ΔΕΞΙΑ ΟΓΚΟΛΟΓΙΚΗ ΠΑΓΚΡΕΑΤΕΚΤΟΜΗ

Εκτομή του Μεσοπαγκρέατος

«Artery – first» Approach

Λεμφαδενεκτομή

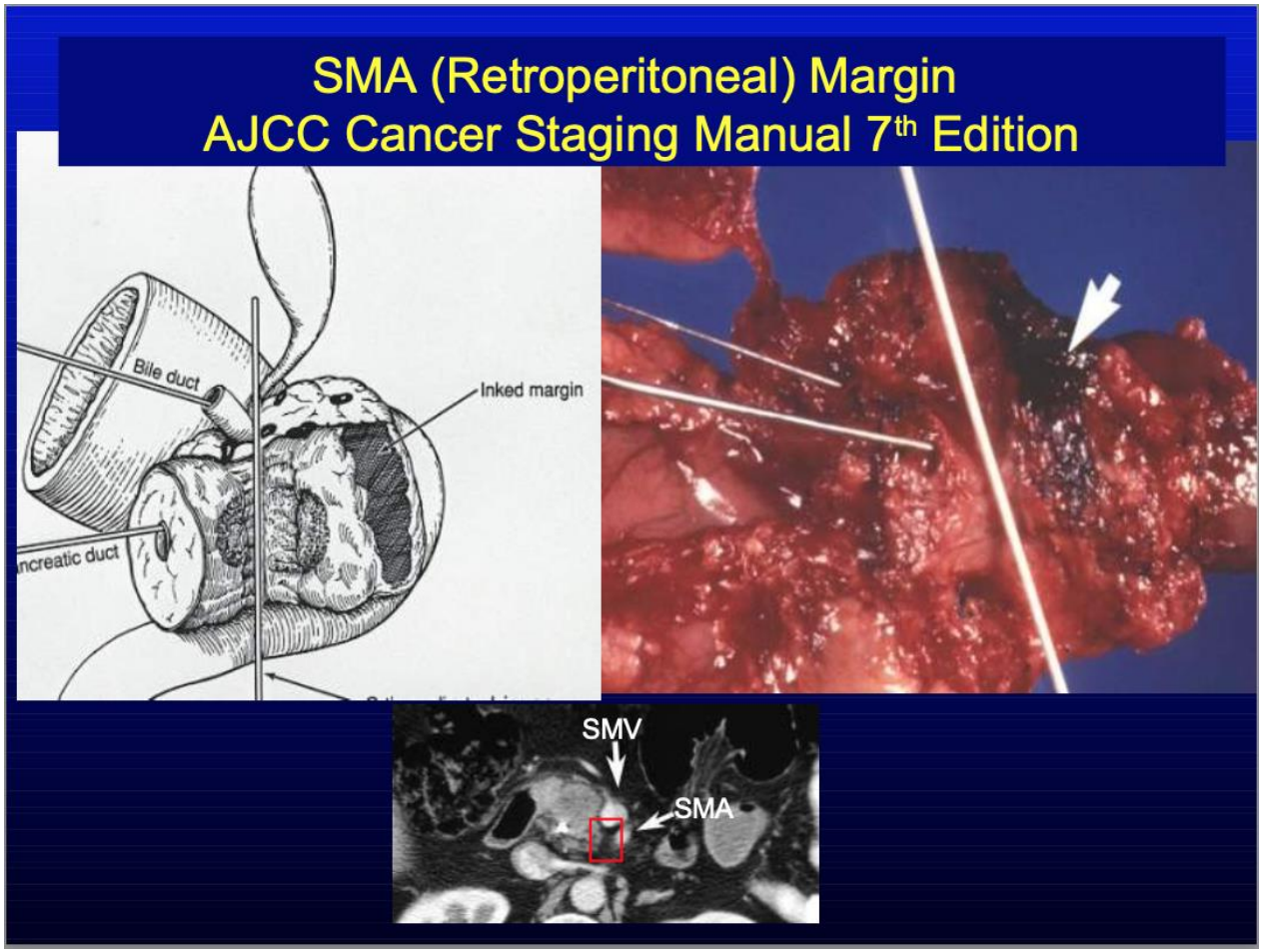
ΔΗΜΗΤΡΗΣ Π. ΚΟΡΚΟΛΗΣ
Διευθυντής Χειρουργικής Κλινικής
ΓΑΟΝΑ «Άγιος Σάββας»

Pancreatic Cancer

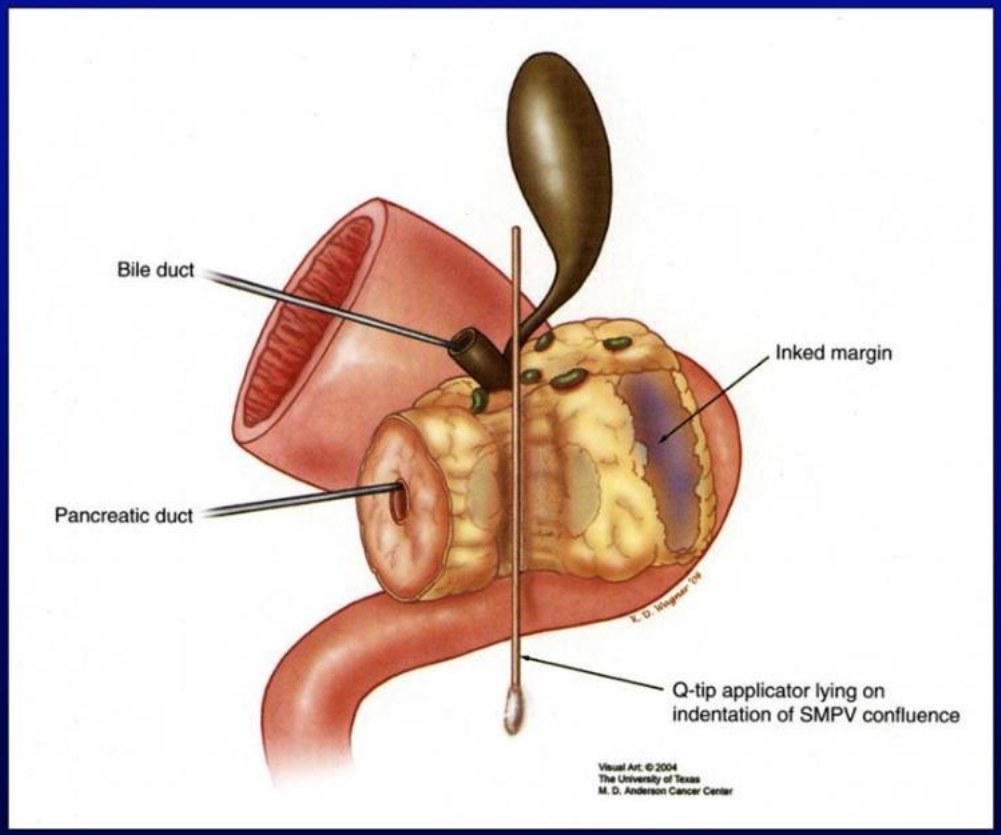
- Most difficult to solve surgical issue
- 4th leading cause of cancer-related death
- 2nd by 2030
- Poor prognosis even after PD + adj chemo
    1. 20-25% 5-yr survival
    2. 15-25 months OS
- R1 resections 20-50% → Early Recurrence 15-60% → Early Death
- Close Anatomy with SMA, SMV, CT
- Median/SMA margin: Most frequent site of rec after PD ± SMV invasion

MESOPANCREAS!!!

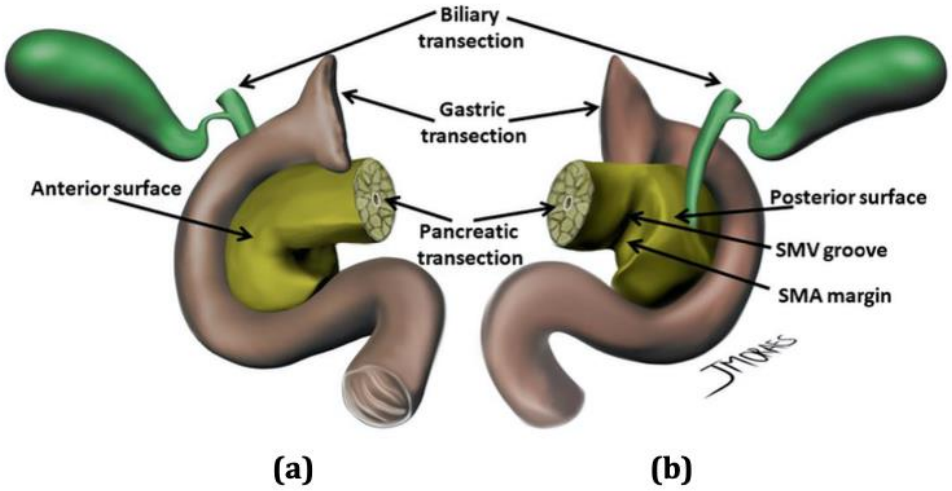
Mesopancreas

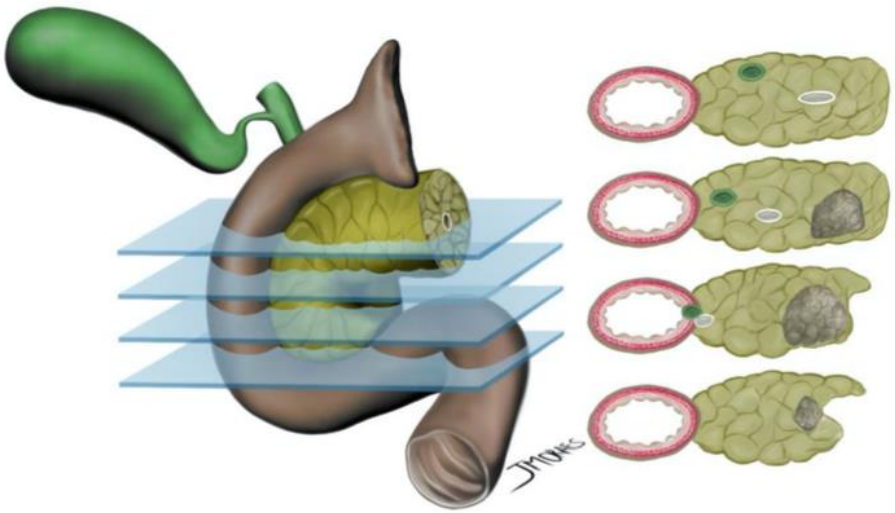


Mesopancreas



Pathology Assessment





The Royal College of Pathologists 2019

Resection Status PDAC

ORIGINAL ARTICLE

Pancreatic Cancer Surgery

The New R-status Counts

Oliver Strobel, MD, Thomas Hank, MD,* Ulf Hinz, MSc,* Frank Bergmann, MD,† Lutz Schneider, MD,* Christoph Springfeld, MD, PhD,‡ Dirk Jäger, MD,‡ Peter Schirmacher, MD,† Thilo Hackert, MD,* and Markus W. Büchler, MD**

561 PDAC patients **2006-2012**

- **standardized pathological workup**
- **circumferential margin**
- **R0 vs. R1 (<1mm) vs. R1 (direct tumor invasion)**

Strobel et al., Ann Surg 2017

Resection Status PDAC

prognostic factors – multivariate analysis

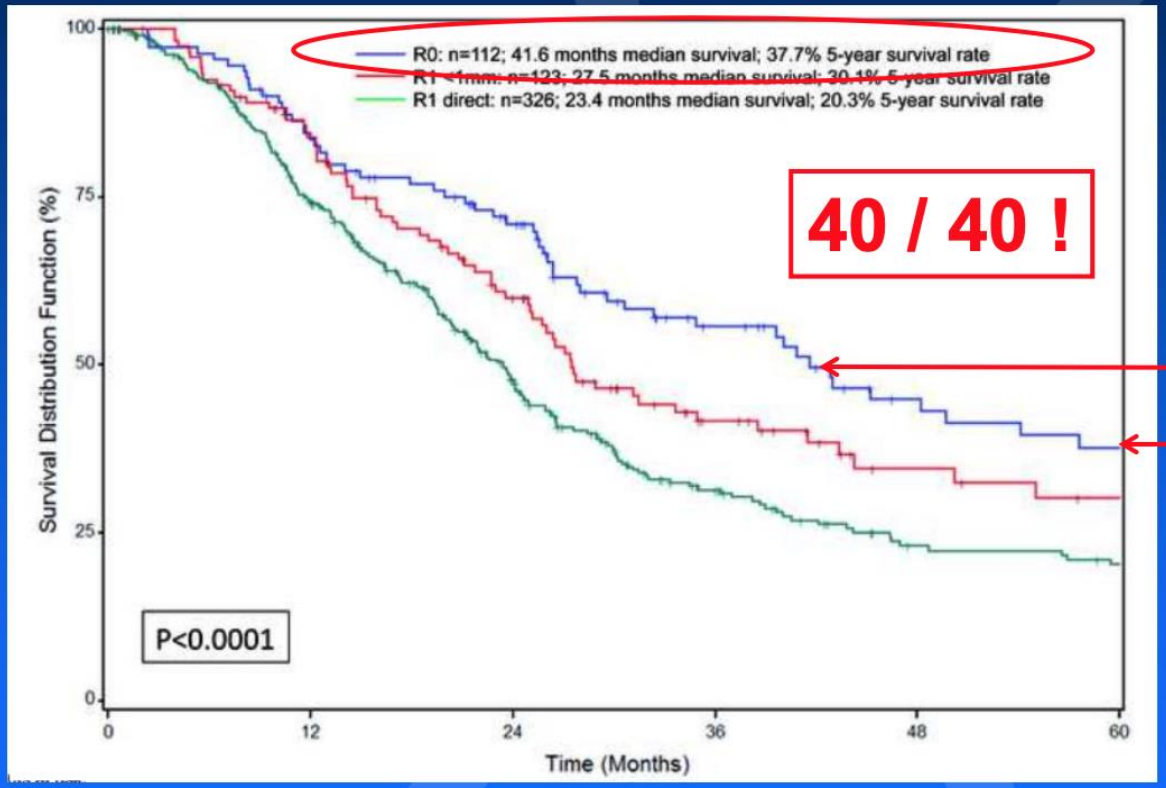
TABLE 2. Multivariate Survival Analysis of 538 Pancreatic Head Adenocarcinoma (Missing Values, N = 23)

Parameter	HR	95% CI	*P*
R0 vs R1 (direct)	0.73	0.54–0.98	0.0391
R1 (≤1 mm) vs R1 (direct)	0.71	0.54–0.95	0.0193
G3 vs G1/2	1.58	1.23–1.98	<0.0001
PLN ≥ 8 vs pN0	3.00	1.97–4.55	<0.0001
PLN 4–7 vs pN0	2.12	1.38–3.25	0.0006
PLN 1–3 vs pN0	1.66	1.11–2.49	0.0138
pT1/2 vs pT3/4	0.24	0.06–0.98	0.0472
CA 19–9 < 37 vs ≥37 [U/mL]	0.73	0.56–0.96	0.0218

