



Achieving Excellence

PANCREATIC CANCER UK NATIONAL STUDY DAY

Surgery for pancreatic cancer, current strategies and borderline cases

Mr. Christian Macutkiewicz

Consultant HPB & Laparoscopic Surgeon

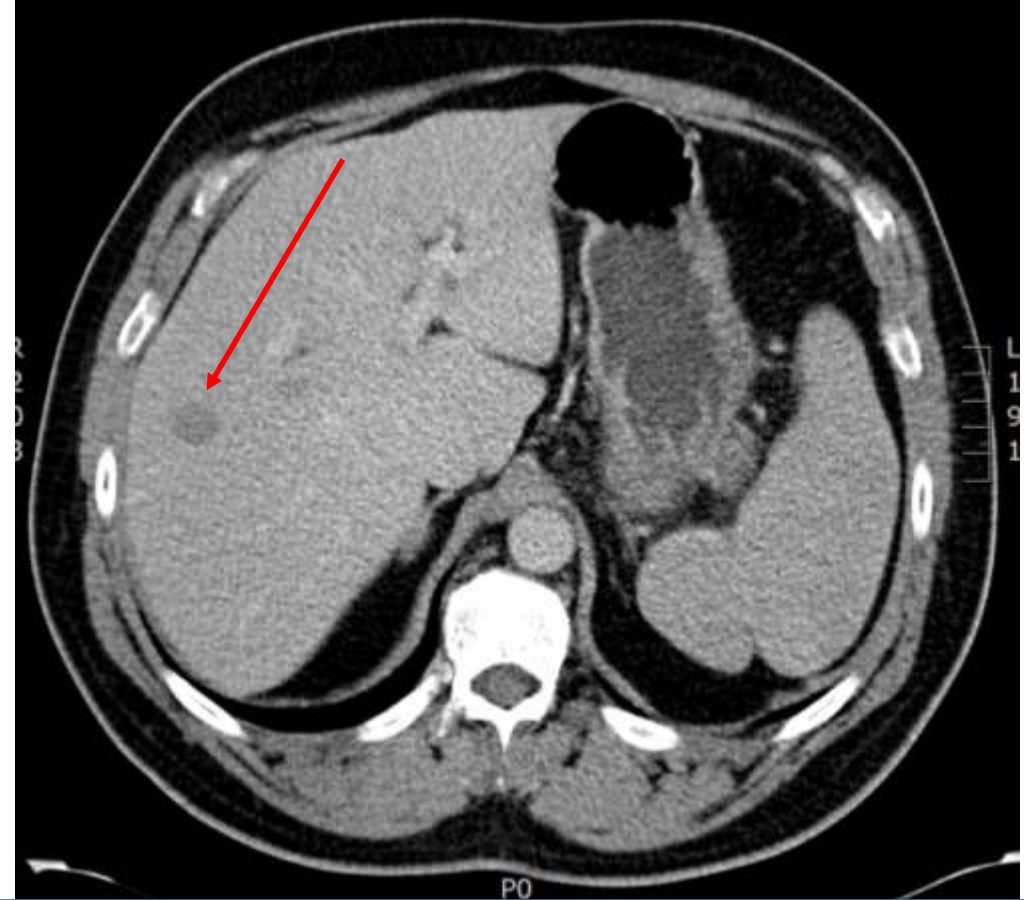


Introduction

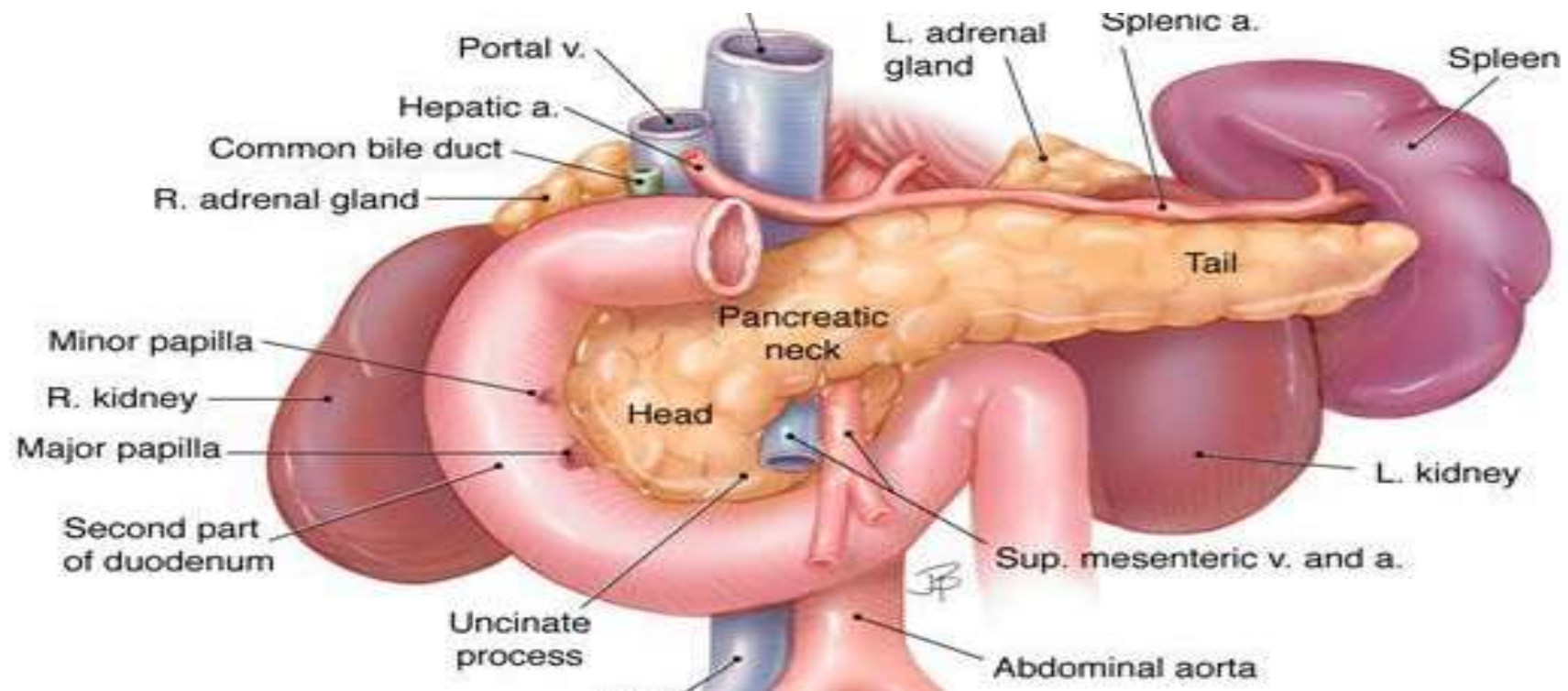
- Traditional approach to pancreatic surgery
- “Fast-track” Whipples
- Borderline operable pancreatic cancer
- Neoadjuvant therapy for pancreatic cancer
- Discuss real-life cases
- Look at future directions

Audience case

- 47 year old male
- Presents with obstructive jaundice
- CT: PDAC with solitary metastasis
- Management:
 - Palliative chemotherapy
 - Neoadjuvant chemotherapy + Surgery?



