

Synchronous arterial resection in pancreatic cancer: A case report

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Abstract. Pancreatic cancer is one of the most lethal malignancies affecting people worldwide. As it is frequently diagnosed in advanced stages of the disease, the 5-year overall survival rate is <10%. Advanced stages are usually characterized by the local invasion of the superior mesenteric axis, celiac axis and portal vein and are considered a sign of unresectable cancer. The association between venous resections and survival outcomes has been widely reported. The effect of arterial invasion remains unclear as only isolated cases have been reported thus far. The present study investigated the preliminary experience in the field of arterial resection for locally advanced pancreatic cancer. Between January 2018 and January 2020 arterial resection was successfully associated

with pancreatoduodenectomy in four cases. The mean age at the time of surgery was 48 years, and in all cases the indication of resection was represented by pancreatic head adenocarcinoma. Different types of venous resections were required in all cases. Postoperative reoperation was required in one case, while histopathological studies confirmed microscopic negative resection margins in all but one case. In selected cases, combined pancreatoduodenectomy with venous and arterial resection may be required to increase the chances of radical surgery.

Introduction

Pancreatic cancer is one of the most lethal malignancies worldwide as it is diagnosed in advanced stages of the disease, when invasion of the surrounding organs is present (1-5). Furthermore, despite significant progress in imaging and diagnostic modalities, <25% of patients with pancreatic head adenocarcinoma are diagnosed in incipient stages of the disease (1). Therefore, cases presenting limited invasion at the level of the venous structures, such as the portal vein, are considered to be borderline resectable lesions, while cases presenting arterial invasion are classified as locally advanced lesions (2,3). After the techniques of vascular surgery improved, vascular resections have been widely implemented and their benefits have been demonstrated, including improved overall survival compared with cases submitted to palliative

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medical treatment (3-7). In cases where venous wall invasion occurs, it has been reported that extended pancreatic and vascular resections are justified, and survival rates similar to standard pancreatoduodenectomy have been reported; however, in cases where arterial invasion is present, the effects remain unclear (2-7). In such cases, per primam resection vs. neoadjuvant chemotherapy followed by resection with curative intent have been widely analyzed so far (3-6). Therefore, studies have focused on investigating whether arterial resection is justified and whether they induce more harm than good for these patients (5-7). The present study aimed to investigate the preliminary experience regarding arterial resection in locally advanced pancreatic head adenocarcinoma.

Case report

After obtaining approval from the Ethics Committee of Fundeni Clinical Institute (approval no. 151/2021), data of patients submitted to surgery for locally advanced pancreatic cancer at Fundeni Clinical Institute (Bucharest, Romania) between January 2018 and January 2020 were retrospectively reviewed. After excluding cases in which surgery with radical intent was not feasible, due to the local extent of the disease or presence of peritoneal or liver metastases, there were four eligible cases. All four cases were submitted to surgery with curative intent followed by adjuvant chemotherapy. In all cases the follow-up method consisted of clinical examination, computed tomography and biochemical tests every 3 months. The age range at the time of initial diagnosis was 43-56 years (mean age, 48 years), while the sex ratio was 3:1 (male to female). Preoperative presumptive diagnosis was established via computed tomography and was demonstrated via endoscopic ultrasound biopsy in all cases. The preoperative details are presented in Table I.

As presented in Table II, neoadjuvant chemotherapy was administered in two cases to shrink the tumor volume and spare more vascular structures; in both cases the tumor volume decreased, and the preoperative imaging studies revealed the absence of arterial invasion. Thus, surgery with curative intent was attempted in both cases; however, at the time of surgery persistent invasion at the level of the arterial and venous structures was still present. Arterial invasion was limited in both cases, and given that the patients did not have other comorbidities, surgery with curative intent was performed. In the other two cases, preoperative investigations revealed the presence of borderline resectable lesions, the tumoral invasion being limited to the portal vein; therefore, these two cases were submitted to surgery with curative intent as first intention treatment. However, limited invasion of the superior mesenteric artery was encountered intraoperatively. In both cases, surgery with curative intent was performed. Intraoperative details of the surgical procedures are presented in Table II. In all but one case, histopathological studies confirmed the presence of negative resection margins, confirming the radicality of the surgical procedure. Positive resection margins were encountered in a 42-year-old male who previously underwent neoadjuvant chemotherapy, in which the inferior stump of the resected portion of the superior mesenteric artery presented microscopic tumoral invasion.