Strobel et al., Ann Surg 2017

Resection Status PDAC

survival **R0 = CRM-**

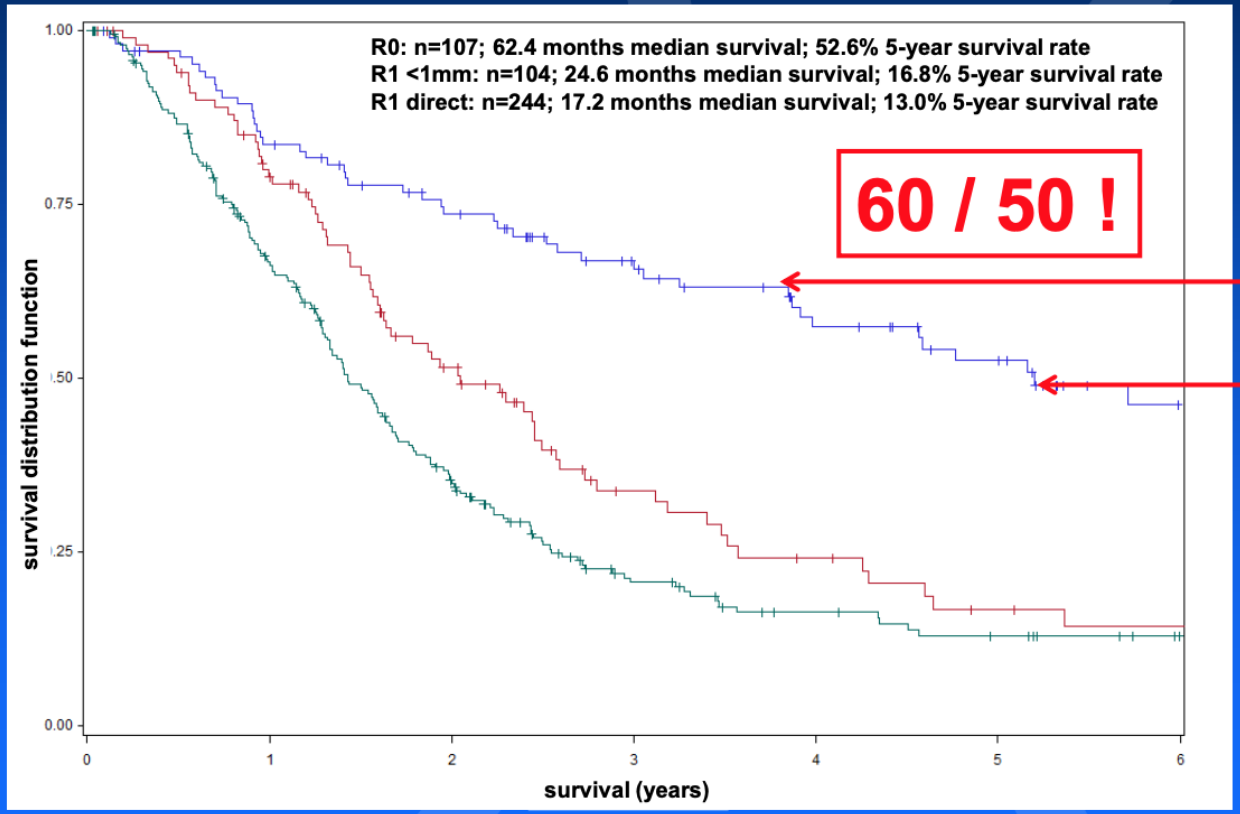


Strobel et al., Ann Surg 2017

Resection Status PDAC

distal & total pancreatectomy

455 PDAC patients, Heidelberg 2006-2014



Resection Status PDAC

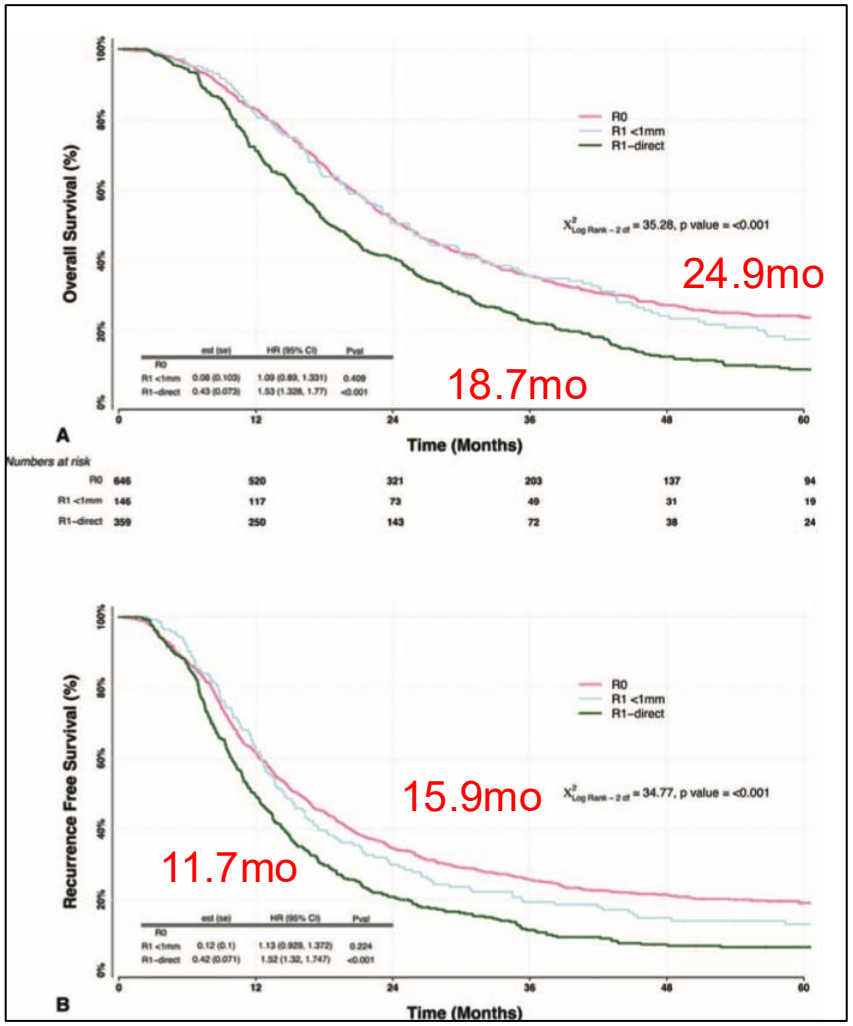
multivariate analysis prognostic factors for survival

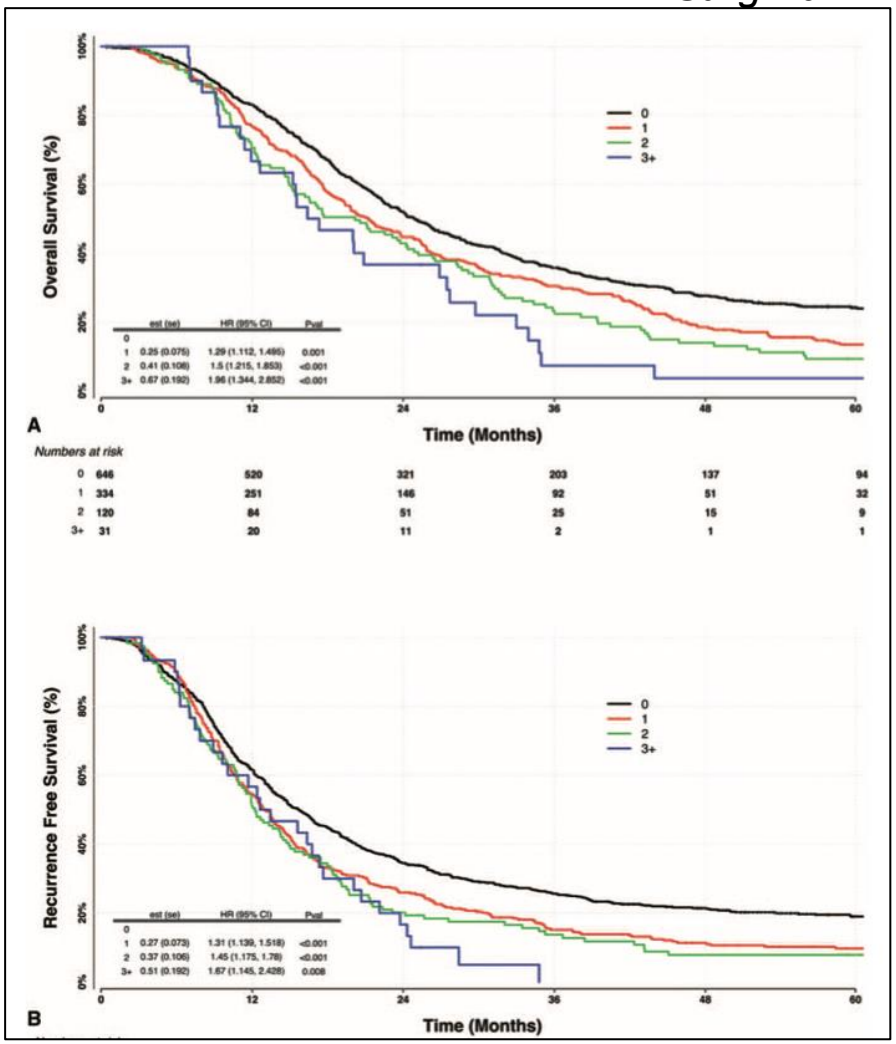
Parameter	HR	95%	P-value
R0 vs. R1 direct	0.45	0.31 – 0.66	<0.0001
R1 <1mm vs. R1 direct	0.79	0.59 – 1.05	0.1089
G3/4 vs. G1/2	1.86	1.47 – 2.37	<0.0001
N1 vs. N0	1.59	1.11 – 2.26	0.0110
age <50 vs. ≥50years	0.59	0.35 – 0.97	0.0373
Distal vs. total pancreatectomy	0.79	0.62 – 0.99	0.0452
CA 19-9 400 vs. <400	1.46	1.14 – 1.86	0.0025

radical resection is the key to long-term survival

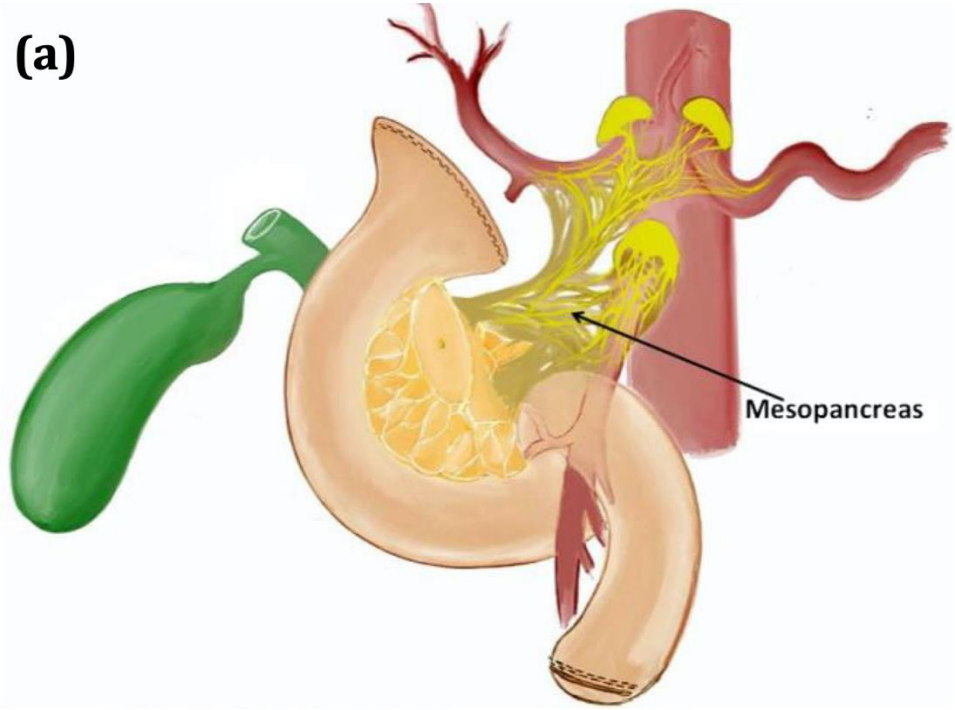
The Impact of Positive Resection Margins on Survival and Recurrence Following Resection and Adjuvant Chemotherapy for Pancreatic Ductal Adenocarcinoma

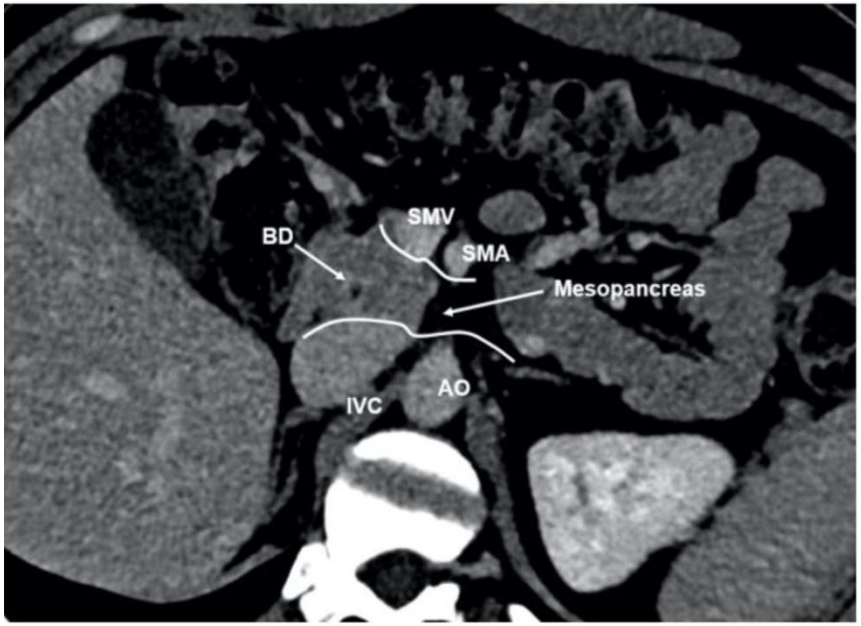
Ann Surg 2017





Mesopancreas

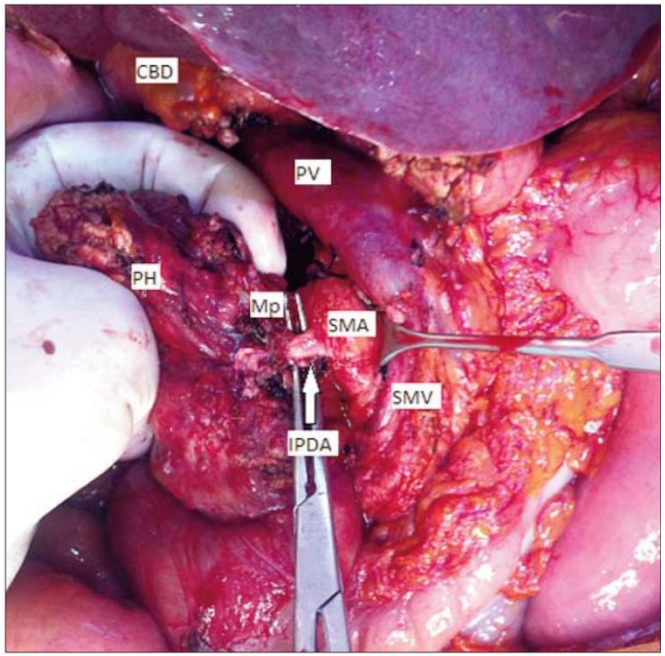


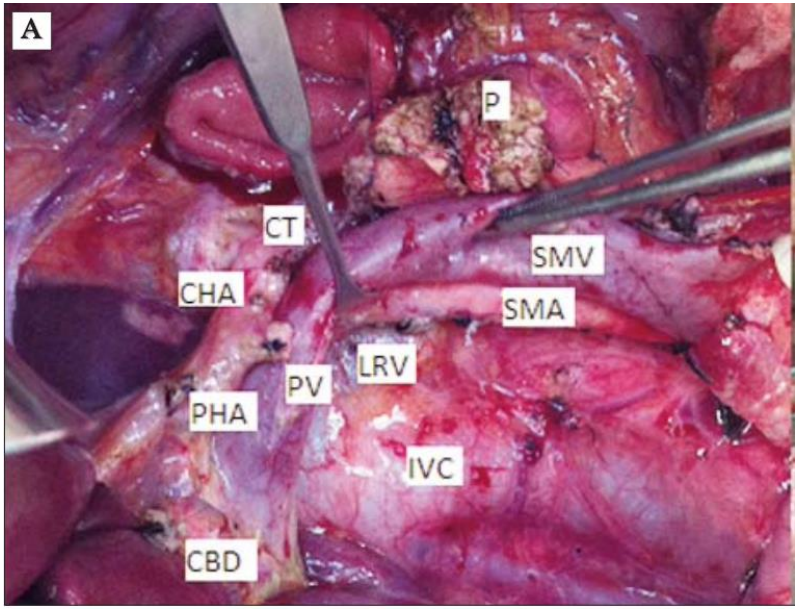


Lateral:	medial and posterior aspect of uncinate process/pancreatic head
Medial:	right aspect of SMV/SMA
Cephalic:	origin of CT
Caudal:	origin of mesenteric root/ IPDA-JA1
Posterior:	left RV

