meetings between January and March 2014. Data collected included age at diagnosis, whether the patient was symptomatic at presentation or had been screened, cancer type, grade and receptor status, FH pedigree and risk stratification, referral to the genetics team, *BRCA* status and imaging surveillance. This was obtained from electronic medical notes.

The initial findings showed less than satisfactory compliance with the NICE standards.² A proforma was developed for history and examination for breast referrals. This had a section for patients/clinicians to construct a FH pedigree as well as a list of the NICE criteria to help the clinician risk stratify individuals. A re-audit was then conducted on a further 200 women with BC between May and July 2016.

All work in this study was reported in line with the SQUIRE (Standards for Quality Improvement Reporting Excellence) criteria.

Results

Between January and March 2014, 200 women were diagnosed with BC in our breast unit. The median patient age was 59 years. FH was taken in only 151 women (76%) assessed in the breast clinic. After the introduction of the proforma, a re-audit was conducted between May and July 2016. This included 200 women diagnosed with BC over this period, with a median age of 60 years. Of these women, 174 (87%) had their FH documented.

Eighty per cent of women in the initial audit presented symptomatically and a fifth (21%) were referred from the NBSP. FH documentation was complete in 88% of symptomatic women and in 27% of women from the NBSP. In the second audit, 71% of women presented symptomatically and 29% were referred from screening. FH documentation was complete in 99% of symptomatic women and 59% of women from the NBSP.

In terms of family structure, in the initial audit, of the 151 women for whom there was FH documentation, 120 (80%) had only a first-degree FH documented in their medical notes, 26 (17%) had first and second-degree relatives documented, and 5 (3%) had FH documentation extending to third-degree relatives. Both second and third-degree FH was better documented in the re-audit. For the 174 women with FH documentation, 16 (9%) included first-degree relatives only, 44 (25%) included FH to second-degree relatives, and 114 (66%) of FH documentation included first, second and third-degree

relatives. Of those women with a positive FH, 43% had age of the relative at diagnosis documented in their medical records in the first audit. This improved to 96% in the re-audit. The results for FH documentation in both audits are summarised in Table 1.

The FH risk stratification (based on the NICE guidance published in June 2013),² used for both of the audits, is shown in Table 2. Of those women with a known FH, 37 (25%) were classified as MR or HR based on their FH (6 MR, 31 HR) in the original audit. Re-audit identified 35 women (20%) of MR or HR based on their FH (12 MR, 23 HR).

Table 3 summarises the findings from both audits for the numbers of women referred for genetic counselling and/or testing. In the initial audit, 13 women underwent gene testing and 4 of these were identified as carriers of a pathogenic *BRCA* mutation gene. The remaining nine women had no gene mutation identified, decreasing their risk to MR. Consequently, in the first audit, the final number of MR women was 15/200 and the final number of HR women was 22/200.

In the re-audit, 16 women underwent gene testing and 3 of these were carriers of the *BRCA* gene mutation. The genetic test results of the remaining 13 women were negative for *BRCA* gene mutations, reducing their risk to MR. In this second audit, the final number of MR women was therefore 25/200 and the final number of HR women was 10/200.

NICE states that all BC patients who are at MR or HR for BC should have imaging annually between the ages of 40 and 59 years (very high risk group until 69 years).² In the initial audit, of the 37 women who were MR or HR according to their FH, almost half ($n=17$, 46%) had inappropriate imaging; this fell to 11% (4/35) in the re-audit. All women in the low risk group had appropriate FUI in both of the audits.

Discussion

Many studies have shown inadequate documentation of cancer FH.^{16–18} Good BC FH documentation in medical records is required in order to ensure that women are referred for genetic counselling and gene testing if indicated. This is particularly important for women with a BC diagnosis with a FH of relevance. This allows the clinician to have discussions regarding appropriate surgical and medical interventions, and additionally planning for FUI surveillance. For this reason, as clinicians, we do our patients a disservice if we neglect the importance of taking account of their FH when treating individuals with BC.¹⁹ The importance of FH and its documentation needs to be reinforced among clinicians by ongoing education and support. Practice related characteristics should also be explored as it is often difficult to find sufficient time to obtain, organise and analyse FH information in a busy breast clinic.

