Breast Cancer Risk Assessment and Screening - Is it a Persistent Problem in a Rural Population?

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Abstract

Trend analysis of breast screening uptake in those meeting screening criteria that were newly diagnosed with breast cancer. Retrospective review of all breast cancer patients diagnosed between 2010 and 2014. Patients' demographics, screening, risk assessment, pathological stages and surgical treatment utilization were recorded. 150 patients, mean ages 55.4 ± 10.2 years (range 29–90), were studied. Overall 65/150 (43.3%) had optimal screening pre cancer diagnosis and 85/150 (56.7%) suboptimal. The trend in optimal screening improved from 30% to 60% over the study period. The mean overall tumour size (excluding DCIS patients) in 131 patients was 32.8 mm; 26.9 mm in optimally and 38.5 mm in the suboptimally screened groups (p = 0.06 x^2 df8). 113/150 (75.3%) diagnosed with early stage breast cancer and 37/150 (24.7%) late stage. Principally late stage at diagnosis was within the group with suboptimal screening; 100%, 100%, 63.6%, 75% and 60% respectively for years 2010–2014. This study identified improving trends in compliance with international screening and risk assessment guidelines. Failure to screen results in more advanced disease; further public health measures to engage appropriate screening may improve stage at presentation and breast cancer outcomes.

Keywords: Breast cancer; Breast cancer detection; Breast screening; Breast outcomes

Introduction

A tailored approach to breast cancer risk assessment is ideal given the prevalence of breast cancer and the lifetime risk between 10% and 12.3% for the female population [1]. The 10-year risk of invasive breast cancer increases from ages 40, 50 and 60 years to 1.5%, 2.3%, and 3.5% respectively. Current breast screening programs tailor to age risk but don't personalise for family history risk [2]. Despite recent controversies, about over diagnosis and the role of screening mammography, early detection of breast cancer optimises outcomes and survival [3-5]. Engagement in health promotion and risk reducing strategies are important but recruitment to programs and tailoring the approach can be difficult [6-8].

In our recent study of newly diagnosed breast cancer patients 69.3% meeting breast screening or family history surveillance criteria did not have a mammogram or risk assessment carried out before their index breast cancer diagnosis [9]. This failure to engage in breast screening and risk assessment resulted in more advanced stage at diagnosis. Optimizing breast care delivery and enhancing recruitment must take into account the trends in screening and assessment uptake over time. With increasing global awareness of breast cancer and more discussion about breast screening the question is whether improved patterns of screening have occurred.

This study analysed the trends in uptake in breast screening in newly diagnosed breast cancer patients. The study specifically looked at those of breast screening age and moderate to high family history risk meeting current mammographic criteria.

Methods

An ethically approved retrospective review of all newly diagnosed, index breast cancer patients, presenting to the Symptomatic Breast Unit of Letterkenny University Hospital over a 5 year period (2010–2014) was undertaken. Patients having breast cancer detected during screening are treated by the Breast Screening Service and are not included in this study. The cohort was divided into those who did (group 1) and those who did not (group 2) meet screening or family history criteria recommendations.

Figure 1: Flow diagram to illustrate the study population.

The International breast screening and risk assessment guidelines adhered to in the study were the National Cancer Screening Service for women in the national screening age-group [10]. Family history risk was determined by use of both the National Institute for Health and Clinical Excellence (NICE) guidelines and IBIS Breast Cancer Risk Evaluation Tool Version 6 [11,12].

Optimal screening and risk assessment was defined as biennial in those of breast screening age (50-65 years old) [10]. Biennial mammography was also considered optimal in those aged 40–49 who met 2006 NICE criteria for a moderate family history risk or had an IBIS (Tyrer-Cuzick) 10 year risk> 3% or a lifetime risk ≥ 17% [11,12]. Suboptimal screening and risk assessment was deemed to have occurred if a mammogram had not been performed within 2 years of diagnosis in those of breast screening age and/or having a moderate or high family history risk.

During the 5 years of this study the breast service treated 358 new breast cancer patients, 208 had no family history or were outside screening age leaving 150 cases eligible for screening and this study (Figure 1). For these 150 patients we determined whether screening was optimal or suboptimal.

