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Use of Total Pancreatectomy and Preoperative Radiotherapy in Patients Undergoing Pancreatectomy with Artery Resection



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We read with great interest the paper from Tee and colleagues.¹ We agree with the authors that, with improved efficacy of neoadjuvant treatments for pancreas cancer, use of pancreatectomy with artery resection will increase in specialized centers for the treatment of patients with locally advanced pancreatic cancer.² Of note, the morbidity and mortality rates are quite high in this article compared with other recent publications.² In particular, looking at the perioperative outcomes of the second period of Tee and colleagues' study and the recent series from Del Chiaro and colleagues,² we see a difference in postoperative severe complication (50% vs 12%) and mortality (9% vs 2.9%) rates. It is possible that this difference in outcomes is related to differences in strategy in performing pancreatectomy with artery resection. In Tee and colleagues' experience, postoperative hemorrhage was the greatest predictor of mortality and postoperative pancreatic fistula, and artery reconstruction with graft/conduit was associated with a high risk of major morbidity. In the article by Del Chiaro and colleagues, the majority of patients who underwent artery resection also underwent total pancreatectomy to both eliminate postoperative pancreatic fistula and rotate the splenic artery for reconstruction of resected arterial segment.³ In that study, use of interposition grafts was also avoided by fully mobilizing the bowel and performing a primary anastomosis without graft.^{4,5} Finally, most of the

patients in Tee and colleagues'¹ series received preoperative radiotherapy, which theoretically could contribute to postoperative hemorrhage.⁶ Of course, there might be disadvantages in performing total pancreatectomy in every patient, as this will lead them to become a relatively brittle diabetic. This will have ramifications for the patients' quality of life and ability to tolerate additional significant chemotherapy. It is also possible that omission of preoperative radiotherapy might not enable R0 resection rate as well. In conclusions, pancreatectomy with artery resection will probably have an increasing role in very carefully selected patients who demonstrate the right biology. We believe that the role of preoperative radiation therapy and total pancreatectomy should be studied further in this very select patient population and that there are pros and cons to their use.

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Arterial Resections During Pancreatectomy In Reply to Del Chiaro and Schulick



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We appreciate the recent thoughtful commentary by Drs Del Chiaro and Schulick about our group's previously published series of arterial resections during pancreatectomy.¹ They appropriately questioned the higher mortality and

morbidity rates in our series in comparison with Dr Chiaro's recent article and asked whether consideration of total pancreatectomy and elimination of preoperative locoregional chemoradiation (CRT) is reasonable, given our findings of increased perioperative risk, specifically postoperative pancreatic fistula (POPF) and postpancreatectomy hemorrhage, in these advanced resection cases. In addition, they noted that interpositional arterial grafts were associated with greater morbidity in our series, and asked whether these can be avoided by additional mobilization and subsequent end-to-end arterial anastomoses or splenic artery transposition.

Our experience with arterial resections continues to increase substantially since our initial publication of 111 cases, largely due to the increased use of total neoadjuvant therapy for pancreatic ductal adenocarcinoma. We have, to date, performed 143 pancreatectomies with arterial resection, which include hepatic artery (-ies), celiac axis, superior mesenteric artery (SMA), or any combination thereof, with most cases requiring formal revascularization, simple or complex. Our perioperative complications continue to decrease with this experience with fortunately no recent additional mortality. We have also gleaned the critical importance of additional perioperative adjuncts beyond intraoperative technical skill sets, to not only decrease the unique set of complications such operations induce, but also mitigate their severity (eg with antibiotics, anticoagulation, enteral/parenteral nutrition, judicious drain management, somatostatin analogues).

We do consider total pancreatectomy in many arterial resection cases, sometimes strictly for anatomical and margin considerations and others specifically performed to eliminate risk of POPF and its attendant risk of abdominal sepsis and/or resulting postpancreatectomy hemorrhage from life-threatening arterial revascularization failure. With significant improvements in diabetes management, such as continuous glucose monitoring and implantable insulin pumps, the historical brittle diabetes and metabolic derangements have not been of significant consequence in our patients; however, there are significant nutritional and absorptive issues with total pancreatectomy, particularly when coupled with total gastrectomy and/or en bloc paravisceral (celiac and/or SMA) arterial resection with combined pancreatic insufficiency and neurogenic postprandial diarrhea sometimes requiring challenging medical management postoperatively; a balanced approach is required. In cases that require hepatic arterial revascularization, there is a higher attendant risk of intrahepatic biliary tract ischemia with resultant stricture, abscess, and ischemic cholangiopathy that is exacerbated with the creation of a biliary-enteric anastomosis due to bacterial contamination of the biliary