Pancreas anatomy



Pancreas Operations

- Head of Pancreas

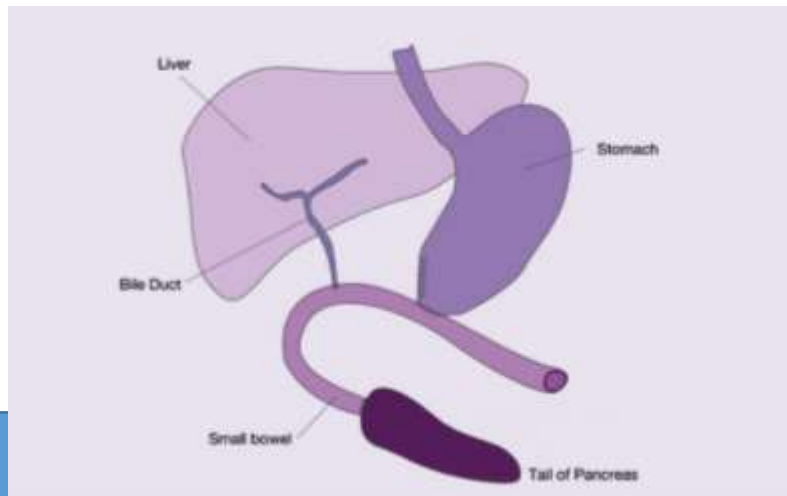
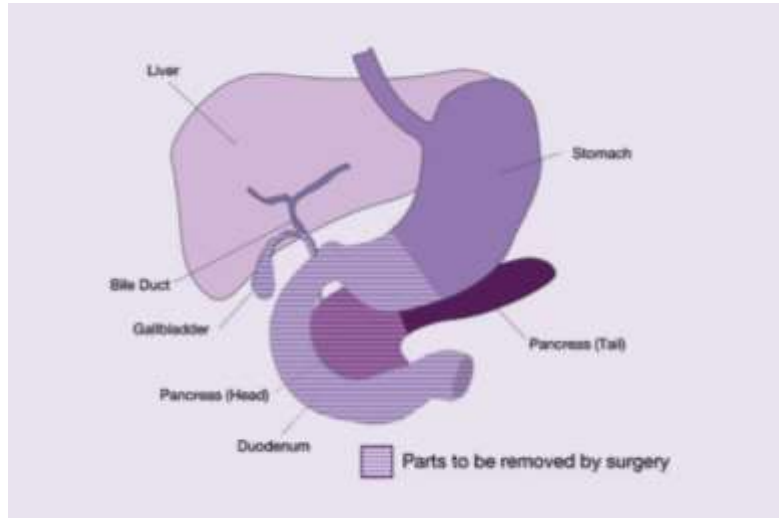
- Whipples (Pancreaticoduodenectomy)
- Pylorus-preserving pancreaticoduodenectomy (PPPD)

- Body & tail of Pancreas

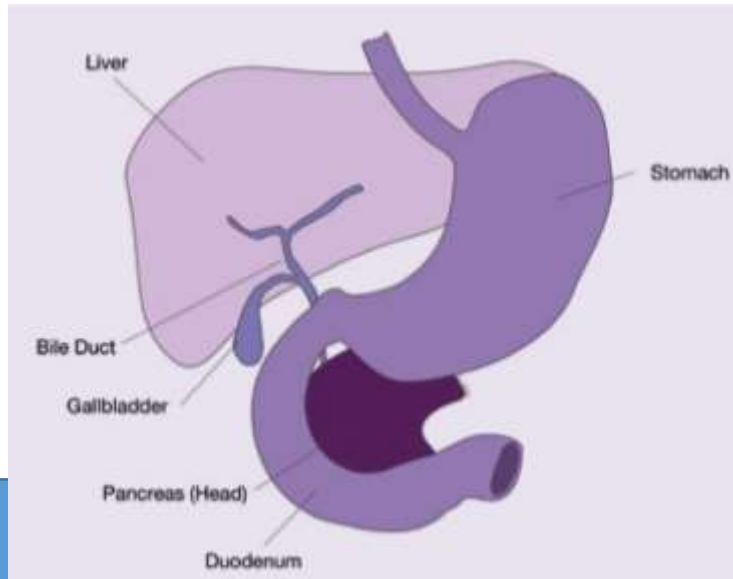
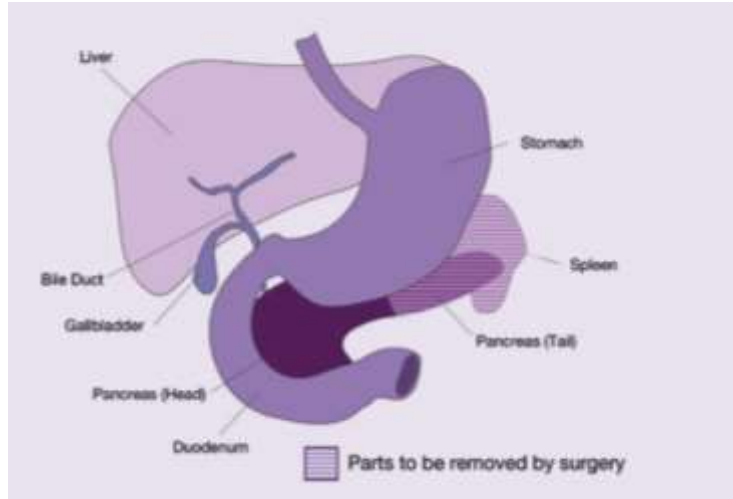
- Distal pancreatectomy +/- Splenectomy

- Total pancreatectomy

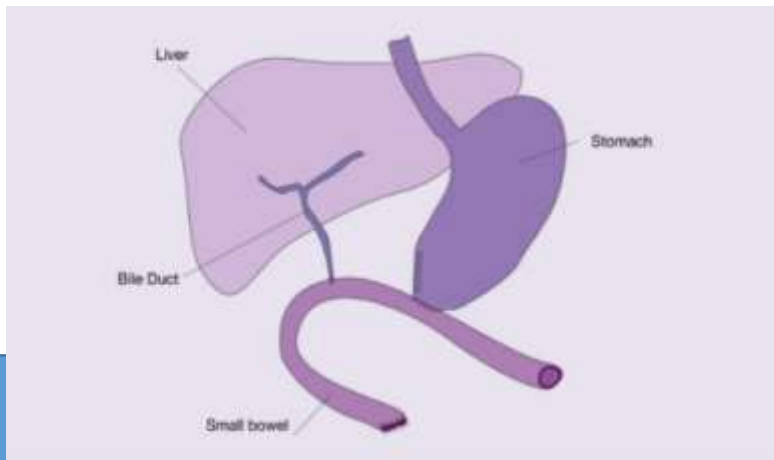
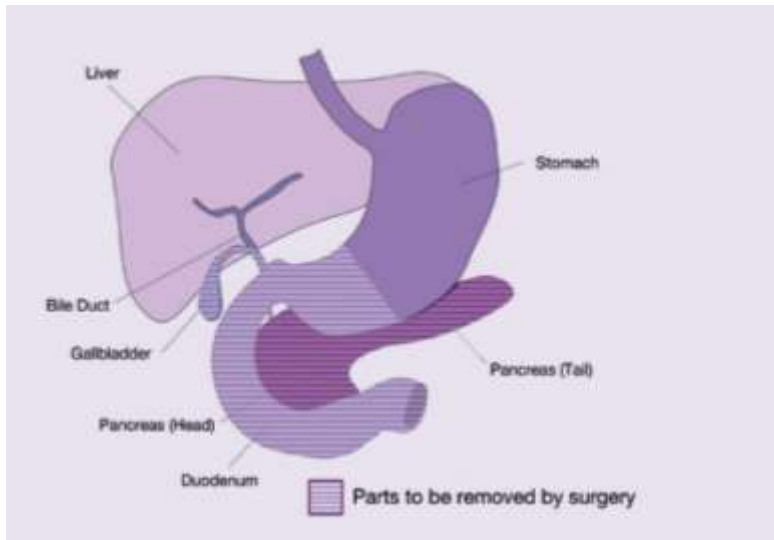
Whipples procedure



