A UK national survey of breast surgeons on primary endocrine therapy of early operable breast cancer

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ABSTRACT

INTRODUCTION A significant proportion of elderly breast cancer patients in the UK have no surgical treatment recorded and appear to be treated with primary endocrine therapy (PET) only. Despite this, PET remains one of the poorly studied areas in breast cancer therapy and very little is known about the practice of PET in the UK.

METHODS A questionnaire comprising 14 questions relevant to PET was sent to 489 breast surgeons who were members of the UK Association of Breast Surgery and returned questionnaires were analysed.

RESULTS Overall, 228 questionnaires (47%) were returned. The vast majority (93%) of surgeons who responded use PET in early operable breast cancer in elderly women unfit for surgery or owing to patient preference but 7% would recommend PET to fit elderly patients. Most (76%) use letrozole. The percentage of elderly patients treated with PET varied from <10% to 70% between surgeons. The majority (77%) of respondents had not formally audited the outcome of their PET patients and over 70% underestimated the expected survival of an 80-year-old woman.

CONCLUSIONS Most UK breast surgeons use PET in elderly patients with surgically resectable breast cancer. While most use it in unfit, frail patients, a minority would treat even fit elderly women with PET. Most surgeons have not formally audited the outcome of their patients treated with PET and underestimate the expected survival of elderly patients, which might have an impact on their decision to offer PET rather than surgery.

KEYWORDS

Breast cancer – Endocrine therapy

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Invasive breast cancers expressing receptors to oestrogen and/or progesterone are amenable to treatment with endocrine therapy. A number of endocrine therapy options such as tamoxifen, luteinising hormone-releasing hormone analogues and oophorectomy are available in younger premenopausal women with functioning ovaries but in older women the usual options are tamoxifen or aromatase inhibitors (AIs). Endocrine therapy is usually offered as adjuvant therapy after surgery or as neoadjuvant therapy to downstage the tumour prior to surgery. Primary endocrine therapy (PET), where the breast cancer is treated with an endocrine agent as sole therapy, is an option in women who are unfit or unwilling to undergo surgery.

Among almost 50,000 breast cancers diagnosed in the UK in 2006, 29% were in patients aged over 70 years; among these, 20% of patients aged 70–74, 30% of those aged 75–79, and 62% of those aged 80 and over had no surgical treatment recorded.¹ As other treatment modalities such as primary chemotherapy are unlikely in this older age group, it is most probable that these patients were treated with PET. PET is also used commonly in Europe.^{2,5} Despite this, relatively little has been published on the use of PET in breast

cancer and not much is known about its current practice in the UK or elsewhere.

The aim of this survey was to look into the practice of PET in the UK with regard to patients aged 70 years or over (referred to as ‘elderly’ in the rest of this paper) presenting with surgically resectable early breast cancer. As PET is usually offered by surgeons, we conducted a national survey of breast surgeons.

Methods

A questionnaire comprising 14 questions relevant to PET was posted to all consultant and associate specialist surgeon members of the UK Association of Breast Surgery. Data from the returned completed questionnaires were collected and analysed.

Results

A total of 489 questionnaires were posted and 228 (47%) were returned. Of these, 220 were from consultant surgeons and 8 from associate specialists. The questions asked and

Table 1 Analysis of 228 returned completed questionnaires

Question	Number answered this question	Answer
1. What is your grade?	228	97% (220/228) Consultant 3% (8/228) Associate Specialist
2. Do you use PET in early operable breast cancer?	228	93% (213/228) Yes 7% (15/228) No
3. If you don't use PET, how do you treat your frail/unfit patients presenting with early breast cancer?	15	80% (12/15) Surgery under LA 7% (1/15) Radiotherapy 13% (2/15) Other
4. If you use PET, how do you use it in relation to ER/PR status?	207	97% (201/207) – In ER or PR +ve tumours 2.42% (5/207) – Only in ER +ve tumours 0.5% (1/207) –Regardless of ER/PR status
5. What are your indications for using PET? (more than one indication allowed)	213	91% (194/213) –Unfit for surgery under GA 35% (74/213) – Patient preference 27% (59/213) – Old age 10% (21/213) – Unfit for surgery under LA 12% (25/213) –Other
6. Would you recommend PET to elderly patients even if they were fit for surgery?	215	7% (16/215) Yes 93% (199/215) No
7. What is your first drug of choice?	216	76% (165/216) Letrozole 13% (28/216) Anastrozole 10% (21/216) Tamoxifen 1% (2/216) Exemestane
8. Once started on PET, how do you follow your patients up?	216	44% (96/216) Clinical follow-up only 54% (116/216) Clinical and Imaging 2% (4/216) Other
9. If you follow up patients clinically, how often do you follow them up?	216	4% (9/216) 2 monthly 38% (82/216) 3 monthly 13% (28/216) 4 monthly 13% (28/216) 6 monthly 32% (69/216) Other

a summary of answers to the questions are presented in Table 1. Ninety-three per cent of respondents said they use PET in elderly patients presenting with early operable breast cancer. Among those who do not use PET, most offer surgery under local anaesthesia (LA) if the patient is not fit for a general anaesthesia (GA).

The main indications for PET were unfit for GA or patient preference but 7% of the respondents said they would recommend PET to elderly patients who are fit for surgery. The majority (82%) said that 10–30% of their elderly patients are treated with PET but the percentage varied from <10% to 70% between surgeons. This was an estimate in most cases as 78% of respondents have not audited the number or the outcome of patients treated with PET. Letrozole is the drug of choice for 76% but 10% still use tamoxifen. When asked to guess the expected survival of a woman aged 80 and of average health living in the UK, over 70% of respondents underestimated the expected survival.