tree. As an example, for patients with body tumors requiring celiac axis resection and hepatic arterial revascularization, although total pancreatectomy would eliminate the risk of POPF, we tend to prefer only subtotal pancreatectomy, as long as the tumor is not invading the pancreatic head, to avoid the consequences of these hepatobiliary complications that can be markedly difficult to manage postoperatively. We have initiated the use of intra-arterial tPA (tissue plasminogen activator) instillation for hepatic artery reconstructions, as currently used by our transplantation colleagues in an effort to minimize these risks. Although we do not routinely perform total pancreatectomy in all cases, we do use Fistula Risk Score calculations to predict POPF risk, with most intermediate- and high-risk patients being considered for total pancreatectomy to specifically avoid this complication.

Our center's current criteria for "resectability" of locally advanced tumors are likely the broadest in the US, with relatively few hard anatomical contraindications barring technical feasibility, and we need to weigh the benefit of these operations in terms of long-term survival, primarily determined by the efficacy of their neoadjuvant therapy, against the risk of revascularization failure, which can be life-threatening, as well as postoperative quality of life. With regard to avoidance of interposition graft, this is not often a choice and is dependent on anatomical constraints and tumor extent. For simple and straightforward short-segment encasement of the common or proper hepatic artery or SMA alone, then yes, we agree that with additional mobilization an end-to-end anastomosis or splenic artery transposition can be done quite easily and this is often done in our practice. However, there are no end-to-end anastomotic options when resecting more extensive tumors: tumors encasing the celiac axis from the aortic origin and extending to the distal proper hepatic artery or beyond to the right/left hepatic artery bifurcation; tumors encasing the SMA from its proximal aortic takeoff and extending deep into the mesentery to the middle colic artery or proximal jejunal branches; tumors involving all of the paravisceral vasculature (celiac axis, common/proper hepatic, SMA, portal vein/superior mesenteric vein). For such cases, only interposition grafts are possible and required for hepatic and visceral revascularization. Furthermore, many cases also require resection of the artery flush with the aorta to obtain a vascular margin and subsequent supra- or infra-celiac partial aortic cross-clamping to create an aorto to distal target artery (proper hepatic, right hepatic, or SMA) interpositional graft and is not achievable by any simpler reconstructive method.

Regarding preoperative radiation therapy, although there have not been rigorously proven "direct" survival

benefits to preoperative locoregional CRT, there are likely “indirect” benefits in the context of surgical resection with increase in margin-negative resection rates. As a negative margin operation is our oncologic contribution as surgeons, we use CRT in essentially all patients that will likely require arterial resection. We favor long-course CRT over stereotactic body radiation therapy for specific concerns beyond this discussion. Although we have anecdotally noticed increased clinically significant stenoses of portal/superior mesenteric venous reconstructions in those with preoperative radiation therapy, we have not necessarily found a similar detriment with arterial reconstructions, and rather most of the arterial anastomotic problems were likely technical in our early experience and improving over time, specifically with increased use of either autologous or cryopreserved arteries to avoid synthetic grafts and issues with infection and pseudoaneurysms and mandating some form of soft-tissue coverage (eg omentum, round ligament patch) of all arterial reconstructions.

This is a critical and exciting time for pancreas cancer surgeons, and with an increase in effective multimodality therapeutics this will likely lead to more complex

resection strategies and potential for improved survival. Having transparent data from multiple specialized global centers with experience with such advanced resections is important not only to learn from each other on how best to perform these custom and often bespoke operations from a technical perspective, but more importantly how to select these patients, how best to treat them preoperatively, and also in assistance in managing these patients postoperatively and beyond, many of whom are living longer than ever before with postoperative concerns not previously addressed, given earlier-era short survival. We look forward to sharing our growing large experience as more data accumulate, as well as descriptions and formal classification of the types and variety of arterial resections and associated consequences that we are learning are as varied as the patients themselves.

REFERENCE

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