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Treatment of Breast Cancer in Two Teaching Hospitals: a Comparison with Consensus Guidelines

Mark McCarthy and Jo Bore

We compared the initial treatment of 383 patients with breast cancer in two central London teaching hospitals during 1986 with the guidelines of the King's Fund Consensus Conference for breast cancer treatment held in London the same year. The majority of patients (68%) received lumpectomy and 18% received mastectomy. Lumpectomy was followed by radiotherapy for 95% of cases but 30% of mastectomy patients also received radiotherapy. Only 42% of the patients had surgical sampling of the axillary nodes. Cytotoxic chemotherapy was recorded for 27% women under 50, but also for 16% women age 50 or more. Tamoxifen was given to 58% of women aged 50 or more, but also to 26% of women under 50. We conclude that there are discrepancies between consensus guidelines and clinical practice. Further study is needed to determine whether these variations are clinically important, and whether similar variations exist elsewhere in Europe.
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INTRODUCTION

BREAST CANCER is the most common malignancy of women in Western industrialised countries. Neither the cause nor a means of primary prevention of breast cancer are known; therefore, management depends on early diagnosis (including screening) and treatment.

Three consensus developing conferences have been held on the management of breast cancer. The 1980 National Institutes of Health (NIH) conference [1] in the USA covered the initial treatment of breast cancer, and described the trend towards more conservative surgery and the use of primary radiotherapy with or without minimum surgery. A second NIH conference [2], held in 1985, looked at the role of cytotoxic drugs and endocrine therapy. In 1986, the King's Fund held a conference [3] in London, which differed in including lay members in the panel. The conference addressed a broad range of issues on breast cancer management and presented guidelines on local and systemic treatment.

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This study compares the initial treatment of patients with breast cancer in two central London teaching hospitals in the same year as the King's Fund consensus statement. The two hospitals, Middlesex Hospital and University College Hospital, both provide radiotherapy and oncology services. Patients are referred directly by general practitioners, and also by other hospitals in surrounding districts. We used the consensus conference statement as our criterion for quality assessment.

METHODS

Four sources were available from which names of patients could be identified: the regional cancer register (held at the Thames Cancer Registry); a register of cancer patients held locally in University College Hospital; histopathology laboratory records; and the routine hospital discharge information system (Hospital Activity Analysis). We wrote to all 18 consultants who had treated patients with breast cancer identified from these sources, explaining the study and seeking their permission to review patient case notes: no consultant refused. The study was approved by the Bloomsbury district ethical committee.

We included in the study patients diagnosed with primary breast cancer. We excluded patients who were male (2), treated privately outside the NHS (21), bilateral (8), referred for a second opinion (1) or having non-carcinomatous breast disease

(2, both lymphomas). We also excluded patients initially seen at clinics within Bloomsbury but who were referred on for definitive treatment outside the district. The case notes of some patients were untraceable: for 17 the case notes were missing (9 dead, 8 alive), and for 12 patients identified by name on the source registers no case notes registration number could be found.

Information was extracted from the notes onto a standardised recording sheet. Problematic coding was discussed between the authors. Because of variations in actual surgical practice, we included all forms of mastectomy (radical, total and partial) together. We also combined axillary sampling and axillary clearance since the case notes were often unclear on the type of surgery performed (no data for 43 cases).

Pre-operative nodal status was not described for 96 cases. Cases were coded for stage using the tumour-node-metastasis (TNM) system. Where possible, TNM data were taken from postoperative, rather than clinical, findings regardless of whether the TNM stage was formally recorded in the notes. Information on whether the patient was included in a clinical trial was collected from the Cancer Research Campaign clinical trials centre for University College Hospital patients, and the breast cancer clinical trials coordinator for Middlesex Hospital patients. The coded data were entered into a microcomputer by two people working jointly to enhance reliability of the data transfer. Statistical analysis with SPSS-PC used χ^2 tests.

Comparison criteria were derived from the published report of the King's Fund consensus conference [3]. The recommendations for management are summarised here for reference.