World J Surg Oncol 2007

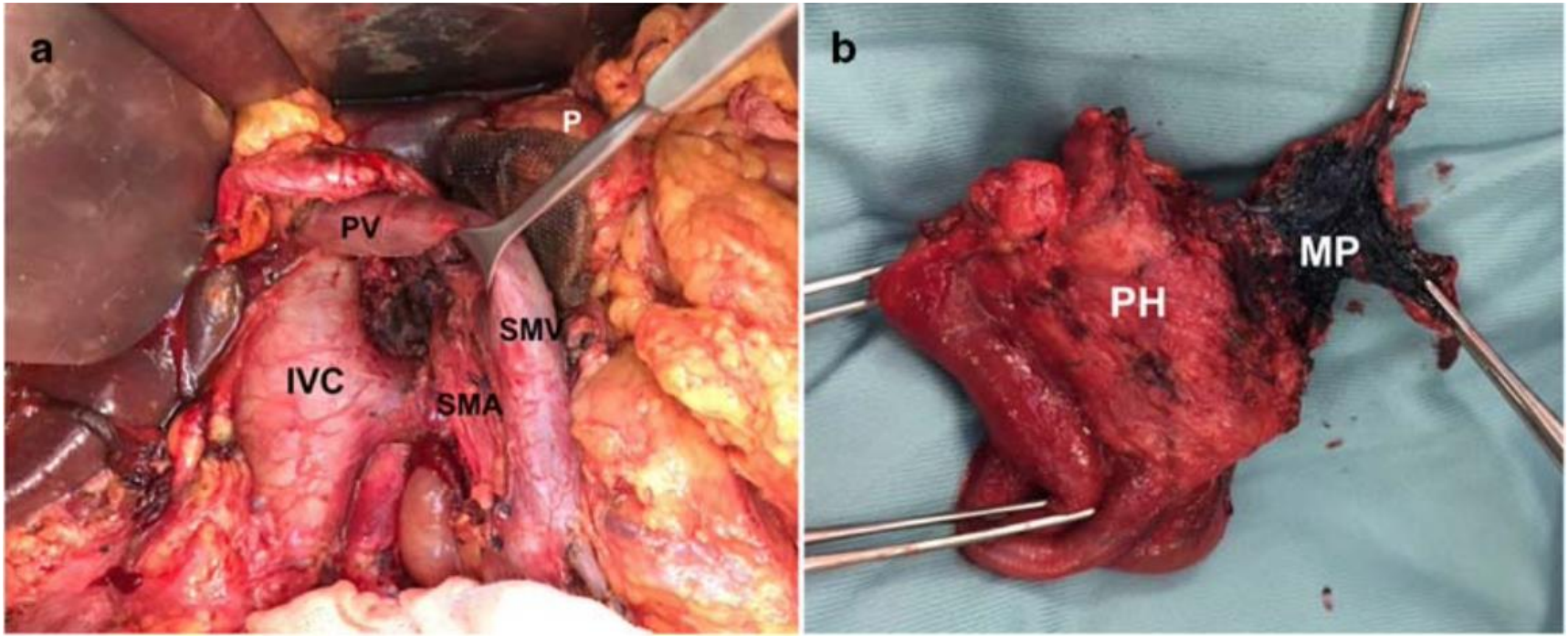
Total Mesopancreas Excision (TMpE)





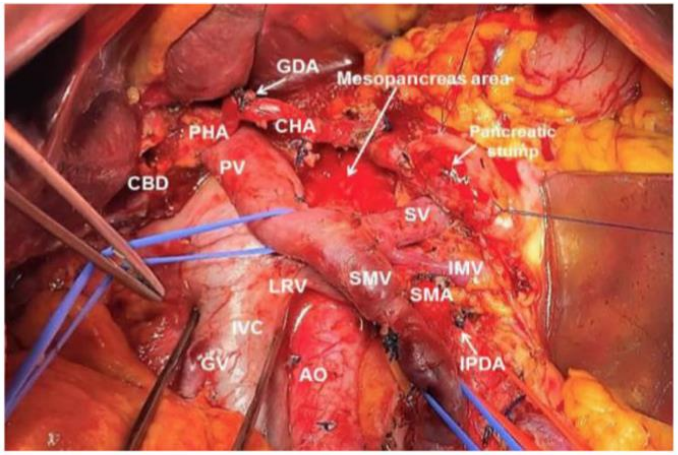
Total mesopancreas excision for periampullary malignancy: a single-center propensity score-matched comparison of long-term outcomes

Giuseppe Quero [1,2,3] · Claudio Fiorillo [1,2] · Roberta Menghi [1,2] · Caterina Cina [1,2] · Federica Galiandro [1,2] · Fabio Longo [1,2] · Francesco Sofo [1,2] · Fausto Rosa [1,2] · Antonio Pio Tortorelli [1,2] · Maria Cristina Giustiniani [4] · Frediano Inzani [4] · Sergio Alfieri [1,2,3]

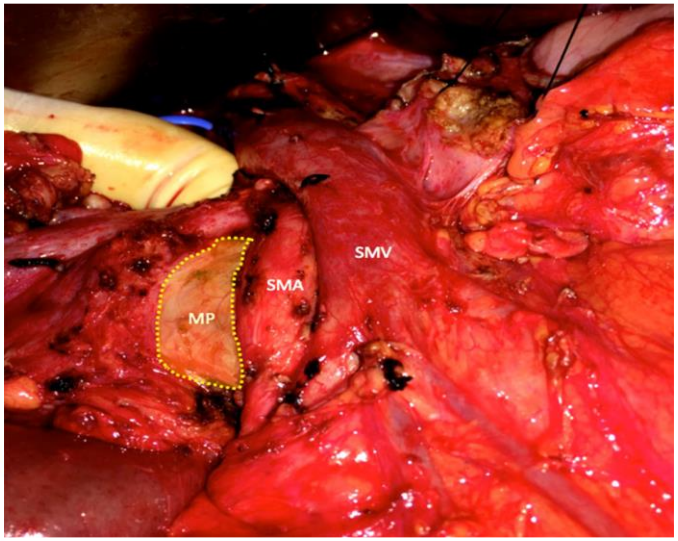


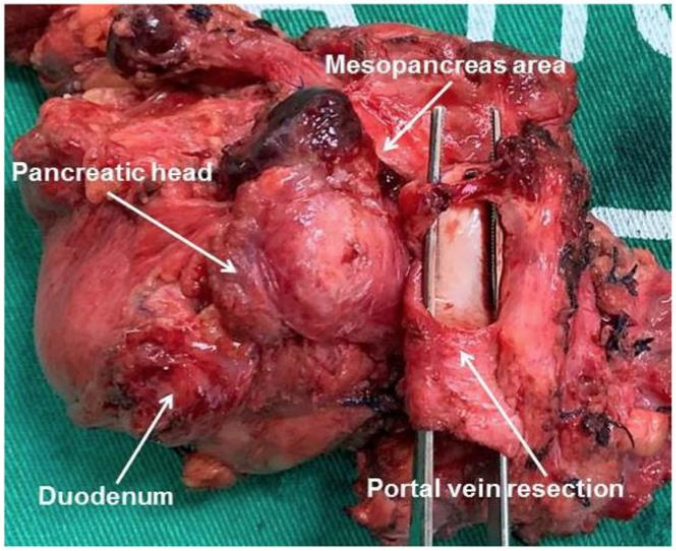
Langenbeck's Archives of Surgery 2021

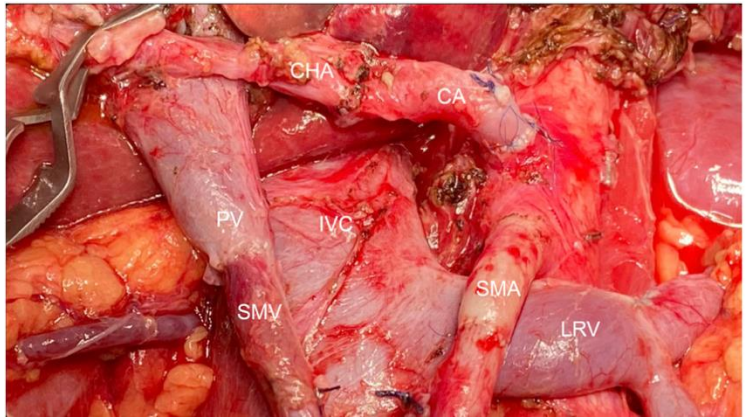
Mesopancreas – Surgical Anatomy



(a)

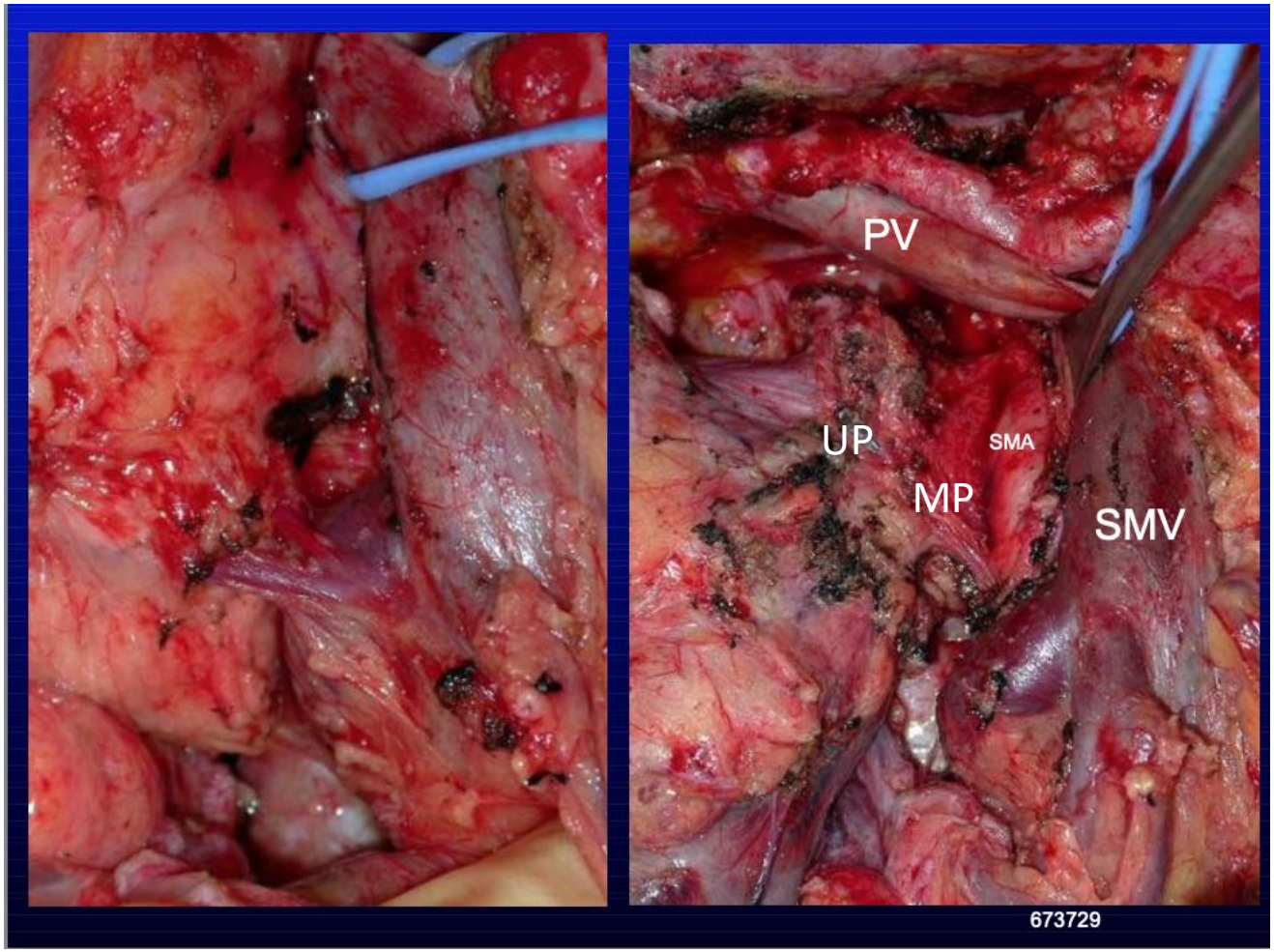






Ann Surg 2017

Total Mesopancreas Excision (TMpE)



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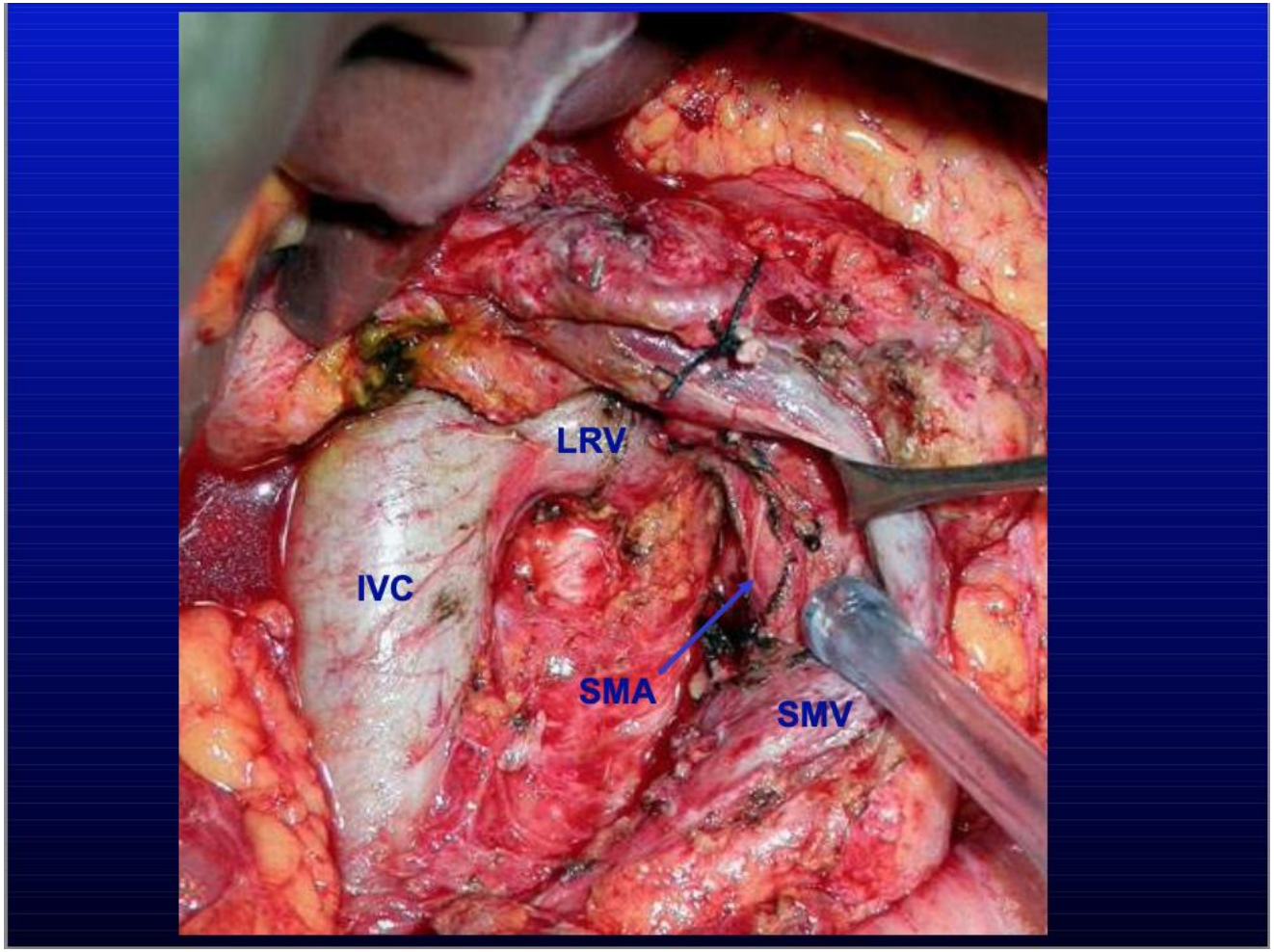

Total mesopancreas excision for periampullary malignancy: a single-center propensity score-matched comparison of long-term outcomes

