

Pancreatoduodenectomy *En Bloc* with Portal and Superior Mesenteric Artery Resection – A Case Report and Literature Review

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Abstract. *Background: Pancreatic cancer is one of the most lethal malignancies and is associated with a very poor overall survival. However, it seems that the only curative option remains an aggressive surgical approach capable of obtaining a radical resection. Unfortunately, this desiderate is even harder to be obtained when it comes to pancreatic tumors with vascular invasion. Case Report: We present the case of a 65-year-old patient who was diagnosed with a cephalo-pancreatic tumor invading both the portal vein and the superior mesenteric artery. Results: Whipple procedure was performed with portal and superior mesenteric artery resection; the continuity of the portal vein was established by an end-to-end anastomosis, while the superior mesenteric artery was re-implanted in the infra-renal aorta. Conclusion: Due to improvements of surgical techniques and postoperative management, the postoperative morbidity and early mortality significantly decreased and enabled the surgeon to perform ultra-radical surgery with better outcome.*

Pancreatic cancer represents an aggressive malignancy with poor overall survival in which the mortality rate almost reaches the same values as the annual incidence (1).

Even in cases diagnosed at an early stage of the disease, when the lesion is perfectly resectable, the 5-year overall survival is still low, ranging between 10-20% (2, 3).

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However, due to the particular anatomy of the pancreatic region and the close contact between the pancreatic head and major vascular structures (portal vein, superior mesenteric vessels), numerous patients already present tumoral vascular invasion at the time of diagnosis making the surgical procedure even more demanding and increasing the rates of postoperative morbidity and mortality. However, in the last decade, due to improvements of surgical techniques and postoperative management, the rate of postoperative major complications became more acceptable encouraging the surgeons in specialized Centers to undertake surgical approaches more often. We present the case of a 65-year-old patient diagnosed with a pancreatic head tumor invading both the portal vein and superior mesenteric artery in whom a pancreatoduodenectomy with arterial and venous resection associated with superior mesenteric artery re-implantation in the aorta and end-to-end venous anastomosis was performed. In the postoperative course, the patient developed a splenic vein thrombosis, which was successfully treated by heparin administration for 5 days. The patient was released in the 17th postoperative day. The Doppler ultrasonography performed one month later revealed patient’s venous and arterial anastomosis and recanalisation of the splenic vein.

Case Report

The 65-year-old patient presented for jaundice associated with vague epigastric discomfort and slight weight loss in the previous few months. The biochemical tests showed the presence of increased values for total and direct bilirubin (5.1 and 2.9 mg/dl, respectively) associated with increased values of transaminases (alanine transaminase (ALT)=1,043 U/l, aspartate aminotransferase (AST) 650 U/l, respectively). The abdominal ultrasonography raised the suspicion of a solid mass at the level of the pancreatic head and, thus, a computed scan (CT) was performed that confirmed the



Figure 1. The preoperative CT scan showing a pancreatic tumor with vascular invasion.



Figure 2. The final aspect after resection.

presence of a pancreatic tumor measuring 4/3.5 cm without demarcation interface with the portal vein and superior mesenteric artery (Figure 1). Due to the good biological status of the patient, the decision was made to attempt radical surgery. A pancreatoduodenectomy *en bloc* with portal vein and superior mesenteric artery was performed and vascular continuity was re-established by end-to-end porto-portal anastomosis, while the mesenteric artery was end-to-side implanted in the infra-renal aorta (Figures 2-7). In the postoperative course, the patient developed a splenic vein thrombosis, which necessitated administration of intravenous heparin for 5 days followed by oral anti-coagulation (Figure 8). The patient was discharged in the 17th postoperative day in good condition. The contrast CT performed prior to discharge revealed a partial recanalization of the portal vein, while the Doppler ultrasonography performed one month after discharge revealed the complete recanalization of the splenic vein.