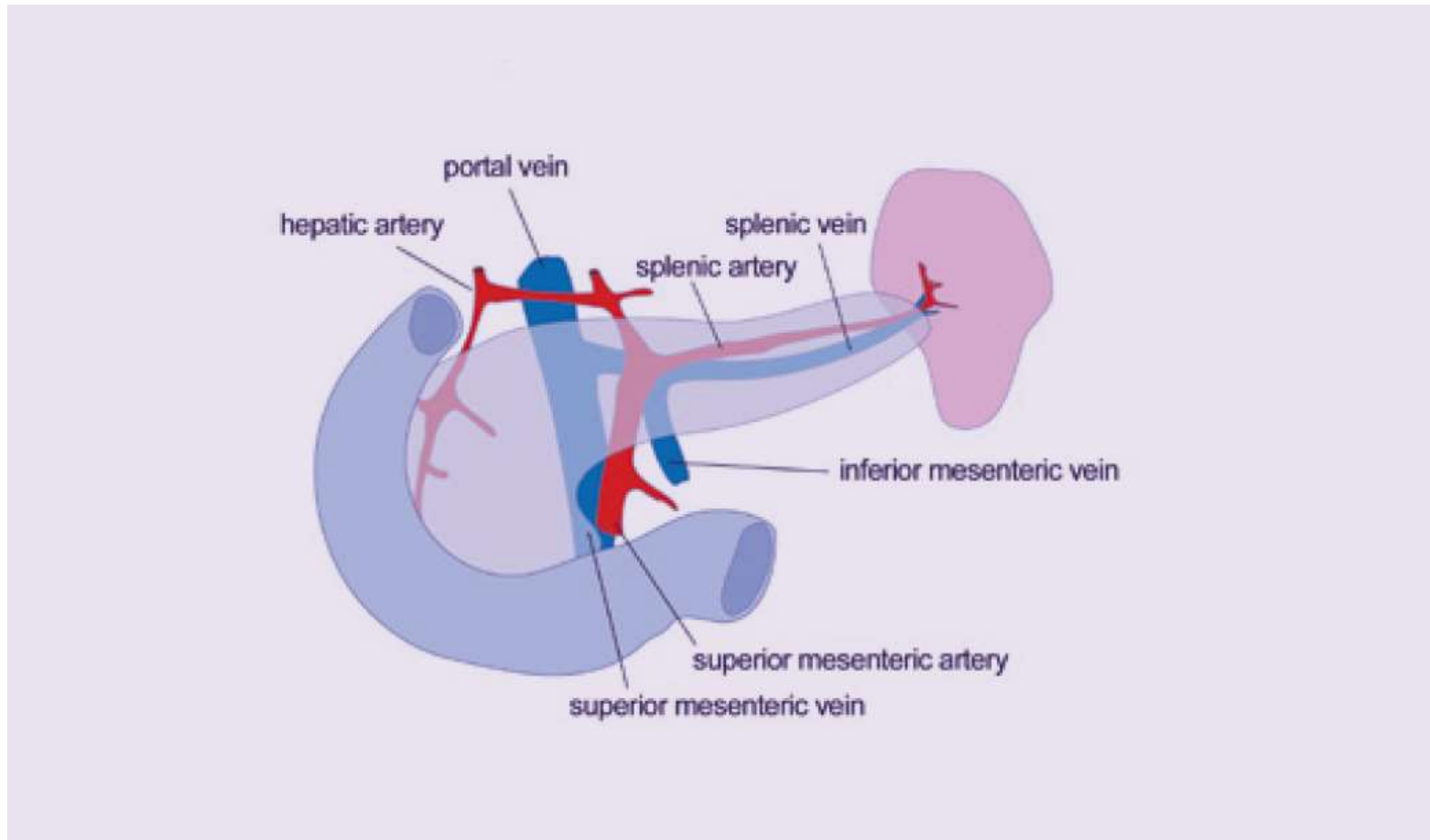
Distal Pancreatectomy & Splenectomy



Total pancreatectomy



Position of the tumour is important!



“Traditional” Surgical Approach

- >180 degree involvement of PV/SMV
- Any tissue around the SMA
- Any tissue around the common hepatic artery
- Any tissue around the coeliac trunk

BYPASS!!

Advanced surgical approach



En Bloc Vascular Resection for Locally Advanced Pancreatic Malignancies Infiltrating Major Blood Vessels: Perioperative Outcome and Long-term Survival in 136 Patients

Yekebas, Emre F. MD*; Bogoevski, Dean MD*; Cataldegirmen, Guellue MD*; Kunze, Christina MD*; Marx, Andreas MD†; Vashist, Yogesh K. MD*; Schurr, Paulus G. MD*; Liebl, Lena MD*; Thieltges, Sabrina MD*; Gawad, Karim A. MD*; Schneider, Claus MD*; Izbicki, Jakob R. MD*

- Even up to 2008 – PV resection controversial
- Hamburg – results of vascular resections
- Median survival similar to standard resections BUT vastly superior to palliative bypass + chemo

Advanced surgical approach



The Royal College of Surgeons of England

controversial topics in surgery

Portal vein resection during pancreaticoduodenectomy for cancer

AAMIR Z KHAN AND ANDREW M SMITH & GRB IRVING AND IAIN CAMERON

- Numerous reviews, no RCTs possible
- Generally accepted that PV/SMV resection beneficial in selected patients to get R0
- SMA generally not accepted as standard

“Fast-Track” Whipples

A reduced time to surgery within a ‘fast track’ pathway for periampullary malignancy is associated with an increased rate of pancreatoduodenectomy

Keith J. Roberts, Pooja Prasad, Yvonne Steele, Francesca Marcon, Thomas Faulkner, Hentie Cilliers, Bobby Dasari, Manuel Abradelo, Ravi Marudanayagam, Robert P. Sutcliffe, Paolo Muiesan, Darius F. Mirza & John Isaac

- Long delays from diagnosis to treatment in the order of 80 days
- Preop biliary drainage has been shown to increase complications
- Patients can become inoperable during the delay in treatment
- Can “Fast-Track” Pancreatoduodenectomy be possible in the NHS?

“Fast-Track” Whipples

Table 2 The pathway from initial CT scan to surgery as defined by key periods

Interval	PBD n = 61	No PBD n = 32	p
CT to referral	16 (1–67)	2 (0–15)	<0.0001
Referral to MDT	4 (0–54)	2 (0–10)	0.003
MDT to clinic	8 (0–43)	1 (-2 ^a -6)	<0.0001
Clinic to surgery	25 (5–153)	7 (2–21)	<0.0001
TOTAL: CT to surgery	65 (9–181)	16 (8–39)	<0.0001

Table 3 Summary of the study cohorts

		PBD n = 61	No PBD n = 32	p
Gender male/female		31/30	19/13	0.679
Age [median (range)]		69 (51–88)	67 (49–82)	0.162
Smoker		2	5	0.045
Asthma		6	3	1
Chronic obstructive lung disease		2	0	0.544
Diabetes		17	10	0.811
Hypertension		33	13	0.276
Myocardial infarction		2	1	1
Cerebrovascular accident		0	2	0.116
CKD (stage 3 or 4)		2	0	0.544
Bilirubin at presentation, median (range)		200 (29–585)	173 (43–347)	0.235
Bilirubin at surgery, median (range)		21 (5–355*)	306 (78–461)	<0.001
Cancer origin	Pancreas	46	29	0.168
	Bile duct	5	2	
	Ampulla	10	1	
Venous involvement on initial CT		7	10	0.025
Venous/arterial involvement surgery		14	11	0.303
Surgical procedure	Resection	46	31	0.009
Venous resection with PD	No	42	21	0.014
	Yes	4	10	

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- Reduction in time to surgery (65 days to 16 days)
- Reduction in palliative bypass rate 25% to 3%
- “Fast-Track” Whipples is POSSIBLE!

Table 3 Summary of the study cohorts

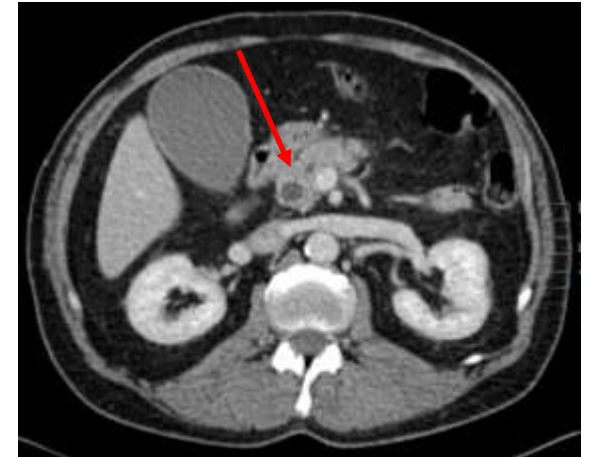
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BUT...

