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EDITORIAL – PANCREATIC TUMORS

Scoring System to Predict Survival After Resection of Locally Advanced Pancreas Cancer: What is Achieved?

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Tanaka et al., from the University of Heidelberg,[1] present an analysis of consecutive patients with locally advanced pancreatic cancer (LAPC) undergoing resection with curative intent after neoadjuvant therapy, with the goal of evaluating prognosis in this patient group. The authors, defining LAPC by National Comprehensive Cancer Network (NCCN) guidelines,[2] highlight that Response Evaluation Criteria in Solid Tumors (RECIST 1.1) is problematic for LAPC. RECIST utilizes change in tumor burden to describe treatment response,[3] but for LAPC, vascular involvement specifically rather than tumor burden alone determines resectability after neoadjuvant treatment.[1] Decision-making about resection in LAPC is notably individualized by surgeon and by center, although there is agreement that neoadjuvant therapy generally is warranted. The authors' goal was to identify, via a single-center, retrospective study, preoperative factors that could predict improved survival for patients with LAPC undergoing resection after neoadjuvant therapy.

The methodology included review of consecutive patients from a single center over a 7 year period. Included patients received neoadjuvant FOLFIRINOX prior to resection of LAPC via partial or total pancreatectomy. The authors utilized a standard measurement on interval computed tomography (CT) to objectively determine response, which was a ratio of tumor size post/pretreatment and density post/pretreatment. Changes in vascular involvement were determined by expressly noting a change in the length and degree of tumor contact for vascular involvement. The study included 62 resected patients, of whom nearly half underwent total pancreatectomy, and in all, 85% required venous and/or arterial resection. The authors proposed a scoring system for prognosis based on factors relating to survival in this cohort of resected patients, with increasing points assigned to factors independently predictive of survival (tumor shrinkage, tumor density, and post-chemotherapy Ca19-9). The authors identified a significantly shorter recurrence-free and overall survival for those patients with a lower score (2 or less) than for those with a score of 3–5, with the median difference in overall survival being 31 months.[1]

Given that the study includes a modest sample size of patients undergoing extremely complex multidisciplinary pancreas cancer care in a high-volume, tertiary care center, generalizability is limited. There is no comparison group of nonoperated patients, nor a validation cohort,[1] thus constraining at this time a broader understanding of the discriminatory capacity of this scoring system. However, should the present study's findings be validated in a subsequent cohort, results may be able to be extrapolated to other similar centers, used to guide referral to tertiary centers for patients seen in smaller centers who may benefit from resection, and/or to facilitate development of guidelines critical to the advancement of care for this patient group. The identification of factors relevant to predicting improved postoperative survival and better delineating which patients would benefit from resection and which patients would not, is of high interest for both pancreatic cancer surgeons and other providers, as well as for patients and families.

The authors highlight the limitations of radiology in suggesting a response to neoadjuvant therapy, and they incorporate a means of accounting for radiologic response by using size and tumor density. This is relevant for

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pancreatic adenocarcinoma, which has a high proportion of stroma and fibrosis. Because perivascular response to neoadjuvant therapy is difficult to predict with current imaging options, many pancreatic surgeons currently do not rely on improvement in the Peri-vascular involvement, but rather look for subjective disease stability in the context of other indicators of successful treatment such as a decline in Ca19-9[4] and tolerance of treatment. The scoring system developed here includes measurable and objective radiologic changes, which, if validated, may facilitate interpretation of interval imaging in this patient group.

