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Letter to the Editor

Comment on "Standard Pancreatoduodenectomy Versus Extended Pancreatoduodenectomy with Modified Retroperitoneal Nerve Resection in Patients with Pancreatic Head Cancer: A Multicenter Randomized Controlled Trial"

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Dear Editor,

Pancreatic head cancer remains one of the most lethal malignancies, with a 5-year overall survival (OS) rate of approximately 10%. In patients with stage I–II disease, radical resection offers the only potentially curative treatment; however, the high risk of local and/or distant recurrence continues to limit its benefit. Consequently, the optimal extent of surgical dissection has long been debated [1,2].

Japanese and Korean randomized controlled trials (RCTs) have demonstrated that 360° circumferential dissection of the celiac and superior mesenteric artery (SMA) plexuses may improve R0 resection rates but results in intractable diarrhea, malnutrition, and impaired quality of life. A subsequent Korean RCT limited the dissection to the right 180° hemicircumference, achieving comparable oncologic outcomes with lower morbidity. Thus, the optimal extent of neural plexus dissection in pancreatoduodenectomy remains controversial [3,4].

A recent multicenter, open-label, phase III RCT conducted in six high-volume Chinese centers randomized 400 patients with stage I–II pancreatic head cancer to standard pancreatoduodenectomy (SPD) or extended pancreatoduodenectomy (EPD) [5]. EPD included right-sided 270° dissection of the celiac-SMA plexus and removal of lymph node (LN) stations 8a, 8p, 9, 12, 14a, 14b, 16a2, and 16b1, with venous resection/reconstruction when necessary. The primary endpoint was OS, with disease-free survival (DFS), morbidity, and mortality as secondary outcomes. Although OS did not differ significantly between the groups (23.0 vs. 20.2 months; $p = 0.10$), DFS was significantly longer in the EPD arm (16.1 vs. 13.2 months; $p = 0.031$). The most notable improvement occurred among patients with preoperative CA19-9 < 200 U/mL, who achieved superior OS and DFS (30.8 vs. 20.9 months; $p = 0.009$). Morbidity rates were comparable. The incidence of diarrhea at 3 months was 5.0% in SPD and 7.5% in EPD, indicating that a functionally limited 270° dissection can balance oncologic radicality and quality of life [5].

A recent meta-analysis of eight studies involving 687 patients reported that extended lymphadenectomy failed to improve OS and may increase morbidity [6]. Nevertheless, the current trial showed that EPD significantly reduced locoregional recurrence (16.5% vs. 35.2%, $p < 0.001$) and mesenteric LN relapse (4.0% vs. 10.1%, $p = 0.022$). Subgroup analysis revealed that patients with CA19-9 ≥ 200 U/mL experienced predominantly systemic recurrence (>80%), suggesting that micrometastasis rather than locoregional failure drives prognosis. In contrast, patients with CA19-9 < 200 U/mL derived clear benefit from EPD. CA19-9 therefore appears to be not only prognostic but also predictive for tailoring surgical extent. Local control with EPD, combined with adjuvant systemic therapy, may provide optimal outcomes [7].

Approximately 86% of patients received adjuvant chemotherapy, with comparable completion rates between groups. Even among these, DFS remained 3.2 months longer in the EPD arm (17.7 vs. 14.5 months; $p = 0.019$) [5].

Modern phase III evidence has confirmed that multi-agent adjuvant therapy particularly modified FOLFIRINOX significantly prolongs OS following resection [8]. Hence, achieving adequate local clearance with EPD, alongside effective systemic control, represents a biologically rational dual strategy. Additional subgroup analyses revealed that patients with well- or moderately differentiated tumors and no PV/SMV resection gained the most DFS benefit from EPD. Conversely, patients requiring vascular reconstruction or with borderline disease did not. These findings indicate that EPD is most beneficial in biologically localized tumors with low metastatic potential.

In conclusion, this multicenter RCT demonstrated that EPD can be performed safely and may improve DFS particularly in patients with preoperative CA19-9 < 200 U/mL, well-differentiated histology, and R0 resection receiving adjuvant chemotherapy. For patients with high systemic risk (CA19-9 ≥ 200 U/mL or vascular invasion), neoadjuvant therapy should remain the preferred strategy before considering EPD. Future studies should explore the role of EPD after neoadjuvant FOLFIRINOX and the safety of minimally invasive EPD techniques in high-volume centers.

Sincerely,

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