Surgery and radiotherapy

The King's Fund consensus statement recognised the recent trend towards less radical surgery, and that breast conservation with radiotherapy has rates of recurrence that are comparable with mastectomy alone. However, mastectomy was regarded as the treatment of choice in certain cases, e.g. if tumours are multifocal or occupy a large proportion of the breast; and patients may request a mastectomy, which reduces the risk of local recurrence and the need for radiotherapy. Local recurrence is reduced substantially with radiotherapy, although it does not prolong life. Patients with locally advanced disease may benefit from radiotherapy.

Axillary surgery

The consensus stated that spread to the axillary nodes cannot be accurately determined by clinical examination, and axillary nodes should be sampled at the time of surgery. Gross spread to the axilla would normally be treated with axillary clearance, with radiotherapy reserved for recurrence.

Adjuvant drug therapy

The consensus statement recognised the use of combination chemotherapy for women under 50, indicating a reduced risk of death in premenopausal women with positive nodes. The benefits for women over 50 years were "substantially less". Chemotherapy could be considered along with radiotherapy and endocrine therapy for patients presenting with locally advanced or metastatic disease. The consensus statement recognised that primary treatment with tamoxifen reduced mortality rates in women over 50 but only reduced the relapse rate in women under 50. Oophorectomy for women under 50 may reduce mortality rates as much as multi-agent chemotherapy.

Table 1. Stage, age and nodal status of home and referred patients

	Home	Referred	Total
Stage			
I	39 (29%)	94 (37%)	133 (35%)
II	62 (47%)	113 (45%)	175 (45%)
III	15 (11%)	23 (9%)	38 (10%)
IV	15 (11%)	22 (9%)	37 (10%)
Age			
<50	35 (28%)	77 (31%)	112 (30%)
≥50	96 (72%)	175 (69%)	271 (70%)
Nodal status			
Node +ve	27 (21%)	68 (27%)	95 (25%)
Node −ve	104 (79%)	184 (73%)	288 (75%)
All	131 (100%)	252 (100%)	383 (100%)

RESULTS

There were 383 cases identified. 131 were both diagnosed and treated in Bloomsbury hospitals ("home" cases), and 252 were diagnosed elsewhere but referred to Bloomsbury for treatment—mainly for radiotherapy ("referred" cases). The two groups of cases showed no significant differences in distributions for stage, age or nodal status (Table 1).

Surgery and radiotherapy

For stage I and II cases, 94% were treated with surgery (4% received no surgery and 3% unknown). Surgery was less common for stage III (79%) and stage IV (35%). Overall, lumpectomy was more common (69%) than mastectomy (18%). Lumpectomy was most frequent for stage I tumours (90% of all stage I cases), reducing for subsequent stages (stage II: 68%; stage III: 37%; stage IV: 30%). Mastectomy was uncommon for stage I tumours (5% of all stage I cases), increasing for stage II (26%) and stage III (42%), but again infrequent for stage IV (5%).

Radiotherapy use showed less decline with advanced disease: it was given to 93% of stage I cases (5% no radiotherapy, 2% not known), 86% stage II, 79% stage III and 65% stage IV cases. For almost all cases receiving lumpectomy, surgery was followed with radiotherapy (95%); but radiotherapy was also given after 30% of mastectomies. There were differences here in clinical practice for home and referred cases. All but one of 179 (99%) referred lumpectomy cases received radiotherapy, but only 69 of 80 (86%) home cases ($\chi^2 = 30.9, P < 0.001$). In contrast, 36 of 38 (95%) referred mastectomy cases received radiotherapy compared with 6 of 24 (25%) home cases ($\chi^2 = 3.5, P = 0.06$).

Axillary surgery

Details of the surgical operation were available for 340 patients. 145 (43%) of these patients had axillary surgery. Data on pre-operative nodal status were available in 287 patients. Of these, axillary surgery was undertaken on 41 (15%) patients with clinical nodes pre-operatively: 28 (10%) were positive on pathology, and 13 (5%) negative. Axillary surgery was also undertaken in 87 (30%) of cases without pre-operative nodes and not undertaken in the remaining 159 (55%) cases.

