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ABSTRACT

Background: Pancreatic ductal adenocarcinoma (PDAC) is associated with poor survival, and complete surgical resection with a negative circumferential resection margin (R0CRM–) remains the only potentially curative treatment. Current resectability criteria primarily stratify patients according to arterial and portomesenteric venous involvement. However, the impact of mesopancreatic infiltration on resection margin status within these classifications remains unclear.

Methods: A consecutive cohort of 271 patients undergoing upfront resection for primarily resectable or borderline resectable PDAC of the pancreatic head was analyzed. Preoperative staging was reassessed according to current NCCN resectability criteria using multidetector CT. Histopathological evaluation followed the LEEPP protocol and 1-mm CRM definition. Mesopancreatic infiltration was correlated with resectability status and margin involvement.

Results: Among 271 patients, 209 (77.1%) were classified as primarily resectable and 62 (22.9%) as borderline resectable. Mesopancreatic infiltration was present in 208 patients (76.9%). Overall, R0CRM– resection was achieved in 143 patients (52.8%), while 128 patients (47.2%) had R1/R0CRM+ margins. In primarily resectable patients, mesopancreatic infiltration was significantly associated with incomplete total resection (p=0.004) and dorsal margin positivity (p=0.026). Across the entire cohort, mesopancreatic involvement increased the likelihood of incomplete resection by 2.71-fold (95% CI 1.35–5.43; p=0.005). In contrast, NCCN-based resectability classification did not significantly correlate with total or dorsal margin status.

Conclusion: Mesopancreatic infiltration is frequent and associated with an increased risk of incomplete oncologic clearance, including in patients classified as primarily resectable. These findings suggest that mesopancreas-related features may merit consideration in future refinements of resectability assessment.

Abbreviations: AHPBA, Americas Hepato-Pancreato-Biliary Association; CA 19-9, Carbohydrate Antigen 19-9; CHA, Common Hepatic Artery; CRM, Circumferential Resection Margin; CT, Celiac Trunk; ECOG, Eastern Cooperative Oncology Group; LEEPP, Leeds Pathology Protocol; MDACC, MD Anderson Cancer Center; MDCT, Multi-Detector Computed Tomography; MP, Mesopancreas; MPE, Mesopancreatic Excision; NCCN, National Comprehensive Cancer Network; PDAC, Pancreatic Ductal Adenocarcinoma; Pn, Perineural Invasion; PV, Portal Vein; SMA, Superior Mesenteric Artery; SMV, Superior Mesenteric Vein; SSAT, Society for Surgery of the Alimentary Tract; SSO, Society of Surgical Oncology; UICC, Union for International Cancer Control.

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Introduction

Despite extensive research, the pancreatic ductal adenocarcinoma (PDAC) remains associated with a poor five-year survival rate and is projected to become the second leading cause of cancer-related death [1]. Surgical resection with true R0CRM- margins (CRM=circumferential resection margin) [2,3] remains the cornerstone of local tumor control and ensures the chance for long-term survival [4,5]. However, achieving this goal is challenging due to the anatomical complexity of the pancreas [6] and the advanced stage at which the PDAC is typically diagnosed. The previous literature revealed that true R0CRM- resections were only possible in about 30% of all PDAC patients, making the dorsal and medial resection margins mostly at risk for a R1 resection [7,8].