Patient demographics, date of diagnosis and previous mammograms were documented. TNM staging was used to classify stage at presentation [13]. Patients with isolated tumour cells were classified as node negative. Breast cancer stages 0-2 were considered to be early and 3–4 late stages. Surgical treatment utilization was categorised as either breast conserving surgery or mastectomy. The potential impact of stage migration on our population was minimal with the same surgical technique, same Consultant Pathologist, same sentinel node sectioning and TNM classification used throughout the entire study.

Data was expressed as mean and standard deviation for normally distributed data and medians and inter quartile range for non-normal data. Chi square test or Student's T-test was used as appropriate for categorical and continuous variables. Data was considered significantly different if p-value was <0.05.

Results

150 female patients, mean age 55.4 ± 10.2 years (range 29–90), were studied. Overall 65/150 (43.3%) had optimal screening pre cancer diagnosis and 85/150 (56.7%) suboptimal. Figure 2 shows the 5 year trend in optimal compared to suboptimal breast screening and risk assessment pre cancer diagnosis. Invasive cancer occurred in 131/150
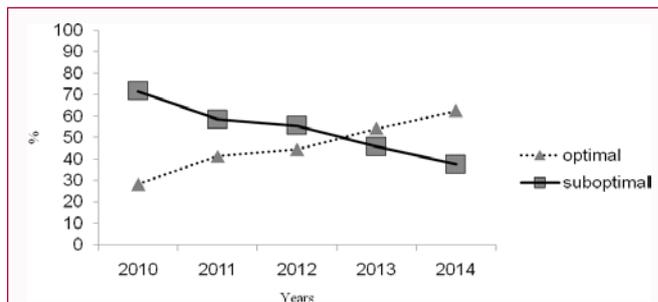
Figure 2: 5 year trend in optimal compared to suboptimal breast screening and risk assessment pre cancer diagnosis (n=150).
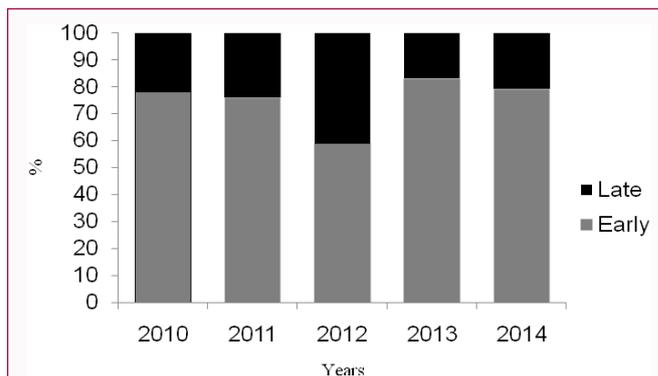
Figure 3: Overall 5 year trend in stage of breast cancer at diagnosis: Early compared to late stage (n=150).

(87.3%) and ductal carcinoma in situ (DCIS) in 19/150 (12.7%). The mean tumour size (excluding DCIS patients) in 131 patients was 32.8 mm ± 28.3 mm (3.5-210). The percentage of invasive cancer increased slightly from 80.4% in 2010 to 87.5% in 2014. The trend in invasive cancer rates and tumour size is shown in Table 1. DCIS occurred in 9/46 (19.6%), 4/29 (13.8%) 1/27 (3.7%), 2/24 (8.3%) and 3/24 (12.5%) respectively for the years 2010–2014.

In the 131 with invasive cancer 73/131 (55.7%) were node positive at time of diagnosis. The 5 year trend in nodal status in both those who had optimal and suboptimal screening pre cancer diagnosis is shown in Table 2. 113/150 (75.3%) were diagnosed with early stage breast cancer and 37/150 (24.7%) late stage. The overall trend in breast cancer stage at diagnosis over the 5 years is shown in Figure 3. Principally late stage at diagnosis was within the group with suboptimal screening; 100%, 100%, 63.6%, 75% and 60% respectively for years 2010–2014.

