Oestrogen receptor activity in breast cancer detected at a prevalence screening examination

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Summary

In view of the possible introduction of screening programmes, this study compares oestrogen receptor (ER) levels in a series of women whose primary tumour was detected by screening and an age-matched consecutive series of women whose tumours were diagnosed after symptomatic presentation. Because of missing data and other statistical considerations, the comparison was made using T1 and T2 categories of tumour only. Some differences were found: the distribution of ER levels was significantly different in the two groups, with more extreme values in the symptomatic series; the screening series, however, had more moderate/rich ER levels than the symptomatic group. Tumours of special pathological type (for example, tubular, cribriform, lobular, medullary, and mucoid) were more likely to be ER-moderate or -rich, and there were more of these tumours in the screening series. The relationship of these findings to tumour growth rate is discussed. The study highlights the difficulty of obtaining sufficient tissue for conventional DCC biochemical assays from the small non-invasive tumours found by screening, and suggests that newer alternative methods employing monoclonal antibodies may be required for such types of tumour.

Methods

Patients studied

The screening group, composed of 82 women, had cancer detected at their first screening examination. They were all 45–65 years of age, and had attended for screening between 1979 and 1983. They had been invited to the clinic within the Edin-
The symptomatic women had attended a hospital diagnostic breast clinic in the same period and were of similar age. None of these consecutive 238 women had been screened, though some were in the study population of the randomised trial, either as controls or having refused an invitation to screening. Cases arising symptomatically among attenders for screening, but in the intervals between screening examinations, were omitted from this study. For the year 1983 only, the case notes of all 79 newly diagnosed patients in the age group at the diagnostic breast clinic were reviewed to obtain the stage of the disease in those who did not have the receptor assay performed as well as in those who did. The information was used to compare the proportions of tumours assayed, by stage, in both symptomatic and screening groups. In both the screening and the symptomatic series, only women who had the assay performed on the primary tumour were included in this study and all were investigated and treated in a similar way. For those women in the randomised trial of screening, histological data were available for analysis from the trial pathology register [8].

Receptor assay

Specimens were transported on ice to the laboratory within an hour of excision. Oestrogen receptor activity was determined by a method previously described [9]. In brief, tumour extract, prepared by homogenisation (100 mg/ml buffer containing Tris 10 mM, sucrose 0.25 M, ethylene diamine tetraacetate 1 mM, glycerol 10% v/v, and monothioglycolic acid 1% v/v, pH 8.0 at 22°C) and centrifugation at low speed (2040 x g), was incubated overnight at 4°C with 0.031 nM [2, 4, 6, 7-3H] oestradiol-17β and varying concentrations of competing, non-radioactive oestradiol-17β, (0.03, 0.09, 0.15, 0.21, 0.28, 0.31, 0.64, and 61.2 nM). Free and bound steroid were separated by the addition of dextran (0.015% w/v) - coated charcoal (0.15% w/v) suspension, and the radioactivity in the supernatant bound fraction was determined by liquid scintillation counting. The concentration of receptor sites and dissociation constant of binding were calculated by Scatchard analysis [10]. The concentration of soluble protein was determined by the dye-binding method of Bradford [11] and receptor site concentration was expressed as fmols oestrogen-binding sites/mg total soluble protein.

In line with previous work allied to a British Breast Group study [12], tissues containing ≥5 fmols receptor/mg protein were classed as ‘receptor-negative’ and tissues containing ≥5 fmol receptor/mg protein were classed as ‘receptor-positive’; those with levels of 5–19 were termed ‘receptor-poor’, those with levels of 20–99 ‘receptor-moderate’ and those with levels ≥100 fmols/mg protein ‘receptor-rich’. These categories derive from previous experience in this laboratory and elsewhere: tissues containing <20 fmol receptor/mg protein rarely respond to endocrine therapy, whilst those with ≥100 fmol receptor/mg protein are the most likely to respond.

Where, after checking by a pathologist, tumour cells accounted for <10% of the sample specimen used for receptor assay, that specimen was designated as ‘inadequate’ and the assay was deemed invalid.

Histological tumour type

The histological type of tumour was assessed using the pathological categories previously described [13]. This approach recognises invasive cancer according to histological appearances identified and named in the standard literature [14, 15], such as tubular, cribriform, lobular, medullary, and mucoid patterns, and places them in three groups: special type (ST) has at least 90% of the tumour showing a designated pattern; variant special type (VST) has <90% but >50% composition as a designated pattern or as a mixture of more than one designated pattern; not of special type (NST) lacks preceding designated features and corresponds with category not otherwise specified (NOS) of Fisher et al. [14].