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REVIEW ARTICLE

Artery First Approach to Pancreatic Cancer Resection: A Review of the Evidence for Benefit

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ABSTRACT

Artery first approach to pancreatic cancer is being increasingly adopted to improve perioperative outcomes. This review summarised the current evidence regarding the role of artery first approach in improving perioperative and long-term oncological outcomes. Several retrospective studies employing artery first approach to pancreatic cancer have shown increase in R0 resection rates, lymph node yield, reduced intraoperative blood loss, and prolong long-term survival. These benefits of artery first approach to pancreatoduodenectomy are worth exploring further, and this will require multi-centre studies with close attention to the consistency of artery first approach to pancreatoduodenectomy techniques and its perceived benefits. Furthermore, the increasing use of neoadjuvant (chemotherapy ± radiotherapy) strategies for pancreatic ductal adenocarcinoma is also relevant to this discussion about artery first approach to pancreatoduodenectomy. Patients who have not developed evidence of metastases are may benefit from a trial dissection using an artery first approach to determine resectability and the ability achieve an R0 margin.

INTRODUCTION

Portal/superior mesenteric vein (PV-SMV) resection is being performed more frequently during pancreatoduodenectomy in order to increase R0 resection rates, although the survival benefit is still debated [1]. The superior mesenteric artery margin is often positive in these patients [1], although this is only identified after transection of the neck of the pancreas and point of no return. Recent imaging analysis has shown that 80% of the pancreatic branches of the SMA come from the right dorsal aspect of the artery, and cancer abutment occurred exclusively from the same direction [2], thereby increasing the likelihood of a R1 resection along this margin. In 1993, Nakao *et al*. first described the technique of isolated pancreatectomy, in which the superior mesenteric vein (SMV) and superior mesenteric artery (SMA) were approached from the mesentery of the jejunum at the base of the transverse mesocolon [3]. This approach allowed earlier division of the inferior pancreaticoduodenal artery (IPDA) to enable meticulous dissection along the SMA. This was the first technical description of approaching the SMA prior to transecting the pancreatic neck. Subsequent to that, the posterior approach to SMA by kocherisation of the duodenum was described by Pessaux and colleagues in 2003 [4]. It was not until 2010 that the 'artery first' term was first used when describing the uncinate first approach to the SMA [5]. Since then there have been four more 'artery first' approaches described, each with a specific indication and technical justification [6]. The term 'artery first' is usually applied to the SMA, although may also refer to other arteries, including the common hepatic artery, depending on the location and relations of the primary tumour.

More recently Inoue *et al* have further stratified the artery first approach by defining three levels based on the extent of dissection along the SMA margin.

Level 1 dissection just resects the pancreatic head without LN dissection

Level 2 dissection resects the pancreatic head, the complete mesopancreas and regional LNs in association with the SMA.

Level 3 dissection resects the pancreatic head, with hemi circumferential pl-SMA dissection just outside the SMA adventitia. The common trunk of IPDA and Jejunal artery is ligated and divided at its root in addition to complete mesopancreas resection.

There is mounting evidence for an artery first approach to pancreatoduodenectomy (AFAPD) and the aim of this

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Abbreviations AFA artery first approach; AFAPD artery first approach to pancreatoduodenectomy; SMA superior mesenteric artery; SMV superior mesenteric vein
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review is summarise this in response to a series of key clinical questions.

Does an AFAPD Improve R0 Resection Rate?

Initial evidence that an AFA increased R0 rates was relatively sparse [7, 8]. More recent studies however have shown an increase in R0 resection rates [9, 10, 11] with the AFAPD. Kawabata *et al* [9] has shown an AFA incorporating the principle of total excision of meso-pancreatoduodenum including a cluster of soft tissue along the IPDA and the first jejunal artery improves R0 resection rates compared with standard PD. The R0 resection rates was 66% for AFAPD compared with 7% for a standard PD. Similarly, other studies using AFAPD approach have shown improved R0 resection rates [10, 11, 12].

Does AFAPD Improve The Lymph Node Yield?