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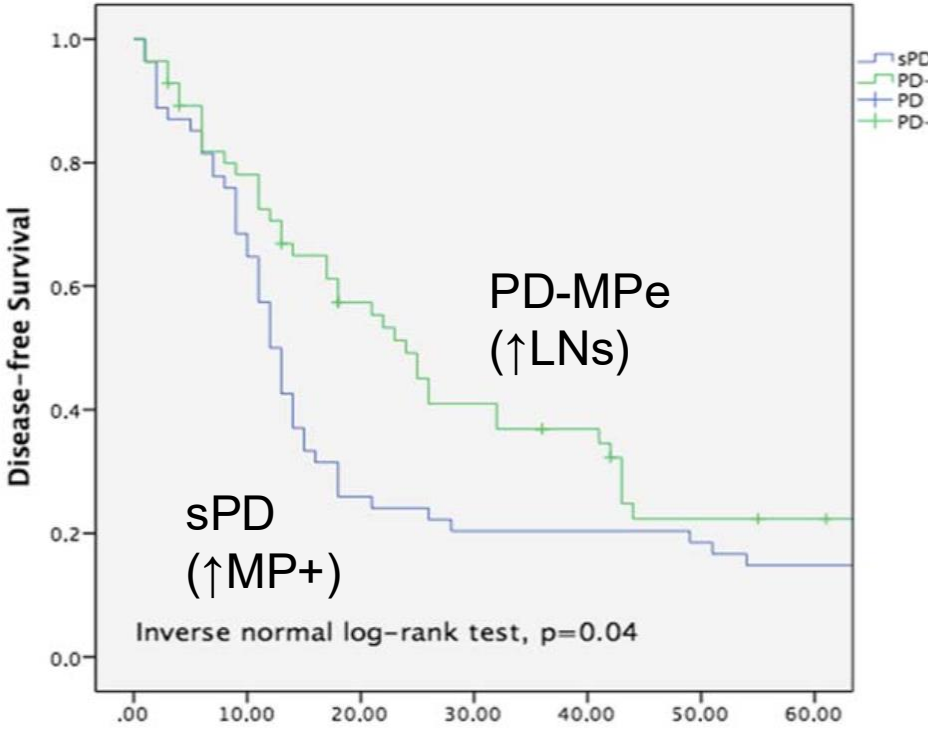
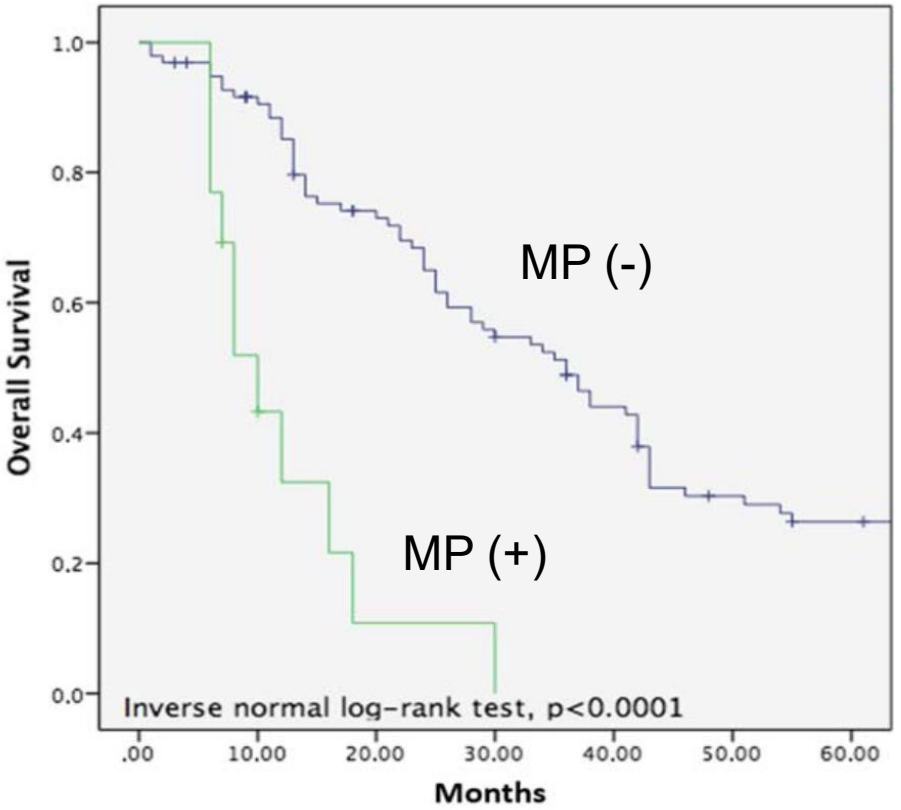
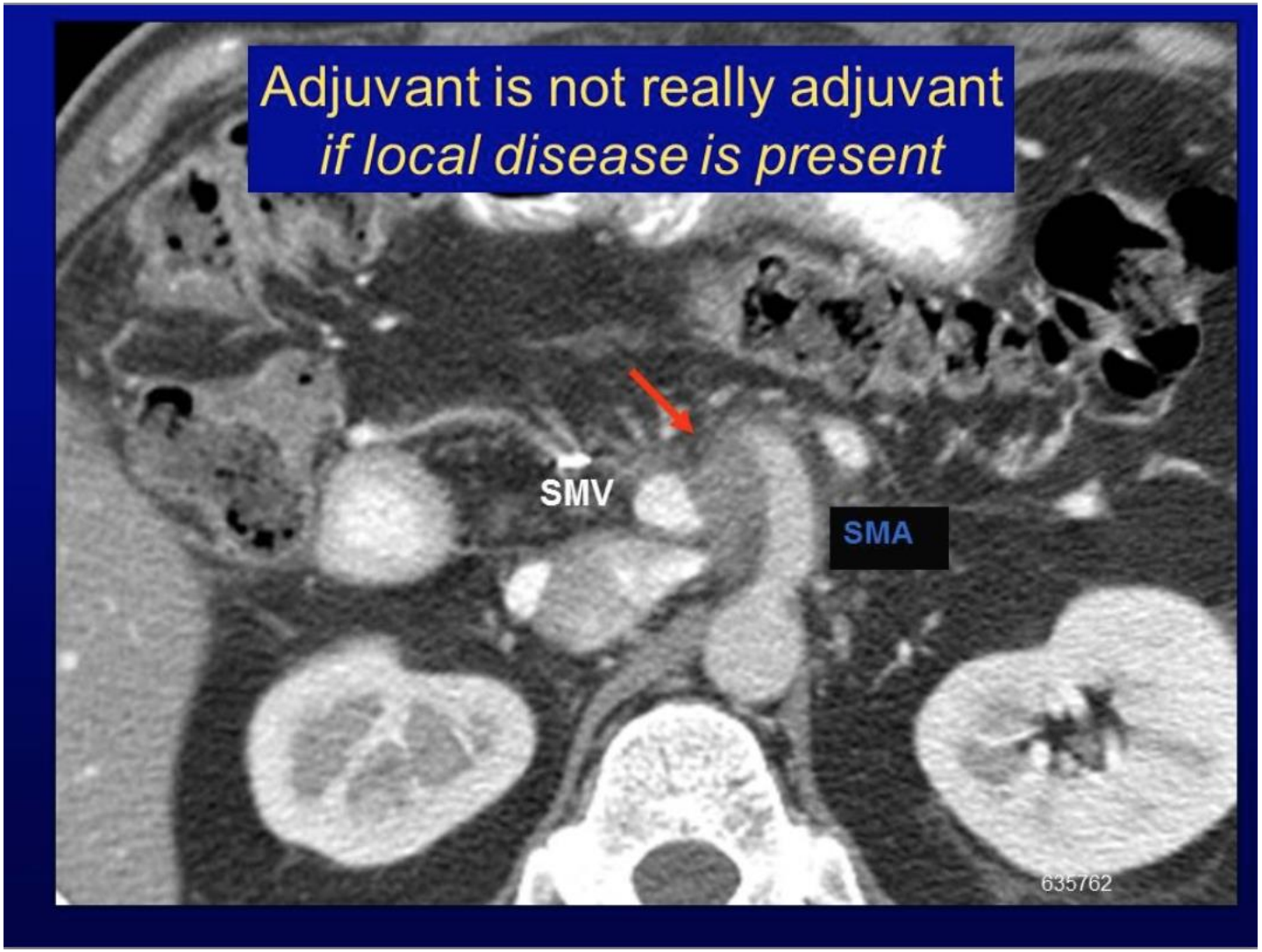
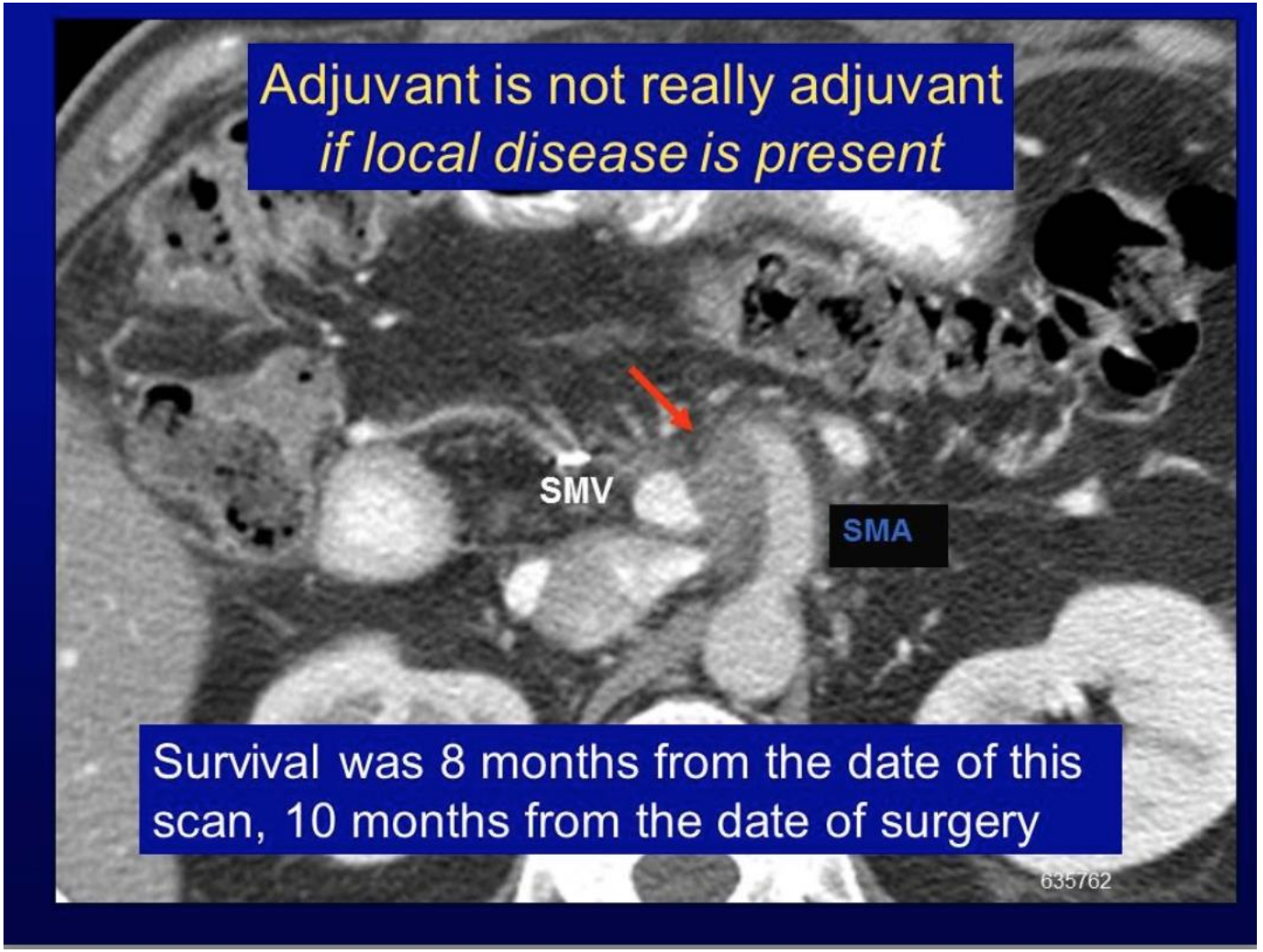




Langenbeck's Archives of Surgery 2021


Adjuvant is not really adjuvant
if local disease is present
SMV
SMA
635762


Adjuvant is not really adjuvant
if local disease is present
SMV
SMA
Survival was 8 months from the date of this scan, 10 months from the date of surgery
635762

What do surgeons need to know about the mesopancreas

Eduardo de Souza M. Fernandes [1,2] · Oliver Strobel [3,4] · Camila Girão [1,2] · Jose Maria A. Moraes-Junior [5,6] · Orlando Jorge M. Torres [5,6]

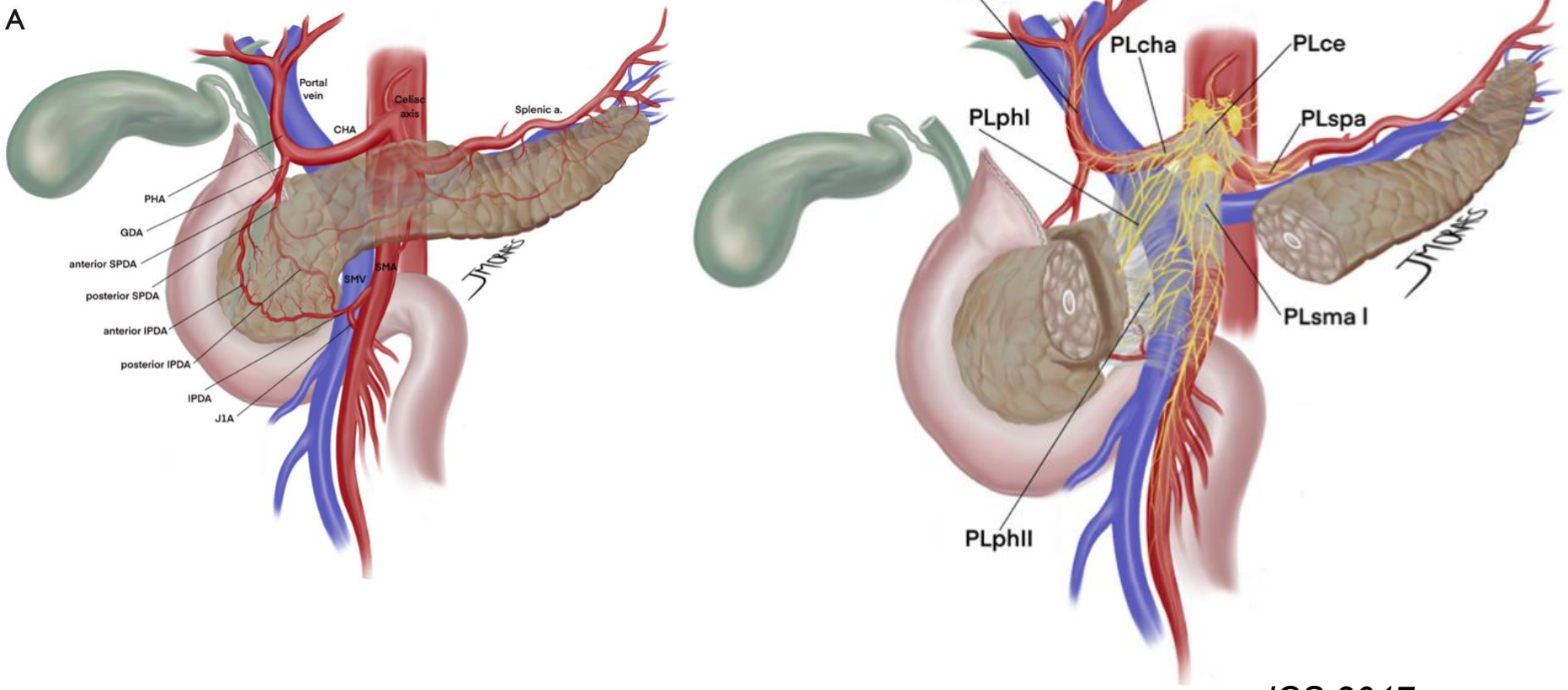
Author	Results	TME	SPD	p
Kawabata et al. (2012)	R0 resection (%)	92.8	60	0.019
	R1 resection (%)	7.2	40	
	Recurrence (%)	14.2	64	0.036
Aimoto et al. (2013)	R0 resection (%)	74	68	NS
	R1 resection (%)	26	30	NS
Xu et al. (2017)	Local recurrence (%)	0	37	<0.01
	Median DFS (Months)	16.9	13.4	0.044
	Median OS (Months)	19.9	22.5	0.176
	1-year total recurrence rate (%)	31.8	55.3	0.054
	1-year local recurrence rate (%)	18.2	39.5	0.018
Quero et al. (2021)	Disease-free survival (%)	22.3	14.8	0.04
	R1 Mesopancreas margin (%)	5.0	16.7	0.04
	Local tumor recurrence (%)	26.8	55.5	0.002