Discussion

Since 1946, when Waugh and Clagett modified the Whipple operation to the current form and established the main rules in surgery for pancreatic malignant tumors in that there should be reasonable opportunity for cure and the risk of death should not outweigh the prospects for cure, these principles became the cornerstones of the balance between surgical radicality and attempt to limit postoperative morbidity and mortality. Once the intraoperative and postoperative management improved, the debate went even further focusing on more extended associated procedures including vascular resections in an attempt to achieve R0 resections. The main ongoing question was whether vascular

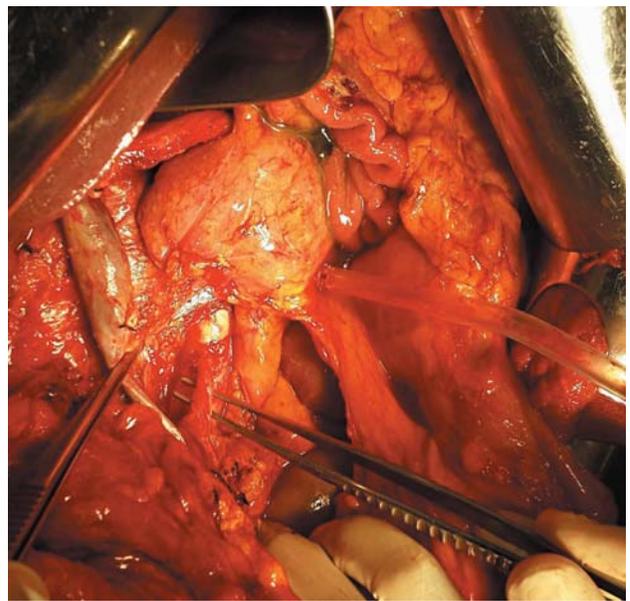


Figure 3. The superior mesenteric artery is re-implanted in the infra-renal abdominal aorta; the continuity of the portal vein is re-established by an end-to-end anastomosis.

resections could be associated to pancreatic resection with acceptable morbidity and mortality rates and possible survival benefit (4-7).

The first series of pancreato-duodenectomies with vascular resection was reported in 1977 by Fortner *et al.*; at that moment, the postoperative mortality reached almost 17% and average hospital stay was 53 days (4).

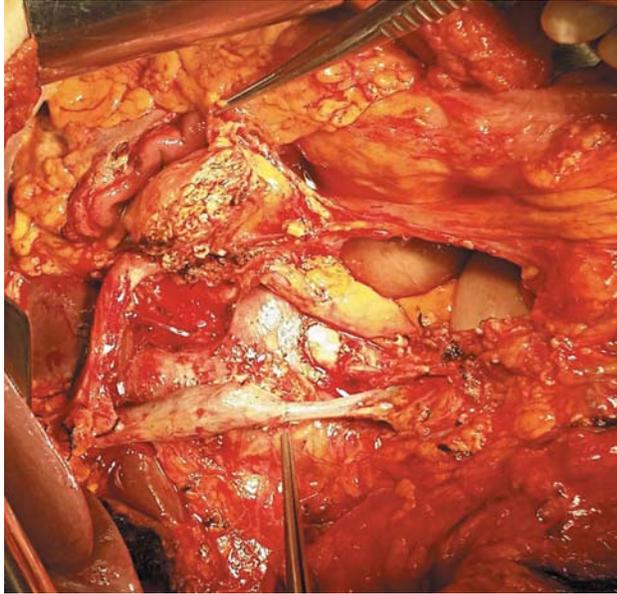


Figure 4. Porto-portal anastomosis; the superior mesenteric artery is re-implanted in the infra-renal aorta.