- “Almost all patients have systemic disease at the time of presentation with PDAC”
- 85% of patients having a “curative resection” succumb to systemic metastases^{*}
- “Fast-Track” surgery doesn’t treat the systemic disease – survival data is pending

Mr JW – 67 yrs old

- Presents with obstructive jaundice
- 30/11/16 - CT shows double duct dilatation
- 6/12/16 - EUS/ERCP – small pancreatic tumour, no vessel involvement
- 12/12/16m – “Fast-track” Pancreaticoduodenectomy

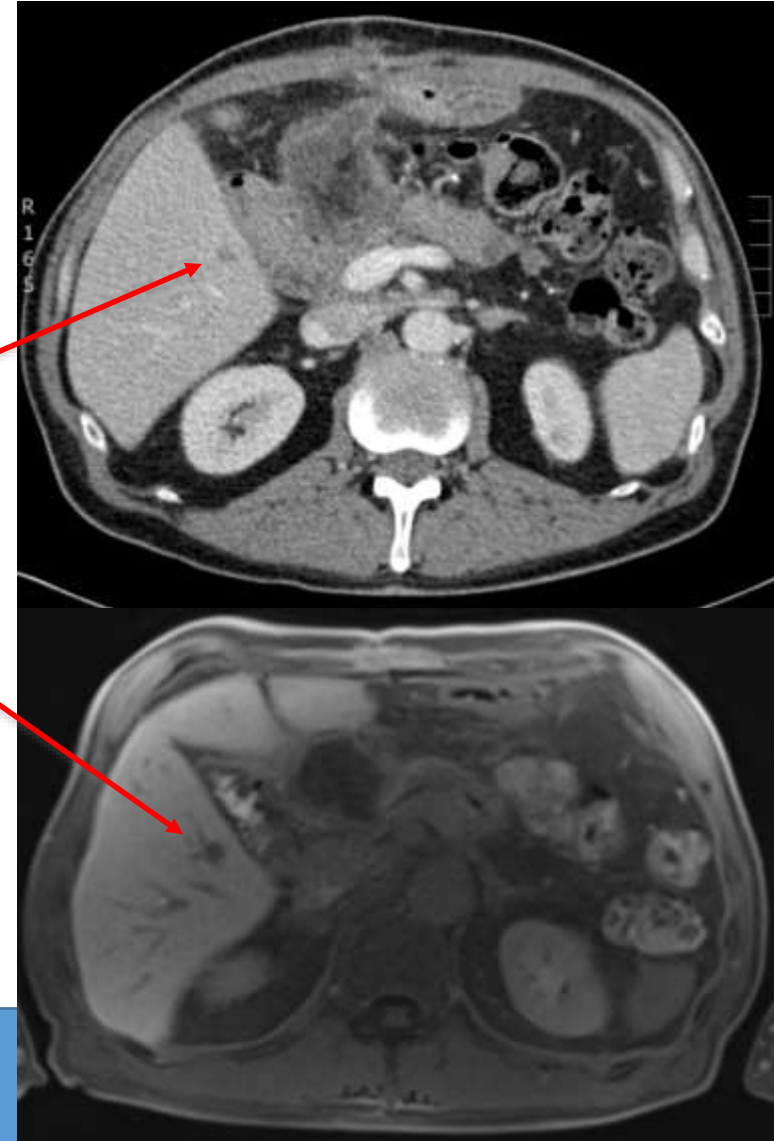


Mr JW – 67 yrs old

- Histology: moderately well differentiated adenocarcinoma
pT3N1(2/10)V1R0
- Post-operative course complicated by pancreatic leak
- Discharged 5/1/17 – LOS 36 days
- Readmitted 3/2/17 – failure to thrive

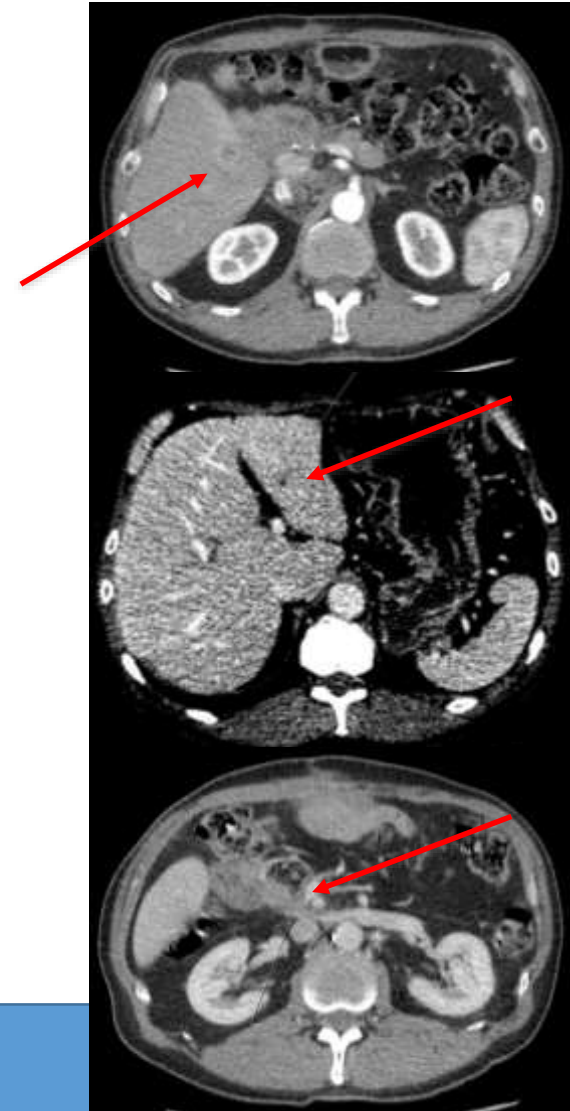
Mr JW – 67 yrs old

- New CT 3/2/17
- New liver lesion
- Confirmed on MRI
- Referred to Oncologists



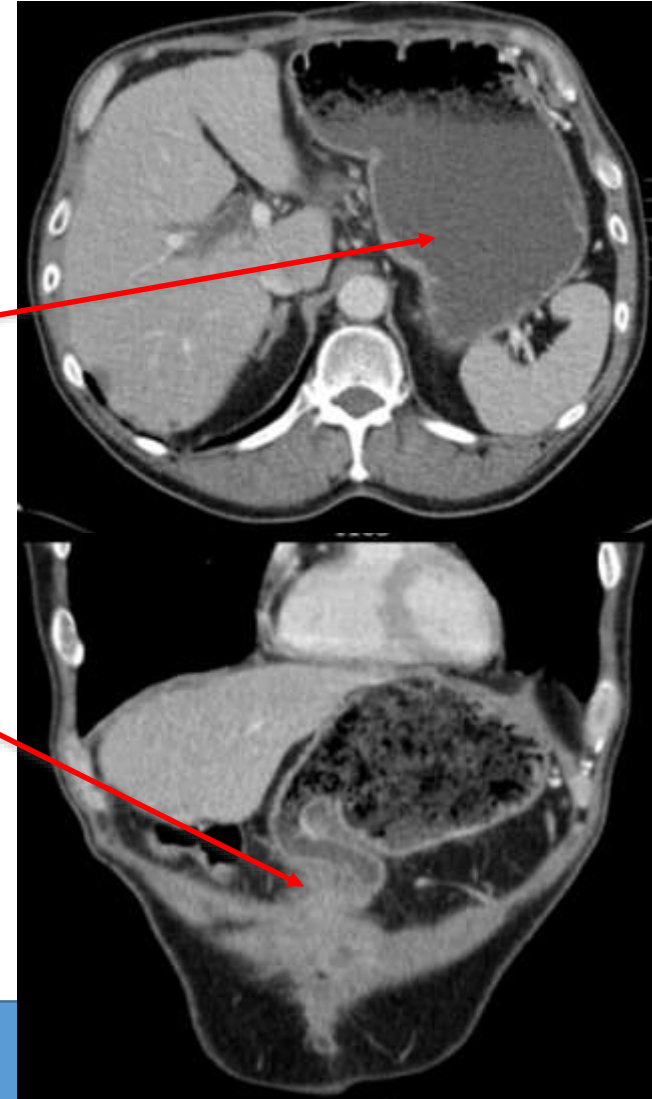
Mr JW – 67 yrs old

- Seen by Medical Oncology
- CT prior to treatment 16/5/17
- Sg V LM bigger, Sg IV met
- Spiculated mass SMV/IVC



Mr JW – 67 yrs old

- Admitted from surgical clinic
- Gastric outlet obstruction
- Local recurrence
- Metal stent
- Palliative care



Discussion

- Did “Fast-Track” surgery work?
- Should all PDAC have neoadjuvant chemo?
- Would chemo have shown this man to have aggressive disease?

Paradigm Shift

The
Oncologist®

Gastrointestinal Cancer

Neoadjuvant FOLFIRINOX for Borderline Resectable Pancreas Cancer: A New Treatment Paradigm?