To improve margin negativity and local tumor control, a pretherapeutic stratification model was implemented to identify patients who are most likely suitable for upfront surgery or neoadjuvant down-sizing therapy [9,10]. Various international committees, including MD Anderson Cancer Center (MDACC) [11], Americas Hepato-Pancreato-Biliary Association/Society of Surgical Oncology/-Society for Surgery of the Alimentary Tract (AHPBA/SSO/SSAT) [12], Intergroup Alliance [13] and National Comprehensive Cancer Network (NCCN) [14] created their own definitions, but these differ only marginally. Primarily resectable PDACs are therefore defined by the absence of arterial (celiac trunk CT, superior mesenteric artery (SMA) and common hepatic artery (CHA)) and low-risk portomesenteric (portal vein (PV)/superior mesenteric vein (SMV)) involvement. Since these criteria are based on the medial axis of the pancreatic head, the current anatomical resectability classification system [9,10] could be unidimensional. Although the current resectability criteria for PDAC are well established and internationally approved, relevant limitations remain. The diagnostic accuracy of venous involvement on preoperative multidetector computed tomography (MDCT) is still questionable. A meta-analysis demonstrated that only 60% of patients with intraoperatively confirmed venous invasion showed corresponding radiographic signs preoperatively [15]. In addition, the assessment of preoperative resectability is affected by a considerable inter-observer bias [16,17], as key definitions such as “venous resectability” or “reconstructability” are interpreted differently across institutions and by individual surgeons, resulting in substantial heterogeneity in staging and treatment decisions [9]. Furthermore the available literature investigating the impact of radiologically defined resectability status on the CRM-status outcome remains limited and heterogeneous. It therefore remains unclear whether the likelihood of achieving an R0CRM–resection—which is known to confer a significant survival benefit—is consistently reduced in patients classified as borderline resectable [17–22]. Beyond the anatomical limitations of vascular staging, current diagnostic pathways in pancreatic cancer are further limited by persistent rates of misdiagnosis and disease misclassification despite the combined use of cross-sectional imaging and biopsy [23] In recognition of these shortcomings, international recommendations have increasingly adopted a multidimensional framework for resectability assessment, incorporating not only anatomical criteria but also biological and conditional factors, as reflected in the “ABC” model. Within this framework, biological parameters such as serum CA 19-9 levels [24,25], together with conditional factors including performance status [25], are considered alongside anatomical vessel involvement to improve patient selection and optimize treatment allocation. However, despite this evolution toward multidimensional staging, anatomical criteria remain the cornerstone of initial surgical decision-making and continue to determine margin-oriented risk assessment. Consequently, further refinement of the anatomical component of resectability assessment remains necessary, particularly with regard to imaging-based risk stratification and prediction of resection margin status.

The oncological benefit of mesopancreatic excision (MPE) has been repeatedly demonstrated by our group and others [6,26–29]. The mesopancreas is an anatomical predefined area which incorporates the dorsal and ventral margins of the pancreas. The Treitz and Fredet fascia [30–33] are known landmarks which define the mesopancreas as a separate anatomical compartment and serve to distinguish the peripancreatic area from the surrounding tissue. These fascia sheets merge medially with the SMA, a result from the embryologic rotation in order to achieve a secondary retroperitoneal nature of the pancreas. Both the Treitz and the Fredet fascia are a result of duplication and fusion. From a neuroanatomical perspective, the mesopancreatic dissection area has been shown to correspond anatomically, at least in part, to components of the extrapancreatic pancreatic head surrounding the superior mesenteric artery [34]. As these neural structures represent established routes of perineural tumor dissemination in PDAC, this neuroanatomical perspective further supports the oncological relevance of the mesopancreatic region.

We revealed that the mesopancreas is frequently involved in PDAC patients and that a positive MP infiltration status was associated with a higher risk for R1/R0CRM+ resection status at the dorsal resection margin [6]. Mesopancreatic excision also resulted in a decline in local recurrence rates when compared to follow up results in the known literature [6], underlining local tumor control is also possible for PDAC patients [8,29,35].

The previous literature on the mesopancreas in PDAC patients did not consider the current resectability criteria during analysis. It remains unknown if primary resectable patients are at risk for cancerous involvement of the mesopancreas and if the mesopancreatic infiltration status in these patients influences the resection margin status of the dorsal area. The aim was to study the mesopancreas in a consecutive treated non selected PDAC cohort, integrating current radiographic and histopathological standards.

Material and methods

Patient selection and demographic data

This study retrospectively analyzed a consecutively treated patient cohort, from a prospectively maintained database, who underwent primary surgical therapy for primary or borderline resectable PDAC of the pancreatic head at the University Hospital of Duesseldorf between January 2016 and January 2024. Treatment decisions were based on a preoperative assessment by a multidisciplinary tumor board. Inclusion criteria were upfront resected primarly resectable PDAC patients and borderline resectable PDAC patients with and without neoadjuvant treatment. In patients with borderline resectable PDAC, systemic therapy was administered according to international guidelines, consisting primarily of multi-agent chemotherapy with FOLFIRINOX or, in patients not eligible for this regimen, gemcitabine plus nab-paclitaxel. Patients with other peri- or ampullary carcinomas, metastatic disease, and locally advanced PDAC were excluded. In this study, the mesopancreas was defined as the firm, fibro-fatty tissue dorsal to the pancreatic head and uncinate process, bordered anteriorly by the Fredet’s fascia, posteriorly by the Treitz’s and Toldt’s fasciae, and medially by the SMA and SMV [6, 36].