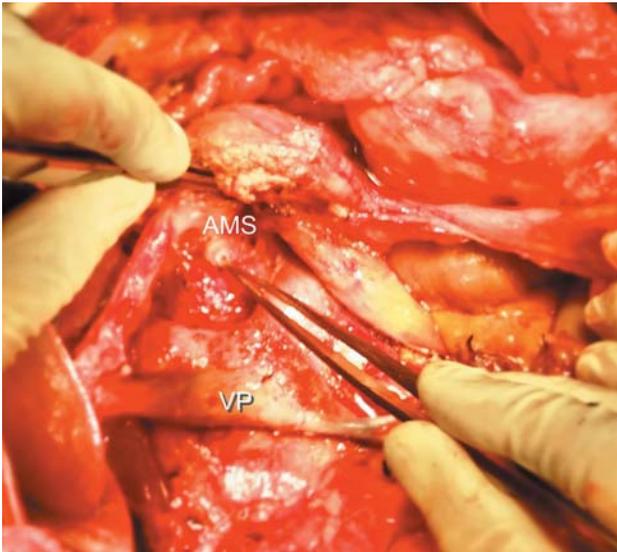


Figure 5. The superior mesenteric artery ligated stump. The portal vein is re-constructed.

Nowadays, the postoperative outcomes significantly improved and led to an important decrease of the postoperative morbidity and mortality to 30% and 3%, respectively, in large experienced Centers (2, 5). While venous resections, involving portal vein, portal confluent or



Figure 6. The specimen: pancreatic head tumor en bloc with the invaded vascular zones.

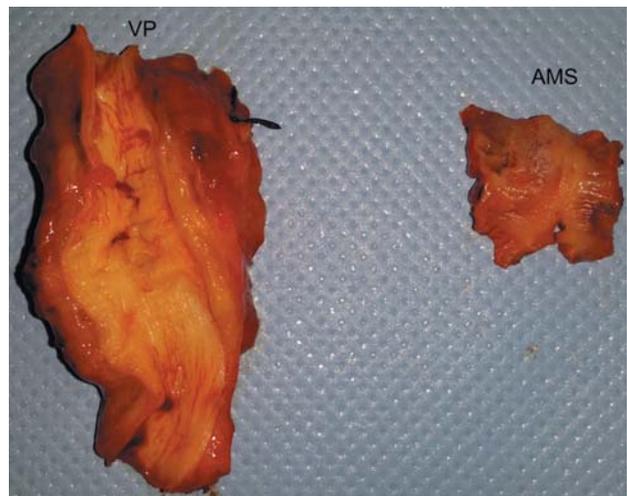


Figure 7. The specimen showing vascular invasion.

superior mesenteric vein, are more often performed, arterial involvement of the celiac trunk, superior mesenteric artery or hepatic artery is more often considered as a limit to resection due to presumed higher morbidity with insignificant effect on survival (6, 7).

For surgeons who still consider that tumor invasion of the superior mesenteric artery is still a contraindication for performing resection, the “artery first” technique might be useful. This consists of dissection of the superior mesenteric



Figure 8. Postoperative CT scan showing the presence of a splenic vein thrombosis.

artery at the beginning of the procedure, while the stomach, the duodenum and the pancreas are transected in the end. In cases in which arterial involvement is present during dissection, the surgeon may decide for abandoning resection or performing resection with remnant tumor around the artery (8, 9). Another possible benefit of this approach is represented by the possibility of early recognition of a particular anatomic situation, such as the presence of a right hepatic artery arising from the superior mesenteric artery, which seems to exist in up to 20% of the normal population (10). In cases in which this anatomic particularity is identified preoperatively and the surgeon estimates that the superior mesenteric artery will be removed *en bloc* with the right hepatic artery, embolization of the superior mesenteric artery has been proposed in order to increase the blood supply through the left hepatic artery and through the neo-formation of collateral vessels, which are going to be developed (10).

Usually, the presence of the tumor invasion of the superior mesenteric artery is located at the level of the uncinate process. In such cases, a partial resection of the artery with end-to-end anastomosis is feasible. In cases in which an adequate mobilization of both sides of the artery, in order to obtain a tension-free suture, is not feasible, a vascular graft can be used. An arterial invasion up to its origin at the level of the abdominal aorta is rarely seen and is usually correlated with voluminous tumors (11).

