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Identification Of Prognostic Markers In Early Onset Pancreatic Cancer

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Background : Early-onset pancreatic cancer (EOPC), defined as age of diagnosis ⟨45 years, is a rare condition with increasing incidence. Little is known about molecular differences between EOPC and average-age-onset pancreatic cancer (AOPC). This study aims to elucidate such differences as well as to identify potential prognostic markers in EOPC.

Methods : In total, 21 EOPC and 36 AOPC patient samples were obtained from the Biobank of the European Pancreas Centre at the Department of General Surgery, Heidelberg University Hospital. Clinical data was obtained from a prospectively maintained database. FOXC2, E-cadherin, N-cadherin, Vimentin were defined as markers of epithelial-mesenchymal transition (EMT), ki67 staining was used to assess proliferation. Immune cell infiltration was assessed using CD3 (T cells), CD20 (B cells), CD56 (natural killer cell), CD68 (macrophage), CD138 (plasma cell) stainings. Immunohistochemistry (IHC) staining were subsequently quantified using QuPath software. Bulk RNA-seq was performed in 10 EOPC samples and CIBERSORT 2.0. applied to identify immune cell enrichment. Statistical analysis was performed using GraphPad Prism 8 and SPSS.22.

Results : No patient of the cohort received neoadjuvant chemotherapy prior to potentially curative resection. In EOPC compared with AOPC, protein expression of FOXC2, N-cadherin and Vimentin was significantly increased ($p<0.001$, $p<0.001$, and $p<0.001$, respectively), while E-cadherin and ki67 was decreased ($p<0.01$, and $p<0.001$, respectively). Furthermore, CD3, and CD20 were decreased ($p<0.01$, and $p<0.01$, respectively), while CD68, CD138 were significantly increased ($p<0.05$, and $p<0.001$, respectively) in EOPC. Higher expression of CD138 was associated with longer overall survival ($p=0.006$) and relapse-free survival ($p=0.024$) in EOPC. CD56 protein expression as assessed by IHC did not differ between AOPC and EOPC, while natural killer cells were decreased in EOPC ($p=0.003$) based on transcript levels.

Conclusions : This study provides evidence that EOPC displays upregulation of EMT markers compared to AOPC. Furthermore, CD138 positive plasma cell infiltrates were identified as prognostic marker in EOPC. Functional studies are needed to elucidate the biological significance of these findings.

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