Epidermal Growth Factor Receptor Overexpression in Resected Pancreatic Cancer

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OBJECTIVES

1) To study the association between cell membrane epidermal growth factor receptor (EGFR) expression and histopathologic features and clinical outcomes in patients with resected pancreatic cancer.

2) To study the association between cytoplasmic EGFR expression and histopathologic features and clinical outcomes in patients with resected pancreatic cancer.

INTRODUCTION

• Pancreatic cancer is the fourth leading cause of cancer death in United States with 36,800 deaths and 43,140 incident cases estimated in 2010.

• Despite therapy, the 5-year relative survival rate is approximately 6%.

• Even in patients who undergo pancreatectomy, the majority of the patients develop recurrence with the 5-year overall survival of only 23.9%.

• Genetic and molecular alterations are being investigated to understand the basis of the disease aggressiveness.

• EGFR is a 170 kDa protein belonging to ErbB family of transmembrane tyrosine kinase growth factor receptors.

• Activation of EGFR in tumors results in increased cell proliferation, reduced apoptosis, increased angiogenesis, increased motility, invasion and metastasis.

• EGFR overexpression is observed in 30% to 90% of pancreatic cancers.

• The association between cytoplasmic expression of EGFR and clinicopathologic features in patients with pancreatic cancer has been reported in only one prior study.

METHODS

Patients

• Ninety patients were included in the study

• All patients underwent surgical resection for pancreatic cancer at Thomas Jefferson University from April 2008 to April 2010.

• All the cases were histologically diagnosed as ductal adenocarcinoma.

• For pathologic and immunohistochemical evaluation, 10% neutral-buffered formalin fixed and paraffin-embedded tissue blocks from surgically resected specimens were processed and 5-µm tissue sections stained into use.

• The tissue sections were stained using routine hematoxylin and eosin for histopathologic diagnosis.

• The study was approved by Institutional review Board at Thomas Jefferson University.

Immunohistochemistry

• Immunohistochemical staining for EGFR was performed using the EGFR Pharmed™ kit (Dako).

• Specimens were evaluated for both cytoplasmic and membranous immunostaining.

• A pathologist blinded to the results at Thomas Jefferson University Hospital.

• Cytoplasmic overexpression was considered positive if EGFR expression was noted in the cytoplasm in ≥10% of tumor cells.

• Cell membrane EGFR staining was divided into four categories based on intensity and completeness of staining as follows:

  • +: no membrane staining or membrane staining < 10% of cells
  • ++: complete, weak or moderate membrane staining in ≥10% of cells
  • +++: complete, strong staining in ≥10% of cells
  • Scores of 2+ and 3+ were considered membranous EGFR overexpression.

RESULTS

• 90 patients were included in the study

• The median age was 68 years (Range: 37-92 years)

• Cell membrane EGFR overexpression was observed in 51 (56.7%) patients.

• Cytoplasmic EGFR overexpression was observed in 64 (71.1%) patients.

• The median follow up time was 15.5 months.

• 52 (58%) patients had either recurrence or death.

• Ninety patients were included in the study.

• Chi-square test was used to determine the association between EGFR overexpression and clinicopathologic features.

• Proportional hazard regression analyses were used to estimate overall survival.

• Descriptive statistics were used to characterize the cohort.

• The association was analyzed using SAS statistical software (SAS Institute, Inc., Cary, NC).

• In patients with resected pancreatic cancer:

  • Cell membrane EGFR overexpression was associated with lymph node involvement by the tumor.

  • Cytoplasmic EGFR overexpression was associated with positive margins.

  • In patients with membrane EGFR overexpression, PFS was significantly shorter (median PFS:15.9 vs. 23.9 months). There was no statistically significant difference in survival, although there was a trend towards poorer survival.

  • There was no statistically significant differences in PFS and OS with cytoplasmic EGFR overexpression.

CONCLUSIONS

• Membrane EGFR overexpression is associated with poorer clinical outcomes in patients with pancreatic cancer receiving adjuvant therapy post resection.

• Cytoplasmic EGFR overexpression is not associated with clinical outcomes.