Overall in the 5 years 133/150 (88.7%) had surgical treatment; 54 (40.6%) had a mastectomy and 79 (59.4%) breast conserving surgery. Of the 54 patients having a mastectomy 29/54 (53.7%) had a simple mastectomy and 25/54 (46.3%) a mastectomy with reconstruction. 18/54 (33.3%) of women having a mastectomy had optimal screening pre diagnosis and 36/54 (66.7%) suboptimal. 10/18 (55.6%) of the optimally screened group had a simple mastectomy and 8/18 (44.4%) a mastectomy with reconstruction. 19/36 (52.8%) of the sub optimally screened group had a simple mastectomy and 17 (47.2%) a mastectomy with reconstruction. 17/150 (11%) did not undergo surgery; 5/65 (7.7%) of the optimally screened group and 12/85 (14.1%) of the suboptimal group (p = 0.3).

Discussion

This study provides an insight into the pattern of optimal breast

Table 1: 5 year trend in invasive cancer rates and tumour size in those meeting screening criteria (n=131).

All cancers		Invasive only		Invasive tumour size (mm) (mean)	
Year	n	n	%	Optimal screening*	Suboptimal screening*
2010	46	37	80.4	27.8	36.3
2011	29	25	86.2	24.2	33.3
2012	27	26	96.3	27.7	38.1
2013	24	22	91.7	24.3	26.6
2014	24	21	87.5	30.9	58.1
Total	150	131	88.4	26.9	38.5

(*p=0.06 χ2 df8)

Table 2: 5 year trend in nodal positivity in optimal versus suboptimal assessed patients (n=131).

Year	Total	Overall positive (n=73)		Optimal Screening* (n=27)		Suboptimal Screening* (n=46)	
		n	n	%	n	%	n	%
2010	37	20	54.1	3	15	17	85
2011	25	12	48	2	16.7	10	83.3
2012	26	18	69.2	10	55.6	8	44.4
2013	22	8	36.4	3	37.5	5	62.5
2014	21	15	71.4	9	60	6	40
Total	131	73	55.7	27	36.9	46	63.1

(*p=0.2 χ2 df8)

care delivery in a single rural region. It identifies improving trends in compliance with international screening and risk assessment guidelines; from 30% to 60%. A failure to screen resulted in more advanced disease stage at diagnosis.

The region is rather unique with only a single hospital providing symptomatic breast care services. The delivery of rural health care in itself poses a significant problem due in part to geographic isolation, access to resources and fear of travel to receive appropriate therapy [14,15]. The study was performed over a 5 year period and while a longer period would have been preferable breast screening was only introduced into the region in 2008.

Patients presenting with breast cancer may fall into the breast screening group, family history risk group or those outside those criteria. High risk genetic groups are relatively rare in presentation to a general breast clinic as opposed to a specific genetic or family history clinic. The Unit has evaluated its family history referrals and has been very proactive with primary care to encourage appropriate screening [16,17]. The region does not provide General Practice access to mammography.

The guidelines for breast screening have varied internationally. The American Cancer Society guidelines make strong recommendations for annual screening for ages 45–54 then biennial until life expectancy is less than 10 years [18]. The British guidelines suggest every 3 years from ages 50–70 with an on-going trial extension rolling out to include 47–73 year olds [19]. A number of other countries have expanded their programme to include 40 year olds and a significant number extending to 69; some even extending to ≤ 74 years [20]. Nationally within Ireland the National Cancer Control Programme has recommended biennial mammography between 50 and 64; this is now being extended to include women up to the age of 69 [21]. International screening criteria for those between 40 and 50 have been controversial and have changed over the years. This study adopted the

current Irish National Cancer Screening Programme guidelines.

To tailor family history risk and need for assessment we used both NICE criteria and the Tyrer-Cuzick IBIS Risk Evaluation Tool version 6 [11,12]. NICE provides a simple easy to use system but has limitations not taking into account some biological, hormonal and metabolic criteria included in Tyrer-Cuzick IBIS Risk Evaluation. This study may have under estimated the family history criteria as it used version 6. IBIS Version 7 has the perception of increasing the likelihood of categorizing patients into moderate or high risk groups [22].

