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# Thyroid function in patients with breast cancer

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**Summary**

*Thyroid function has been assessed in 40 patients with breast cancer and compared with an age-matched control female population. The free thyroxine index was lower and the level of thyroid-stimulating hormone in the serum higher in the cancer group and these changes became more marked at 6 months. It is concluded that patients with breast cancer show more evidence of hypothyroidism as time progresses.*

## Introduction

The clinical impression that thyroid disease occurs frequently in patients with breast cancer has prompted many clinicians to investigate the association. Repert[1] studied life assurance tables and found that the incidence of breast cancer was much higher in hypothyroid patients. An autopsy study[2] demonstrated marked thyroid atrophy in patients who had died of breast cancer and Ellerker[3] showed the incidence of breast cancer to rise in patients following partial thyroidectomy. Throughout the next decade many authors[4-6] looked at crude measures of thyroid function and intimated that those patients with advanced malignant disease had the more abnormal results. Emery and Trotter[7] treated patients with thyroxine in addition to conventional therapy but found no improvement in survival. Moossa and his colleagues[8] drew attention to the importance of goitre in the long-term survival of patients with breast cancer, these patients having done particularly badly. The advent of more sophisticated methods of assessing thyroid function allowed Mittra[9] to show that serum thyroid-stimulating hormone levels, both basally and after the administration of thyrotrophin-releasing hormone, were elevated in breast cancer patients.

The importance of timing of thyroid function tests has been reported recently[10]. Most hormonal levels rise with operative treatment and the need for investigations to be done before any form of treatment is emphasised.

## Patients and methods

Forty consecutive patients admitted to St Bartholomew's Hospital, London, with carcinoma of the breast were entered into the study. Eighteen patients had clinical Stage I disease, 9 had Stage II, 8 had Stage III, and 5 had evidence of distant metastases at presentation. An age-matched group of female inpatients acted as the control group. Most of this latter group were patients with vascular disease or benign breast disease. Figure 1 shows the age distribution of the two groups of patients.

The investigations were carried out preoperatively and at 10 days and 6 months after operation. Patients who did not have a mastectomy were not studied at the intermediate stage and 11 patients were not studied at 6 months; 7 of the latter were undergoing treatment at the time, 2 had died, and 2 were lost to follow-up.

### INVESTIGATIONS

Serum thyroid-stimulating hormone (TSH) activity was measured by a radioimmunoassay using a double antibody separation technique and the results expressed as mU of the MRC 68/58 standard per litre; the total serum thyroxine (T4) concentration was measured by a competitive protein-binding method

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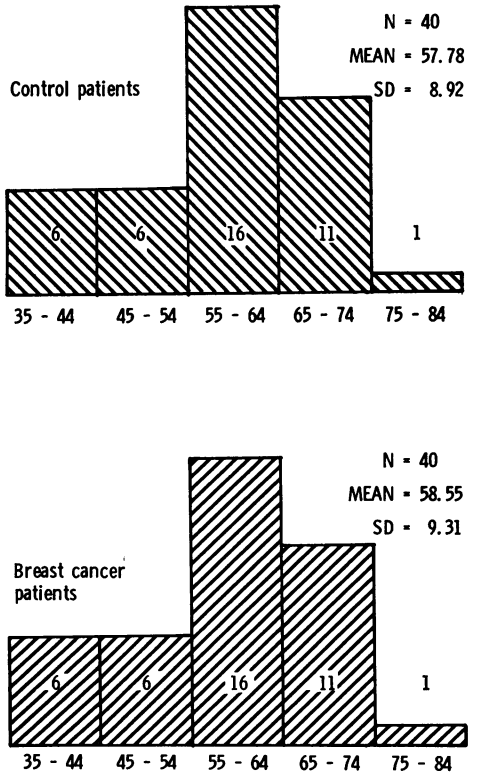


FIG. 1 *Age ranges, control and breast cancer patients.*

(Thyopac-4) and the results expressed as μg $T_4$/100 ml serum. The thyroid hormone uptake test (THUT) to measure unoccupied binding-site concentration was performed by the Thyopac-3 method. The free thyroxine index ($FT_4I$) was calculated from the $T_4$ and THUT results. All blood samples were taken between 8 a.m. and 11 a.m. and stored at 4°C.