KATHLEEN K. CHRISTIANS,^a SUSAN TSAI,^a ANNA MAHMOUD,^a PAUL RITCH,^b JAMES P. THOMAS,^b LAUREN WIEBE,^b TRACY KELLY,^c
BETH ERICKSON,^c HUAMIN WANG,^d DOUGLAS B. EVANS,^a BEN GEORGE^b

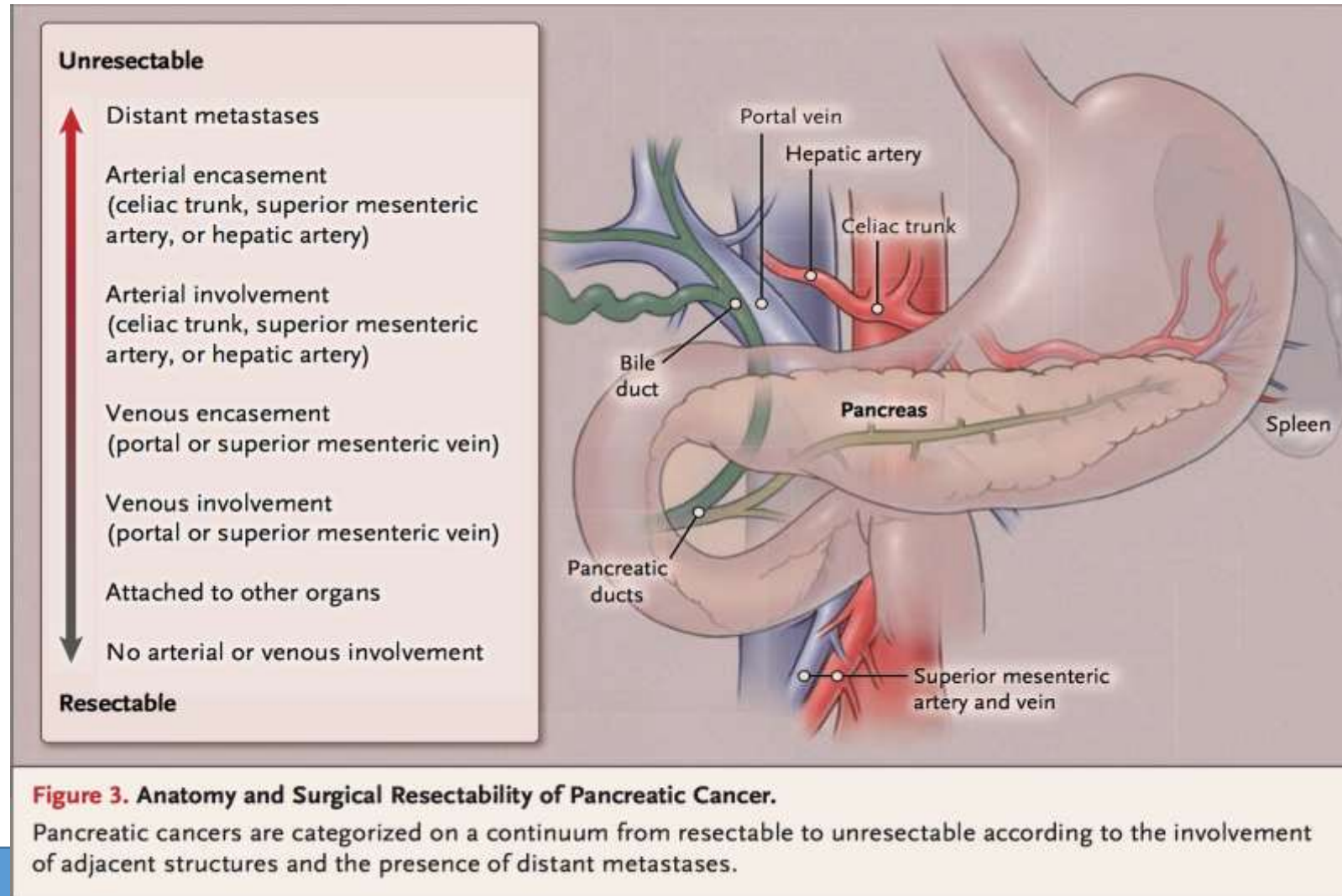
^aDepartment of Surgery, Division of Surgical Oncology, ^bDepartment of Medicine, Division of Medical Oncology, and ^cDepartment of Radiation Oncology, Pancreatic Cancer Program, Medical College of Wisconsin, Milwaukee, Wisconsin, USA; ^dDepartment of Pathology, University of Texas MD Anderson Cancer Center, Houston, Texas, USA

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Neoadjuvant therapy • FOLFIRINOX • Pancreatic adenocarcinoma • Borderline resectable pancreas cancer

- Borderline resectable tumours
- Chemotherapy followed by Chemoradiotherapy
- 67% of patients went on to surgery
 - 100% R0 resection
 - 17% positive lymph nodes
 - 58% of patients alive at 22 months

Borderline & Locally Advanced Disease

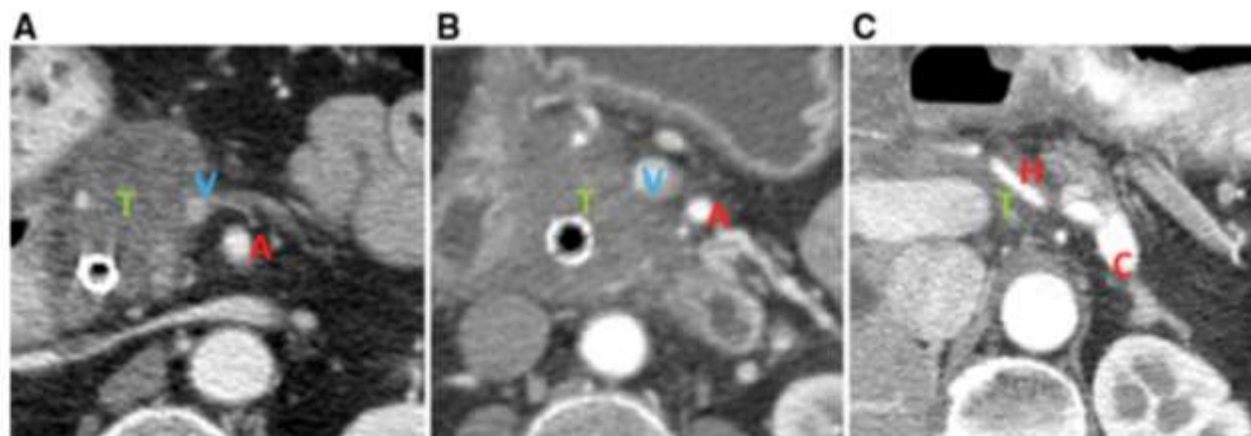


Borderline Resectable Disease

Table 1 Comparison of radiographic differences in common definitions for borderline resectable pancreatic cancer

Effected vessel	AHPBA/SSAT/SSO/NCCN ^[29]	MD Anderson ^[28]	Alliance ^[26]
SMV/PV	Abutment, impingement, encasement of the SMV/PV or short segment venous occlusion	Occlusion	Tumor-vessel interface $\geq 180^\circ$ of vessel wall circumference, and/or reconstructable occlusion
SMA	Abutment	Abutment	Tumor-vessel interface $< 180^\circ$ of vessel wall circumference
HA	Abutment or short segment encasement	Abutment or short segment encasement	Reconstructable short segment interface of any degree between tumor and vessel wall
CA	Uninvolved	Abutment	Tumor-vessel interface $< 180^\circ$ of vessel wall circumference

