TheGMS
The Gazette of Medical Sciences
https://www.thegms.co ISSN 2692-4374 DOI https://www.doi.org/10.46766/thegms

Oncology | Retrospective Study

A retrospective analysis of Estrogen Receptors in Breast Cancer and its comparison with national standards

Zaibun Nisa[1*], Soha El Shiekh[2]

[1]Consultant Histopathologist, Queen's hospital, Romford.
[2]Consultant Histopathologist, Royal Free Hospital.

Submitted: 06 February 2022
Approved: 01 March 2022
Published: 02 March 2022

Address for correspondence:
Dr Zaibun Nisa, Consultant Histopathologist, Queen's hospital, Romford.

How to cite this article: Nisa Z, Shiekh SE. A retrospective analysis of Estrogen receptors in Breast Cancer and its comparison with national standards. G Med Sci. 2022; 3(1): 070-073. https://www.doi.org/10.46766/thegms.oncol.22020601

Abstract

Estrogen receptor (ER) positive tumours are more common than ER negative tumours and tend to have a better prognosis. These tumours respond well to endocrine therapy as compared to ER negative tumours, thus avoiding the harmful effects of chemotherapy. Moreover, since ER positive tumours are associated with slow tumour growth and low histology grade, it increases the overall survival.

Due to the aforementioned reasons, ER testing should be done in 100% of breast cancer cases. It is also vital that low ER positive tumours are not erroneously reported ER negative or vice versa.

Stringent protocols and strict quality control is maintained under the UK NEQAS to avoid false positive or false negative results. Also, regular audits were advised by CQC in a report published in April 2013. In order to meet the requirements and maintain standards, a five-year analysis of the ER audit was done in Royal Free hospital.

Keywords: Pathology, surgical, Breast Cancer, Estrogen receptors, Endocrine therapy

Introduction

Hormone receptor assay in breast cancer act as a predictive and prognostic marker. It helps in predicting whether endocrine therapy or chemotherapy should be given to patients [1]. The prognostic significance of ER testing is that ER positive tumors are usually low-grade tumors and are associated with slow tumor growth. However, accurate ER testing is essential and is crucial to the correct management of the patients.

Regular audits on hormone positivity rates and to benchmark against other laboratories was advised by the Care Quality Commission (CQC). All UK clinical laboratories utilizing immunohistochemical assays for Estrogen Receptors (ER) and Progesterone Receptors (PR) as predictive or prognostic markers must participate in an appropriate External Quality Assurance (EQA) programme, such as that run by the UK National External Quality Assessment Scheme for Immunocytochemistry and in situ hybridization (UK NEQAS ICC and ISH) [2].

This was done following an incident in Nottingham hospital in April 2013, where wrong ER interpretation was made in 120 women which affected their treatment strategies. In the report above, a target level of 300 breast cancer ER assays per year for screening cases was identified. This number was recommended to identify any outliers in ER positivity rates and enable appropriate prompt action to be taken to ensure patient safety and protect patients [3].

Therefore, in order to meet the requirements, set out by CQC, regular audits were carried out in the Department of Cellular Pathology, Royal Free Hospital over a 5-year

period (2010-2013, 2018, 2019). The aim of the audit was to ensure ER testing standards were maintained consistently and to show comparability of ER testing with the national standards.

Methodology

A retrospective Winpath search was done and all women who had ER tested on biopsy or resection with primary or metastatic breast carcinoma and screening cases were included. The exclusion criteria were no tissue such as FNA diagnosis and ER testing done on other organs as a diagnostic panel.

ER testing was done by automated immunohistochemical methods using either ER (Dako) or ER (Ventana) clone. Appropriate positive and negative controls were used. ER scoring was done by Allred scoring system [4] which is as follows:

Score for proportion	Score for intensity
0 = no staining	0 = no staining
1 = <1% nuclei staining	1 = weak staining
2 = 1-10% nuclei staining	2 = moderate staining
3 = 11-33% nuclei staining	3 = strong staining
4 = 34-66% nuclei staining	
5 = 67-100% nuclei staining	

- Only nuclear staining is assessed
- The scores are summed to give a maximum of 8
- The cut off for positivity is score ≥ 3
- Only invasive component is considered for scoring.

Results

- Total number of samples investigated for breast carcinoma in the 5-year period: 1892
- Number of cases tested for ER: 1475.
- Number of cases not tested for ER: 18. The reasons for this included microinvasive carcinomas, metastatic carcinomas and cases which were tested but no supplementary was added.
- The number of cases tested for ER was 216 in 2010, 221 in 2011, 181 in 2012, 184 in 2013 and 673 in 2019. The proportion of ER testing was 98% in 2010, 100% in 2011, 99% in 2012, 100% in 2013 and 98% in 2019 (Table 1).
- The number of cases tested positive for ER ranged from 80% in 2012 to 90% in 2011. It was 82% in 2013, 83% in 2010 and 85% in 2019 (Table 2).
- Overall, ER positivity rate was 85% with 86% for primary & 64% for metastatic breast cancer.
- Screening detected invasive breast cancer cases under North London Breast Screening Service (NLBSS): 30% with ER positivity: 98-99%.

