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Role of Surgery in Patients with G1-G2 Pancreatic Neuroendocrine Tumors and Synchronous Liver Metastases

Valentina Andreasi, Stefano Partelli, Anna Battistella, Domenico Tamburrino, Nicolò Pecorelli, Stefano Crippa, Massimo Falconi.

Pancreatic and Transplant Surgery Unit, Pancreas Translational and Clinical Research Center, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy.

BACKGROUND

The liver represents the most common site of metastatic involvement in patients with pancreatic neuroendocrine tumors (PanNET). While surgery remains the cornerstone of treatment for localized disease, its role in the metastatic setting is still debated. Notably, there is a lack of robust comparative data evaluating the outcomes of surgical intervention versus systemic therapy in patients with metastatic PanNETs. The aim of this study was to compare progression-free survival (PFS) and overall survival (OS) in patients with G1-G2 PanNENs and liver metastases (LMs) who underwent either surgical or medical treatment.

METHODS

This is a retrospective cohort study that included patients with histologically confirmed G1-G2 PanNENs and synchronous LMs treated between 2010 and 2024 at San Raffaele Hospital (Italy). Patients were divided into two groups based on initial treatment strategy: surgery versus systemic treatment. A propensity score matching (PSM) was performed to minimize baseline differences between the groups.

RESULTS

Overall, 82 patients were included. Of these, 48 (58%) underwent surgical resection and 34 (42%) received medical treatment as first-line therapy. A higher proportion of females was observed in the surgical group (60%) compared to the medical treatment group (32%) ($p=0.012$). The surgical group had also a significantly longer follow-up, with a median of 62 months, compared to 23 months in the non-surgical group ($p<0.001$). After a median follow-up of 44 months, disease progression occurred in 56 patients (68%), and 18 patients (22%) died during the study period, with 17 deaths attributed to PanNET progression. A trend towards a longer PFS in the medical treatment group was observed ($p=0.119$), whereas OS was comparable between the two groups ($p=0.419$). After PSM (based on gender and follow-up duration), the medical treatment group exhibited a significantly longer PFS compared to the surgical group: 20 months vs. 9 months, respectively ($p=0.033$). No statistically significant difference in OS between the two groups ($p=0.567$) was confirmed after PSM.

CONCLUSIONS

The present study demonstrated that patients with G1-G2 PanNENs and LMs who were managed

with medical therapy experienced longer PFS compared to those who underwent surgery. Also, no significant OS benefit was observed in the surgically treated group. These findings suggest that the role of surgery in the metastatic setting is uncertain and likely restricted to highly selected cases, especially when complete oncological clearance cannot be reached. Further prospective, ideally randomized, trials are needed to define optimal treatment strategies and identify subgroups of metastatic patients that may benefit the most from surgery.

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