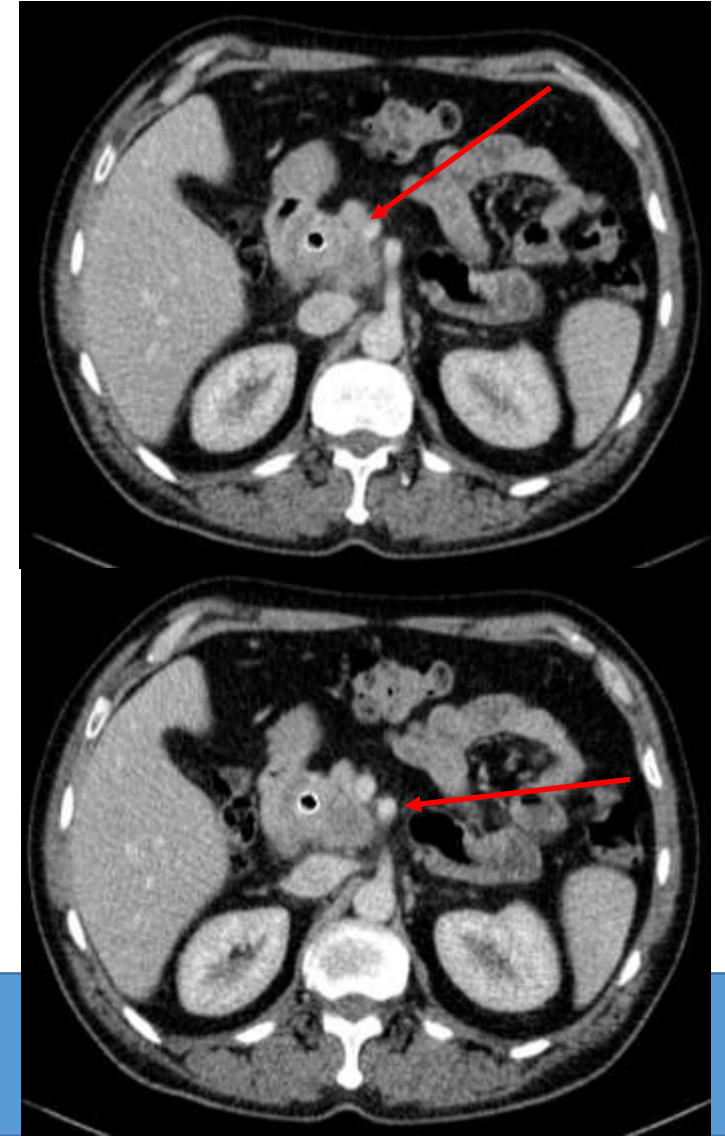
AHPBA/SSAT/SSO/NCCN: Americas Hepatopancreaticobiliary Association/Society for Surgery of the Alimentary Tract/Society of Surgical Oncology/National Comprehensive Cancer Network; SMV/PV: Superior mesenteric vein/portal vein; SMA: Superior mesenteric artery; HA: Hepatic artery; CA: Celiac artery.





Case Presentation – Mr KP, 56 years old

- Patient presents with obstructive jaundice
- Locally advanced tumour
 - 5cm mass
 - PV/SMV strictured
 - Loss of SMA fat plane
- EUS: adenocarcinoma

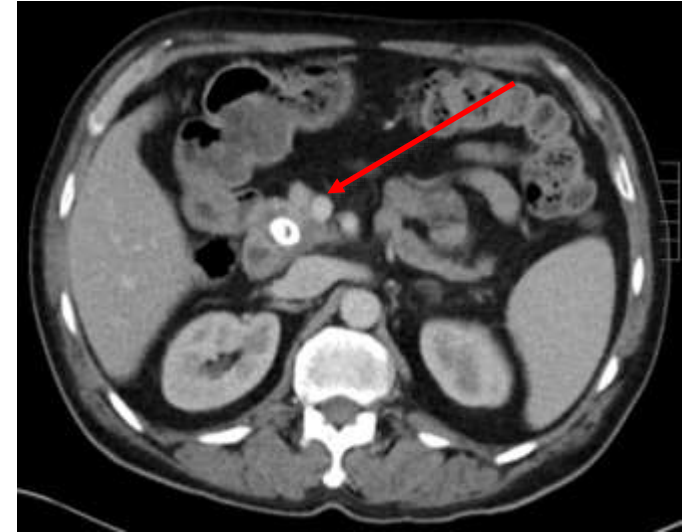


Case Presentation – Mr KP, 56 years old

- MDT: For FOLFIRINOX
- Started IrOxMdG → OxMdG (3 months)
- Reaction to Irinotecan
- Grade 1 paraesthesia in hands and feet
- Post-treatment CT

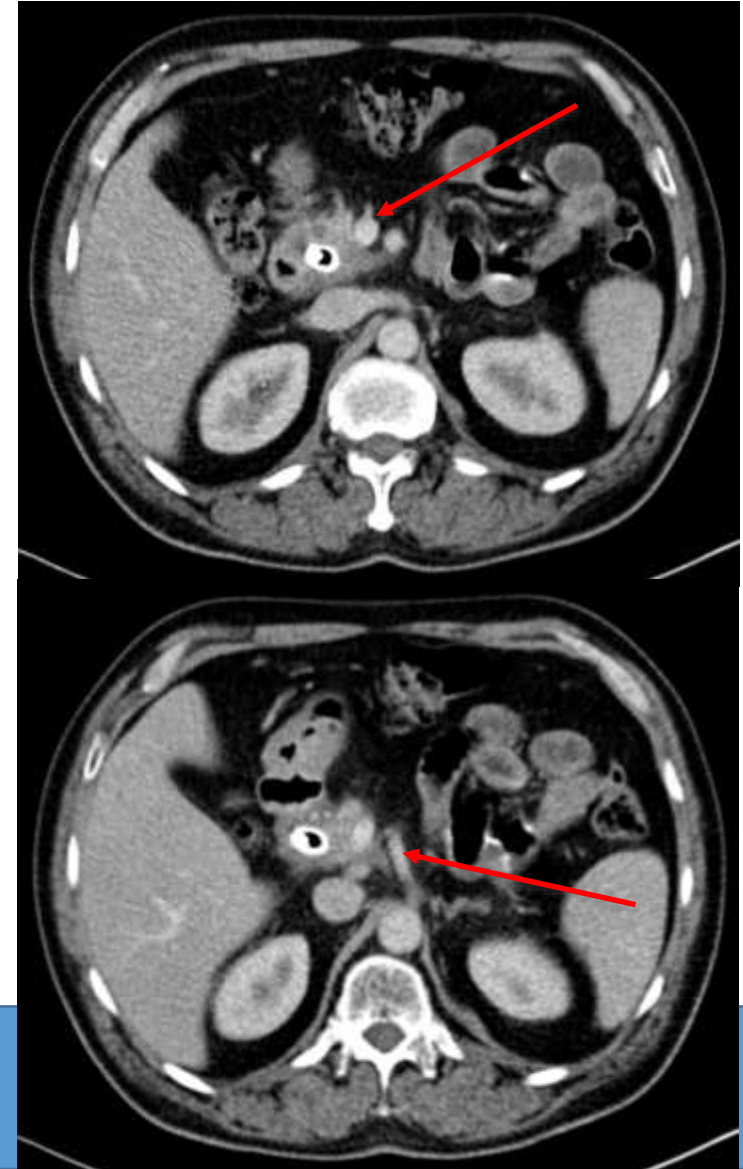
Case Presentation – Mr KP

- Significant response to treatment
- PV/SMV no longer strictured
- Fat plane between SMA
- Referred for ChemoRad



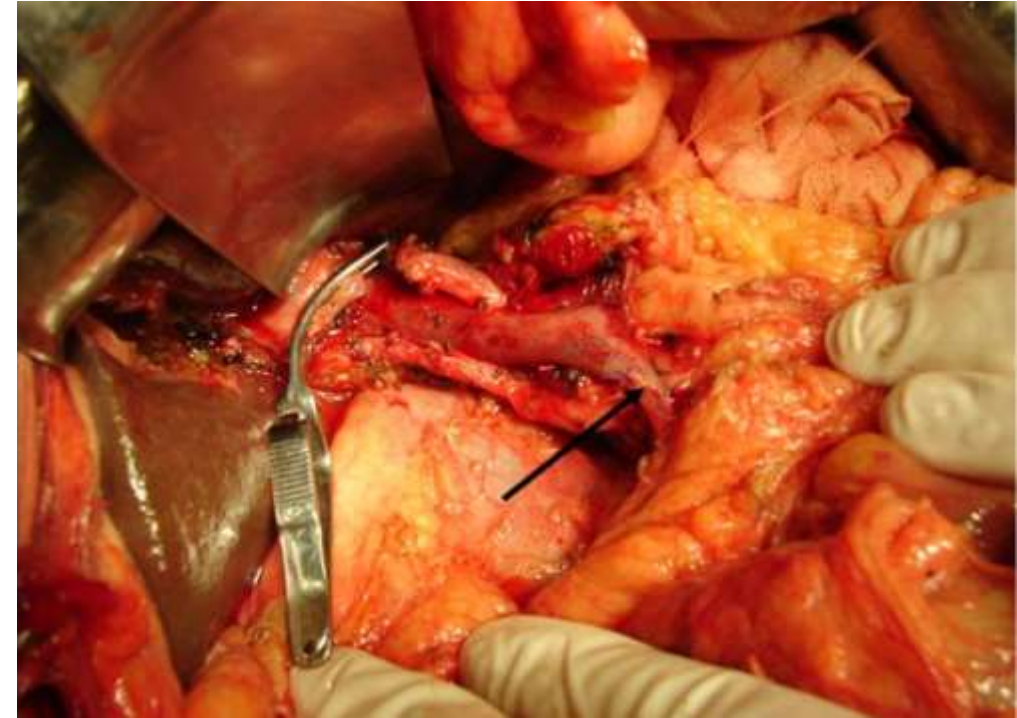
Case Presentation – Mr KP

- 54Gy in 30 fractions
- Post chemoradiotherapy
- Good response
- Small contact with SMA
- Over very short distance
- Offered trial dissection