Discussion

This survey shows that over 93% of breast surgeons use PET to treat elderly women presenting with surgically re-

sectable breast cancer, with 82% estimating that 10–30% of their patients aged ≥70 years are treated this way. PET should therefore now be considered an important treatment modality in breast cancer in the UK.

While endocrine therapy is often used to downstage the tumour in elderly patients presenting with locally advanced, hormone-sensitive breast cancer, treating patients presenting with surgically resectable disease with endocrine therapy only is questionable. Most would agree that surgery, followed by appropriate adjuvant therapy, should be the standard of care in breast cancer regardless of age as it provides better long-term local control of disease. Consequently, it is of some concern that 7% of surgeons would offer it to women fit for surgery. Such concern is unwarranted if there is evidence to suggest PET has equal efficacy with regard to local control and survival compared with standard therapy. A number of randomised trials have compared tamoxifen given as PET with surgery and a review of these trials showed tamoxifen was associated with inferior local disease control but similar overall survival.⁴ However, these trials are now old, patients received tamoxifen regardless of hormone receptor status in most trials, and the quality of surgery and radiotherapy received by the surgical group

10. How often do you do the imaging?	143	18% (26/143) 3 monthly 8% (11/143) 4 monthly 25% (35/143) 6 monthly 17% (24/143) Yearly 33% (47/143) Other
11. Have you formally audited your patients treated with PET?	212	22% (46/212) Yes 78% (166/212) No
12. What proportion of your elderly patients are treated with PET?	208	8% (17/208) <10% of patients 39% (81/208) 10% 23% (47/208) 20% 20% (42/208) 30% 4% (9/208) 40% 3% (6/208) 50% 1% (2/208) 60% 2% (4/208) 70%
13. The figure given above – was it accurate or an estimate?	208	8% (17/208) Accurate 92% (191/208) Estimate
14. What do you do if the tumour is growing on the first endocrine therapy you prescribed?	216	51% (110/216) Change to a different endocrine agent 18% (39/216) Surgery 13% (28/216) Change to a different endocrine agent and perform surgery 2% (4/216) Radiotherapy 16% (35/216) Other
15. Can you guess the expected average survival of a woman aged 80 and of average health living in the UK (cohort expectation of life)?	209	0.5% (1/209) 0–1 year 4.3% (9/209) 2–3 years 15.3% (32/209) 4–5 years 27.2% (57/209) 6–7 years 25% (52/209) 8–9 years 24.4% (51/209) 10–11 years (correct answer) 3.4% (7/209) 12–13 years

PET = primary endocrine therapy; LA = local anaesthesia; ER = oestrogen receptor; PR = progesterone receptor; +ve = positive; GA = general anaesthesia

was mostly not in line with modern day standards. In addition, AIs have now largely replaced tamoxifen in the management of breast cancer in postmenopausal women owing to proven superior efficacy in other clinical scenarios such as adjuvant^{5,6} and neoadjuvant⁷ therapy as well as metastatic/advanced disease.⁸ This survey confirms that AIs have also mostly replaced tamoxifen in the PET setup. Few papers confirming the efficacy of AIs as PET have been published^{9–11} and AIs have not been compared with surgery in a prospective randomised fashion. One trial that attempted to do this closed early owing to poor recruitment.¹² At present, there is therefore no evidence to suggest PET with AIs is of equal efficacy to surgery (and appropriate adjuvant therapy afterwards).

There is general consensus that breast cancer patients should not be treated with endocrine therapy only unless their expected survival (owing to co-morbidity) is relatively short. National Institute for Health and Care Excellence guidelines state: ‘Treat patients with early invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery.’¹⁵ This is because tumour progression occurs in a large number of patients with time. A large retrospective study of 616 PET patients, in

which tamoxifen was used for the majority (69%) but an AI was used for others, with a median follow-up duration of 41 months, reported tumour progression in 45% of patients with a median time to progression of 49 months.¹⁰ In another study of 101 patients treated with letrozole, with a median follow-up duration of 56 months, 18% of patients with hormone receptor positive tumours did not respond and another 18% responded initially but later progressed.¹¹ This makes PET even with an AI decidedly inferior to surgery in terms of local control. Women with a reasonable life expectancy may outlive the effectiveness of PET, and this will lead to surgery and other treatment modalities at a later stage and at a more advanced age. In this regard, it was notable that the majority of the surgeons in the survey underestimated the expected survival of an 80-year-old woman of average health living in the UK, which, in 2011 (based on national population projections from 2008), was 10.8 years.¹⁴ Over 70% of the respondents underestimated the expected survival. If the expected survival is perceived to be low by the surgeon, there is a larger likelihood of the patient being offered PET rather than surgery.

The estimate of the number of elderly patients treated with PET varied widely between surgeons. We have shown

previously that even in a limited geographical area of a 'cancer network' in the UK, the number of elderly women treated with PET varied considerably between multidisciplinary teams.¹⁵ This variation noted in the survey may also be due to the fact that most surgeons were estimating the proportion of their elderly patients treated by PET as most have not formally audited the number or outcome of these patients.

Conclusions

PET with an AI is used widely by breast surgeons in the UK to treat elderly unfit breast cancer patients. A small proportion of surgeons would use it even in elderly patients fit for surgery. There is a need for surgeons to audit these patients so they are aware of the number treated with PET and the outcome. Surgeons should be aware of the increasing life expectancy of elderly women, which might influence their decision to offer PET to elderly women. There are no national guidelines on PET at present and these are required urgently to standardise its practice.

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