In the family history risk group biennial mammography was the standard in this unit at study commencement. In the absence of global gold standards in optimal screening the criteria adopted for this study were chosen as they were considered balanced and reasonable. Increasing evidence has seen a paradigm shift from recommending biennial to annual screening in women age 40–49 years with a moderate risk of breast cancer [18,20,23,24]. For these reasons the risk assessment classification and optimal screening criteria for both breast screening and family history patients were relatively conservative in this study.

The numbers in the study are relatively small leading to statistical analysis somewhat short on power in showing a difference. This study focused only on those of breast screening age and those with a family history therefore 60% of the newly diagnosed were not included in this study. There are no missing data in this relatively small sampled study unlike other similar papers where data is incomplete [25,26].

During the study period there were no male breast cancer patients; this is relative to the 1% general prevalence of male breast cancer [27].

Previous work from our Unit identified significant issues in enrolment of patients into screening and risk assessment programmes [16,17]. This had been previously identified to result in breast cancer stage at diagnosis being more advanced in those failing to engage in proactive screening [9,28]. Outcomes in breast cancer, while controversial, have been shown to be improved with appropriate breast screening [29].

The current study of 150 breast cancer patients identified only 43% having optimal screening however the trend had improved from 30% to 60% over the study period. It is truly hard to qualify why the change has occurred but may be partially linked to a general national trend improvement in the percentage of eligible women acceptance rates from 73.9% in 2010 to 76.5% in 2014 [30,21]. Local initiatives relating to engagement with the community, proactive approaches supporting breast recruitment to breast screening and a series of public forums may also have played their part.

A key issue to improving breast cancer outcomes are earlier diagnosis and resultant less advanced stage and with associated lower rates of nodal positivity. This study identified that nodal positivity in sub optimally screened patient's remains particularly high. Overall the group has a high positivity rate with 48.7% of the group node positive. Other studies involving non screening detected breast cancers report nodal positivity rates of 44% and 40% [31,32]. It is clear from our study that failure to screen appropriately tends to result in a much higher nodal positivity, 63.1% versus 36.9%. The unique regional rural, relatively isolated geographical location of the study centre may, in part, account for the overall high positivity rate of 48.7%. Inequality by place of residence, mainly rural areas compared to cities,

is reported in the literature [33,34]. In contrast Leung et al. [35] found an absence of urban-rural differences in attendance at screening mammography both in Scotland and Australia. Similar to Hofvind et al. [25] the trend in stage distribution was more favourable in women who had had optimal screening carried out pre cancer diagnosis. Stage migration (down staging) is an expected outcome of screening [36]. The trend over the study period regarding proportions diagnosed at early versus late stages was fairly consistent. The potential impact of stage migration on our population due to subtle disease classifications was minimised as outlined in the methods section. The 7th edition of the TNM Classification system became effective in January 2010 when this study commenced. Sobin and colleagues report no basic changes in this classification from the previous 6th edition [13,37].

The percentage of women with invasive breast cancer who did not undergo surgery in our study is around 12% for the entire period; 4/55 (7.3%) and 12/76 (15.8%) in optimally and sub optimally screened groups respectively. Again failure to appropriately screen will reduce surgical options; further compounded by reduced reconstructive options.

On-going attempts to improve breast cancer outcomes are multifaceted and include new national strategies to fast track cancer diagnosis; efforts to optimise mammography interpretative processes and screening technologies as well as public health measures aimed at reducing known breast cancer risks by managing lifestyle factors such as alcohol and diet [38-43]. In Norway all inhabitants are given a unique Personal Identification Number (PIN) by birth or immigration, allowing for identification of women of age-appropriate cohorts [25]. This assists the compilation of a screening database which includes women's screening invitation status, their history of screening activity and screening outcome. A similar system is being developed in Ireland and may assist in future recruitments [44]. It would appear from this study, despite the improvements in screening, that there is still a significant public health issue to be addressed. The National uptake rate for 2014 was 76.5 % and the programme standard is 70 percent [21]. This standard has not been achieved in this study.