Study endpoints

The primary objective of this study was to evaluate whether histopathological mesopancreatic infiltration is associated with incomplete oncologic clearance (R1/R0CRM+) in patients according to current NCCN anatomical criteria. Secondary objectives were to examine (i) the relationship between radiologically defined resectability status and mesopancreatic infiltration, (ii) the association between resectability classification and resection margin status, including its predictive performance, and (iii) the correlation between resectability status and established clinicopathological parameters such as T-stage, N-stage, grading, perineural invasion, lymphovascular invasion, and peripancreatic fat infiltration.

Computertomographic analysis

All radiological MDCT scans were retrospectively analyzed by a radiologist (FZ) with expertise in the pancreaticobiliary system, with a particular focus on reclassifying cases as either primarily resectable or borderline resectable. To minimize bias, the radiologist was blinded to the resection status as well as preoperative and postoperative staging. Each scan was systematically evaluated between tumor contact and the extent of involvement of the major pancreatic arteries (CT, SMA, CHA) and veins (PV/SMV). Resectability criteria were incorporated from the NCCN guidelines [9,10]. Imaging was performed using a MDCT with a slice thickness of 2 mm with an intravenous contrast administration, and all analyses were conducted using Sectra Workstation IDS7 (Version 25.2.13.7617).

Histopathological analysis

The histopathological specimens from the included patients were taken from the histopathological reporting. Following this, the findings were documented and incorporated into our database. Since September 2015, the University Hospital of Duesseldorf has applied the '1mm rule' for circumferential resection margin (CRM) assessment, defining R0CRM- as a minimum clearance of 1mm, to determine the resection status in patients undergoing pancreatic surgery. All pancreatic ductal adenocarcinoma specimens included in this study were analyzed following the LEEPPs criteria [2,3].

Surgical therapy

All resections during the study period were performed by a dedicated hepatopancreatobiliary team led by WTK. At our institution, MPE is routinely incorporated into all oncological pancreatic head resections as a standardized surgical principle.

In accordance with our previously described surgical concept, the mesopancreas was defined as a fascially delineated peripancreatic compartment containing fibro-fatty, lymphatic, and perineural tissue located dorsal and medial to the pancreatic head and uncinate process. The dorsal boundary is formed by the fascia of Treitz, which is followed during mobilization of the pancreatic head in the course of the Kocher maneuver. Ventrally, the compartment is limited by the duplication fascia of Fredet, preserved during mobilization of the right colonic flexure and dissection along the mesocolon. Medially, the dissection proceeds along the perivascular plane of the superior mesenteric vessels while maintaining fascial integrity. This region represents the retroperitoneal attachment zone of the pancreatic head and contains the neurolymphatic structures relevant for tumor spread. Cranially, the compartment extends toward the level of the celiac trunk and common hepatic artery, whereas caudally it reaches the mesenteric root at the inferior border of the uncinate process; the exit area of the inferior pancreatoduodenal artery.

The objective of MPE is the comprehensive removal of this compartment in an en bloc fashion together with the pancreatic head specimen. In all patients, a uniform compartment-oriented dissection was performed, aiming at complete clearance of the mesopancreatic tissue up to the periadventitial plane of SMA and SMV. The extent of resection did not vary between cases. Particular emphasis was placed on meticulous clearance of the perivascular neurolymphatic tissue along the SMA axis, as this region represents a critical site for microscopic tumor spread and margin involvement.

Reconstruction was performed using a standardized three-limb jejunal configuration. End-to-side pancreaticojejunostomy and hepaticojejunostomy were constructed using retrocolic jejunal limbs. Gastrointestinal continuity was restored via an antecolic duodenojejunostomy or gastrojejunostomy. The jejunal limbs were connected by two side-to-side jejunojejunal anastomoses in Roux-en-Y configuration [6,36] (Fig. 1).

