

Abstracts for Presentation at the BASO ~ The Association for Cancer Surgery Annual Scientific Meeting 17th- 18th November 2019

Ronald Raven Prize Papers

Sunday 17th November 2019, 09.00 to 10.00

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PREDICTING RESPONSE TO NEOADJUVANT THERAPY IN OESOPHAGEAL ADENOCARCINOMA PRE-TREATMENT BIOPSIES

Megan Lloyd, Fereshteh Izadi, Rob Walker, Annette Hayden, Jack Harrington, Ben Grace, Jo Horne, Maria Machado, Irina Fesenko, Saqib Rahman, Tim Underwood. *University of Southampton, Southampton, UK*

Background: We urgently require tools to predict response to neoadjuvant therapy (NAT) in oesophageal adenocarcinoma. This pilot study aims to identify differentially expressed genes in pre-treatment biopsies between responders and non-responders to NAT.

Method: Diagnostic formalin fixed paraffin embedded tissue from 26 responders (Mandard Tumour Regression Grade (TRG) 1-2) and 30 non-responders (TRG 4-5) underwent gene expression profiling with two nuclease protection assays (EdgeSeq, HTG – Oncology Biomarker Panel and Precision Immuno-Oncology Panel). Analysis of clinical characteristics and gene expression was performed in “R”.

Results: There were no differences in pre-treatment characteristics between responders and non-responders. Responders had better mean overall survival than non-responders (3.76 years and 2.95 years, respectively. $p=0.047$).

Genes significantly up-regulated in responders were involved in apoptosis and cell cycling whilst those upregulated in non-responders were involved in cytokine signalling and the immune response. Using a threshold of log2 fold change >1 and $p < 0.05$, we identified 26 and 11 differentially expressed genes between responders and non-responders from the Oncology Biomarker Panel and Immuno-Oncology Pane, respectively. Using the 26 differentially expressed genes from the biomarker panel, we created a model to predict response to NAT, which had an overall accuracy of 73% with sensitivity of 80% and specificity of 70%.

Conclusion: Accurate prediction of response to NAT would allow non-responders to be diverted straight to surgery or to receive an alternative treatment. Further study using widely available stored tissue may allow us to improve the performance of our model to predict response to NAT in the clinic.

21.

SYMPTOMATIC BREAST CANCERS AND WHY BREAST PAIN MAY NOT ALWAYS NEED CLINICAL REVIEW

Jeremy Batt, Nicola Cook, Clare Fowler. *Cheltenham General Hospital, Cheltenham, UK*

Background: Breast pain contributes a heavy burden to the symptomatic breast clinic, accounting for a large number of referrals due to patient/clinician subjective anxiety and unclear aetiology. We assess the link between breast pain and cancer with a view to easing the demand on breast services.

Methods: All new breast cancer diagnoses were identified from the MDT outcomes for the 12 months between October 2017 and 2018. Presenting symptoms were identified from the GP and consultant letters. Examination findings were checked with details on imaging requests.

Results: 434 new symptomatic cancer diagnoses were made in patients with an average age of 68. 332 patients were referred by GPs as two-week waits. New lumps accounted for 294 ipsilateral cancer diagnoses, nipple symptoms for 28 and pain with normal examination for 4 (screening aged patients). Incidental cancers in the contralateral, non-symptomatic breast were identified via mammography alone in 5 cases. 3 further cases were detected when previously unfound lumps were identified in clinic by the consultant and were subsequently confirmed via mammography.

Conclusions: Pain does not appear a reliable symptom in breast cancer

presentation. It was more common for patients to have incidental, contralateral asymptomatic cancer than it was for patients with pain alone to have underlying ipsilateral cancer. All cancers were identified accurately on mammography. There is little benefit in repeated clinical examination by a Breast Specialist in patients presenting with pain as an isolated symptom. Direct to test with mammography could be safe, effective and efficient alternative practice.

25.

MACHINE LEARNING TO PREDICT EARLY RECURRENCE AFTER OESOPHAGEAL CANCER SURGERY

Saqib Rahman¹, Robert Walker¹, Megan Lloyd¹, Ben Grace¹, Gijs van Boxel², B Feike Kingma², Jelle Ruurda², Richard van Hillegersberg², Scott Harris³, Simon Parsons⁴, Stuart Mercer⁵, Ewen Griffiths⁶, J.Robert O'Neill⁷, Richard Turkington⁸, Rebecca Fitzgerald⁹, Timothy Underwood¹. ¹*Cancer Sciences Unit, University of Southampton, Southampton, UK;* ²*University Medical Centre, Utrecht, Netherlands;* ³*Public Health Sciences & Medical Statistics Department, University of Southampton, Southampton, UK;* ⁴*Department of Surgery, Nottingham University Hospitals NHS Trust, Nottingham, UK;* ⁵*Department of Surgery, Portsmouth Hospitals NHS Trust, Portsmouth, UK;* ⁶*Department of Upper Gastrointestinal Surgery, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK;* ⁷*Cambridge Oesophagogastric Centre, Addenbrookes Hospital, Cambridge University Hospitals Foundation Trust, Cambridge, UK;* ⁸*Centre for Cancer Research and Cell Biology, Queen's University Belfast, Belfast, UK;* ⁹*Hutchison/Medical Research Council Cancer Unit, University of Cambridge, Cambridge, UK*

Background: Early cancer recurrence after oesophagectomy is a common problem with an incidence of 20-30% despite the widespread use of neoadjuvant treatment. Quantification of this risk is difficult and existing models perform poorly. Machine learning techniques potentially allow more accurate prognostication in areas of complex variable interaction. This study aimed to develop a predictive model for early recurrence using machine learning techniques and routinely available clinico-pathologic characteristics in a large, international, multi-centre cohort.

Methods: Consecutive patients who underwent oesophagectomy for adenocarcinoma and had neoadjuvant treatment in 6 UK and 1 Dutch oesophago-gastric units were analysed. Using clinical characteristics and post-operative histopathology, models were generated using elastic net regression (ELR) and the machine learning methods random forest (RF) and XG boost (XGB). Finally, a combined (Ensemble) model of these was generated. The relative importance of factors to outcome was calculated as a percentage contribution to the model.

Results: In total 812 patients were included. The recurrence rate at less than 1 year was 29.1%. All of the models demonstrated good discrimination. Internally validated AUCs were similar, with the Ensemble model performing best (ELR=0.785, RF=0.789, XGB=0.794, Ensemble=0.806). Performance was similar when using internal-external validation (validation across sites, Ensemble AUC=0.804). In the final model the most important variables were number of positive lymph nodes (25.7%) and vascular invasion (16.9%).

Conclusions: The derived model using machine learning approaches and an international dataset provided excellent performance in quantifying the risk of early recurrence after surgery and will be useful in prognostication for clinicians and patients.

30.

BREAST SCREENING AGE EXTENSION; HIGH CANCER PICK UP RATE OF SMALL BREAST CANCERS AMENABLE TO BREAST AND AXILLARY CONSERVATION

Lucy Cielecki, Sian Burley, Blossom Lake, Sue Williams, Donna Appleton. *Shrewsbury & Telford Hospital NHS Trust, Telford, UK*

Background: In 2012, Public Health England (PHE) extended the age range for breast screening up to 73. For screening to be an effective tool, one of