STATISTICAL ANALYSIS

Comparison between the group means was carried out using Student's *t* test. A TSH value of 0.3 mU/l was arbitrarily used for levels below the sensitivity limit of the assay (0.4 mU/l).

## Results

Four patients showed clear evidence of clinical hypothyroidism at presentation: one had had a partial thyroidectomy and a second radioactive iodine therapy for thyrotoxicosis, while the

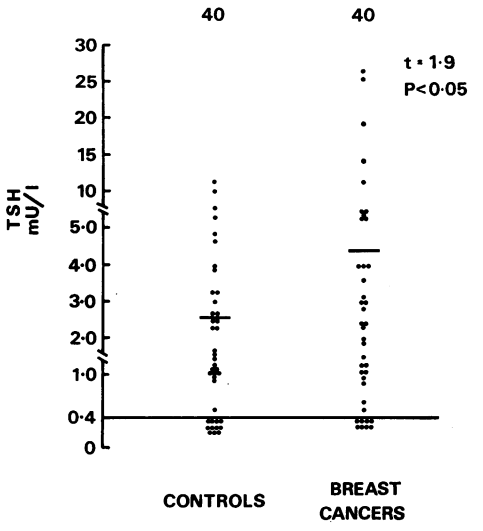


FIG. 2 *Preoperative serum TSH activity, control and breast cancer patients.*

other 2 patients had gross myxoedema at their first outpatient attendance.

The mean preoperative serum TSH level (± SE of mean) in patients with breast cancer (Fig. 2) was higher (4.31 ± 0.62 mU/l) than in the control group (2.57 ± 0.52 mU/l) ($P<0.05$). This was matched (Fig. 3) by a significantly lower mean $FT_4I$ value in the patients with cancer (8.1 ± 0.21) than in the controls (9.2 ± 0.32) ($P<0.02$). TSH levels were even higher (6.4 ± 0.5 mU/l) at 6

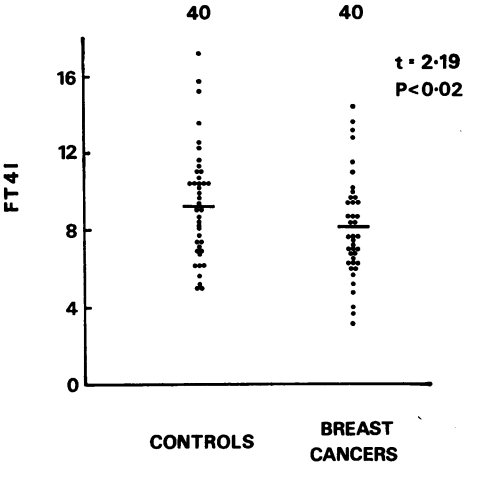


FIG. 3 *Preoperative $FT_4I$ values, control and breast cancer patients.*

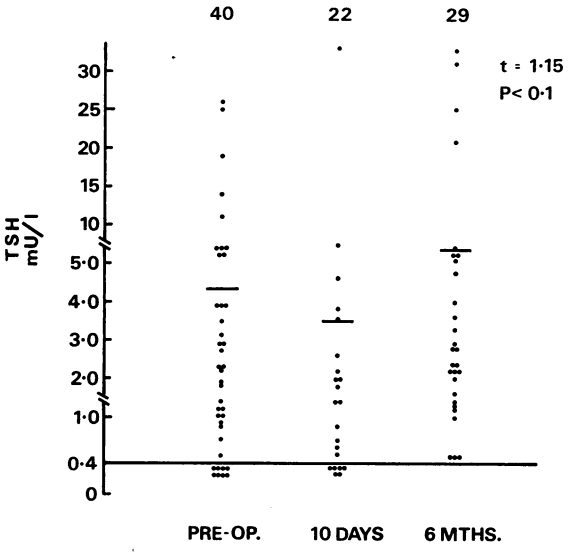


FIG. 4 *Serum TSH activity, breast cancer patients.*

months (Fig. 4), though this increase was shown not to be statistically significant. There were no patients with an unmeasurable level of TSH activity at this time. This rise in TSH activity at 6 months was matched by a further significant fall in FT4I (Fig. 5), the mean level at 6 months being 6.15 ± 0.25 ($P<0.01$).