Postoperatively, a single patient developed pancreatic leak and required emergency reoperation consisting of totalization pancreatectomy to minimize the risk of postoperative cataclysmic bleeding from the vascular anastomoses. The postoperative hospital stay ranged between 7-28 days, and there were no postoperative mortalities. In all cases, anticoagulant treatment was administered for the next 3 months, followed by computed tomography to detect the patency of the vascular reconstructions.

Postoperative follow-up consisted of clinical examination, laboratory tests, abdominal ultrasound and computed tomography every 3 months.

The treatment outcomes were as follows: At the 3 months follow-up, there were no vascular complications, all the grafts and reconstructed segments being functional. Furthermore, no signs of local or distant recurrence were observed. At the 6 months follow-up one of the two cases presented a recurrent tumor invading the celiac axis, while, at the 1 year follow up, another case was diagnosed with multiple peritoneal and hepatic metastases, both cases being further submitted to chemotherapy with palliative intent.

Discussion

Locally advanced pancreatic cancer involving the vascular structures has been considered for a long period of time as unresectable and therefore patients were submitted to palliative treatment (1-3). However, once the surgical technique and the preoperative imaging techniques improved, vascular resections became more frequently performed, the best results in terms of survival being obtained in cases in which arterial resections were not needed, invasion being limited to the venous structures (4-6). Furthermore, in certain cases local invasion of the arterial structures was observed intraoperatively and arterial resections were therefore associated with promising results. Initially, such cases were diagnosed with arterial invasion only intraoperatively and radical surgery was further performed due to the low level of invasion (5,6). Similarly, in the present study, in two out of the four cases, arterial invasion was solely observed intraoperatively and, due to the limited area of invasion, radical surgery was performed, including arterial resections. In the other two cases, arterial invasion was diagnosed initially and decreased due to the administration of the neoadjuvant chemotherapeutic treatment. In this respect, in these two cases, radical surgery, including arterial resection, was performed. In all four cases, the early postoperative course was uneventful, thus demonstrating the feasibility and efficacy of the method.

The role of arterial resection in locally advanced pancreatic head adenocarcinoma has been widely debated thus far, with contradicting results (8,9). Some studies have reported that arterial resection can significantly improve survival, while others suggest that surgery should be avoided when arterial resection is present (7-9). Barreto and Kleeff (7) suggested that this may be due to the association with perineural invasion; therefore, as opposed to cases where venous invasion is present, presence of the arterial wall is expected to have malignant cells at the level of the anatomical neural plexus surrounding the arteries, resulting in apparition of locoregional metastases irrespective to the type of procedure performed. In addition, presence

Table I. Demographic features and preoperative evaluation of the four patients diagnosed with locally advanced pancreatic cancer.

No.	Age, years	Sex	CA19-9, U/ml	Histopathological type	Degree of differentiation	Neoadjuvant chemotherapy
1	43	M	39	PDAC	Poorly differentiated	Yes
2	56	M	412	PDAC	Poorly differentiated	No
3	42	M	28	PDAC	Moderately differentiated	Yes
4	51	F	386	PDAC	Poorly differentiated	No

F, female; M, male; CA19-9, carbohydrate antigen 19-9; PDAC, pancreatic ductal adenocarcinoma.

Table II. Intraoperative details of the patients submitted to arterial and venous resection in association with pancreatoduodenectomy.