Adjuvant drug therapy

70 (18%) cases definitely received chemotherapy, while chemotherapy was possibly used but not recorded clearly in the case notes of 10 (3%) patients. Only 30 (27%) women under 50 years of age had chemotherapy recorded, while 40 (16%) women

Table 2. Use of chemotherapy by node status and stage

	Nodes	Chemotherapy	No chemotherapy	Total
Age				
<50	+ve	11 (44%)	14 (56%)	25 (100%)
	−ve	19 (22%)	68 (78%)	87 (100%)
≥50	+ve	15 (21%)	55 (79%)	70 (100%)
	−ve	25 (12%)	176 (88%)	201 (100%)
Stage				
I		23 (17%)	110 (83%)	133 (100%)
II		27 (15%)	148 (85%)	175 (100%)
III		8 (21%)	30 (79%)	38 (100%)
IV		12 (32%)	25 (68%)	37 (100%)
All	70 (19%)	313 (81%)	383 (100%)	

of 50 years or more also did (Table 2). Even for node positive patients, 56% of women under 50 did not receive chemotherapy. Chemotherapy was not significantly related to stage ($\chi^2 = 6.2$, $P = 0.1$).

187 (48%) patients received tamoxifen: 58% of those aged 50 and over, and 26% of those under 50. 4 (13%) of the cases aged 50 or less treated with tamoxifen were recorded as being in clinical trials, and 27 (17%) of the cases over 50 were in trials. 19 (5%) patients received oophorectomies, 7 (2%) in combination with tamoxifen.

There were differences in adjuvant drug treatment betweeen home and referred cases. Home cases (15, 11%) received chemotherapy less frequently than referred cases (55, 22%) ($\chi^2 = 5.5$, $P = 0.02$). Similar proportions of patients under 50 received tamoxifen treatment: 13 (35%) home and 17 (19%) referred cases ($\chi^2 = 1.6$, $P = 0.19$); but for patients age 50 and over, proportionately more home cases (72, 75%) than referred cases (85, 49%) received tamoxifen ($\chi^2 = 16.7$, $P < 0.001$).

DISCUSSION

This study indicates differences in clinical practice in the treatment of breast cancer in two London teaching hospitals in 1986 compared with the statement from a consensus conference also held in London in the same year. Equivalent data exist for only one other European country, Italy [4, 5], where breast cancer treatment of patients in 63 hospitals in the early 1980s was compared with Italian Breast Cancer Task Force guidelines. Italian clinical practice at that time was markedly different to our findings for Britain: 46% of stage I and II patients at that time received a modified radical mastectomy, and less than 1% a lumpectomy. In the USA, 76% of patients more than 50 years of age in 7 Californian hospitals were considered to be treated in accordance with standard practice derived from text books [6]. For example, these criteria approved either a radical or modified radical mastectomy, or local excision with radiotherapy for stage I and I cancers; but adjuvant drug therapy was excluded on the grounds of being "controversial".

A high proportion of patients were treated with conservative surgery and radiotherapy, a finding in line with the trend indicated in the consensus statement [3] and other evidence of surgical practice in Britain [7, 8]. Radiotherapy was given to 13% of locally diagnosed stage I and II cancers treated by mastectomy; the much higher proportion (95%) of referred patients first treated with mastectomy and then receiving radiotherapy must reflect the effect of referral selection, but most of these cases were also only stage I and II. It is, of course, difficult for a receiving clinician to advise a patient against radiotherapy, even after mastectomy, if the patient has been referred for that treatment by another doctor.

The proportion (43%) of patients undergoing axillary surgery did not follow the consensus guidelines, but does reflect British surgical practice for limited intervention [7]. Node sampling is needed to distinguish between stage I and stage II spread, and positive node status has been suggested as an indication for chemotherapy [9]; but the consensus statement recommended the same treatment for both stages, and choice of drug therapy by age rather than node status. It is possible that axillary surgery is avoided when the patient is to have radiotherapy since it may increase the incidence of oedema of the arm.

Adjuvant drug therapy also differed from the consensus guidelines. For women under age 50, 73% of all patients (and even 44% of node positive patients) received no chemotherapy, while 26% received tamoxifen. For women aged 50 or over, 42% received no tamoxifen while 15% received chemotherapy. Entry within clinical trials did not appear to be an explanation, although it is possible that these data were incomplete. Support for the consensus guidelines on adjuvant therapy has become stronger through publication of an overview on randomised trials of adjuvant drug treatment [10]. For patients under 50, clinicians must weigh the improvement in survival for a minority against the costs and morbidity incurred in giving chemotherapy to all [11].