The present study raises several points of interest as to the estimation of which LAPC patients are appropriate candidates for extensive resections. To offer technically feasible and safe resections when vascular, particularly arterial, reconstruction is performed, the authors undertook a much higher rate of total pancreatectomy (42%) than is typically performed for pancreas cancer. Since this study focuses solely on preoperative factors that predict postoperative survival, ample questions arise that should be included in subsequent studies. For example, consideration of total pancreatectomy requires preparation and then long-term support for both brittle diabetes and exocrine insufficiency. Not all patients are able to manage being a-pancreatitic; some patients may thus be excluded from resection whose score would otherwise suggest possible success in this scenario. Additionally, nearly half of patients experienced major morbidity, which also warrants further investigation and delineation. This complication burden is particularly relevant in terms of the quality of life of the patient as well as in terms of one of the authors' stated goals, which is to determine which patients may benefit from adjuvant therapy. Patients experiencing major morbidity are likely to be delayed in initiation of, or excluded from, adjuvant therapy, which in turn may prove to impact survival in larger series.[5]

One other interesting point presented here is the margin status of patients undergoing resection in this study. As noted, the vast majority had a vascular reconstruction as well. The margins are reported as R0 > 1 mm (which is the standard definition of R0[2]) and the remainder reported as R0 direct, which includes those with close margins as well as the > 1 mm group. Thus, 31% of patients had an R0 margin according to the margin classification standards, leaving many attributed as close or directly microscopically positive. Yet, there was no difference in margin status between the low and high groups in the scoring system, further supporting the utility of the scoring system for this scenario, in which patients have been fully treated preoperatively. This finding also highlights the current lack of clarity or standardization of margin reporting for pancreas cancer and underscores that the impact of the margin status is unclear in patients receiving neoadjuvant therapy.[6]

So, what is achieved with the proposed scoring system? Despite the limitations noted by the authors, the study by Tanaka et al.[1] is thought provoking and raises interesting questions, given that the proposed scoring system distinguishes recurrence-free and overall survival remarkably well between the low- and high-scoring groups. In this highly lethal disease, a recurrence-free survival difference of 10 months and overall survival difference of 31 months is impressive. More patients previously or initially considered unresectable are now being taken for potentially curative resection. Even with optimal staging and evaluation, it is challenging to identify which patients will most benefit, and certainly it is important to exclude from major surgery those who will not benefit from it.

The scoring system requires validation in a separate and larger cohort but shows promise as a straightforward, easy-to-apply tool that can be calculated entirely based on preoperative information. Its ultimate application has yet to be determined in the absence of confirmatory studies but could be considered as support for attempted resection in patients with a high score, as well as guidance for discussions with patients and families as to whether resection is indicated.

DISCLOSURES The author declares no conflicts of interest.

REFERENCES

1. Tanaka M, Heckler M, Mihaljevic AL, et al. Induction Chemotherapy with FOLFIRINOX for Locally Advanced Pancreatic Cancer: A Simple Scoring System to Predict Effect and Prognosis. *Ann Surg Oncol*. 2022. https://doi.org/10.1245/s10434-022-12569-y.
2. NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. Version 1. (2022). Accessed 11/20/22.
3. Eisenhauer EA, Therasse P, Bogaerts J, et al. New Response Evaluation Criteria in Solid Tumours: Revised RECIST Guideline. *Eur J Cancer*. 2009;45:228–47. https://doi.org/10.1016/j.ejca.2008.10.026.
4. Van Veldhuisen E, Vogel JA, Klompmaker S, et al. Added Value of Ca19-9 Response in Predicting Resectability of Locally Advanced Pancreatic Cancer Following Induction Chemotherapy. *HPB*. 2018;20:605–11. https://doi.org/10.1016/j.hpb.2018.01.001.
5. Mintziras I, Wächter S, Manoharan J, et al. Postoperative Morbidity Following Pancreatic Cancer Surgery is Significantly Associated with Worse Overall Patient Survival; Systematic Review and Meta-analysis. *Surg Oncol*. 2021;38:101573. https://doi.org/10.1016/j.suronc.2021.101573.
6. Schmocker RK, Delitto D, Wright M, et al. Impact of MARGIN status on Survival in Patients with Pancreatic Ductal Adenocarcinoma Receiving Neoadjuvant Therapy. *J Am Coll Surg*. 2021;232:405–13. https://doi.org/10.1016/j.jamcollsurg.2020.11.018.