The immunocytochemical versus cytosol measurement of the oestrogen receptor in invasive breast cancer tissue

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Abstract

To compare two methods of measurement of oestrogen receptor (ER)-expression in invasive breast cancer tissue. Sections from 299 breast cancer cases were stained for the ER by immunocytochemical assay (ICA), using mouse monoclonal antibody (MAb) NCL-ER-6SF11, and by the dextran-coated charcoal assay (DCC). Concordant results were observed in 230 of the 299 cases (77%), 69 patients had discordant results (kappa = 0.537). We found a moderate concordance between ICA and DCC for ER measurement in breast cancer tissue. If we change the golden standard from DCC to ICA, 23% of patients would receive a different therapeutic approach.

Keywords: Breast cancer; Oestrogen receptor; Dextran-coated charcoal; Immunocytochemistry

1. Introduction

It is well known that the oestrogen receptor (ER) is important for predicting endocrine response in breast cancer therapy [1–3]. For many years, ER measurements were performed by cytosol-based ligand binding techniques, like the dextran-coated charcoal (DCC) assay. There are, however, some pit-falls associated with this method. They require large amounts of fresh-frozen tissue, so that measurements on fine needle aspirates are impossible, as are retrospective studies. Other problems include difficulties in distinguishing heterogeneity of ER-expression within one tumour, possible interference with benign cells and competition with endogenous or exogenous hormones. It was realised that these problems could be overcome by the use of specific antibodies against the ER protein. More recently, immunocytochemical assay (ICA) is being used as an alternative method and it is proven to be as accurate as the ligand binding assay for receptor determination and predicting the response to adjuvant endocrine therapy [1,3]. The purpose of this study was to calculate the concordance between ICA and DCC in ER measurement in invasive breast cancer tissue.

2. Materials and methods

Over a period of 3 years, we collected 299 cases of breast cancer. These cases were stained for ER expression by both DCC and ICA. From each breast cancer case, a fresh frozen section was sent for DCC assay. Tumours with an ER status of >10 fmol/mg protein as measured by DCC were considered ER-positive. For the ICA, we used mouse MAb NCL-ER-6SF11 on paraffin-embedded tissue. The ICA is a semiquantitative method, scored between 0 and 300, also known as the H-score. The pathologist, therefore, counted 100 cells in three different high power fields and each nucleus was given a value between 0 and 3 depending on the intensity of ER expression. A score of '0' was given for an ER-negative cell, '1' for an ER with weak intensity, '2' for an ER with moderate intensity and '3' for a strong ER-positive cell. All these were added up, resulting in a maximum score of 300 (when all cells were strong receptor-positive). As a cut-off value for an ER-positive tumour we used 30. We searched for a relationship between DCC (after logarithmic transformation) and ICA by means of linear regression. Kappa statistic was used for comparing the two methods of measurement.

3. Results

Although concordant results were observed in 230 out of 299 cases (77%), 69 patients had discordant results.

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17 cases were positive by ICA but negative by DCC assay, although 5 showed some ER-activity in the DCC assay but this was below the >10 fmol/mg protein cut-off level. 52 cases were negative by ICA but positive by DCC assay; 17 of these 52 (33%) did show some ER-immunoreactivity but the H-score was well below 30. Agreement between the two methods was moderate (kappa = 0.537).

4. Conclusion

We found only a moderate concordance between ICA and DCC analyses of ER measurement in breast cancer tissue. If we change the golden standard from DCC to ICA, 23% of our breast cancer patients would have got a different therapy, if one limits hormonal therapy to patients with ER-positive breast cancer tissue. The ultimate usefulness of ER status assessment by ICA, however, resides in its ability to predict clinical outcome, especially response to hormonal therapy. It is clear that further studies are required to determine the predictive value of ICA.

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How best to express oestrogen receptor activity

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Abstract

Oestrogen receptor (ER) activity, detected and expressed in a variety of ways, is important in breast cancer. Experience in Edinburgh (1973–1996) showed that [1] no single mode of expression was entirely satisfactory, [2] the probability of a good 'outcome' (prognosis or response to endocrine therapy) increased with increasing activity (either fmol ER sites/mg protein or per cent cells staining for ER). Thus the use of a single 'cut-off' should be avoided and activity quantified, or stratified into categories.

Keywords: ER; Biochemical assay; Immunocytochemical assay; Response; Quantitation; Cut-off

1. Introduction

The oestrogen receptor (ER) protein, best established of the biological factors relating to 'outcome' in breast cancer, has been detected by a variety of biochemical methods and expressed as, e.g. fmol binding sites/mg protein or /μg DNA, or after immunocytochemical assay (ICA) as, e.g. per cent cells staining for ER, or 'histoscore'. Here, I review our experience in Edinburgh to help assess how best to express ER.

2. Methods

2.1. Patients and assessment of outcome

Five studies are considered:

1. A prospective study of 215 patients with operable disease followed up at 4–6 monthly intervals and by annual mammography [1].
2. Premenopausal patients with advanced disease, treated by surgical oophorectomy.
3. Patients with large (>4 cm), operable tumours, pretreated, after wedge biopsy, by neoadjuvant therapy.

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