Our study has demonstrated that a proforma allowing patients/clinicians to record their BC FH can improve data collection and risk stratification. Introduction of such a proforma improved FH documentation to 87%. This is unlikely to be due to bias such as the Hawthorne effect (where clinicians may function differently when monitored) as this was a retrospective study.

The re-audit highlighted that FH documentation was still incomplete in a number of women (13%). The majority of these (24/26) were women referred from the NBS. At cancer diagnosis, having a multidisciplinary team treatment plan in place (as these cases would have been discussed before their clinic visit) and pressure of timely treatment may have resulted in the FH being overlooked.

In the initial audit, breast clinicians documented first-degree FH in 80% of women with BC but this reduced when extended to second and third-degree relatives. The second audit saw a significant improvement with 66% of individuals having FH to a third-degree

Table 1 Extent of family history (FH) documentation in medical records of patients with breast cancer

FH documented	Initial audit ($n=151$)	Re-audit ($n=174$)
Up to third-degree relatives	5 (3%)	114 (66%)
Documentation of age at diagnosis in relative	65 (43%)	167 (96%)

Table 2 Family history (FH) risk stratification

Risk stratification	Initial audit (known FH = 151)	Re-audit (known FH = 174)
Low risk	114 (76%)	139 (80%)
Moderate risk	6 (4%)	12 (7%)
High risk	31 (21%)	23 (13%)
Unknown (no FH taken)	49/200 (25%)	26/200 (13%)

Table 3 Referral of women with personal and family history of breast cancer for genetic counselling and/or testing

	Initial audit ($n=31$)	Re-audit ($n=23$)
Referred for genetic counselling and/or testing	13 (42%)	16 (70%)
<i>BRCA</i> +	4 (31%)	3 (19%)
<i>BRCA</i> -	9 (69%)	13 (81%)

relative documented. Documentation of age at BC diagnosis in relatives improved by 53 percentage points in the re-audit. Being a retrospective study, one of the difficulties is the interpretation of electronic records. Absence of documentation of FH in the records may be due to omission of FH being taken. However, another reason is that it may not have been recorded if the FH was negative as clinicians are unlikely to record information in letters that is not clinically relevant.

At the first audit, 46% of women with MR or HR had inappropriate FUI as recommended by the NICE guidance.² This fell to 11% in the re-audit, indicating that there was an improvement in the planning for FUI. All patients in the low risk group had appropriate FUI in both of the audits.

In the original audit, 42% of women with BC were referred for genetic counselling and/or testing and this increased to 70% on re-audit. Despite an improvement of 28 percentage points in the number of women being referred, almost one in three HR women were not referred. A dedicated FH clinic led by a FH nurse specialist has since been set up and this may improve this aspect of care. A further audit will be undertaken.

Our study is not the first to conclude low referral numbers of eligible individuals for assessment of genetic testing,^{20–25} and explanations for this range from clinician knowledge and time pressures to patient awareness of FH.²⁴ Offering gene testing by guidelines is liable to result in missing women with significant pathogenic mutations and in 2019, the American Society of Breast Surgeons recommended that genetic testing should be made available to all women diagnosed with BC.²⁵ Until this becomes the standard of care internationally, the reliance is still on a detailed FH assessment and documentation. Our study has shown that a simple intervention such as the FH proforma helps with this aspect, ensuring appropriate referrals for genetic counselling/testing and adequate FUI surveillance.

Conclusions

FH is essential in recognising women at risk of BC. This is of particular importance in women diagnosed with BC. Risk stratification helps identify women likely to benefit from genetic counselling and/or testing and allows for appropriate referral. Additionally, this information may influence surgical management and FUI surveillance.

