

Prognosis of resected pancreatic cancer: is the refined resection margin status dispensable?

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Pancreatic cancer is a tumor entity which is generally characterized by a poor prognosis. The only hope for cure lies in the radical resection of circumscribed tumors, or even better in the resection of precursor lesions, such as not-yet malignant intraductal papillary mucinous neoplasms. Despite radical resection, patients with supposedly completely resected pancreatic carcinomas encounter local recurrences in many cases. The high recurrence rate does not correspond with the high R0 resection rates, which were reported to be about 70 % for pancreatoduodenectomies in most large surgical series. Some specialized pathologists for pancreatic diseases established a detailed 3-dimensional analysis of pancreatic resection specimen combined with a new R1 resection status, as defined as microscopic evidence of tumor within 1 mm from a resection margin [1, 2]. Just recently, our group confirmed the relevance of the refined R1 definition in a series of 1,071 consecutive patients with resected primary pancreatic adenocarcinomas [3]. Whereas R0 and R1 resections were associated with similar prognosis in the time period prior to the revised R1 definition, the revised R0 status was one of three independent positive predictors of patient survival (the others were Tis/T1/T2 status and G1 grading).

The study presented by Janot et al. [4] investigated the prognostic relevance of the revised R1 definition in their own patient cohort of 62 potentially curative resected pancreatic head ductal adenocarcinomas. The authors did not identify significant survival differences between R0 and R1 resections when the revised R1 definition was applied, and concluded that the refined resection margin status has no impact on the prognosis of patients with pancreatic ductal adenocarcinoma (PDAC). When discussing the results of our study, Janot et al. commented that the subsumption of different species of pancreatic adenocarcinomas and the heterogeneous tumor localization including pancreatic head, body, and tail supposedly did not allow a valid conclusion. However, PDAC, undifferentiated adenocarcinomas (equals PDAC with G4 grading), and intraductal papillary mucinous carcinomas (which had similar stage-related prognosis as compared to PDAC, as demonstrated by multivariate analysis) accounted for 97.3 % of patients. More importantly, the authors' opinion that head tumors require a separate evaluation compared to body or tail tumors is not convincing. Pancreatic body and large tail tumors require a dorsal retroperitoneal mobilization plain as well as a medial transection plain dividing the lympho-vascular tissue of the mesopancreas. Apart from the respective side to the mesenteric vessels, these plains are similar to those of head tumors. Based on our study cohort [3], we can demonstrate that the refined resection margin status is relevant for all tumor locations within the pancreas. Whereas survival differences between R0 and R1 using the conventional

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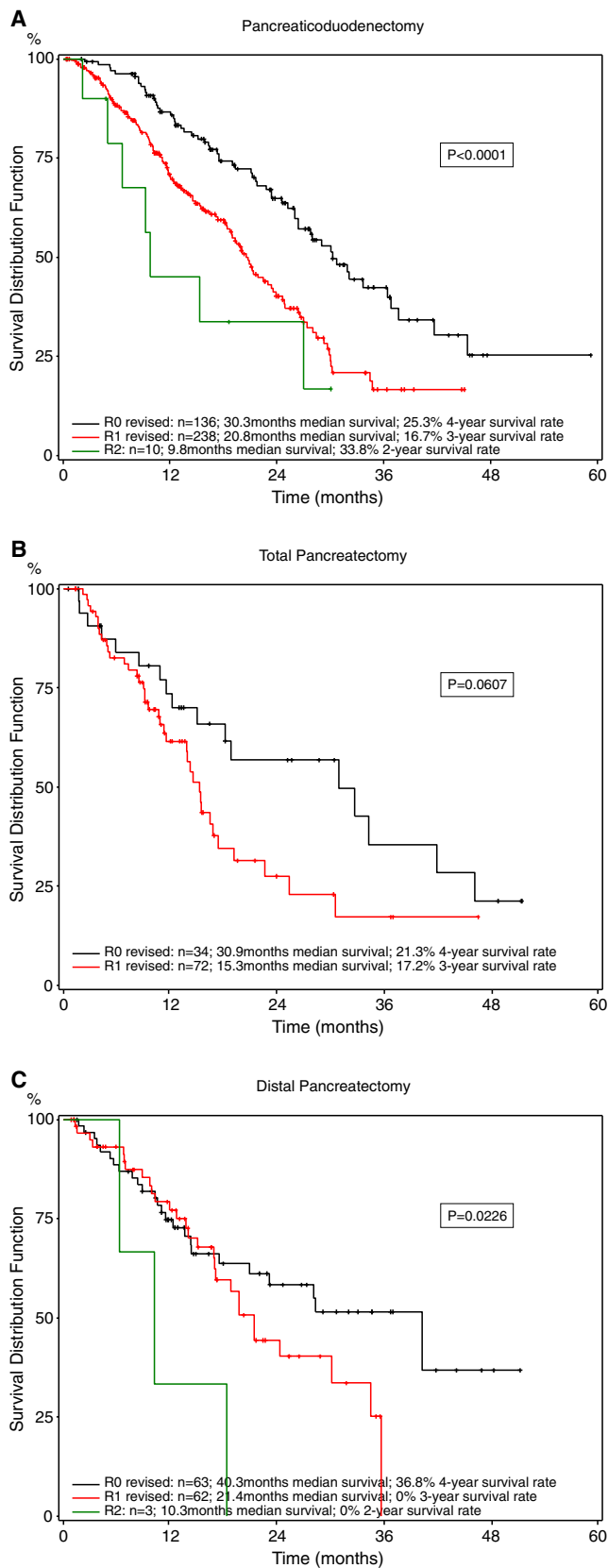


Fig. 1 Prognostic differences that were present for all resection procedures using the revised definition

definition were non-significant for pancreaticoduodenectomies ($p=0.83$), total pancreatectomies ($p=0.09$), and distal pancreatectomies ($p=0.41$), prognostic differences were present for all resection procedures using the revised definition (Fig. 1a–c).

How to proceed from here? Refining the pancreatic specimen assessment, the Glasgow group further stratified resection margins into so-called mobilization margins along the anterior or posterior aspect of the pancreas, which have no influence on survival, and transection margins of the pancreas and mesopancreas, which do influence survival [5]. Since cut-off levels for resection margin clearance are controversial [6], the inclusion of the minimal distance between tumor and resection margin into the R classification, as known from rectal cancer, may be a further option. Importantly, therapeutic regimens to prevent or adequately respond to tumor positive transection margins located along the mesenteric vessels, e.g., by the “artery first” [7] or “uncinate first” [8] approach or possibly by adjuvant chemoradiation therapy, will demand our future attention to improve survival of patients with resectable pancreatic cancer.

Conflicts of interest None.

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