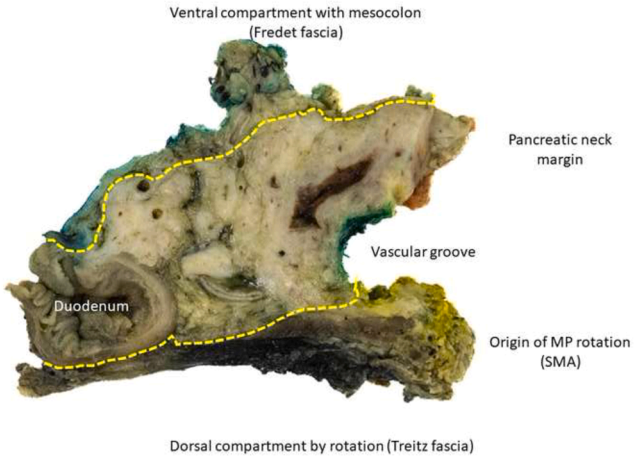

Fig. 1. The specimen was processed with axial slicing to illustrate anatomical orientation. Relevant landmarks were marked to facilitate a standardized evaluation: posteriorly, the Treitz fascia defines the boundary, while anteriorly the Fredet fascia is visible. The vascular groove outlines the trajectory of the superior mesenteric vein (SMV), and the dorsal medial pedicle indicates the embryological pivot point of mesopancreatic rotation.

Statistical analysis

All statistical analysis were carried out using SPSS® Statistics for Windows (version 26.0; SPSS, Inc., Chicago, IL, USA), considering a p-value below 0.05 as the threshold for statistical significance.

Statistical analyses were conducted to evaluate numerical and categorical data using appropriate methods. The Mann-Whitney U test and Pearson correlation test were applied to assess numerical variables, while categorical data were analyzed using the Chi-squared test and fisher exact test. To determine predictive factors, binary logistic regression modeling was performed, with results expressed as hazard ratios alongside their respective confidence intervals.

This research adhered to the principles of Good Clinical Practice (GCP) and the ethical standards set forth in the Declaration of Helsinki. Approval for the study was granted by the Institutional Review Board (IRB) of the Medical Faculty at Heinrich Heine University Düsseldorf (IRB No. 2019-473_1).

Results

Demographic data

The histopathological assessment and demographic data are summarized in Table 1. In all 271 PDAC patients, histopathological assessment included CRM status and mesopancreatic infiltration, whereas preoperative resectability classification was based on radiological evaluation according to current NCCN criteria. In 208 (76.9%) patients the MP was infiltrated by the PDAC. 209 (77.1%) patients were preoperatively classified as primarily resectable and 62 (22.9%) as borderline resectable. Among the borderline resectable patients, 37 (59.7%) received neoadjuvant therapy prior to surgery. A true R0CRM− resection was achieved in 143 of 271 patients (52.8%). Among the remaining 128 patients (47.2%) with incomplete oncologic clearance, 87 cases (32.1%) were classified as R0CRM+ whereas 41 patients (15.1%) exhibited a R1 resection. For further analysis, we sub grouped the total R-status into the dorsal and medial resection status separately.

Correlation analysis of radiographic and histopathological results

Correlation between resectability status and histopathology variables

Notably, preoperative resectability status (resectable vs borderline resectable) did not significantly correlate with conventional staging

Table 1
Demographic table of all 271included patients. Staging is revised to the 8th edition of the UICC TNM classification of malignant tumors.

Age in years		
Median (range)	69.5 (17-90)	
Gender	**N**	**%**
Male	159	58.7
Female	112	41.3
T-stage		
T1	15	5.5
T2	134	49.4
T3	115	42.4
T4	7	2.6
N-stage		
N0	58	21.4
N1	148	54.6
N2	65	24.0
Grading		
G1	10	3.7
G2	134	49.4
G3	127	46.9
Pn		
Pn0	42	15.5
Pn1	229	84.5
L		
L0	123	45.5
L1	148	54.5
V		
V0	182	67.0
V1	89	33.0
R-status total		
R1/R0CRM+	128	47.2
R0CRM-	143	52.8
R-status dorsal		
R1/R0CRM+	76	28.0
R0CRM-	195	72.0
R-status vascular groove		
R1/R0CRM+	68	25.1
R0CRM-	203	74.9
MP-status		
MP negativ	63	23.1
MP positiv	208	76.9
Resectability status		
Primary resectable	209	77.1
Borderline resectable	62	22.9

CRM: circumferential resection margin; MP-status: mesopancreatic infiltration status; Pn: perineural invasion; V: venous invasion

variables, especially T- or N-status (*p=0.406; p=0.132*) according to the 8th UICC classification. Among all analyzed clinicopathological parameters, only perineural invasion (Pn+) showed a statistically significant association with resectability status ($p = 0.025$) (Table 2). Specifically, borderline resectable tumours demonstrated a high positive predictive value for Pn+ status, with an odds ratio (OR) of 3.23 (95% CI 1.10–9.46, $p = 0.032$). However, resectable tumours also frequently exhibited perineural infiltration, resulting in low sensitivity of 25.33% (Supplementary Table I).