Further public health programmes are required to engage women at risk, families at risk and involve primary care providers in ensuring enrolment. The National Cancer Control Programme should be proactive to help reduce the tumour size which in this study was 32.8 mm. This in turn will improve outcome by reducing stage at presentation plus reducing the cost and social burden of the disease. A larger series across different health and geographic regions is urgently required to determine if the results of this study are translated and validated. If that is the case culture change introduction of newer aids in recruitment and health promotion could make significant improvements in breast cancer care way beyond advances in adjuvant or other forms of therapy which attempt to optimise late stage treatments.

References

1. Rojas K, Stuckey A. Breast Cancer Epidemiology and Risk Factors. ClinObstet Gynecol. 2016;59(4):651-72.

2. Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast cancer screening decisions. JAMA. 2014;311(13):1327-35.

3. Swain M, Jeudy M, Pearlman MD. Controversies in Screening Mammography. ClinObstet Gynecol. 2016;59(2):351-61.

4. Kopans DB. Breast cancer screening panels continue to confuse the facts and inject their own biases. CurrOncol. 2015;22(5):e376-9.

5. Webb ML, Cady B, Michaelson JS, Bush DM, Calvillo KZ, Kopans DB, et al. A failure analysis of invasive breast cancer: most deaths from disease occur in women not regularly screened. Cancer. 2014;120(18):2839-46.

6. Nadalin V, Maher J, Lessels C, Chiarelli A, Kreiger N. Breast screening knowledge and barriers among under/never screened women. Public Health. 2016;133:63-6.

7. Hall P, Easton D. Breast cancer screening: time to target women at risk. Br J Cancer. 2013;108(11):2202-4.

8. Onega T, Beaber E, Sprague B, Barlow W, Haas J, Tosteson AN, et al. Breast Cancer Screening in an Era of Personalized Regimens: A Conceptual Model and National Cancer Institute Initiative for Risk-Based and Preference-Based Approaches at a Population Level. Cancer. 2014;120(19):2955-264.

9. Johnston A, Curran S, Sugrue M. Failure to Engage in Breast Screening and Risk Assessment Results in More Advanced Stage at Diagnosis. Adv Breast Cancer Res. 2015;4(2):53-62.

10. http://www.breastcheck.ie/.

11. National Institute for Health and Clinical Excellence. Familial Breast Cancer: The Classification and Care of Women at Risk of Familial Breast Cancer in Primary, Secondary and Tertiary Care. Nice Clinical Guideline 41. 2006.

12. http://www.ems-trials.org/riskevaluator/.

13. Edge S, Byrd D, Compton C, Fritz A, Greene F, Trotti A. American Joint Committee on Cancer (AJCC). Cancer Staging Manual. 7th ed. New York: Springer-Verlag; 2010.

14. Ambroggi M, Biasini C, Del Giovane C, Fornari F, Cavanna L. Distance as a Barrier to Cancer Diagnosis and Treatment: Review of the Literature. Oncologist. 2015;20(12):1378-85.

15. Bennett KJ, Olatosi B, Probst JC. Health disparities: a rural-urban chartbook. Columbia (SC): South Carolina Rural Health Research Center; 2008.

16. Gorman A, Sugrue M, Ahmed Z, Johnston A. An Evaluation of FaHRAS Computer Programmes' Utility in Family History Triage of Breast Cancer. Adv Breast Cancer Res. 2014;3(2):17-21.

17. Thomas J, Sugrue M, Curran S, Furey M, Sugrue R. Are family doctors compliant with breast family history guidelines? Adv Breast Cancer Res. 2013;4(2):149-53.

18. Oeffinger KC,Fontham ET, Etzioni R, Herzig A, Michaelson JS, Shih YC, et al. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. JAMA. 2015;314(15):1599-614.

19. ISRCTN33292440. Nationwide cluster-randomised trial of extending the NHS breast screening age range in England. 2009.

20. Altobelli E, Lattanzi A. Breast cancer in European Union: an update of screening programmes as of March 2014 (review). Int J Oncol. 2014;45(5):1785-92.

21. Breast check programme report 2014-2015. National Cancer Screening Service (NCSS). 2015.

22. http://www.ems-trials.org/riskevaluator/.