↑LNs ↑OS
↓Blood loss ↑RFS

Langenbeck's Archives of Surgery 2020

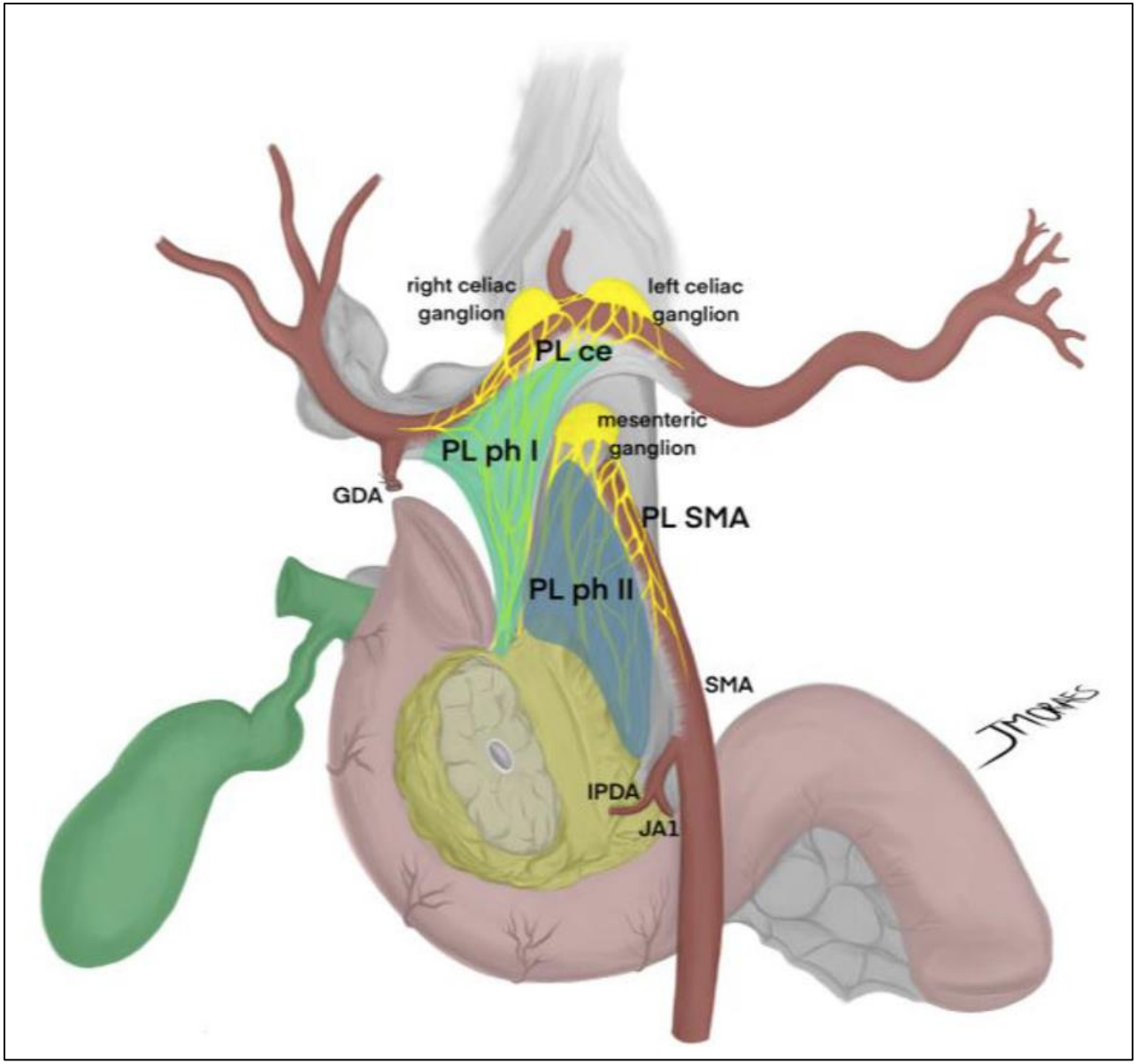
MESOPANCREAS – Main Nerve Structures

Japan Cancer Society (Pancreatic Head Plexus)



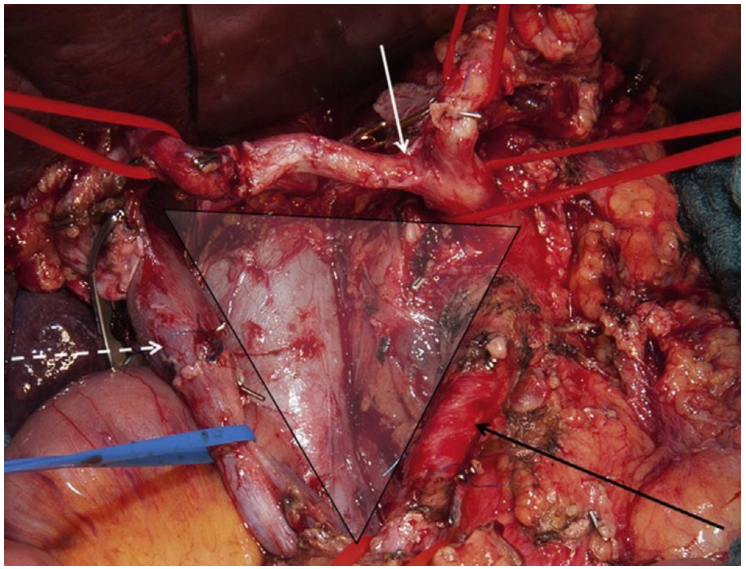
JCS 2017

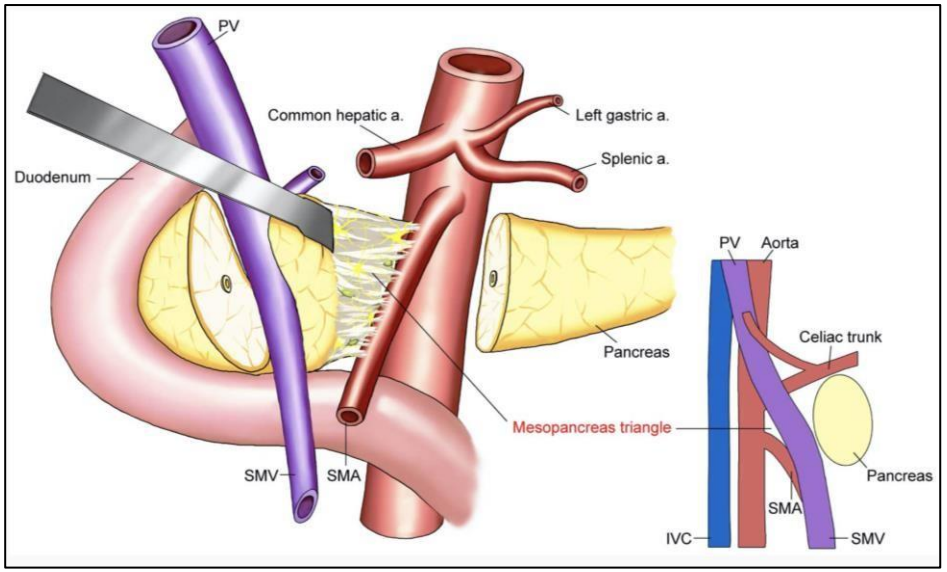
MESOPANCREAS – Japan Pancreas Society



How to assure a high possibility of R0 resections in BR
Surgical strategy

Step 1:
En bloc resection of the mesopancreas
TMpE





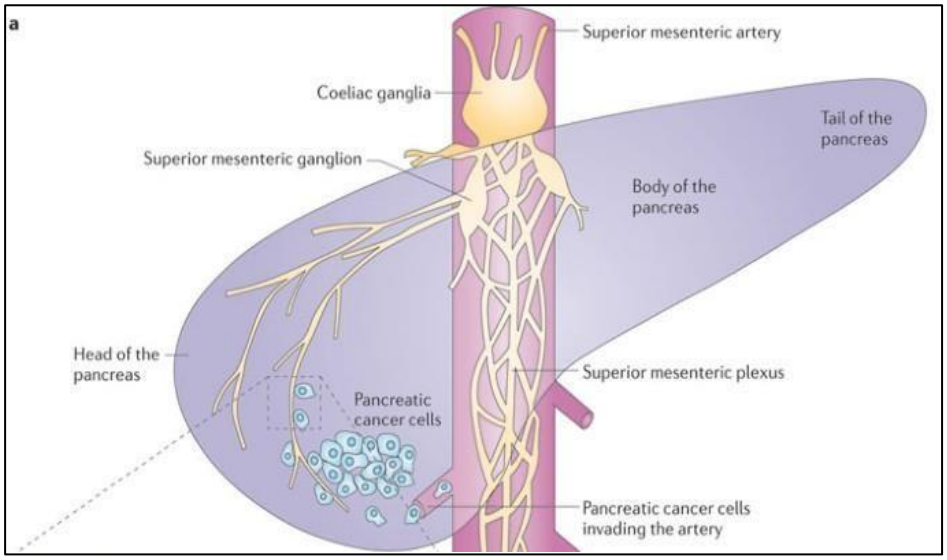
Hackert et al. 2017, Hirono et. al. 2017

How to assure a high possibility of R0 resections in BR
Surgical strategy

Step 2:
Minimize the risk of local recurrence –
focus on perineural invasion

Perineural invasion:

- Early spreading to the retroperitoneal space, along the arterial vessels and to the Lymph nodes
- Non-continuous spreading



Schorn et. al. 2017, Takahashi et. al. 1997, Bapat et. al. 2011

How to assure a high possibility of R0 resections in BR Surgical strategy

Step 3: Minimize the risk of local recurrence – focus on perineural invasion

- Level 1 LV1: Not for PDAC
- Level 2 LV2:

Ligation of IPDA+JA1+JV1 and systemic resection of correspondent lymph nodes incl. mesopancreas

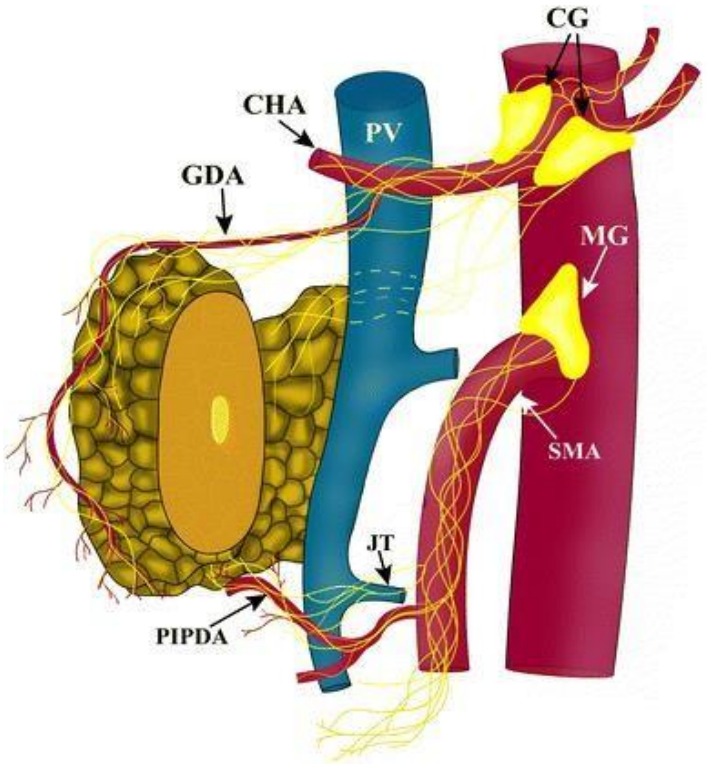
- Level 3 LV3:

Hemicircumferential resection of the plexus

- Extended Level 3 ExtLV3:

Completed peri SMA plexus resection (diarrhea)

Periarterial divestment

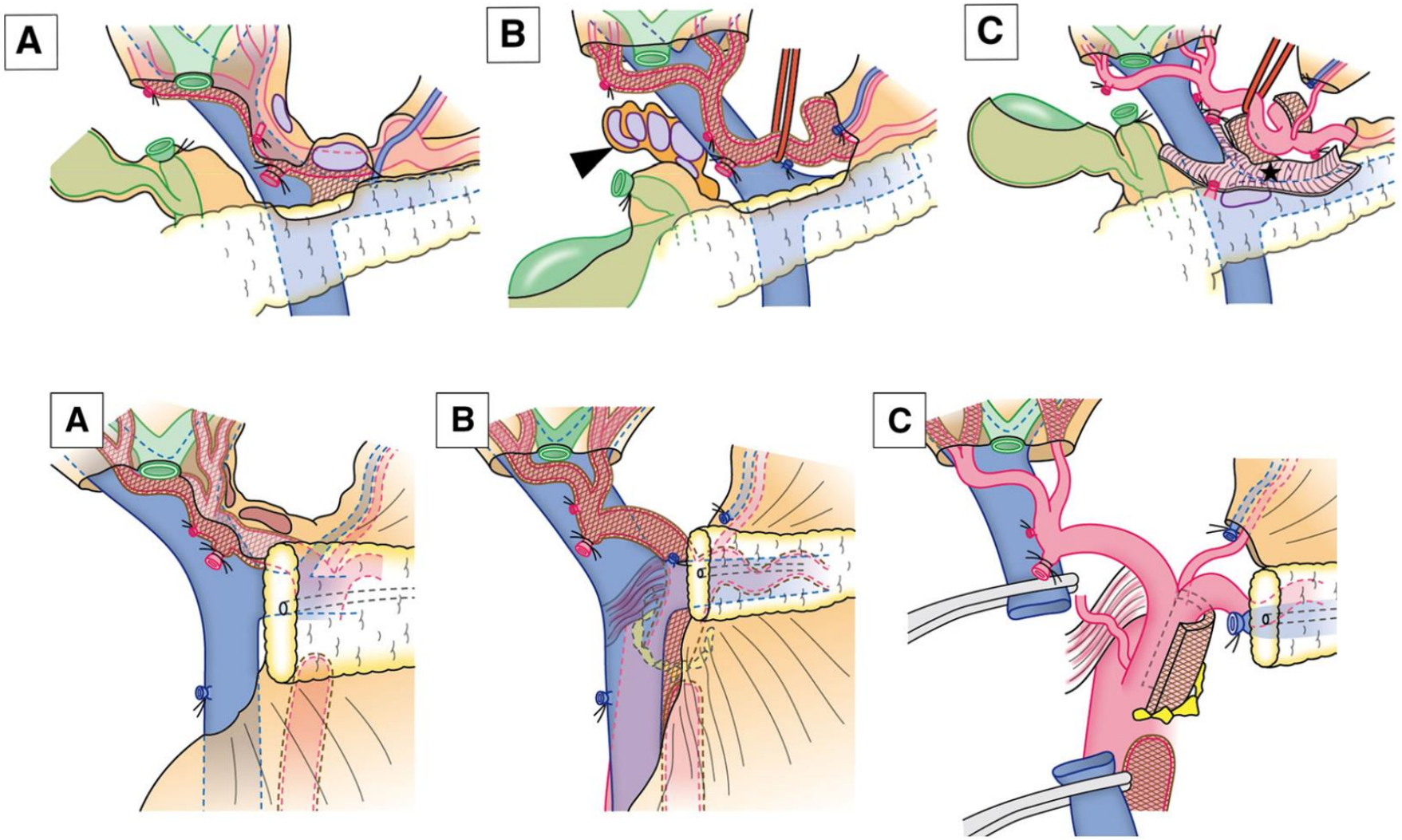


Inoue et. al. 2018

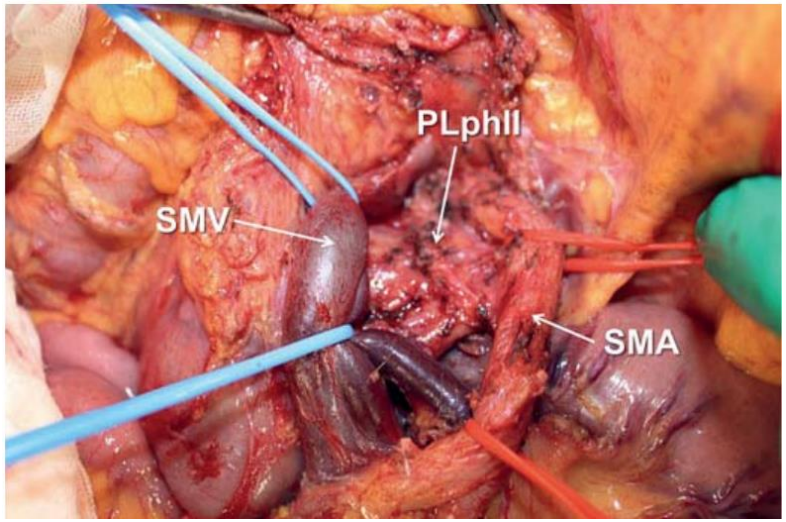
A Novel Classification and Staged Approach for Dissection Along the Celiac and Hepatic Artery During Pancreaticoduodenectomy

