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The borders of borderline resectable pancreatic cancer (BRPC)

Speaker: Chetan Kantharia, Mumbai

Understanding the resection margins in standard pancreatic oncologic resections:

The pancreas lies over the critical blood vessels of the upper alimentary tract - the celiac axis, common hepatic artery and the gastroduodenal artery - all of which lie on the upper border of the pancreas. The second crucial vascular pedicle is the superior mesenteric artery which lies just to the left of the pancreatic neck. The portal vein-mesenteric vein axis lies within the two lines and is the third vital fact to remember.

When one understands the resection margins of a right-sided pancreatic resection (Whipple) or a left pancreatic resection, it forms the template from which BR PDAC can be easily understood. The upper border of the resection is at the gastroduodenal artery take-off at the common hepatic artery, and the left resection margin is at the IPDA take-off at the superior mesenteric artery. The superior margin - the gastroduodenal artery is a gateway to the anterior surface of the portal vein. The pancreatic neck is transected, and the resection line skirts the portal vein's right border and reaches the SMA's right edge. This is the standard resection margin in right-sided pancreatic resections.

The anatomical definition of BR PDAC will involve a breach of one or more of the borders or the resection line. The anatomical description aims to predict the possibility of margin-positive resection in pancreatic cancer. Standard imaging guidelines define identification that these borders are breached. The report hinges on the anatomical proximity of the tumour to the blood vessels. Proximity is determined by the abutment of the ship that defines the borders of the resection.

In addition, the IAP guidelines consider additional criteria for predicting the presence of extrahepatic disease and patient factors that preclude resection treatment options. This is known as the ABC criteria and will add to the decision-making process.

The current classification of pancreatic cancer based on resectability is given below:

Borderline resectable pancreatic cancer for pancreas head cancers - BR PDAC					
Anatomical definitions					
	Arterial			Venous	
Defining organisation or Center	SMA	CA	CHA	SMV/PV	IVC
MD Anderson Cancer center	< 180 degree contact	< 180 degree contact	Short segment around the GDA origin	Short segment occlusion Suitable vessel for	

				reconstructi on	
AHPBA/SSA T/SSO	< 180 degree contact		Short segment around the GDA origin	Abutment , without impingemen t or narrowing of the lumen Encasemen t of the vein, with no involvement of the adjacent arteries Short segment occlusion	
NCCN 2021	< 180 degree contact		Solid tumour contact, but no extension to CA or the hepatic artery bifurcation	> 180 degree abutment or < 180 degree abutment with contour irregularity of the vein or thrombosis with a good reconstructi on option	Solid tumour contact
			Solid tumour contact with variant arterial anatomy - aRHA or rRHA		
Japanese pancreas society 7th edition	< 180 degree contact		Tumour contact or invasion without showing		

	No stenosis or deformity noted		tumour contact or invasion of the hepatic artery proper and/or CA		
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International consensus on definition and criteria of borderline resectable pancreatic ductal adenocarcinoma 2017

Type of definition	Anatomical	Biological	Conditional
R	R-Type A	No: R-Type A	No: R-Type A
		Yes: BR-Type B	Yes: BR-Type C
BR	BR-Type A	No: BR-Type A	No: BR-Type A
		Yes: BR-Type AB	Yes: BR-Type AC
Locally advanced: LA	LA-Type A	No: LA-Type A	No: LA-Type A
		Yes: LA-Type AB	Yes: LA-Type AC

Biological definition:

- CA 19-9 more than 500 IU/ml
- Regional lymph node metastasis (biopsy or PET-CT)

Conditional host-related definition: • Depressed performance status (PS: 2 or more)

Tumor is classified based on combination of A, B, and C (for example, a patient with both Type B and Type C features would be classified as Type ABC).

What does it imply?

A borderline resectable pancreatic cancer means there is a high chance of margin-positive resection or an increased risk of extrahepatic disease or inability of the patient to withstand major surgery.

The definition aims to identify a subset of tumours with more aggressive biological features, on which a neoadjuvant approach could be preferable instead of classic upfront surgery. There are some advantages of neoadjuvant therapy, like early systemic treatment for undetected micrometastases, increased R0 resection rate, and reduced postoperative pancreatic fistula. Current NCCN guidelines suggest neoadjuvant chemotherapy for this subset of patients.

What are the solutions?

There are limited evidence-based recommendations and debate on neoadjuvant treatment for BR PDAC is wide open. In an intention to treat analysis following neoadjuvant chemotherapy for BR PDAC, Jang et al noted improved 1 and 2 year survival in the neoadjuvant treatment group. However, the PREOPANC study did not reveal a significant difference in the median overall survival between neoadjuvant chemotherapy and upfront surgery for BR PDAC. These studies have not shown us robust results and the treatment algorithm remains open to debate.

There are 6 meta analyses addressing these issues (Gillen et al., Tang et al., Dhir et al., Verstijne et al., Pan et al. and Cloyd et al.) but only one of them analyses patient with BR PDAC alone. So the data still is unclear. However, with the limited evidence available, neoadjuvant chemotherapy is considered the gold standard in this group of patients. Newer RCTs are designed to address these issues and hopefully, they will provide much better answers.

Surgery in BR PDAC

In addition to the use of NACT in BR PDAC, two surgical options are advised: venous resection and periadventitial dissection. Venous resection performed concomitantly with pancreas resection in patients with vascular involvement seems to result in similar surgical mortality and perioperative morbidity rates when compared to standard pancreas resections. The complication rates and morbidity are similar in both venous resection and those without venous resection.

The subadventitial dissection of the SMA is gaining favour among pancreatic surgeons, but the question is being addressed in the DISSECT trial which is ongoing.

The TRIANGLE operation is another surgery which removes the tissue upwards of the SMA and between SMA and the CA. This also gives better clearance after NACT for BR PDAC.

Key points:

1. BR PDAC indicates lesions with a higher chance of treatment failures - either R1 resections or distant failures.
2. Diagnosis is established by anatomical, biologic or conditional criteria. For anatomical criteria, there are well-defined radiologic criteria for diagnostic classification.
3. NACT is recommended in most patients, but there is no robust evidence of its benefit.
4. Surgical resection is possible with specialised surgical techniques. While venous resection has become a technical standard, arterial resections are limited to left-sided cancers.

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**Summary prepared by
Rapporteur**

**Ilango Sethu
MIOT, Chennai**