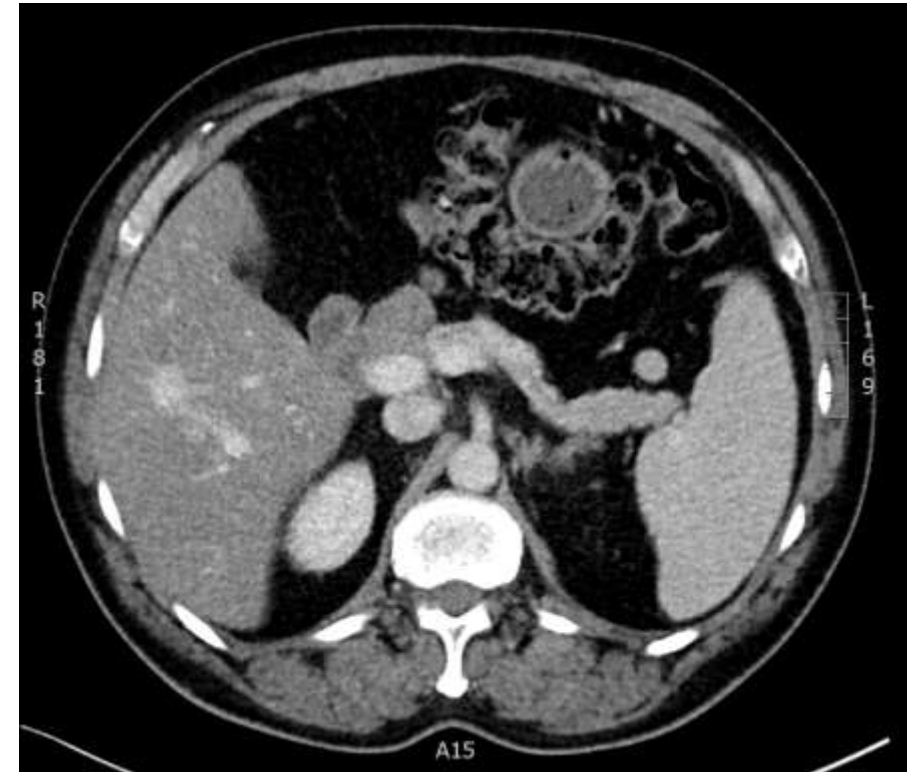
Case Presentation – Mr KP

- Two Consultant operation
- Difficult resection, dense fibrosis
- Wedge vein resection needed
- Drain amylase 50 iu/L
- Length of stay 13 days
- Histology – no residual tumour, no LN mets



How's he doing?

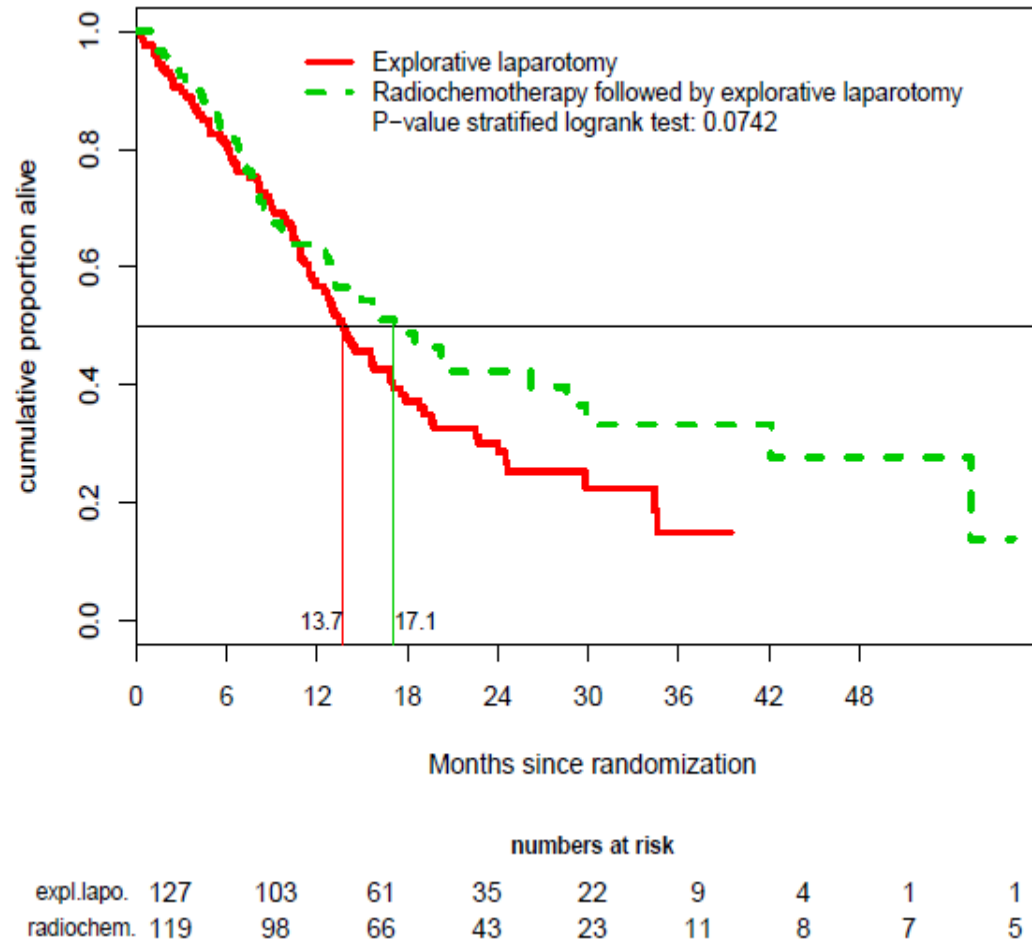
- Post-op 3 years now
- No recurrence
- No metastatic disease



**Preoperative radiochemotherapy versus
immediate surgery for resectable and
borderline resectable pancreatic cancer
(PREOPANC) :
A randomized, controlled, multicenter phase III
trial of the
Dutch Pancreatic Cancer Group**

- Geertjan van Tienhoven, radiation oncologist, AMC, Amsterdam
- Eva Versteijne ¹⁾, Mustafa Suker ²⁾, Karin B Groothuis ³⁾, Olivier R Busch ⁴⁾, Bert A Bonsing ⁵⁾, Ignace H de Hingh ⁶⁾, Sebastiaan Festen ⁷⁾, Gijs A Patijn ⁸⁾, Judith de Vos -Geelen ⁹⁾, Aeilko H Zwinderman ¹⁰⁾, Cornelis J Punt ¹¹⁾, Casper H van Eijck ²⁾

Overall survival (ITT)