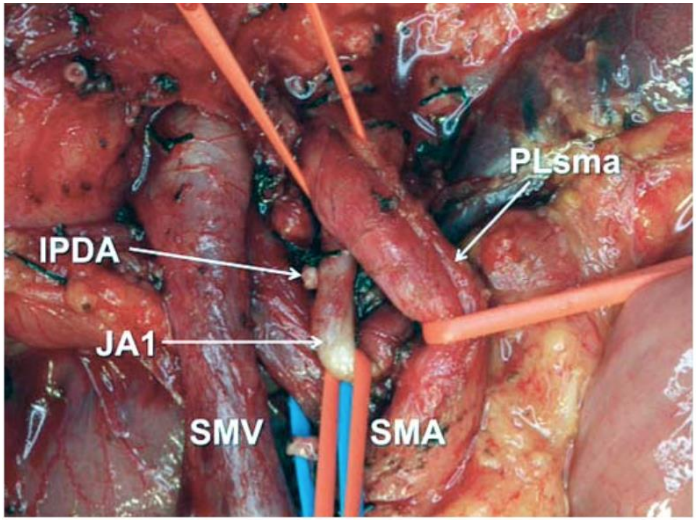
Yosuke Inoue[1] · Akio Saiura[1] · Yu Takahashi[1]

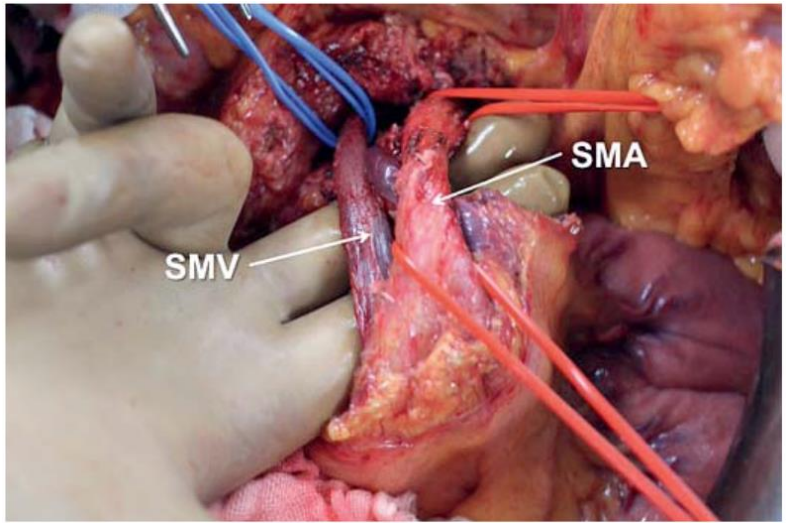
World J Surg 2018

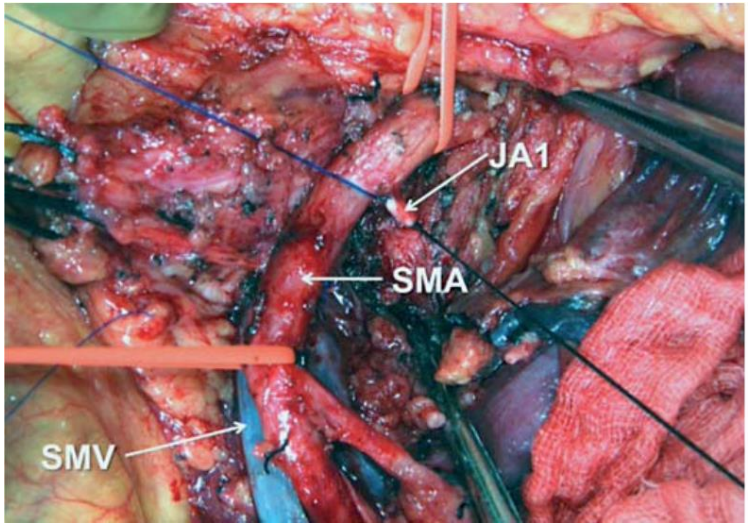


TMPe



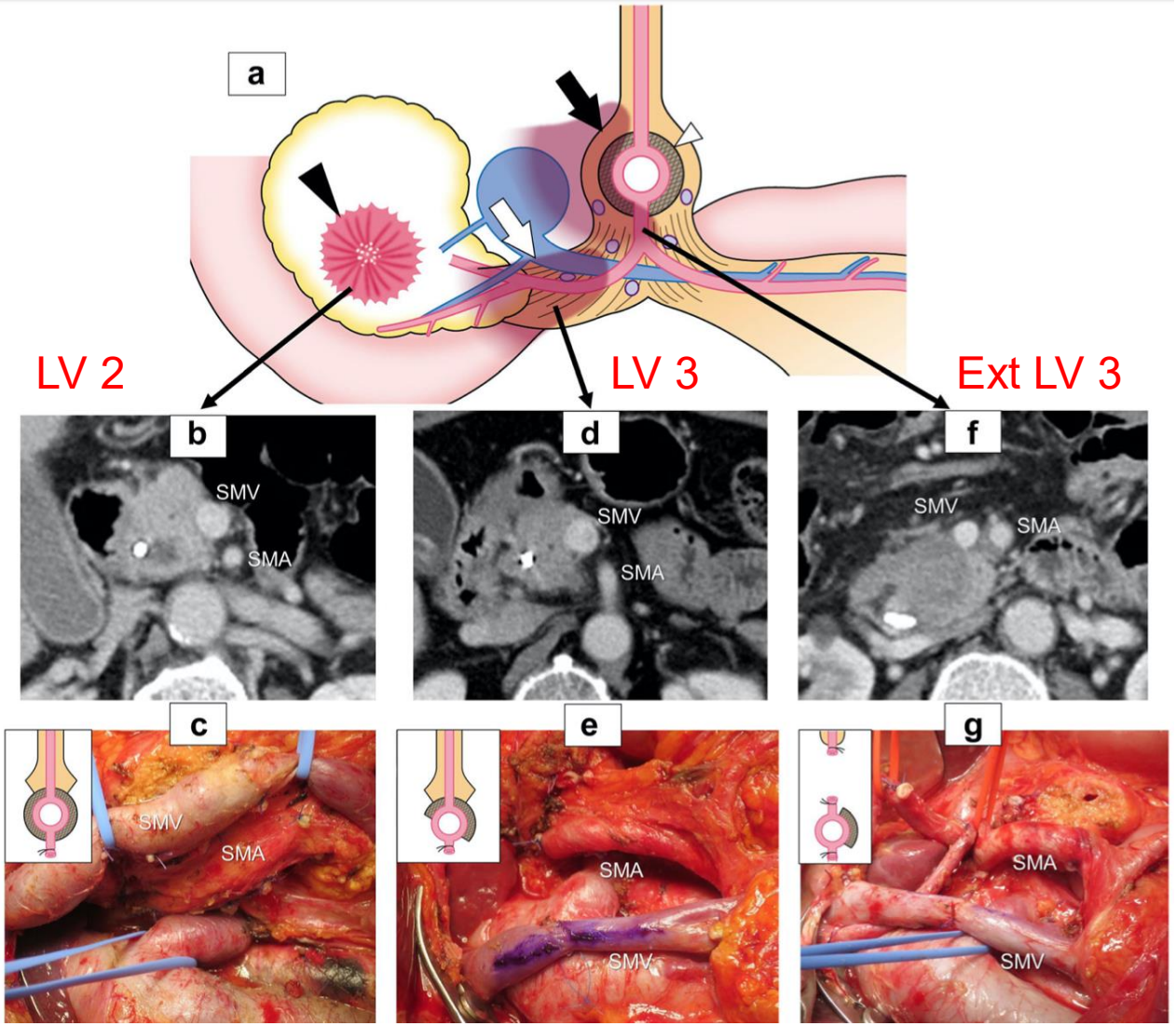






Optimal Extent of Superior Mesenteric Artery Dissection during Pancreaticoduodenectomy for Pancreatic Cancer: Balancing Surgical and Oncological Safety

Yosuke Inoue[1] · Akio Saiura[1] · Atsushi Oba[1] · Shoji Kawakatsu[1] · Yoshihiro Ono[1] · Takafumi Sato[1] · Yoshihiro Mise[1] · Takeaki Ishizawa[1] · Yu Takahashi[1] · Hiromichi Ito[1]



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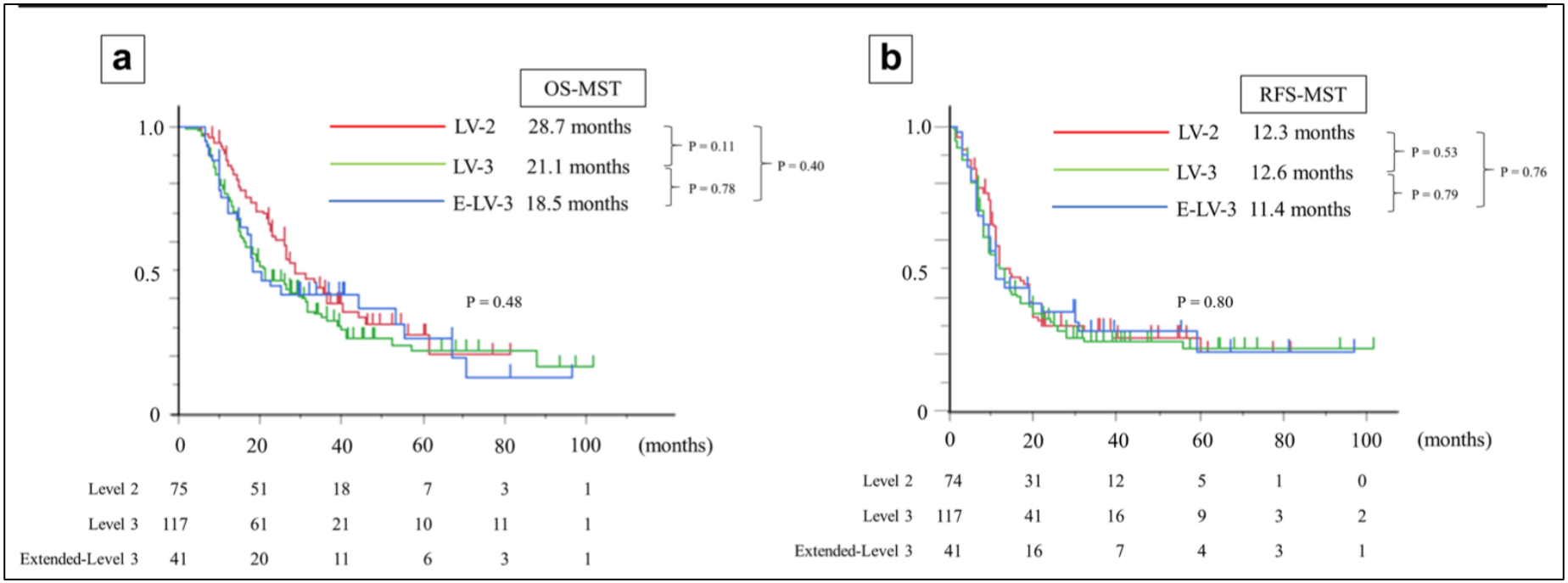


R1 <1mm resections: 0%!!!

J Gastrointest Surg 2018

How to assure a high possibility of R0 resections in BR Surgical strategy

Step 1: Artery first

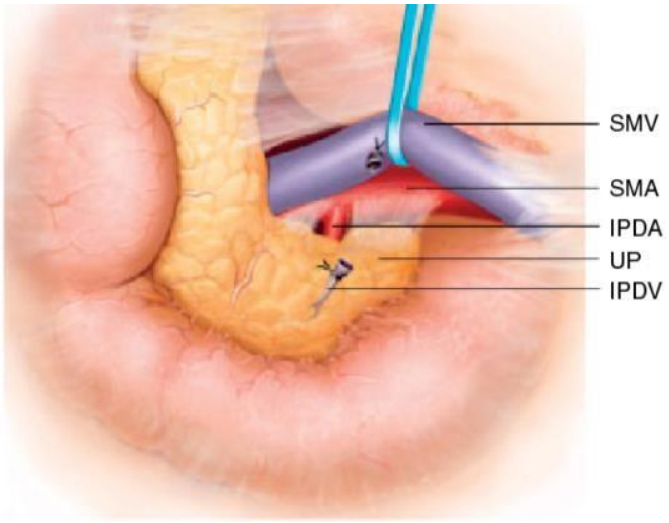
Systematic review

Meta-analysis of an artery-first approach *versus* standard pancreatoduodenectomy on perioperative outcomes and survival

N. Ironside[1], S. G. Barreto[3,4], B. Loveday[1,2], S. V. Shrikhande[5], J. A. Windsor[1,2] and S. Pandanaboyana[1,2]

[1]Department of Surgery, Faculty of Medical and Health Sciences, University of Auckland, and [2]Hepatobiliary and Pancreatic Unit, Department of General Surgery, Auckland City Hospital, Auckland, New Zealand, [3]Hepatobiliary and Oesophagogastric Unit, Division of Surgery and Perioperative Medicine, Flinders Medical Centre, and [4]School of Medicine, Faculty of Medicine, Nursing and Health Sciences, Flinders University, Bedford Park, South Australia, Australia, and [5]Gastrointestinal and Hepatopancreatobiliary Unit, Department of Surgical Oncology, Tata Memorial Hospital, Mumbai, India

Correspondence to: Mr S. Pandanaboyana, Department of Hepatobiliary and Pancreatic Surgery, Auckland City Hospital, Park Road, Grafton, Auckland 1023, New Zealand (e-mail: spandanaboyana@adhb.govt.nz; @sanjay_p99)