Table 2
Correlation analysis of radiographic and histopathological variables. Statistical difference was calculated by Pearson analysis. Logistic regression analysis was performed for prediction assessment.

	Primary resectable n= 209	Borderline resectable n=62	*p-value*
T1/T2	117	31	*0.406*
T3/T4	92	31	
N0	49	9	*0.132*
N1/N2	160	53	
G1-G2	113	31	*0.836*
G3	96	31	
Pn0	38	4	***0.025***
Pn1	171	58	
L0	94	29	*0.936*
L1	115	33	
V0	145	37	*0.128*
V1	64	25	

Correlation analysis between resectablity stauts, resection margin status and mesopancreatic Infiltration

We explored whether resectability status correlates with surgical margin involvement or mesopancreatic (MP) fat infiltration. There was a trend toward association with medial margin positivity, particularly along the vascular groove ($p = 0.066$) which did not reach statistical significance. Resectability status neither correlated with the total nor the dorsal margin status ($p = 0.172$ and $p = 0.844$, respectively). Predictive models for medial R-status based on resectability demonstrated limited discriminatory performance, with a sensitivity of 30.88%, specificity of 79.80%, PPV of 33.87%, and NPV of 77.51% (Supplementary Table II). The logistic regression did not reach statistical significance (p = 0.071; OR 0.57, 95% CI 0.31–1.05). Additionally, resectability status did not relate to peripancreatic fat invasion ($p=0.231$) (Table 3).

Correlation analysis between mesopancreatic infiltration status and resection status PDAC patients

Notably, in the subgroup of primarily resectable PDAC patients, positive MP status was significantly associated with incomplete dorsal ($p = 0.026$) and total resection margins ($p = 0.004$) (Table 4). In the subgroup of borderline resectable PDAC patients, no statistically significant correlation was observed between MP infiltration and individual resection margin involvement (medial: $p = 0.249$; dorsal: $p = 0.642$; total R status: $p = 0.154$) (Table 5). Mesopancreatic infiltration was present in 51 patients (82.3%) and absent in 11 patients (17.7%). Of the 51 MP-positive patients, 29 (56.9%) had received neoadjuvant therapy, whereas 22 (43.1%) underwent upfront resection. In contrast, among the 11 MP-negative patients, 8 (72.7%) received neoadjuvant treatment and 3 (27.3%) proceeded directly to surgery. Across the entire cohort, MP infiltration was associated with a 2.71-fold increased likelihood of incomplete local tumour control (R0CRM+/R1) (95% CI 1.35–5.43; $p = 0.005$) (Supplementary Table III).

Discussion

Pre-therapeutic staging primarily utilizes computed tomography in PDAC patients and continues to be the radiographic modality of choice. During tumor staging a detailed evaluation of the possible carcinomatous infiltration of the major peripancreatic vessels and, based on this, stratification into primary, borderline resectable and locally advanced is carried out [9]. The current literature that defined these criteria is scares, to our knowledge limited data is available that analyzed the

Table 3
Correlation analysis of histopathological mesopancreatic fat infiltration and resection status. Statistical difference was calculated by Fisher's exact test.

	Primary resectable n= 209	Borderline resectable n=62	*p-value*
Total R-status			
R1/R0CRM+	94	34	*0.172*
R0CRM-	115	28	
Dorsal R-status			
R1/R0CRM+	58	18	*0.844*
R0CRM-	151	44	
Vascular groove R-status			
R1/R0CRM+	47	21	*0.066*
R0CRM-	162	41	
MP Infiltration status			
MP negative	52	11	*0.231*
MP positive	157	51	

Table 4
Correlation analysis between mesopancreatic infiltration status and resection status in the 209 primary-resectable PDAC patients. Resection status was evaluated by the LEEP protocol. Statistical significance was calculated by the chi-squared test and fisher exact test ($p \leq 0.05$ is significant).