23. National Institute for Health and Care Excellence. Familial breast cancer: classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer. Clinical guideline 164.2013.

24. Moss S, Wale C, Smith R, Evans A, Cuckle H, Duffy SW. Effect of mammographic screening from age 40 years on breast cancer mortality in the UK Age trial at 17years' follow-up: a randomised controlled trial. Lancet Oncol.2015;16(9):1123-32.

25. Hofvind S, Lee CI, Elmore JG. Stage specific breast cancer incidence rates among participants and non-participants of a population-based mammographic screening program. Breast Cancer Res Treat. 2012;135(1):291-299.

26. Colonna S, Halwani A, Ying J, Buys S, Sweeney C. Women with breast cancer in the Veterans Health Administration. Demographics, breast cancer characteristics and trends. Med care. 2015;53(4):S149-S55.

27. Yalaza M, Ä°nan A, Bozer M. Male Breast Cancer. J Breast Health (2013). 2016;12(1):1-8.

28. Paap E, Verbeek AL, Botterweck AA, van Doorne-Nagtegaal HJ, Imhof-Tas M, de Koning HJ, et al. Breast cancer screening halves the risk of breast cancer death: a case-referent study. Breast. 2014;23(4):439-44.

29. Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. Lancet. 2012;380(9855):1778-86.

30. Breast Check-Programme report 2010-2011. National Cancer Screening Service (NCSS). 2011.

31. Burke JP, Power C, Gorey TF, Flanagan F, Kerin MJ, Kell MR. A comparative study of risk factors and prognostic features between symptomatic and screen detected breast cancer. Eur J SurgOncol. 2008;34(2):149-53.

32. Sprague BL, Gangnon RE, Hampton JM,Egan KM, Titus LJ, Kerlikowske K. Variation in breast cancer–risk factor associations by method of detection: results from a series of case-control studies. Am J Epidemiol. 2015;181(12):956-69.

33. Nguyen-Pham S, Leung J, McLaughlin D. Disparities in breast cancer stage at diagnosis in urban and rural adult women: a systematic review and meta-analysis. Ann Epidemiol. 2014;24(3):228-35.

34. Williams F, Thompson E. Disparity in breast cancer late stage at diagnosis in Missouri: does rural versus urban residence matter? J Racial Ethn Health Disparities. 2016;3(2):233-9.

35. Leung J, Macleod C, McLaughlin D, Woods LM, Henderson R, Watson A, et al. Screening mammography uptake within Australia and Scotland in rural and urban populations. Prev Med Rep. 2015;2:559-62.

36. James TA, Wade JE, Sprague BL. The impact of mammographic screening on the surgical management of breast cancer. J SurgOncol. 2016;113(5):496-500.

37. Sobin LH, Compton CC. TNM seventh edition: what's new, what's changed: communication from the International Union Against Cancer and the American Joint Committee on Cancer. Cancer. 2010;116(22):5336-9.

38. NHS England. Achieving World Class Cancer Outcomes: Taking the strategy forward. 2016.

39. Taylor-Phillips S, Wallis M, Jenkinson D, Adekanmbi V, Parsons H, Dunn J,et al. Effect of using the same vs different order for second readings of screening mammograms on rates of breast cancer detection-A randomized clinical trial. JAMA. 2016;315(18):1956-1965.

40. Burnside ES, Sickles EA, Duffy SW. A Pragmatic Approach to Determine Components of Optimal Screening Mammography Practice. JAMA. 2016;315(18):1951-3.

41. Hodgson R, Heywang-Köbrunner SH, Harvey SC, Edwards M, Shaikh J, Arber M, et al. Systematic review of 3D mammography for breast cancer screening. Breast. 2016;27:52-61.

42. Union for International Cancer Control (UICC). Knowledge summaries of comprehensive breast cancer: breast cancer risk factors and prevention. 2015.

43. Key TJ, Reeves GK. Alcohol, diet, and risk of breast cancer. BMJ. 2016;353:i2503.

44. Health Information and Quality Authority. Draft information governance and management standards for the health identifiers operator in Ireland. – Public consultation document. 2015.