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ASO AUTHOR REFLECTIONS

ASO Author Reflections: Recurrence Following Post-neoadjuvant Pancreatectomy: How Can We Do Better?

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PAST

The very high rate of early recurrences following upfront pancreatectomy for pancreatic adenocarcinoma is one of the main reasons for the ongoing shift towards a chemotherapy-first policy.[1] However, the extent to which neoadjuvant therapies prolong the recurrence-free interval following pancreatectomy is ill defined.

PRESENT

In a comprehensive analysis of 315 patients with initially resectable and borderline resectable tumors, the median recurrence-free survival following post-neoadjuvant pancreatectomy was 15.7 months, with 1-year and 3-year recurrence rates of 41.9% and 74.2%, respectively. Remarkably, 83.3% of recurrences were at distant sites. The only preoperative factors independently associated with prolonged recurrence-free survival were Ca 19.9 normalization, ΔCa 19.9 $>$ 50%, and post-treatment tumor size $<$ 20 mm. Interaction analysis suggested a more robust risk reduction when biochemical response occurred in patients with initially elevated baseline values. A Ca 19.9 drop $>$ 50% was a protective factor even in patients with tumors $>$ 20 mm. In a model incorporating pathologic variables, R-status, T-status, and N-status were all associated with disease recurrence.[2]

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FUTURE

The very high rate of early recurrences following post-neoadjuvant pancreatectomy for initially resectable and borderline resectable tumors warrants future investigation to enucleate patients who really benefit from resection. Interestingly, the timing and pattern of recurrence was comparable to pre-neoadjuvant era, although a positive impact relative to upfront resection would likely become evident accounting for the immortal time equal to the duration of preoperative treatment. In our study, the value of baseline resectability status, chemotherapy regimen, radiation therapy, and RECIST response as surrogate endpoints for recurrence could not be proven. While post-treatment gross tumor size and Ca 19.9 normalization and its percentage variation were associated with recurrence, their clinical utilization remains somewhat unrefined, calling for better and more personalized approaches. In the foreseeable future, detection of circulating tumor cells and circulating tumor DNA could allow real-time monitoring of treatment effects, while radiomics could exploit the latent information present in radiological examinations, linking quantitative imaging data with response to systemic therapy.[3, 4]

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