	MP negative n= 52	MP positive n=157	*p-value*
Total R-status			
R1/R0CRM+	15	79	***0.004***
R0CRM-	37	78	
Dorsal R-status			
R1/R0CRM+	9	49	***0.026***
R0CRM-	43	108	
Vascular groove R-status			
R1/R0CRM+	9	38	*0.253*
R0CRM-	43	119	

Table 5
Correlation analysis between mesopancreatic infiltration status and resection status in the 62 borderline resectable PDAC patients. Resection status was evaluated by the LEEP protocol. Statistical significance was calculated by the chi-squared test and fisher exact test ($p \leq 0.05$ is significant).

	MP negative n= 11	MP positive n=51	*p-value*
Total R-status			
R1/R0CRM+	8	26	*0.249*
R0CRM-	3	25	
Dorsal R-status			
R1/R0CRM+	3	15	*0.642*
R0CRM-	8	36	
Vascular groove R-status			
R1/R0CRM+	5	16	*0.154*
R0CRM-	6	35	

preoperative radiographic staging outcome with the redefined 8th edition UICC staging variables and resection status according to the *Royal College of Pathologist* and the LEEPP protocol [10,17–21]. It further remains unknown if current staging and resectability stratification predicts a possible infiltration into the mesopancreas. Although the oncological relevance of the mesopancreas continues to be controversially discussed, there is increasing evidence in the literature that can no longer be dismissed [37–40].

In our opinion, the current recommendation for anatomical categorization of resectability in PDAC patients takes into consideration one unique anatomical facet, although the anatomy is highly sophisticated, and therefore the criteria are too unidimensional, which need to be reconsidered. The aim of a resectability classification is to provide PDAC patients with the best possible prediction to either perform upfront surgery in case of primary resectable or utilize neoadjuvant treatment strategies if otherwise. The current anatomical criteria have already been complemented by conditional [13,41] and biological [42–44] criteria to enable better preoperative stratification of PDAC patients. Therefore a neoadjuvant concept, consisting FOLFIRINOX or gemcitabine-based chemotherapy for borderline resectable patients is already state of the art and implemented into the international guidelines [9,10,45–47].

Our study demonstrates that the anatomical resectability status does not correlate with most of the 8th UICC staging variables and, most importantly, not with the total R-status or the dorsal R-status. These findings are in line with the results of Bolm et al. [21], who likewise reported no significant association between the radiologically defined resectability status and the histopathological margin status. However, a plausible association, but not significant, was observed for the medial R-status (vascular groove). Surprisingly, a positive mesopancreatic infiltration status in the group of primarily resectable patients demonstrated a clear association with both the total R-status and the dorsal R-status. In addition, the positive MP infiltration within all included PDAC patients had a 2.7-fold increased chance of incomplete resection.

The oncological significance of mesopancreatic excision and, as previously described, contribute to improved local tumor control [6,29]. The surgical principles are comparable to the well-established gold-standards of total mesocolic and mesorectal excision. The standardization of mesorectal and mesocolic excision has led to a significant increase in the rate of negative resection margins and has enhanced treatment outcomes [48–50], which is urgently needed for PDAC patients as well. The mesorectal area is not only an anatomical landmark, which is utilized as a resection plane, but serves radiographically to stratify patients for either multimodal treatment path (upfront resection vs. neoadjuvant therapy). Taken the secondary retroperitoneal nature of the pancreas and the current literature into consideration supports the idea to implement the mesopancreas for treatment strategies as well. Nevertheless, it must be acknowledged that MPE remains a matter of ongoing debate [6,36,38,40]. A universally accepted anatomical definition of the MP has not yet been established, and different conceptual frameworks exist. While some authors describe the MP region based on fascial boundaries and embryologic planes [6,36,37], others define it in neuroanatomical terms as corresponding to components of the extrapancreatic pancreatic head plexus [51]. This heterogeneity in definition has led to criticism regarding its anatomical distinctiveness and reproducibility. However, regardless of the underlying conceptual model, the dorsal-medial retropancreatic compartment consistently emerges as a region at high risk for microscopic tumor spread and margin involvement [3,7,40].

