PAPERS AND ORIGINALS

Failure to detect intra-abdominal metastases from breast cancer: a case for staging laparotomy

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Summary and conclusions

Two studies were performed to assess the accuracy of non-invasive methods in detecting intra-abdominal metastases from breast cancer. Firstly, the sites of spread detected at the time of first presentation with metastases were compared with the sites of spread shown at necropsy in the same patients. Although about two-thirds of the patients with bone and lung metastases at necropsy had had metastases detected at these sites when they first presented with metastases, only a third of the patients with liver metastases and none of those with other intra-abdominal metastases had had evidence of disease at first presentation with metastases. The second study confirmed a poor detection rate of liver and other intra-abdominal metastases in patients with breast cancer undergoing laparotomy and oophorectomy who were staged immediately before operation.

Pre-mastectomy staging laparotomy should be considered in those patients with primary breast cancer who are most likely to have disseminated disease beyond the regional nodes. In the presence of occult gross metastases detected by staging laparotomy, mastectomy will not provide additional protection against loca recurrence of disease. Patients with occult gross metastases should also be excluded from studies on adjuvant chemotherapy (designed to treat micrometastases). Aggressive methods of staging are justified to protect the patient as far as possible against unnecessary mastectomy and to identify those patients who should be treated by therapeutic chemotherapy rather than adjuvant chemotherapy.

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Introduction

About 20% of patients with primary breast cancer develop metastases within 18 months of mastectomy and 40-50% within five years.[1 2] Some of these patients may have detectable metastases which are missed at presentation because of the inadequacy of preoperative screening procedures, particularly those for detecting intra-abdominal metastases. We therefore examined this problem, firstly, by comparing the sites of metastases detected by staging tests with subsequent necropsy findings and, secondly, by comparing the operative findings at laparotomy (for oophorectomy) with the results of preoperative staging tests.

Methods and results

Patients were investigated before primary treatment, when they first presented with metastatic disease, and at intervals thereafter. Investigations included estimation of the serum bilirubin, alkaline phosphatase, and serum alanine transferase concentrations. A gamma-camera (Pho-Gamma HPIII) was used to perform liver scanning 20 minutes after intravenous injection of 5 mCi of ^{99m}Tc sulphur colloid and bone scanning one to two hours after intravenous injection of 10 mCi of ^{99m}Tc polyphosphate or ^{99m}Tc MDP. Grey-scale ultrasonography by the method described by Taylor *et al*[3] was used to examine the liver. The bones were also examined by radiological skeletal survey, and all patients underwent chest radiography and cytological examination of bone marrow aspirate from the iliac crest.

In the first study of 33 patients who had died from breast cancer

the extent of disease at necropsy was compared with the extent of disease detected in the same patients when they had first presented with metastatic disease (table I). Bone metastases were found in 32 patients at necropsy and had been detected in 20 at the time of first presentation with metastases. Lung metastases were found in 20 patients at necropsy and in 13 at first presentation. Liver metastases, however, were found in 29 patients at necropsy but had been detected in only 11 when the patients first presented with metastases. The efficacy of the different clinical tests used is shown in table II.

TABLE I—*Comparison of detection of metastases at different sites in 33 patients at first presentation of metastases and at necropsy*

	No (%) of patients with metastases		Ratio
	At necropsy	At first presentation of metastases	
Bone	32 (97)	20 (60)	0·63
Lung	20 (61)	13 (39)	0·64
Liver	29 (88)	11 (33)	0·38
Retroperitoneal lymph nodes	18 (55)	0	0·0
Ovaries and/or adrenals	17 (50)	0	0·0
Peritoneum	13 (38)	0	0·0

TABLE II—*Methods of detecting bone and liver metastases in 33 patients at first presentation with metastatic breast cancer*

	No tested	No (%) metastatic
Bone scan	30	18 (60)
X-ray survey	29	11 (38)
Bone marrow	26	10 (38)
Total bone	33	20 (60)
Palpable liver	33	5 (15)
Liver ultrasound	21	5 (23)
Liver function tests	33	9 (27)
Liver scan	24	7 (29)
Total liver	33	11 (33)

Metastases were also found in ovaries or adrenals, or both, and peritoneum at necropsy but none had been detected at these sites at first presentation. The surprising finding was the high incidence of disease of retroperitoneal nodes found at necropsy, since no metastases had been detected at this site before death.