Comparison with NHS National breast screening program

In our audit, the overall ER positivity rate was 85%, with 86% for primary & 64% for metastatic breast cancer. This was comparable with the UK NEQAS which showed 82.6% overall ER positivity with 86% for primary breast cancer and 69.7% for metastatic breast cancer [5].

Screening detected invasive breast carcinoma cases under NLBSS was 30% with 98-99% ER positivity. This was comparable with the NHS National breast screening program with 41.5% invasive cancers showing 91.4% ER positivity [6].

So, the proportion of ER testing was maintained between 98-100% and the rate of ER positivity ranged between 80-85% in the 5-year period.

As semiquantitative predictive tests, ER and PR require a greater degree of technical and interpretive accuracy than routine immunohistochemistry analyses which are purely diagnostic (positive or negative) and used as part of a panel. False positive and false negative results can lead to direct patient harm as a consequence of lack of benefit and unnecessary side effects from use of inappropriate treatment and denial of benefit from appropriate treatment, respectively.

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It is also essential that quality checks are regularly made in the laboratory to get accurate ER results [2]. This is maintained by:

- Fixation: 6-8hrs (core biopsy); 24-48hrs (excision)
- Clone of antibody used
- Tissue control: Composite tumour blocks containing receptor rich, receptor poor and negative tissues cell lines.
- Internal control assessment is important if fixation is suboptimal
- Automated staining: stringent compliance to standard operating procedures developed in assay validation should be adhered to and QC documentation must be in place.
- Participation in NEQAS on a quarterly basis.

Conclusion

In conclusion, all breast cancer cases should be tested for ER and documented. ER positivity rates should be comparable to UK NEQAS and National breast screening services. In case of significant variations, individual training and laboratory procedures should be reviewed. Regular audits should be performed annually to ensure that the performance standards are maintained.

Acknowledgements

We express our gratitude to all the laboratory staff for their constant hard work in preforming the immunohistochemical testing.

Author contributions

Dr Nisa collected and compiled the data while Dr El Sheikh did the calculations and compared the data with the national standards.

Conflict of interest: None declared.

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Table 1. Number of cases tested for ER and cases not tested for ER in 5 years