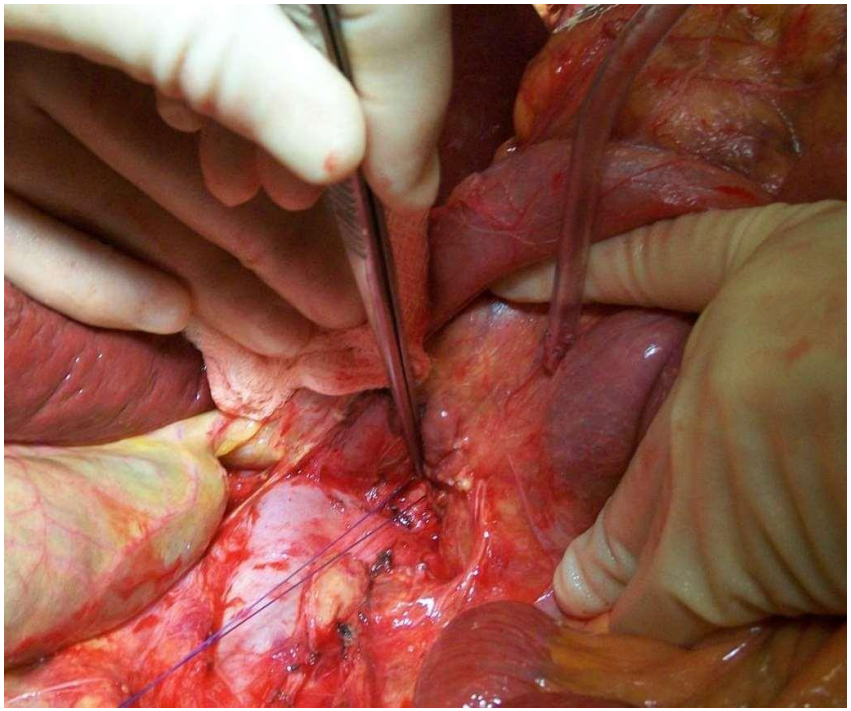


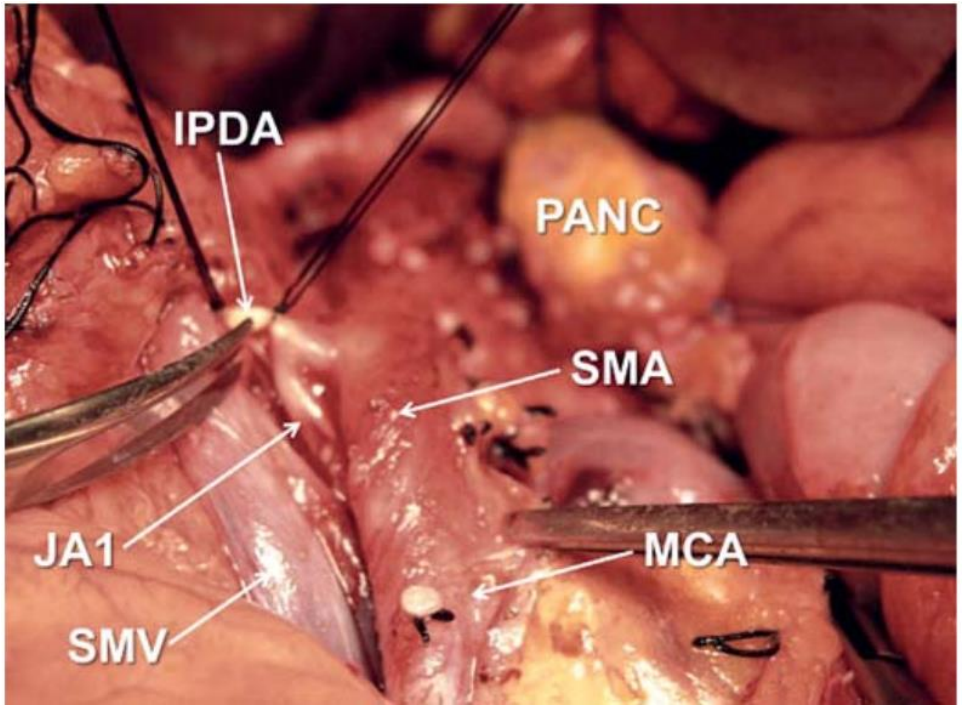
771 artery-first PDs vs. 701 standard PDs

lower blood loss mortality equal morbidity lower R0: 76% vs. 67%

Br J Surg 2018

“Artery first” approach





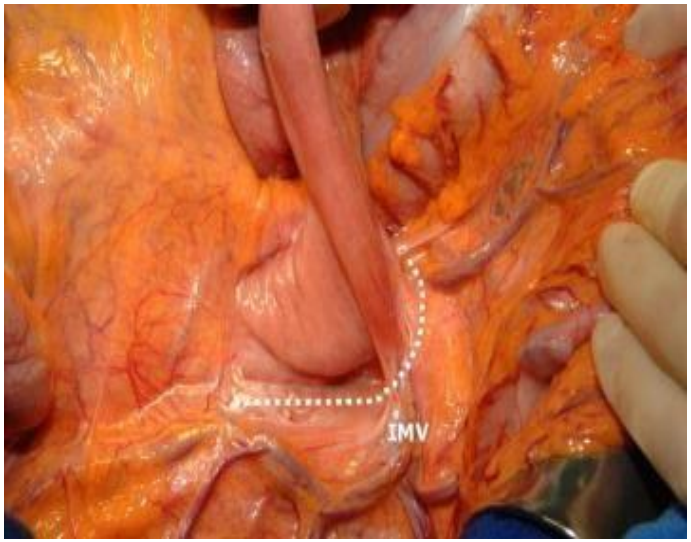
Artery First Approach

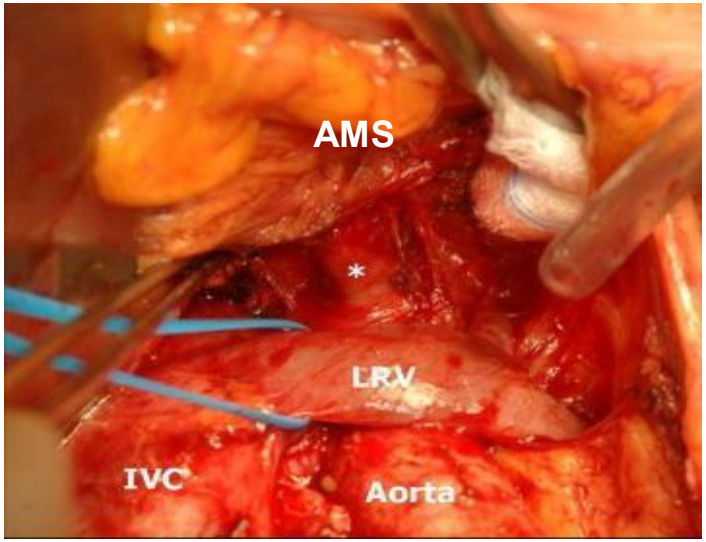
SURGEON AT WORK

The "Artery First" Approach for Resection of Pancreatic Head Cancer

Jürgen Weitz, MD, Nuh Rahbari, MD, Moritz Koch, MD, Markus W Büchler, MD

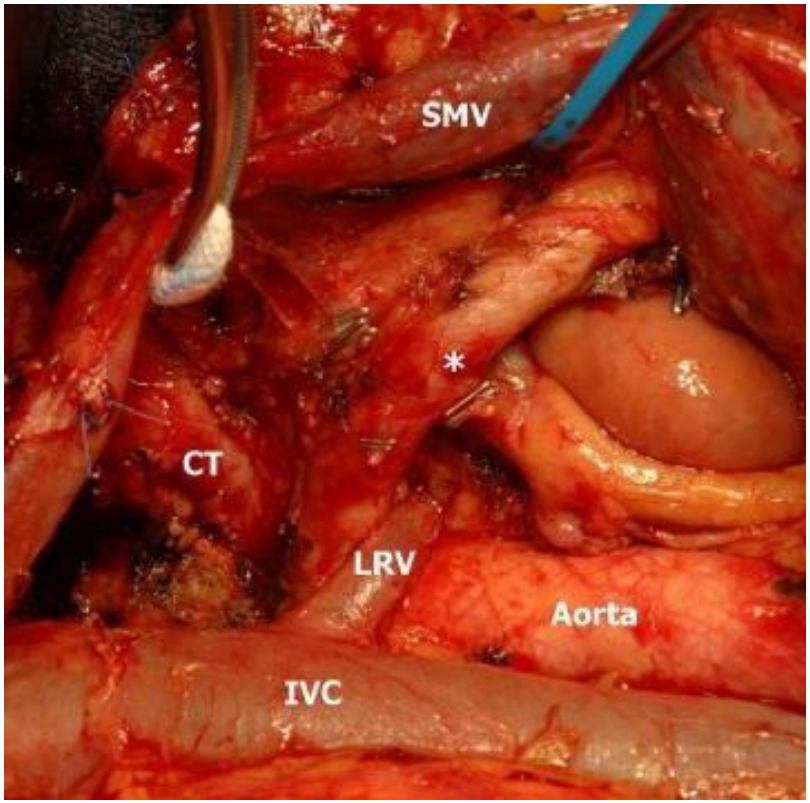
evaluation of arterial infiltration

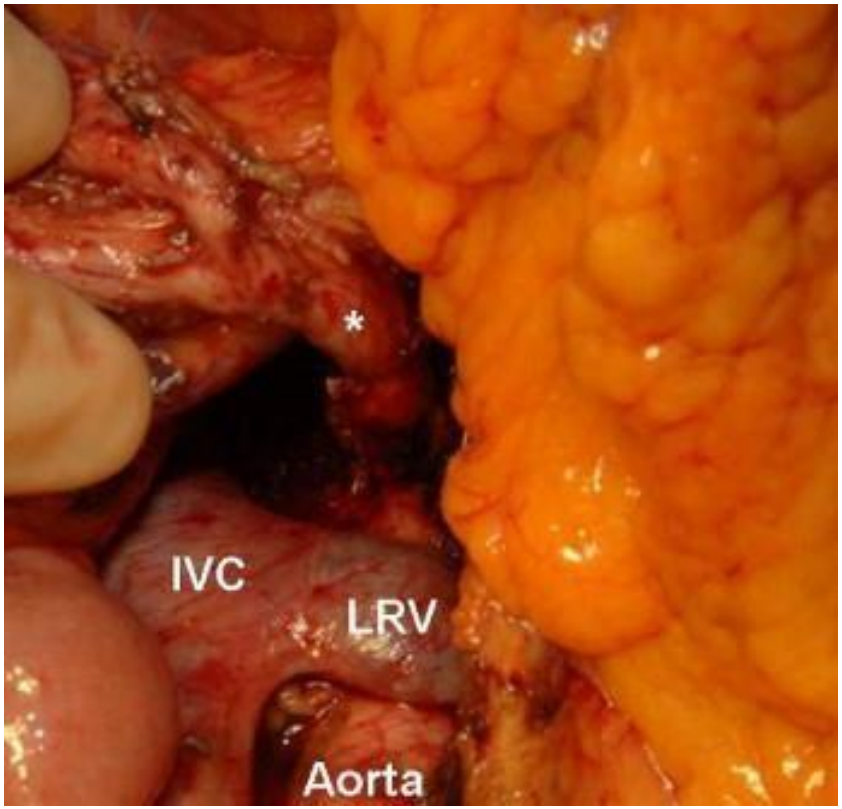




Weitz et al., JACS 2010

Artery First





preparation celiac trunk & SMA

Weitz et al., JACS 2010

Artery First Overview

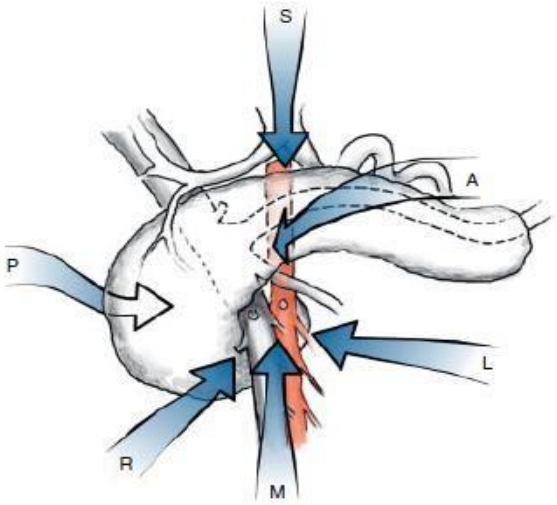
Review

'Artery-first' approaches to pancreatoduodenectomy

P. Sanjay[1,6], K. Takaori[3], S. Govil[4], S. V. Shrikhande[5] and J. A. Windsor[1,2]

[1]Hepatopancreatobiliary/Upper Gastrointestinal Unit, Department of General Surgery, Auckland City Hospital, and [2]Department of Surgery, School of Medicine, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand, [3]Division of Hepato-Biliary-Pancreatic Surgery and Transplantation, Department of Surgery, Kyoto University Graduate School of Medicine, Kyoto, Japan, [4]Division of Gastrointestinal Oncology, Bangalore Institute of Oncology, Bangalore, and [5]Department of Gastrointestinal and Hepatopancreatobiliary Surgical Oncology, Tata Memorial Centre, Mumbai, India, and [6]Department of Surgery, Ninewells Hospital and Medical School, Dundee, UK

Correspondence to: Professor J. A. Windsor, 12th floor, Support Building, Auckland City Hospital, Park Road, Grafton, Auckland, New Zealand (e-mail: j.windsor@auckland.ac.nz)