In the second study the immediate preoperative assessment of 43 consecutive patients who were treated by oophorectomy for advanced breast cancer was compared with the extent of disease found at laparotomy (table III). At laparotomy 16 of the 43 patients were found to have intra-abdominal spread of disease at 28 sites, compared with six patients detected by preoperative assessment as having disease at six sites. Metastases were found in the liver of 13 patients at laparotomy compared with six detected at preoperative assessment. Furthermore, false-positive evidence of liver metastases had been reported in three patients. Metastases were detected in the peritoneum in four patients and the ovaries or adrenals, or both, in 11 patients at laparotomy, none of which had been detected by preoperative staging.

TABLE III—*Comparison of number of sites affected by metastases detected by preoperative staging compared with subsequent findings at laparotomy in 43 patients with metastatic breast cancer*

	Preoperative staging assessment	Operative findings
Liver	6*	13
Peritoneum	0	4
Ovaries and/or adrenals	0	11
Total No of sites affected	6	28
Total number of patients with at least one site affected	6	16

*Liver metastases were incorrectly diagnosed in a further three patients.

Discussion

Development of metastases after mastectomy suggests that either undetectable micrometastases were present at the time of mastectomy or relatively gross disease was not detected by present staging techniques.

The results of the first study show that the pattern of sites affected by metastases in patients who were staged by the methods outlined above when first developing metastases was not the same as that found at necropsy. Although about two-thirds of the patients who had evidence of bone and lung metastases at necropsy had had metastases detected at these sites at first presentation, only one-third of those with liver metastases and none of those with other intra-abdominal metastases had had evidence of disease at first presentation. There are three possible reasons for this discrepancy. Firstly, metastases may develop later in intra-abdominal sites but grow more quickly; secondly, bone or lung metastases may metastasise to intra-abdominal sites; or, thirdly, potentially detectable metastases may have been present in all sites but the present method of staging failed to identify them in the abdomen.

The last hypothesis is supported by the results of the second study, where metastases were found at 28 sites in 16 patients out of the 43 who underwent laparotomy and oophorectomy. Preoperative staging tests had correctly indicated the presence of intra-abdominal metastases in only six patients, and a further three were falsely diagnosed as having liver metastases. This indicates that the present methods of detecting intra-abdominal metastases, and particularly liver metastases, are inadequate.

The high incidence of retroperitoneal lymph node metastases is of interest because this site has not been reported as common for breast cancer. The mechanism for such metastasis is uncertain. Haematogenous spread seems unlikely, and retrograde lymphatic spread from the mediastinum should therefore be considered.

Failure to detect metastases in patients with primary breast cancer has several consequences. Firstly, the detection of occult gross metastases would dictate against mastectomy, which is unlikely to provide additional protection against local recurrence in the presence of distant metastases. Secondly, patients with occult gross disease need palliative cytotoxic or endocrine treatment. Thirdly, patients with occult gross metastases should not be included in adjuvant chemotherapy studies designed to treat micrometastatic disease. The number of patients in adjuvant trials with true micrometastases may in fact be much smaller than previously suspected, and adjuvant chemotherapy for patients with occult gross disease will induce only temporary remission and not cure. This might account for the difference in recurrence rate seen in the first year of adjuvant chemotherapy trials and not reflect the treatment of micrometastases with the implications of cure.[4–6]

This prevalence of intra-abdominal metastases not detected by present staging techniques, together with the clinical implications outlined above, raises the possibility of laparotomy as part of the premastectomy staging assessment. Staging laparoscopy is unlikely to provide enough information, for in a similar situation—when the liver is macroscopically normal in Hodgkin's disease—it has been shown[7] that occult metastases are detected twice as often by wedge liver biopsy than by peroperative four-quadrant Menghini needle biopsy. Furthermore, it is impossible at laparoscopy to assess the retroperitoneal nodes, which may be important.