When it comes to venous resection, direct tumor invasion is not the only possible indication; other situations in which resection is needed are represented by a highly adherent tumor with no clear invasion but with high risk of venous tear-up during dissection or perivenous and perineural microscopic invasion (7).

In order to determine the factors associated with an improved survival, Nakao *et al.* and Ishikawa *et al.* tried to classify the venous invasion depending whether one or both lateral walls of the portal vein are involved and whether venous occlusion with collateral circulation is already present (12, 13). Nakao *et al.* concluded that the presence of bilateral narrowing and venous occlusion with collateral circulation are poor prognostic factors (12). However, cases presenting circumferential involvement of the superior mesenteric vein/ portal vein have a high risk of microscopic involvement through contiguity of the superior mesenteric artery or retroperitoneal tissues, thus inducing a higher risk of microscopic residual disease after resection and consecutive lower rates of survival (13).

Although arterial resection is technically more difficult and has been considered for a long time as a formal contraindication, several studies demonstrated that pancreatoduodenectomy with arterial resection became a safe operation despite its technical complexity (14-16).

In order to decide how far the surgical team should go when dealing with a patient with good biological status and vascular invasion, the International Study Group for Pancreatic Surgery (ISGPS) established a consensus in February 2014. Extended pancreatoduodenectomy was defined as standard pancreatoduodenectomy associated with extended resection of the antrum or distal half of the stomach, colon and/or mesocolon *en bloc* with the main vessels (ileocolic, right or middle colic vessels), small bowel beyond the first segment of jejunum, portal, superior mesenteric and/or inferior mesenteric vein, hepatic artery, celiac trunk and/or superior mesenteric artery, inferior vena cava, right adrenal gland, right kidney and/or its vascularisation. Once resection is performed, an adequate perfusion of the remnant viscera should be ensured by vascular reconstructions or, if it is not already present, by already existing induced collaterals. The same panel recommends performing of '*en bloc* resection' in order to impede intraoperative tumor dissemination (17).

In order to evaluate the oncologic significance of arterial invasion, two theories have been developed: the first one sustains that the presence of arterial invasion is a marker of an aggressive biological tumor behavior associated with poor prognosis, while the second theory considers that local vascular invasion appears only due to a specific location of the tumor, nearby the involved vessels and it is not associated with a more aggressive biology. Secondary, the partisans of the two theories have different points of view regarding the most appropriate treatment: while those who sustain the first theory consider that an R0 resection is not beneficial due to the high risk of development of local recurrences or distal metastases (18, 19), the followers of the second theory strongly support the radical resection *en bloc* with the involved blood vessels (19, 20).