References

1. Cancer Research UK. Breast cancer statistics. <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer> (cited April 2020).
2. National Institute for Health and Care Excellence. *Familial Breast Cancer: Classification, Care and Managing Breast Cancer and Related Risks in People With a Family History of Breast Cancer (CG164)*. London: NICE; 2013.
3. Eberl MM, Sunga AY, Farrell CD, Mahoney MC. Patients with a family history of cancer: identification and management. *J Am Board Fam Pract* 2005; **18**: 211–217.
4. Sifri R, Gangadharappa S, Acheson LS. Identifying and testing for hereditary susceptibility to common cancers. *CA Cancer J Clin* 2004; **54**: 309–326.
5. Wooster R, Bignell G, Lancaster J *et al*. Identification of the breast cancer susceptibility gene BRCA2. *Nature* 1995; **378**: 789–792.
6. Weitzel JN, McCaffrey SM, Nedelcu R *et al*. Effect of genetic cancer risk assessment on surgical decisions at breast cancer diagnosis. *Arch Surg* 2003; **138**: 1323–1328.
7. Weitzel JN. Genetic cancer risk assessment. Putting it all together. *Cancer* 1999; **86**: 2483–2492.
8. Chew HK. Genetic evaluation of cancer: the importance of family history. *Tex Med* 2001; **97**: 40–45.
9. Antoniou AC, Hardy R, Walker L *et al*. Predicting the likelihood of carrying a BRCA1 or BRCA2 mutation: validation of BOADICEA, BRCAPRO, IBIS, Myriad and the Manchester scoring system using data from UK genetics clinics. *J Med Genet* 2008; **45**: 425–431.
10. van Dongen JA, Voogd AC, Fentiman IS *et al*. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. *J Natl Cancer Inst* 2000; **92**: 1143–1150.
11. Chen Y, Thompson W, Semenciw R, Mao Y. Epidemiology of contralateral breast cancer. *Cancer Epidemiol Biomarkers Prev* 1999; **8**: 855–861.
12. Acton RT, Byrns NM, Casebeer L *et al*. Knowledge, attitudes, and behaviors of Alabama's primary care physicians regarding cancer genetics. *Acad Med* 2000; **75**: 850–852.
13. Schroy PC, Barrison AF, Ling BS *et al*. Family history and colorectal cancer screening: a survey of physician knowledge and practice patterns. *Am J Gastroenterol* 2002; **97**: 1031–1036.
14. Sifri RD, Wender R, Paynter N. Cancer risk assessment from family history: gaps in primary care practice. *J Fam Pract* 2002; **51**: 856.
15. Murff HJ, Byrns D, Syngal S. Cancer risk assessment: quality and impact of the family history interview. *Am J Prev Med* 2004; **27**: 239–245.
16. Flynn BS, Wood ME, Ashikaga T *et al*. Primary care physicians' use of family history for cancer risk assessment. *BMC Fam Pract* 2010; **11**: 45.
17. Murff HJ, Greevy R, Syngal S. The comprehensiveness of family cancer history assessments in primary care. *Community Genet* 2007; **10**: 174–180.
18. Sweet KM, Bradley TL, Westman JA. Identification and referral of families at high risk for cancer susceptibility. *J Clin Oncol* 2002; **20**: 528–537.
19. Acheson LS, Wiesner GL, Zyzanski SJ *et al*. Family history-taking in community family practice: implications for genetic screening. *Genet Med* 2000; **2**: 180–185.
20. Meyer LA, Anderson ME, Lacour RA *et al*. Evaluating women with ovarian cancer for BRCA1 and BRCA2 mutations: missed opportunities. *Obstet Gynecol* 2010; **115**: 945–952.
21. Overbeek LI, Hoogerbrugge N, van Krieken JH *et al*. Most patients with colorectal tumors at young age do not visit a cancer genetics clinic. *Dis Colon Rectum* 2008; **51**: 1249–1254.
22. Trivers KF, Baldwin LM, Miller JW *et al*. Reported referral for genetic counseling or BRCA 1/2 testing among United States physicians: a vignette-based study. *Cancer* 2011; **117**: 5334–5343.
23. Wong C, Gibbs P, Johns J *et al*. Value of database linkage: are patients at risk of familial colorectal cancer being referred for genetic counselling and testing? *Intern Med J* 2008; **38**: 328–333.
24. Wood ME, Flynn BS, Stockdale A. Primary care physician management, referral, and relations with specialists concerning patients at risk for cancer due to family history. *Public Health Genomics* 2013; **16**: 75–82.
25. American Society of Breast Surgeons. *Consensus Guideline on Genetic Testing for Hereditary Breast Cancer*. Columbia, MD: ASBrS; 2019.