Our data further suggests that a possible MP infiltration may considered to be included in oncological decision-making, in order to improve stratification. Previously, we and others were able to demonstrate that preoperative evaluation using MP fat stranding in MDCT correlated with an actual involvement of the mesopancreas, underlining that current radiographic modalities during PDAC staging are reliable to access the mesopancreatic fat [52–54].

Subsequently, in this study we were able to show that primarily resectable patients remained at risk of suffering from a true mesopancreatic infiltration, which was consecutively associated with an increased rate of incomplete local tumour control (R0CRM+/R1). Although survival analysis was not part of the present study, it is well established that an R1 situation in PDAC represents a major adverse prognostic factor and significantly limits long-term survival [4]. Our findings therefore suggest that mesopancreatic infiltration, which was strongly associated with positive margins, may likewise contribute to impaired oncologic outcomes. A more detailed analysis of survival endpoints in relation to mesopancreatic involvement would be desirable in future studies. Futhermore this finding supports the hypothesis that currently defined “primarily resectable” PDACs are not sufficiently stratified in terms of their biological and anatomical risk profile. Other studies have similarly suggested that the addition of further criteria may improve risk stratification in primarily resectable PDACs, for example by incorporating factors such as a tumour size >4 cm or even a venous contact <180°, both of which have been reported to be associated with an increased risk of positive resection margins [21,22]. The risk for mesopancreatic infiltration clearly declined when neoadjuvant treatment principles were implemented [27]. Nevertheless, MPE represents a standardized surgical principle at our institution and was performed uniformly in all patients, irrespective of prior systemic therapy. its impact on the technical complexity of mesopancreatic excision remains unclear. Therapy-associated fibrosis and inflammatory alterations may theoretically increase the difficulty of dissection along the vascular and fascial planes; however, systematic data addressing this issue are currently lacking. This aspect warrants further investigation. Thus, even primary resectable patients with a probable involvement of the peripancreatic fat might benefit from neoadjuvant treatment rather than

upfront resection to achieve both local and systemic tumor control. A retrospective study by Papalezova et al. [55] showed an extended median survival after neoadjuvant treatment vs. upfront resection in primary resectable PDAC patients. This could support our hypothesis, that current resectability criteria are not precise enough to stratify patients for the most suitable treatment path. Naturally, the risk of local and systemic progression of pancreatic cancer during the course of chemotherapy cannot be denied [9]. Including mesopancreatic fat infiltration in the current resectability criteria may lead to better stratification, although it's challenging character. This hypothesis requires further validation through prospective randomized trials, containing lager patient cohorts.

The study has inherent limitations. The single-centre and retrospective nature cannot be denied. Furthermore, it is a large investigation period and the lack of inclusion of the conditional - (ECOG status) and biological factor (CA19-9 levels). While these variables are unquestionably relevant for overall patient stratification, the present study was specifically designed to assess the anatomical and surgical dimensions of resectability and their implications for margin status.

Conclusion

Current PDAC staging primarily relies on computed tomography but remains limited in accurately assessing mesopancreatic infiltration. In our cohort, mesopancreatic involvement was frequently observed and was significantly associated with an increased risk of incomplete resection, particularly in patients classified as primarily resectable. These findings suggest that mesopancreas-related features may warrant consideration in future refinements of resectability assessment. Prospective validation in larger, multicenter studies is required to further define their clinical relevance.

Ethics approval and consent to participate

This study was approved by the local institutional review board (Heinrich Heine University, Duesseldorf, Germany; study-no.: 2019-473-1. All procedures performed in this study were in accordance with the ethical standards in the 1964 Declaration of Helsinki and its later amendments. Informed consent was waived because no data regarding the cases were disclosed.

Consent for publication

Not applicable

Availability of data and materials

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

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CRediT authorship contribution statement

Stephan O. David: Writing – original draft, Formal analysis, Data curation, Conceptualization. **Andrea Alexander:** Supervision. **Farid Ziayee:** Formal analysis, Data curation. **Ahmad B. Sultani:** Investigation. **Christoph Roderburg:** Supervision, Investigation. **Irene Esposito:** Validation, Supervision. **Lena Haeberle-Graser:** Formal analysis. **Sascha Vaghiri:** Supervision, Formal analysis. **Wolfram T. Knoefel:** Validation, Supervision. **Sami A. Safi:** Writing – review & editing, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no competing interests.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ctarc.2026.101176.

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