In order to demonstrate whether arterial invasion in pancreatic cancer can be a poor prognostic factor, Bachellier *et al.* realized a matched case-control study in which they introduced all patients who underwent pancreatoduodenectomy with arterial resections in Strasbourg Hospital between January 1990 – December 2008. They concluded that 26 patients were eligible for this study and matched with similar cases submitted to classic resection without any arterial involvement. The matched parameters were age, sex, study period, tumor site, lymph nodes status, presence of perineural invasion and association of portal vein resection. Two group studies, each one involving 26 patients, were formed and compared. In the arterial resection group, involvement of the superior mesenteric artery was seen in 4 cases, with the arterial stump being re-implanted in the abdominal aorta after resection in all of them. The tumor was located at the level of the pancreatic head in 21 cases in each group; portal vein resection was associated in 21 cases in the arterial resection group and in 20 cases in the standard group. The average tumor size was 51 mm in cases with arterial invasion and 40 mm in the standard group ($p=0.06$), while the lymph node status and perineural invasion were similar between the two groups ($p=1$ for both variables). At the end of the surgical procedure, R0 resection was achieved in 21 cases in each study group. The operative duration was higher in the arterial resection group (518 min vs. 440 min, $p=0.112$), while the need of blood transfusion was significantly higher in the first group (it was performed in 25 cases in the first group and only in 15 cases in the second group, $p=0.0005$). When it came to the evaluation of post-operative-related morbidity and mortality, no significant differences were seen: 14 cases in the arterial resection group and 10 cases in the standard group experienced post-operative complications ($p=0.264$), while postoperative mortality was reported in 2 cases in the first group and in one case in the second group ($p=1$). In univariate analysis, arterial resection did not seem to have a negative impact on survival (the median survival was even higher, 17 months, in the first group and 12 months when compared to the standard group, $p=0.581$). However an important prognostic factor was the degree of arterial wall invasion revealed by the histopathological examination: cases presenting a perineural invasion reported a median survival of 18 months, while those with arterial wall invasion reported a median survival of only 9 months ($p=0.002$). Neither the association of portal vein resection nor the presence of portal wall invasion on histopathological studies significantly impacted on survival ($p=0.35$ and $p=0.265$, respectively). In multivariate analysis, only the presence of histopathological arterial wall invasion, perineural invasion and a number of resected lymph nodes, more than 15, were associated with a worse prognosis in terms of survival (21).

Another study, which concluded that arterial resection can be done in safe conditions and bring a benefit in terms of survival, was conducted by Stizenberg *et al.* on 12 patients

who were submitted to pancreatic resections *en bloc* with portal and superior mesenteric artery resection and who reported a median survival of 20 months, comparable to those who underwent pancreatic resection without vascular resection. However, an important aspect of this study was the utilization of neo-adjuvant chemotherapy and irradiation (22).

Contrarily to these studies, Nakao *et al.* reported 14 cases of arterial resection in 201 patients and obtained no benefit in terms of survival when compared to the unresected cases. He concluded that these results are related to the advanced stage of the disease associated with probably positive peripancreatic resection margins and microscopic invasion of the surrounding arterial structures (6).

Mollberg *et al.* (16) wrote a review on literature data published between February 1973 and November 2010 and selected 26 studies including 366 patients who were submitted to pancreatic resection *en bloc* with arterial resections. This meta-analysis concluded that arterial resections were associated with a significantly higher rate of postoperative mortality ($p<0.0001$). In order to determine whether the arterial resection can offer an improved oncological outcome, survival was analyzed after 1, 3 and 5 years. The median 1-, 3-, and 5-year survival rates of patients who were submitted to arterial resections were 49.1% (range=16%–83%), 8.3% (range=0%–30%) and 0% (range=0%–42%), respectively, which were significantly lower compared to those submitted to standard pancreatoduodenectomy. Due to these unfavorable long-term outcomes, further analyses were performed in order to determine whether patients who underwent pancreatic resections *en bloc* with vascular resection reported an improved outcome when compared to those who did not experience surgical resections. Meta-analysis of these studies revealed a higher chance of 1-year survival ($p=0.03$) for patients undergoing arterial resection whereas the difference in 2-year survival did not reach statistical significance ($p=0.23$). However, this study involved all types of arterial resections (including superior mesenteric artery, celiac trunk, right, left, common hepatic artery), with this aspect also being responsible for the overall poorer outcomes (16).

Conclusion

Although vascular invasion of the superior mesenteric artery has been considered for a long time as a criterion of unresectable disease, nowadays, due to improvement of surgical techniques and postoperative management, this surgical procedure has become safer. Further studies are required in order to establish which patients benefit the most from extended resections and who can benefit more solely from oncologic palliation. Integration of invasive surgical procedures in the current multimodal treatment of pancreatic cancer and, in the future, with further development of new

agents is mandatory. In selected cases, for patients with good biological status, extended pancreatic resections should be attempted until more refined selection criteria become available.

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