Preliminary: 149/176 events

Median survival:
13.7 vs 17.1
months
HR 0.74
p=0.074

Conclusion

Results are preliminary with only 149/176 events

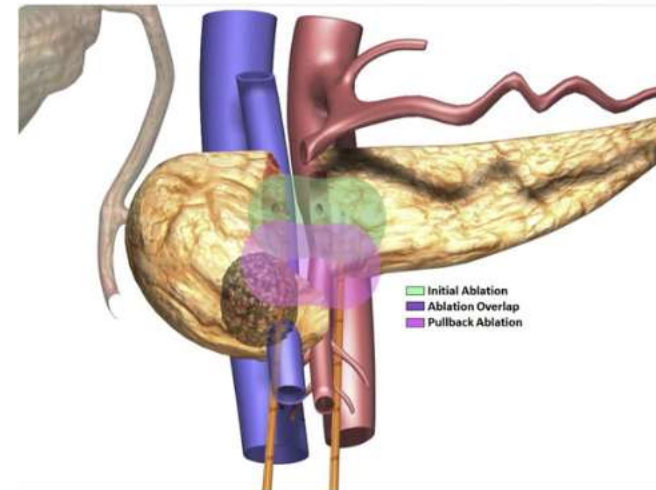
These results of the PREOPANC trial suggest a benefit of neoadjuvant radiochemotherapy over upfront surgery

IRE Margin Accentuation

Borderline and locally advanced pancreatic adenocarcinoma margin accentuation with intraoperative irreversible electroporation

David Kwon, MD, FACS,^a Kelli McFarland, MD, FACS,^a Vic Velanovich, MD, FACS,^b and Robert C. G. Martin, II, MD, PhD, FACS,^c *Detroit, MI, Tampa, FL, and Louisville, KY*

- R0 resection delivers optimal survival
- R1 resection associated with increased local recurrence and decreased survival
- IRE margin accentuation with view to increasing R0 resection



IRE Margin Accentuation

- 48 patients underwent pancreatic resection
- 54% required vascular resection
- 6% local recurrence
- Median survival of 22.4 months
- Median follow-up 24 months
- Promising early results but trial needed (King's)

Metastatic Pancreatic Cancer

Radical surgery of oligometastatic pancreatic cancer

T. Hackert ^a, W. Niesen ^a, U. Hinz, C. Tjaden, O. Strobel, A. Ulrich,
C.W. Michalski, M.W. Büchler*

Department of Surgery, University of Heidelberg, Im Neuenheimer Feld 110, 69120 Heidelberg, Germany

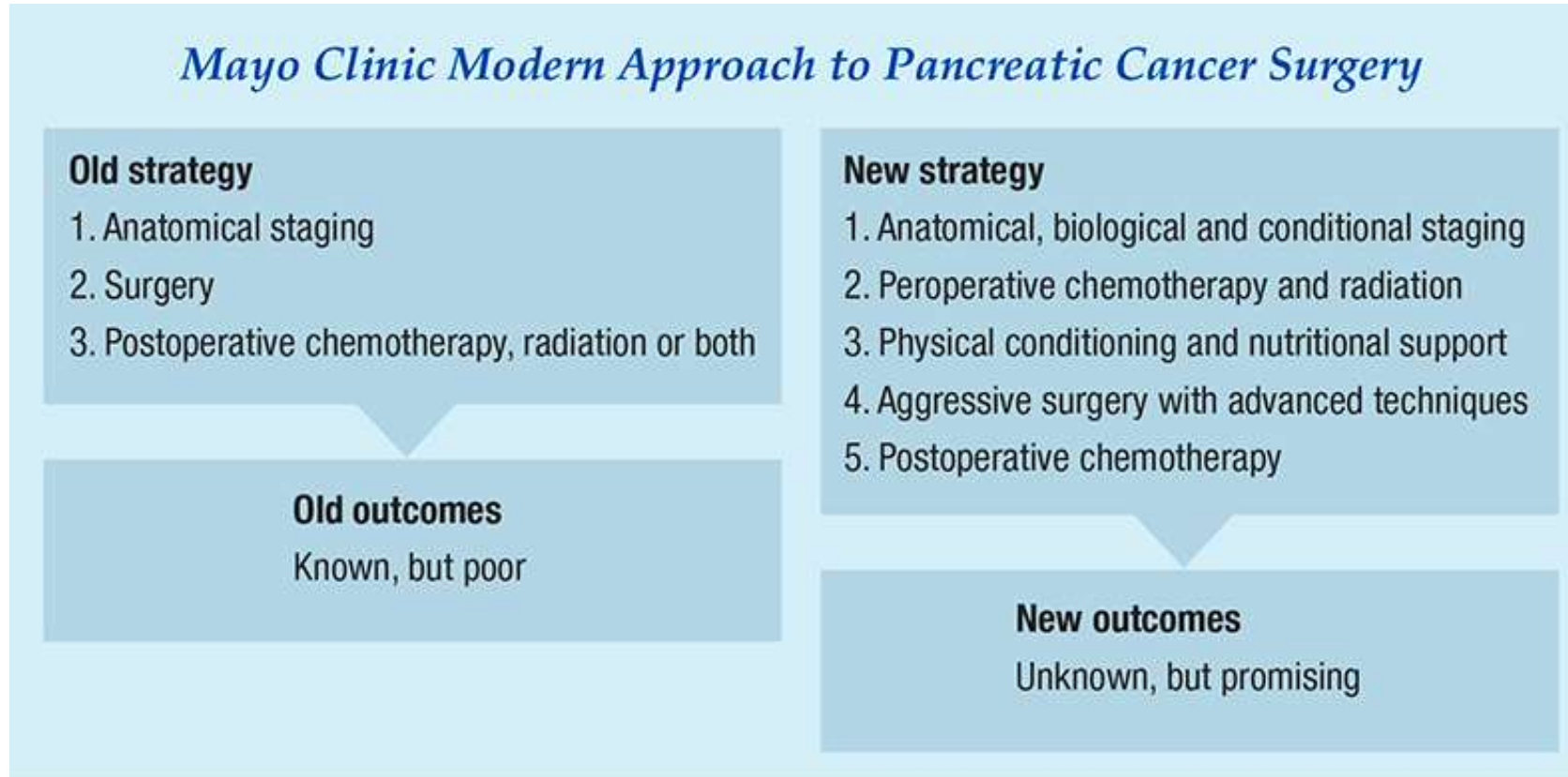
- Stage IV PDAC (n=128, LM: 85, ILN: 43)
- 30 day morbidity: 45%, Mortality: 2.9%
- Overall median survival: 12.3 months
- 5 year survival:
 - LM: 8.1%
 - ILN: 10.1%

Potential future strategy

- Patients with borderline disease and ?resectable disease
- Neoadjuvant FOLFIRINOX then ChemoRad
- Any patients with regression, stable disease, no mets – SURGERY
- Any PV/SMV involvement – RESECTION
- Patients with stable liver mets - ?RESECTION?

Possible sea change in outcomes!

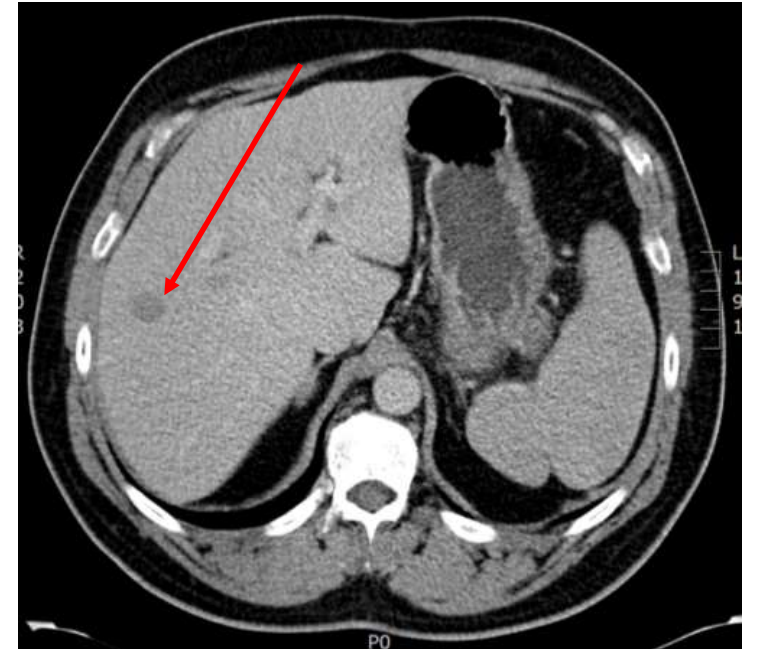
Potential future strategy



“This is a really exciting time in pancreatic cancer surgery. We now have effective chemotherapy, improved radiation and advanced surgical techniques for a multimodality team approach.” – Dr Mark Truty

Audience case

- 47 year old male
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Thank you!



@SurgeryHPB