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Hormone receptor status in primary breast cancer—time for a consensus?

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Abstract

In a previous study, we demonstrated wide variability in the access to oestrogen receptor (ER) measurement, patient selection, choice of technique and the cut-off point for positivity. The aim of this study was to update information on the current use of ER and progesterone receptor (PR) measurement in the United Kingdom (UK). Questionnaires, asking about availability, use and technique of ER and PR measurement, were returned from 170 (74%) units in the UK. Where ER positivity was determined using the percentage of cells staining positive (33%), the absolute cut-off point for positivity varied widely from 5 to 80% of cells. Of the 170 responding units, 107 (63%) felt that PR measurement was important. This study confirms considerable variability in both the technique of ER measurement and the absolute cut-off point for positivity (5–80%). It is essential that a consensus be reached regarding the choice of technique, as well as the threshold for positivity. © 2002 Published by Elsevier Science Ltd.

Keywords: Breast cancer; Adjuvant therapy; Oestrogen receptors; Progesterone receptors

1. Introduction

In patients with breast cancer, oestrogen receptor (ER) status, measured by the ligand binding assay (LBA), is a powerful predictor of response to adjuvant endocrine therapy [1]. More recent evidence suggests that immunohistochemical detection of ER, as well as the progesterone receptor (PR), provides a similar predictive value and is easier and cheaper to perform [2]. In a previous study, we demonstrated that although measurement of ER status in primary breast cancer is generally perceived to be important by the majority of UK breast surgeons, there was a wide variability in patient selection, access to ER measurement, choice of technique and the cut-off point for positivity [3]. The availability of ER status strongly influences the selection of adjuvant systemic therapy [4], and may therefore contribute to differences in outcome between units. The aim of this study was to assess the impact of our previous work and update information on the use and availability of ER and PR measurement in Breast Cancer Units in the UK and the Republic of Ireland.

2. Patients and methods

A postal questionnaire was sent to the lead breast surgeon of all the Breast Cancer Units listed in the 1999 Macmillan Directory of Breast Cancer Services in the United Kingdom ($n=229$) and the Republic of Ireland ($n=96$). The surgeons were asked to give their opinion on the importance of the measurement of ER status in the management of patients with primary invasive breast cancer. Questions were also asked about the availability, use, technique of measurement and threshold of positivity of the technique. In addition, their opinions were sought about the importance, use and availability of PR status in the same group of patients. These results were compared with the previous study carried out in 1997 [3].

3. Results

Completed questionnaires were received from 170 (74%) units in the UK and these results, compared with

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Table 1
Results of postal survey: ER status

Questions	Answers	1997 (%)	2000 (%)
Do you believe that measurement of ER status is important in the management of your patients with primary invasive breast cancer?	Yes	87.5	99.0
	No	12.5	1.0
Do you have access to ER measurement?	On site	60	79
	Elsewhere	24	21
	No	16	0
Do you determine ER status on all new breast cancers?	Yes	38	84
	No	16	0
	Selective policy	46	16
Which technique do you currently use to measure ER status?	Ligand binding assay	2	1
	Enzyme immunoassay	3	0
	Immunohistochemistry	77	85
	Unknown/not given	18	14
If you use immunohistochemistry what is your threshold for positivity?	Absolute no of cells staining	41 ($n=45$)	33 ($n=47$)
	5–20%	$n=28$	$n=26$
	25–40%	$n=7$	$n=6$
	50%	$n=6$	$n=4$
	70–80%	$n=4$	$n=4$ (7 not tested)
	Histoscore	34 ($n=37$)	44 ($n=63$)
	Unknown/not given	25 ($n=27$)	23 ($n=34$)

ER, oestrogen receptor.

Table 2
Results of postal survey: PR status

		(%)
Do you believe that measurement of PR is important in the management of your patients with primary invasive breast cancer?	Yes	63
	No	37
Do you have access to PR measurement?	On site	49
	Elsewhere	24
	No	27
In which patients do you measure PR?	All	35
	None	34
	Selective	31

PR, progesterone.

those from the 1997 study, are presented in Table 1. Of these, 99% stated the measurement of ER status was important in the management of their patients, an increase of 11.5% from the previous study. Access to ER measurement was available in 100% of units, although this facility was off-site in 21%. ER status was determined on all new breast cancers in 84% of units while the remaining 16% used a selective policy. Nearly all units used an immunohistochemical technique (85%), with only one unit (1%) using a LBA. The remaining 14% did not reveal how their assays were performed. ER positivity was determined using either the percentage of cells staining positive alone (33%) or in combination with the intensity of staining (44%). In the former group, the absolute cut-off point for positivity varied widely from 5 to 80% of the cells. Although the majority of units used a cut-off point in the range 5–50% (36/40), the remaining four units used a much higher value (70–80%) as in the previous study. The reasons for this are not clear.

The results of questions relating to PR measurement are shown in Table 2. Of the 170 responding units, 107 (63%) felt that PR measurement was important with access to PR measurement on-site in 49% and off-site in 24%. PR was not measured in 34% of units, while the remainder used it selectively (31%) or on all new patients (35%).

The response rate from Ireland was poor with 31 (32%) completed questionnaires returned. Of these, all units felt that ER measurement was important with ER being measured in 94%, and PR in 48%, of newly diagnosed breast cancers.

4. Discussion

This study confirms that ER measurement is increasingly recognised by breast surgeons as being important in the management of patients with primary breast

cancer. Furthermore, all responding units now have access to this facility, compared with 84% previously, and measure ER either on all new patients (84%) or use a selective policy (16%).

These results highlight an increased use of immunohistochemistry (IHC) when compared with the previous study (85% versus 77%). These figures are likely to be even higher since most of the 14% who failed to reveal their assay technique almost certainly use IHC also.

There is still variability, however, not only in the technique of measurement used, but also in the absolute cut-off point for positivity. If the cut-off point for defining ER positivity is set too high, a substantial number of patients will be denied the known benefits of adjuvant hormone therapy [1]. Furthermore, it is essential the laboratories adopt a protocol which allows semiquantitative reporting of results, and participate in an external quality assurance (EQA) scheme, since values are meaningless if the quality of their assay can not be validated. A protocol and scoring system, currently used in several UK and European laboratories, has recently been proposed as a way of providing results which are highly reproducible and suitable for EQA [5]. Adoption of such a protocol would allow units to reach a consensus regarding the choice of technique as well as the threshold for positivity.

The measurement of PR status by the majority of Breast Units in the UK (63%) will allow the identification of patients with ER- and PR-negative tumours who are unlikely to benefit from adjuvant tamoxifen [6].

Since ER status strongly influences the choice of adjuvant systemic therapy, and accrual to clinical trials [4], the measurement of ER ± PR status in all primary, invasive breast cancers should become the standard of care. This, together with the standardisation of the technique of measurement, as well as the threshold for receptor positivity, is essential if we are to move towards more appropriate and individualised treatment for all women with breast cancer.

Acknowledgements

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