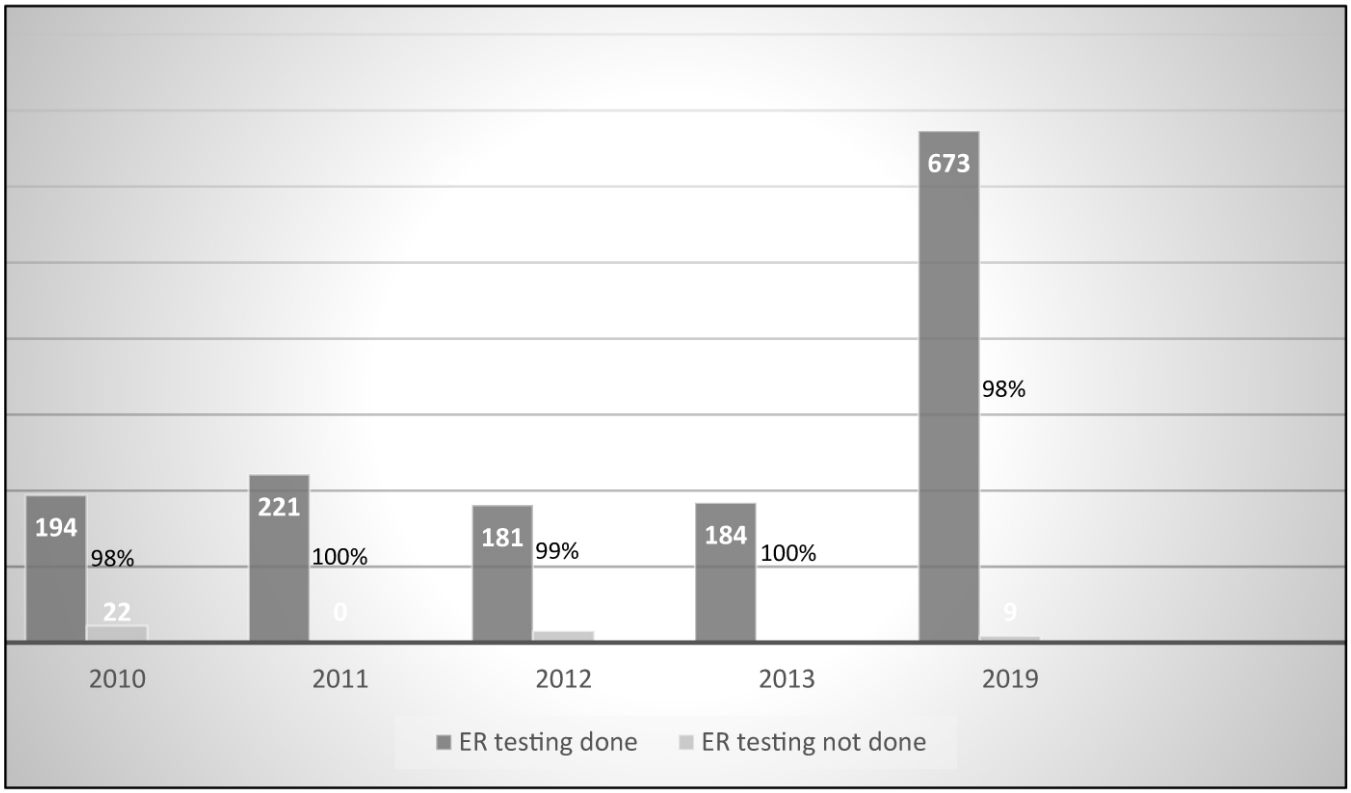
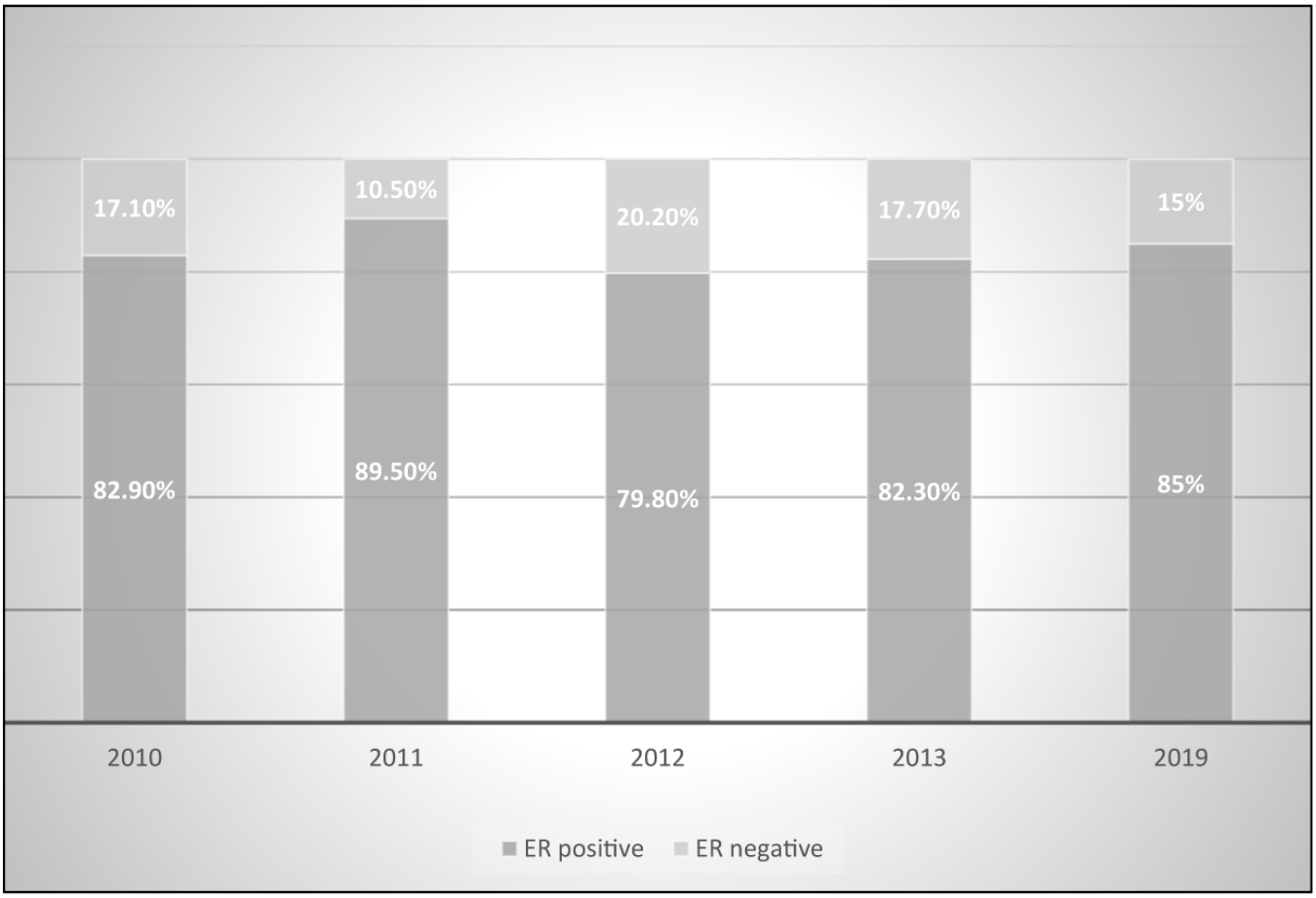


Table 2. ER positivity rates in 5 years



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