No.	Type of arterial resection and reconstruction	Type of venous resection and reconstruction	Estimated blood loss, ml	Length of surgery, min	Type of resection
1	Superior mesenteric artery resection, patch placement	Circumferential portal vein resection, end to end anastomosis	650	420	R0
2	Superior mesenteric artery resection, patch placement	Circumferential portal vein resection, end to end anastomosis	700	510	R0
3	Superior mesenteric artery resection, patch placement	Circumferential portal vein resection, patch interposition	850	490	R1
4	Superior mesenteric artery resection, patch placement	Circumferential portal vein resection, end to end anastomosis	800	380	R0

of arterial invasion is a sign of a more aggressive tumoral biology, which decreases the chances of achieving negative resection margins (10). The Japanese Society of Pancreatic Surgery reported that the presence of arterial involvement acts as an independent prognostic factor associated with lower rates of radical resections, negative margins and survival rates. Furthermore, similar survival rates were reported in cases in which negative resection margins were not reached and cases presenting locally advanced, not surgically treated pancreatic cancer or those with metastatic disease (11).

With regards to cases where neoadjuvant systemic chemotherapy has been performed, it has been suggested that initial investigation via the 'artery first' approach should be applied, followed by frozen biopsy from the surrounding tissues at the level of the celiac axis/hepatic artery/superior mesenteric artery. Furthermore, it has been suggested that surgery should not be performed when remnant tumor is present (12). It has also been suggested that a personalized approach should be taken into consideration for each case, and arterial invasion should not be considered as a formal contraindication for resection (13).

However, patients undergoing neoadjuvant chemotherapy followed by surgery remains controversial. Some have reported the superiority of this therapeutic approach compared with chemotherapy alone. A study by Sonohara *et al* (14) included 44 cases diagnosed with locally advanced pancreatic cancer, who underwent surgery with curative intent following neoadjuvant chemotherapy. The most performed arterial resections were hepatic artery resection in 21 cases, followed by celiac

trunk resection in 12 cases, superior mesenteric artery in six cases and splenic artery in five cases. The authors compared the intraoperative and postoperative outcomes of this study group to those reported in a group of 686 patients who underwent standard pancreatoduodenectomy. Cases where arterial resection was required were frequently associated with positive microscopic resection margins. In addition, performing arterial resection was significantly associated with longer intraoperative times and increased requirement for intraoperative blood transfusion, while the rates of intraoperative blood loss were similar between the two groups. With regards to severe postoperative complications, such as pancreatic leaks, the same study group demonstrated that performing arterial resection did not increase the risk of developing such complications. As for the long-term outcomes, the authors demonstrated that in the last decade, once the surgical technique improved and new chemotherapeutic agents were identified, survival outcomes significantly improved; therefore, the overall survival of patients submitted to arterial resection was similar to those submitted to standard pancreatoduodenectomy. Multivariate analysis demonstrated that neoadjuvant and adjuvant chemotherapy were the most significant prognostic factors that influenced long-term outcomes. Furthermore, neoadjuvant systemic chemotherapy was associated with increased rates of negative resection margins, which in turn improved the long-term outcomes (14).

In conclusion, the role of arterial resection in maximizing the radicality of surgery in locally advanced pancreatic cancer remains controversial. Although it has been suggested that the

presence of arterial invasion should be considered as a formal contraindication for resection, others suggest that this procedure should be performed with neoadjuvant chemotherapy to shrink the tumor volume.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

NB, FF, FG, DR and MD conceived the present study. CB, IB and IC performed the relevant literature research. FF, DR, CSa, VB, CB, IC and FG performed formal analysis. CD, OS and CSa performed the investigation. OS, CB and IC acquired the resources. CSt, CB, IC and IB curated the data. IB drafted the initial manuscript. CSa, FF, IB, IC, CB and VB drafted, reviewed and edited the manuscript for important intellectual content. DR, CSt, CB and IC visualized the data, while VB and IC supervised the present study. NB, CSt, IC, CB and IB participated in the entire review process and contributed to the analysis and critical interpretation of the data. NB, IB, CSa, CSt, VB, IC, FF and FG confirmed the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Fundeni Clinical Institute (approval no. 151/2021) and performed in accordance with the Declaration of Helsinki. Written informed consent was provided by all patients prior to the study start.

Patient consent for publication

Written informed consent was provided by all patients to publish this paper.

Competing interests

The authors declare that they have no competing interests.

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