## Discussion

The clinical impression that patients with breast cancer are more likely to be hypothyroid at presentation is borne out by this prospective study of 40 patients. The biochemical changes

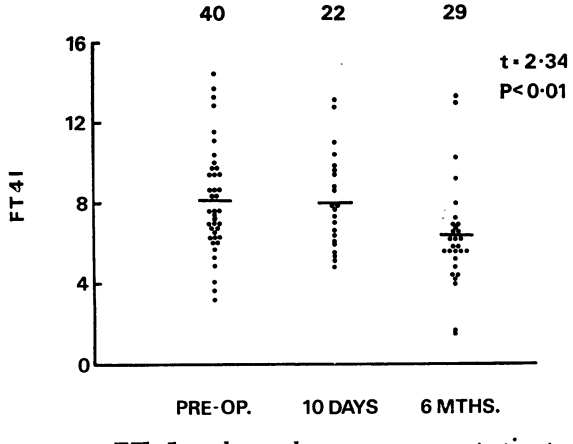


FIG. 5 *FT4I values, breast cancer patients.*

are more marked at 6 months after the diagnosis has been confirmed. This suggests that the patients are becoming progressively more hypothyroid. The need to treat overt hypothyroidism with thyroxine does not permit this group to be followed up indefinitely without treatment. The fact that 11 patients were not studied owing to death or non-attendance at follow-up or because they were undergoing treatment of recurrent disease implies that the fitter patients were investigated. One may speculate that if all the patients had been tested the changes might have been more marked. Thyroxine therapy does not influence the survival of patients with breast cancer[7]. This implies that whatever the stimulus to the combination of cancer and hypothyroidism occurring in the same patient, once the malignancy is recognisable the changes appear irreversible. This factor was recognised by Eskin in his experiments on rats[11]. DMBA-induced tumours were more numerous in iodine-deficient or hypothyroid animals, but dissemination of the tumour could not be prevented when the diets of the animals were corrected.

The association of hypothyroidism and the development of a breast cancer poses many problems. Is the tumour altering the thyroid status of the patient? This would seem to be unlikely as removal of the tumours was not shown to be accompanied by any improvement of thyroid function. The epidemiological studies of Finley and Bogardus[12] drew attention to the increased incidence of breast cancer in areas of endemic goitre throughout the world. Could there be a dietary factor in patients in Britain? Perhaps our patients eat less iodine and more 'goitrogens' than a 'control' population. This and other factors need careful evaluation before any conclusions can be reached concerning the aetiology of a breast cancer.

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## References


1 Repert, R W (1952) *Journal of the Michigan Medical Society, 51,* 1315.

2 Sommers, S C (1955) *Laboratory Investigation, 4,* 160.

3 Ellerker, A G (1956) *Medical Press, 235,* 280.

4 Edelstyn, G, Lyons, A R, and Welbourn, R B (1958) *Lancet, 1,* 670.

5 Humphrey, L J, and Swerdlow, M (1964) *Cancer, 17,* 1170.

6 Backwinkel, K, and Jackson, A S (1964) *Cancer, 17,* 1174.

7 Emery, E W, and Trotter, W R (1963) *Lancet, 1,* 358.

8 Moossa, A R, Price Evans, D A, and Brewer, A C (1973) *Annals of the Royal College of Surgeons of England, 53,* 178.

9 Mittra, I, and Hayward, J L (1974) *Lancet, 1,* 889.

10 Kirby, R, Clark, F, and Johnston, I D (1973) *Clinical Endocrinology, 2,* 89.

11 Eskin, B A (1970) *Transactions of the New York Academy of Sciences, 32,* 911.

12 Finley, J W, and Bogardus, G M (1960) *Quarterly Review of Surgery, Obstetrics and Gynecology, 17,* 139.