Is a consensus statement expected to influence practice? In the USA, an evaluation of four NIH consensus conferences (not only of cancer care) showed no overall impact on clinicians' practices, although sub-analysis suggested some changes after the NIH breast surgery consensus conference [12]. The authors argued that better information on current clinical practice was needed before a consensus conference, because some of the recommendations do not imply change, and so that "deliberations and recommendations can take into account both the state of science and the state of practice". There have been fewer British consensus statements, and they have not been formally evaluated.

British practice in initial management of breast cancer differs from the USA and Italy in using less extensive surgery [5, 13]: are there are also variations in radiotherapy and drug treatment? And do these variations translate into differences in survival, quality of life or acceptability of care to patients? There is a need for national studies in Britain to determine the population effectiveness of breast cancer treatment, and cross-national studies to explore whether differences in survival and quality of life are related to medical care.

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History of Selected Diseases and the Risk of Colorectal Cancer

Carlo La Vecchia, Barbara D'Avanzo, Eva Negri and Silvia Franceschi

The relationship between selected aspects of medical history and the risk of colorectal cancer was analysed using data from a case-control study of 673 cases of colon cancer, 405 of rectal cancer and 1501 controls in hospital for acute, non-neoplastic, non-digestive tract conditions, unrelated to known or suspected risk factor for large bowel cancer. Significantly elevated risks (RR) were observed for history of cholelithiasis (RR = 1.5 [95% confidence interval (CI) 1.1–2.1] for colon; 1.6 [1.2–6.4] for rectum) and diabetes (1.6 [1.1–2.3] for colon; 1.3 [0.8–2.0] for rectum), and a significant protection emerged for history of drug allergy (0.6 [0.4–0.9] for colon; 0.6 [0.5–1.0] for rectum). No significant association was found with thyroid disease, gastroduodenal ulcer, liver cirrhosis, hepatitis, pancreatitis, gastrectomy, appendicectomy, treatment with cimetidine/ranitidine, treatment with chenodesoxycholic acid or with blood transfusions. The associations with cholelithiasis, diabetes and drug allergy were not materially modified by allowance for major identified potential confounding factors, and were not restricted to the diseases diagnosed within 5 or 10 years before large bowel cancer diagnosis. Thus, the analysis of this large dataset offered further quantitative evidence suggesting a possible, however moderate, association between gallbladder disease and colorectal cancer risk, which may be related to enhanced or continuous secretion of secondary bile acids. The associations with diabetes and drug allergy were unexpected, and probably indirect, lacking previous epidemiological support or any obvious biological interpretation. Thus, they should be simply regarded as working hypotheses worthy of further consideration.
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INTRODUCTION

COLORECTAL cancer is the second most common cancer site in Italy, as in most western countries [1, 2] but its causes are still largely undefined. Besides diet, which is likely to play an important role in large bowel carcinogenesis, even in the absence of a clear association with specific nutrients [3], other factors which have been related to colorectal cancer risk include reproductive and menstrual factors [4, 5] and medical history.

Among medical conditions known to be associated with the incidence of colorectal cancer, there are diseases of the large bowel, such as adenomatous polyps [6, 7] and ulcerative colitis [8], but also conditions, such as Barrett's oesophagus [9], which probably reflect common predisposing factors. Other associations, such as those with cholelithiasis or cholecystectomy [10–17] and pernicious anaemia [18], have emerged in some studies, but there is at present no clear consensus on them [19–24]. Some of the associations between aspects of medical history and colorectal cancer may be of potential interest from an aetiological viewpoint, since they may shed light on possible aetiopathogenic mechanisms.

Thus, in order to provide further information on this issue, we considered information on history of selected diseases in a large case-control study conducted in northern Italy.

SUBJECTS AND METHODS

The data were derived from an ongoing study of digestive tract neoplasms, based on a network including major teaching and general hospitals in the Greater Milan area. Recruitment of

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