An AFAPD can include a circumferential lymphadenectomy around the SMA while preserving pl-SMA to prevent postoperative diarrhoea. Lymph node metastases to the left of the SMA (lymph node station 14) are a feature of advanced PDAC, and resection of these nodes is not included in standard PD. AFAPD appears to facilitate resection of these nodes and improving the lymph node yield [9, 10, 11]. Aimoto *et al* [10] have recently shown that AFAPD increased he lymph node yield as well as improving the R0 resection rates with the expectation that this will reduce locoregional recurrence rates. Several other studies have shown improved lymph node yield with an AFAPD [9, 11].

Does AFAPD Improve Perioperative Outcomes?

An AFAPD allows early identification and ligation of the IPDA before ligation of the corresponding afferent veins of the pancreatic head. This may significantly reduce the congestion of the head of the pancreas, resulting in reduced intraoperative blood loss and transfusion requirements. Several studies comparing AFAPD (with early IPDA ligation) to standard PD have demonstrated a lower intraoperative blood loss and transfusion requirements with AFAPD [2, 13, 14]. In addition, several recent studies have shown that AFAPD is associated with reduced overall morbidity compared to standard PD, althought this may be secondary to reduced blood loss, a risk factor for postoperative complications after PD [2, 13, 14].

Does AFAPD Improve Long Term Survival?

Recent data has suggested improved survival after AFAPD [15, 16]. The left posterior approach [15] has been shown to be associated with fewer recurrences (10 *vs.* 37 per cent; p=0·006) and improved survival compared to the standard PD [1- and 3-year survival rates 90 and 53 % (AFA) versus 80 and 16 % (standard PD); p=0·004]. Similarly the Inferior supracolic approach (anterior approach) [16, 17] has been shown to achieve an R0 rate of 82 % for pancreatic adenocarcinoma and 91 % for biliary adenocarcinoma, with a combined overall 2-year survival rate for these subgroups of 75%. Similarly a posterior AFAPD has shown a trend towards improved disease free survival (median 13 *vs.* 19 months) and overall survival (median 19 *vs.* 30 months), although this was not statistically significant (p=0.19 and p=0.18) [11].

It appears that AFAPD improves overall survival in patients and the contributing factors appear to be the higher R0 resection rates, lower blood loss and postoperative morbidity.

Role of AFA for Body of Pancreas Cancer

More recently the AFA has been described for resectable and borderline resectable pancreatic cancer of the body of the pancreas during the RAMP (radical antegrade modular pancreatectomy) [18, 19], especially when there are concerns about the status of the medial and posterior margins. An AFA enables the identification and dissection of the SMA behind the body of the pancreas. The R0 rate after AFA RAMPS has been published as 82% and 100% [18, 19]. There was also a higher lymph node yield (26 (range 9 to 80) compared with published data after standard RAMPS [20]. At the median follow-up after surgery of 12.4 months (range 3.5 to 16.4 months), the overall survival rate was 100% at 1 year. The 1-year disease-free survival rate was 91%. No long term survival data is currently available.

DISCUSSION

It is clear that there is mounting evidence that AFAPD can improve R0 resection rates, increase lymph node yield, reduce intraoperative blood loss, and prolong long-term survival. None of these data are derived from randomised controlled studies comparing AFAPD and PD, meaning that these findings must remain provisional. These benefits of AFAPD are worth exploring further, and this will require multi-center studies with close attention to the consistency of AFAPD techniques. The alternative techniques for AFAPD have never been compared and in most cases the choice is based on the location and relations of the primary tumour.

The increasing use of neoadjuvant (chemotherapy ± radiotherapy) strategies for PDAC is also relevant to this discussion about AFAPD. It is well recognized that the ability to re-stage PDAC after neoadjuvant chemotherapy and the ability to predict resectability is compromised. Current approaches to imaging cannot reliably distinguish cancer extension, desmoplastic reaction, and inflammation associated with cancer that has responded to treatment. Patients who have not developed evidence of metastases are may benefit from a trial dissection to determine resectability and the ability achieve an R0 margin. The overall trend is that more patients are undergoing surgery in this setting. The ability to define resectability before reaching the point of no return therefore becomes even more important, especially because there are highly successful approaches to non-resectional palliation of biliary and duodenal obstruction with endostenting [21]. For these reasons the AFA is assuming a more important role in the surgical management of pancreatic cancer.

Conflicts of Interest

All authors have no conflicts of interest to disclosure. Neither research grants nor commercial financial supports were received for this study.

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