The presence of lymph node metastasis puts patients with resectable esophageal squamous cell carcinoma (ESCC) at a high risk of disease recurrence, and these patients would benefit from neoadjuvant treatment. However, current clinical staging is not enough to capture all patients with high-risk disease, and novel diagnostic tools are required to improve the accuracy of treatment planning. We tried to explore a better prediction using genomic features from large-scale gene mutation data.

The major public data repositories of whole-exome sequencing for ESCC were involved in this study. The absolute differences in gene mutation frequency were calculated using Fisher’s exact test in nodal negative versus nodal positive patients. The classification of gene mutation status was dichotomized as wild-type and mutant type. To find a reliable gene panel that could provide sufficient population coverage, we set the cut-off level above 85% in both nodal phenotypes. The genomic classifier for nodal metastasis risk prediction was further generated by LASSO logistic regression analysis with 10-fold cross-validation based on the topmost significantly different genes.

Above the threshold values, a total of 120 differentially mutated genes were identified in the 561 ESCC genomic sequencing data. The population coverage rates were 85.97% in the nodal positive group (n = 335) and 88.05% in the nodal negative group (n = 226), respectively. According to the LASSO logistic regression approach, a panel of 112 topmost relevant genes (termed LNM112) was selected. The receiver operating characteristic curve of the LNM112 predictive model was plotted with an area under the curve value of 0.95 (95% CI: 0.93–0.96). The sensitivity and specificity of the LNM112 model were 96.72% (324/335) and 71.24% (161/226), respectively.

We identified a genomic signature (112 genes) from the large-scale genomic repertoires capable of predicting lymph node metastasis in ESCC. It can be incorporated into the current staging modalities to help inform treatment decisions, and external validation is warranted in different populations.

Diagnostics of esophageal adenocarcinoma, or Barrett’s esophagus, a pre-malignant condition associated with an increased risk of the adenocarcinoma, currently requires expensive and invasive endoscopy-based procedures, which are often only performed when obvious symptoms have manifested (usually at a late stage of the disease). A targeted mass spectrometry-based method was developed to analyse serum samples for esophageal adenocarcinoma.

Panels of lectin-pulled down serum protein biomarkers were identified that correlate with the presence of early stage esophageal adenocarcinoma (high grade dysplasia). The method was automated and optimised the methodology to measure 33 target peptides in the lectin pulldown in a short 20 minute mass spectrometry run. Analysis of an initial cohort (n = 50) shows the method to be robust and reproducible with an average intra-day CV of 9.3% across the 33 peptides and an average inter-day CV of 11.5%. A larger cohort (n = 266) showed consistent results and was used to build statistical models which distinguished between disease status, using protein biomarker measurements and simple clinical parameters. Several models achieved good discrimination with AUROC values ranging from 0.89–0.97. Model validation was undertaken in the smaller cohort, with the two best performing models achieving AUROC values of 0.82 and 0.87.

The assay has the potential to produce a clinically viable diagnostic test to support screening and early detection in populations at high risk of esophageal adenocarcinoma and Barrett’s esophagus.

Oesophageal adenocarcinoma (OAC) is a deadly disease with an increasing incidence globally. Treatment outcomes with traditional therapy have largely plateaued and responses to immunotherapy are modest at best, necessitating the need for better biomarker driven selection. We aimed to unravel the tumour neoantigen landscape and immune microenvironment in OAC patients to aid improved patient selection and inform novel immunotherapy trials.

To characterise the tumour immune microenvironment and neoantigen landscape of OACs, we performed DNA sequencing (n = 117) and RNA sequencing (n = 115) on biopsies taken at pre-treatment endoscopy. Using expression-based computational methods we analysed transcriptomic data to profile infiltration levels of 28 immune cell populations and their functional orientation, as well as stromal signatures and immune checkpoint molecules. TCGA data was used for as a validation cohort. Tumour neoantigens were predicted using the pVAC-Seq pipeline.

Using an immune based classification based on the tumour microenvironment composition, we identified three distinct phenotypes, immune-enriched (IE), heterogeneously-infiltrated (HI), and immune-cold (IC). The IE group showed improved survival compared to both HI and IC, with HI showing the worst survival. The HI-group showed no difference in stromal scores to the IE group, but showed significantly decreased adaptive-immune cell infiltration, indicating that an immunosuppressive stromal compartment may be driving outcomes for these patients. No difference was seen in total or quality neoantigen load between groups, but high correlation with antigen processing machinery is seen.

Our analysis expands the knowledge of the relatively unknown tumour immune microenvironment of OAC. We have identified three immune TME-phenotypes with prognostic utility with current standard of care therapies; which may also act as potential immunotherapy biomarkers. This is being explored further in ongoing immune microenvironment research and will guide future translational studies.

Transmediastinal radical esophagectomy (TME) is a new minimally invasive approach without thoracotomy. However, transcervical dissection of subcarinal lymph nodes (SCCLN) is challenging. The shape or narrowness of the mediastinal space, especially around the aortic arch to tracheal bifurcation, may affect the difficulty. The present study aimed to clarify predictors for the difficulty of transcervical SCCLN dissection.

Patients who underwent TME between 2016 and 2019 were included (n = 126). Four indicators, the cervical angle, carina distance, aorta distance, and sternum distance, were defined as indicators of the mediastinal narrowness by 3D-CT. The relationship between the difficulty of the transcervical SCCLN dissection and clinicopathological features, including the above indicators, were investigated.

In a univariate analysis, the cervical angle (p = 0.023), aorta distance (p = 0.002), and middle thoracic tumor (p = 0.040) correlated with the difficulty. The median cervical angle (degree) and aorta distance (mm) were