We therefore recommend that staging laparotomy should be considered in some patients with primary breast cancer. The factors that indicate the likelihood of metastases would need to be determined before mastectomy. The site, size, and the rate of development of the primary tumour will influence prognosis.

Excision of the lump to determine the malignancy grade, lymphoplasmocytic infiltration, and vascular invasion within the primary tumour will improve the prognostic accuracy, as will premastectomy axillary node biopsy to confirm gross disease of axillary nodes. Some or all of these factors may be combined to indicate a high likelihood of occult metastases in some patients who could be considered for staging laparotomy before primary treatment.

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Comparison of performance of various sphygmomanometers with intra-arterial blood-pressure readings

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Summary and conclusions

Seven types of sphygmomanometer were used in random order on each of nine hypertensive patients and the readings compared with simultaneous intra-arterial blood-pressure recordings. All the devices gave significantly different values for systolic pressure, and only two measured diastolic pressure without significant error. Systolic pressure was consistently underestimated (range 31-7 mm Hg), and all but one instrument overestimated diastolic pressure (range 10-2 mm Hg). The variability of readings was least with the standard mercury sphygmomanometer and the random-zero machine, while with some of the more automated devices single readings were in error up to −68/33 mm Hg.

The strong correlations found between intra-arterial and cuff systolic pressures with all devices tested and significant correlations for diastolic pressure with all but one device indicate that, with one possible exception, the sphygmomanometers would give accurate results where a change in blood pressure was the main concern.

Introduction

Indirect measurement of blood pressure is undertaken with many more-or-less automated devices whose performance characteristics are poorly documented. In some cases the principle of their operation is not stated and it may not be clear whether they use phase IV or phase V of the Korotkoff sounds for the diastolic end-point. This second factor is highly relevant in exercise, pregnancy, and other high-output states. Reports on antihypertensive and vasoactive agents increasingly refer to automated sphygmomanometers that can provide results in hard-copy form.[1-3] They imply that eliminating the human observer has preserved or even increased the accuracy of the traditional sphygmomanometer.

Labarthe *et al*[4] assessed the performance characteristics of various sphygmomanometers but did not use direct readings as a basis for comparison and omitted newer, simple, and relatively cheap semiautomatic devices, some of which are aimed at self-measurement. Several newer devices have features such as audiovisual signalling of end-points, adjustable preset deflation rate, elimination of observer bias and error, and results in hard-copy form. Any of these features may make one or other model the instrument of choice for particular purposes, such as self-measurement of blood pressure, semiautomated pressure monitoring, epidemiological surveys, or assessment of antihypertensive agents, provided that a given standard of accuracy can be assumed or demonstrated.

We have tested a sample of sphygmomanometers, including the common clinical mercurial model, which varied widely in cost and the amount of training needed by users. They represented mercurial and aneroid models based on human detection of Korotkoff sounds, sound filters, and an ultrasound principle. The study was designed to correspond to everyday clinical application and we did not consider the ease of use or accuracy of the instruments in untrained hands.

Materials and methods

We used seven different types of sphygmomanometer (see table I) in random order on nine patients aged 25-80 years, while simultaneously recording direct intra-arterial blood pressure. The patients were receiving various drug regimens for hypertension and presented a range of blood pressure levels. All gave consent to the study. One patient (case 1) had frequent ventricular ectopic beats, and one other (case 9) was in controlled atrial fibrillation.

Supine blood pressure was taken as the average of two readings, phase V being used as the diastolic end-point when observer auscultation was used. In one patient (case 2) there was no disappearance of sounds down to zero, and in this case muffling (phase IV) was used for the diastolic end-point. Intra-arterial pressure was determined as the average of 15 complexes immediately preceding cuff inflation.

The blood-pressure cuff was applied to the arm containing a 50 mm 17-gauge Teflon cannula (Dwellcath, TUTA Laboratories, Lane Cove, Australia) inserted into the brachial artery. Intra-arterial blood pressure was measured by a Siemens model 746 pressure transducer and a Philips amplifier type XV 1505, direct calibration of the system being carried out on the day of the procedure. The resonant frequency of the whole system was 13·8 Hz with a damping factor of 0·37. Zero reference level was taken as midthorax in the supine position and was

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