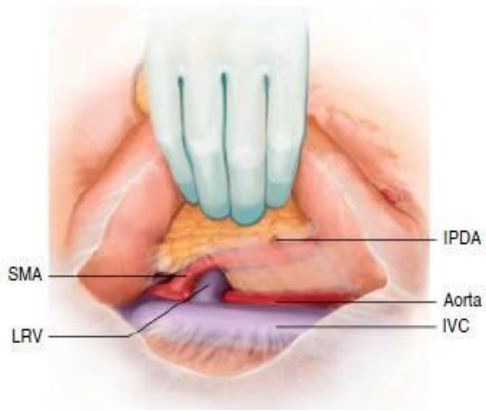


literature search

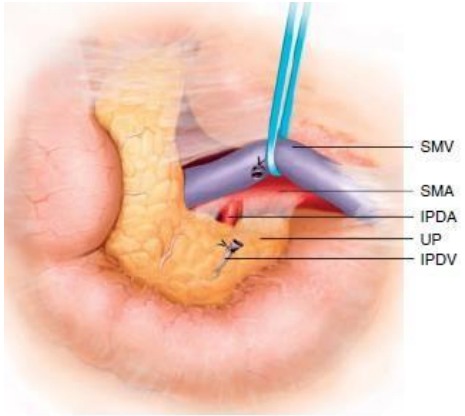
6 different approaches

Sanjay et al., Br J Surg 2012

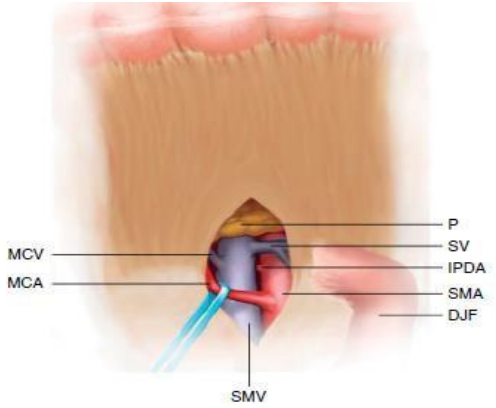
Artery First Overview



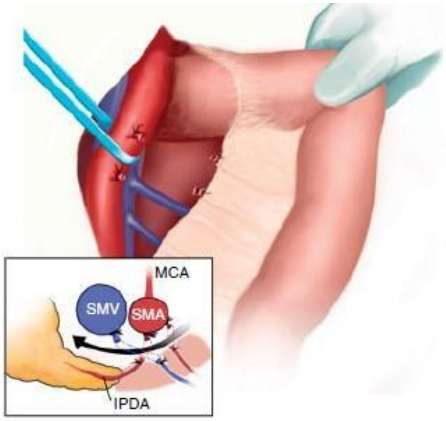
posterior



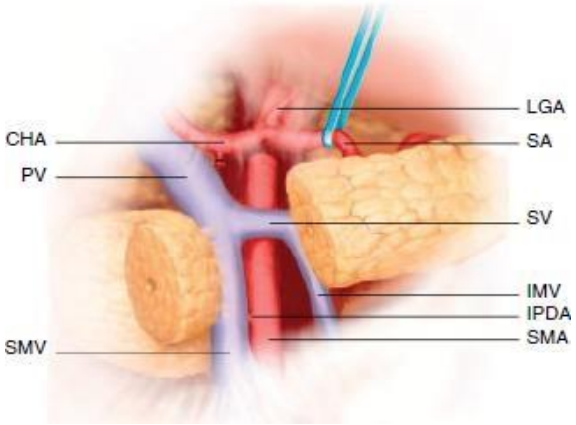
medial uncinate



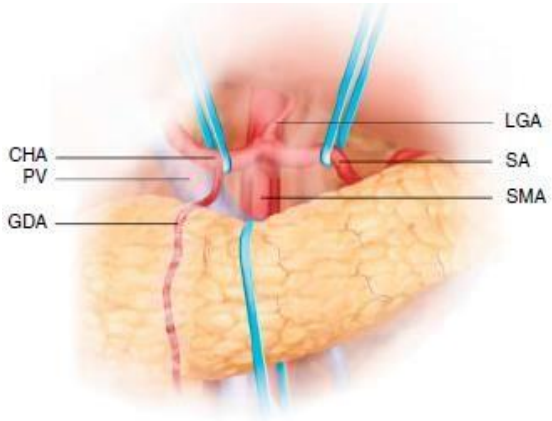
inferior infracolic



left posterior



inferior supracolic



superior

Uncinate First Approach

HOW TO DO IT

Uncinate process first—a novel approach for pancreatic head resection

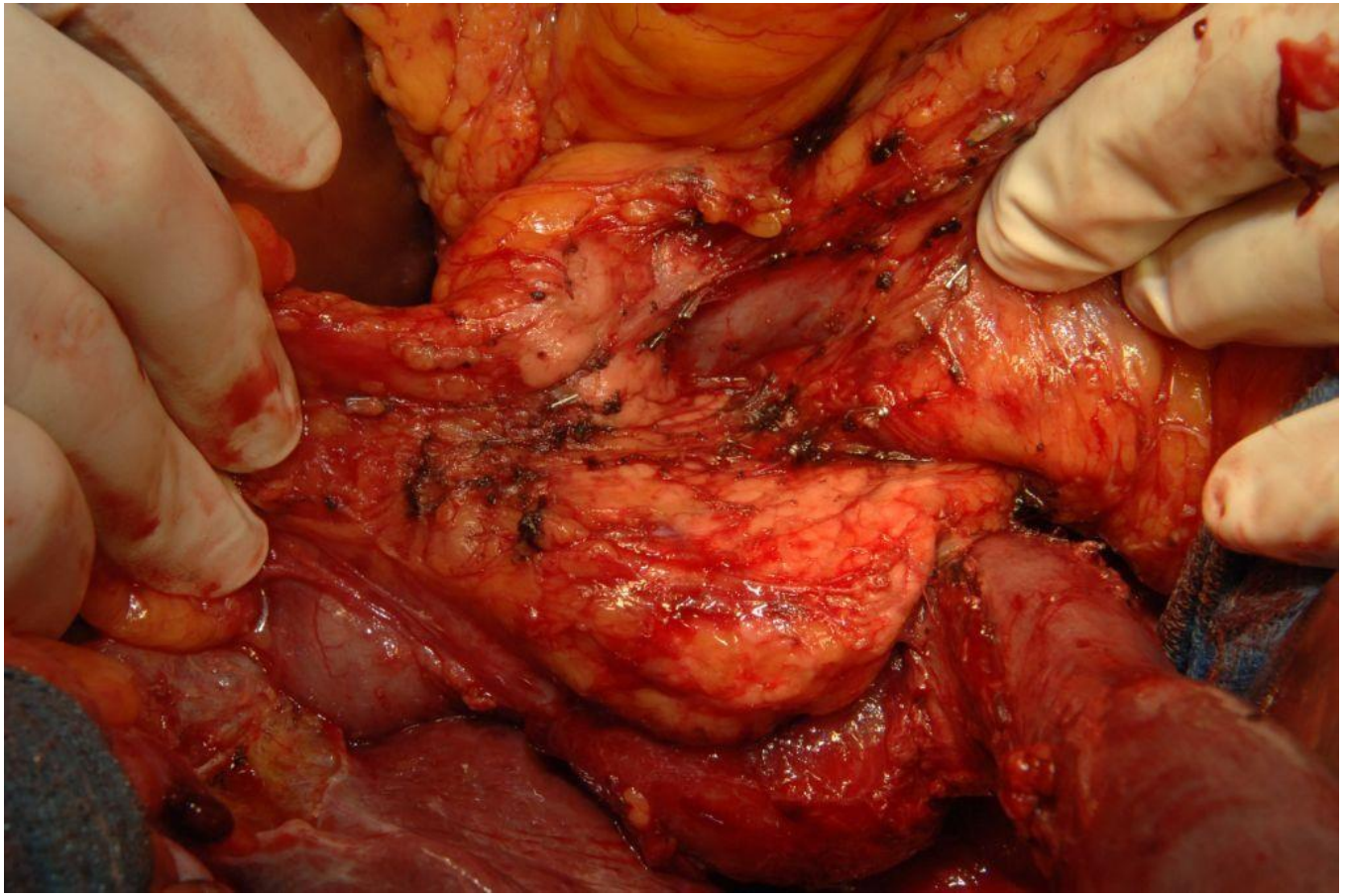
Thilo Hackert · Jens Werner · Jürgen Weitz · Jan Schmidt · Markus W. Büchler

Retrograde resection:

good vessel control (PV & SMA)
convenient situs during resection
standard technique in Heidelberg
can be combined with artery first approach

Hackert et al., LAS 2010

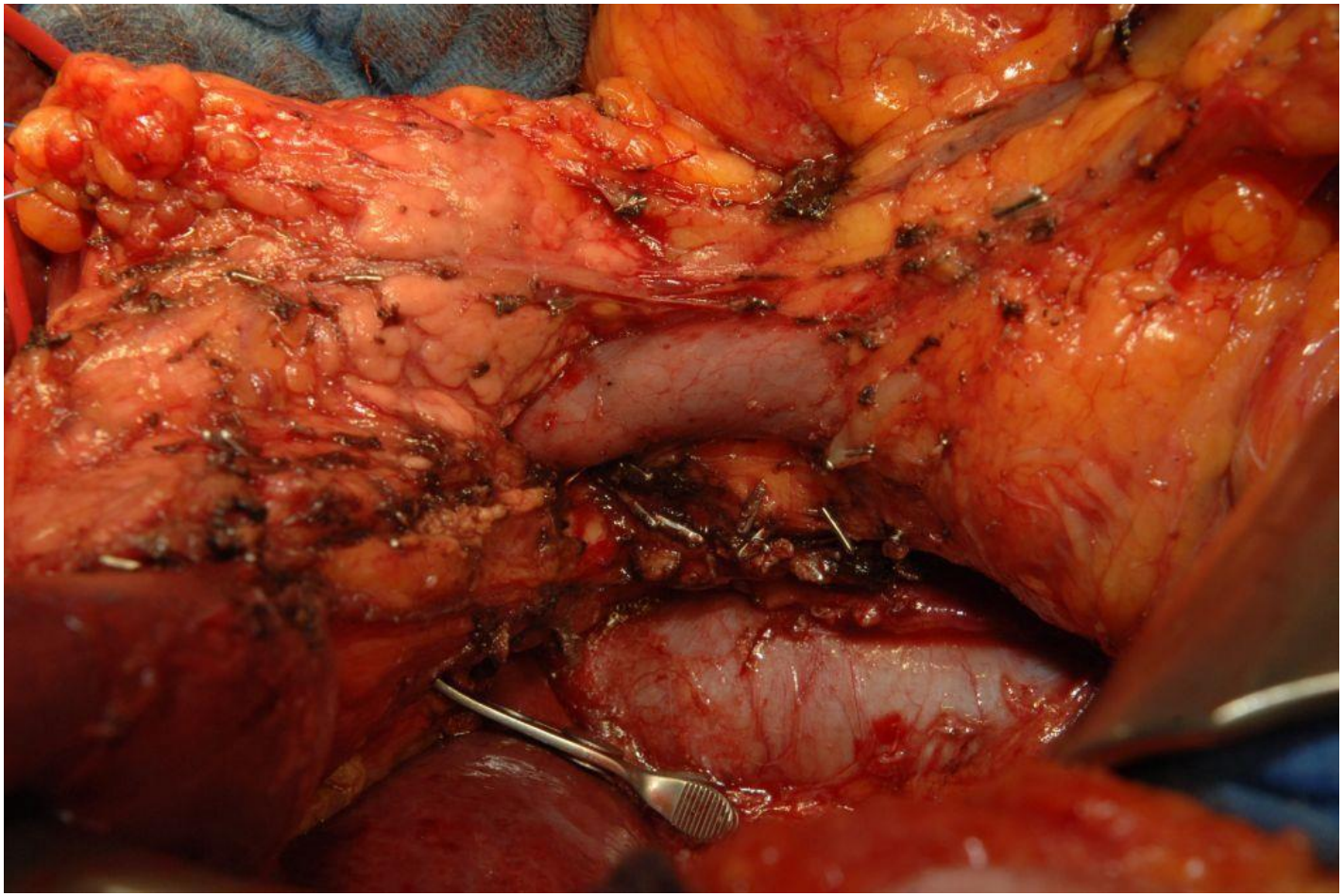
Uncinate First



starting dissection caudally

Hackert et al., LAS 2010

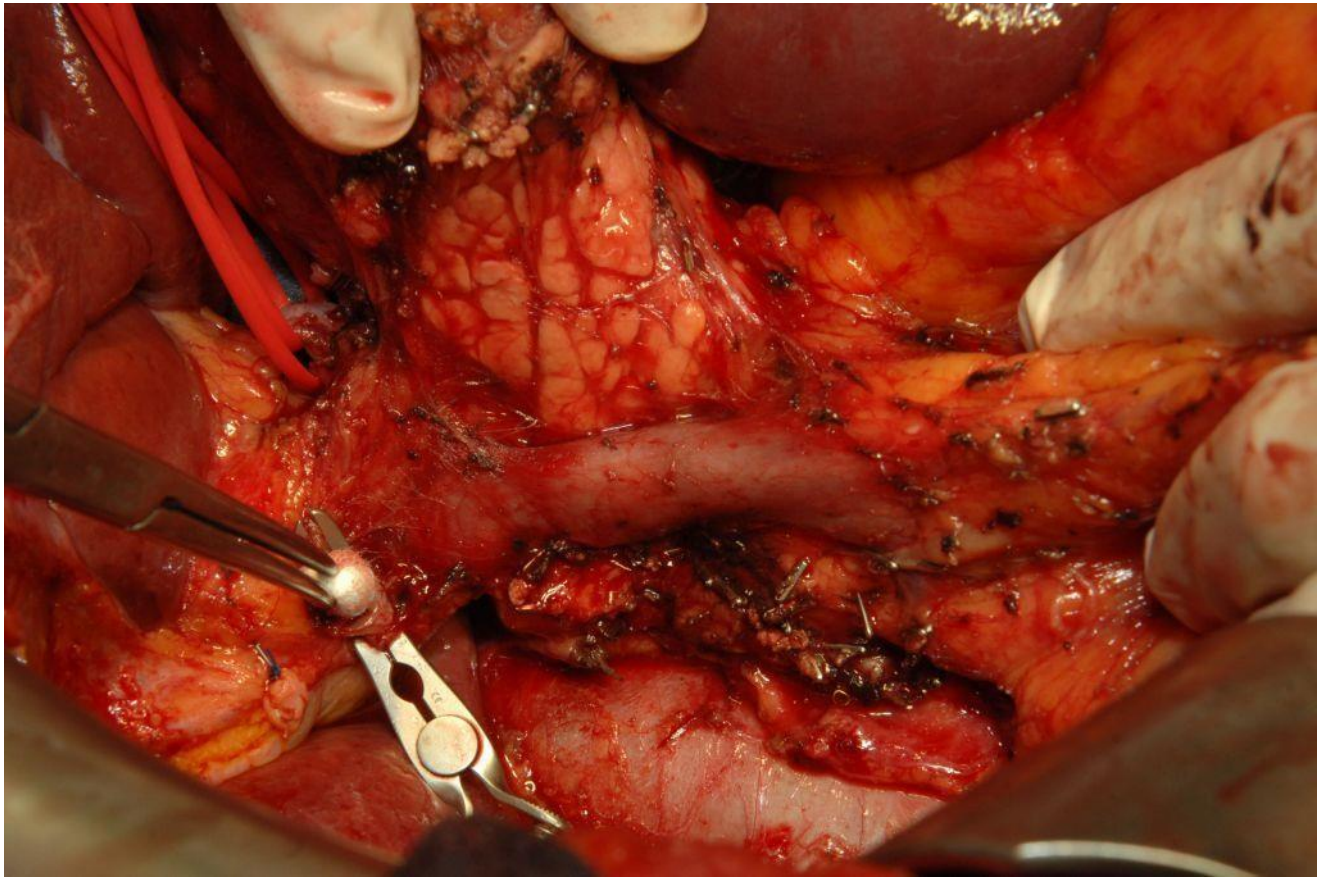
Uncinate First



preparation along SMA & PV

Hackert et al., LAS 2010

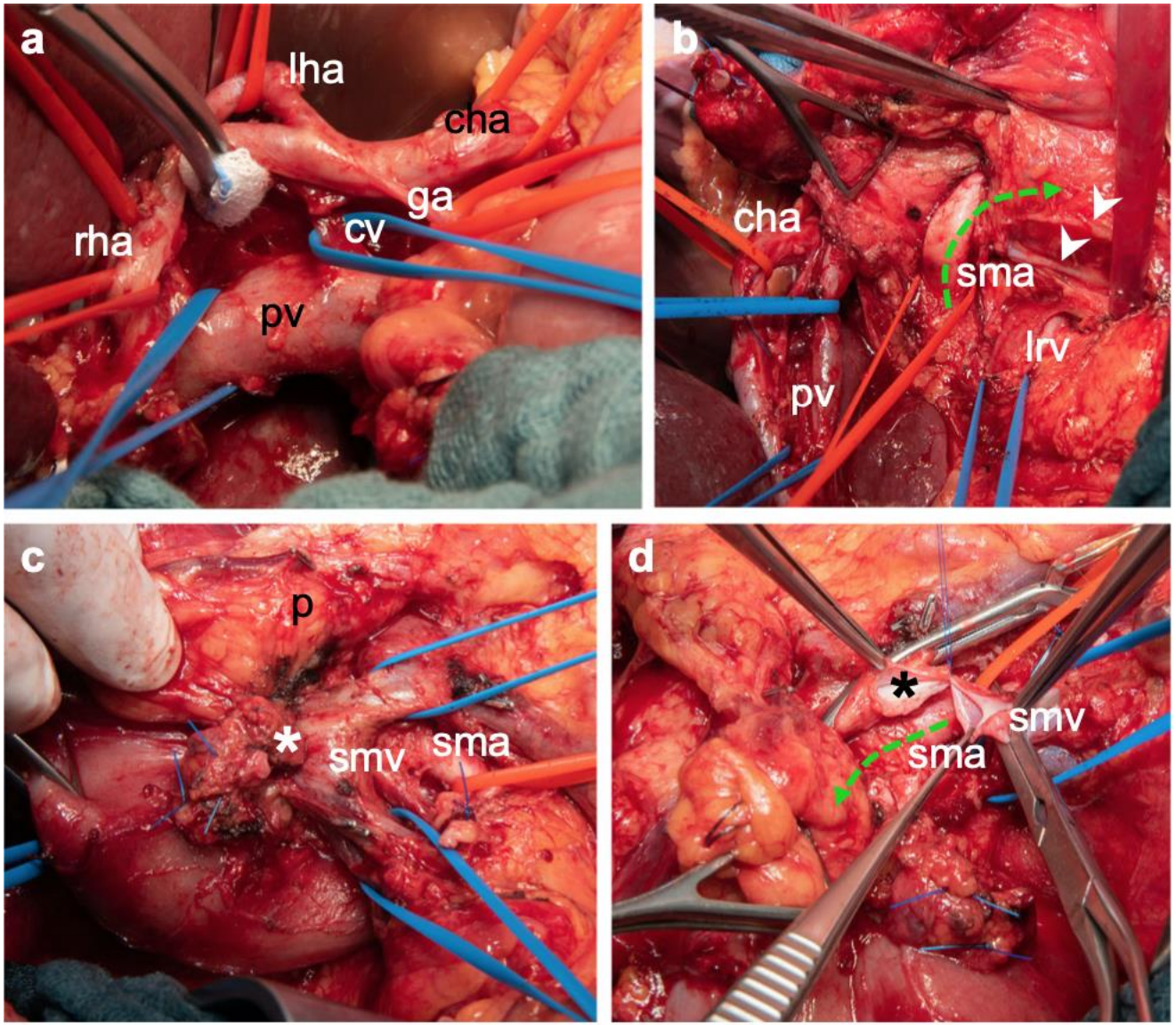
Uncinate First



complete retrograde mobilisation of the pancreatic head

Hackert et al., LAS 2010

TMPE – Surgical Technique



Artery First Approach - Advantages

Resection without breaching tumor planes
NO cell spillage!

↑R0 resection, ↓local recurrence

Complete resection of peripancreatic retroperitoneal tissue TMpE

↑RLNs

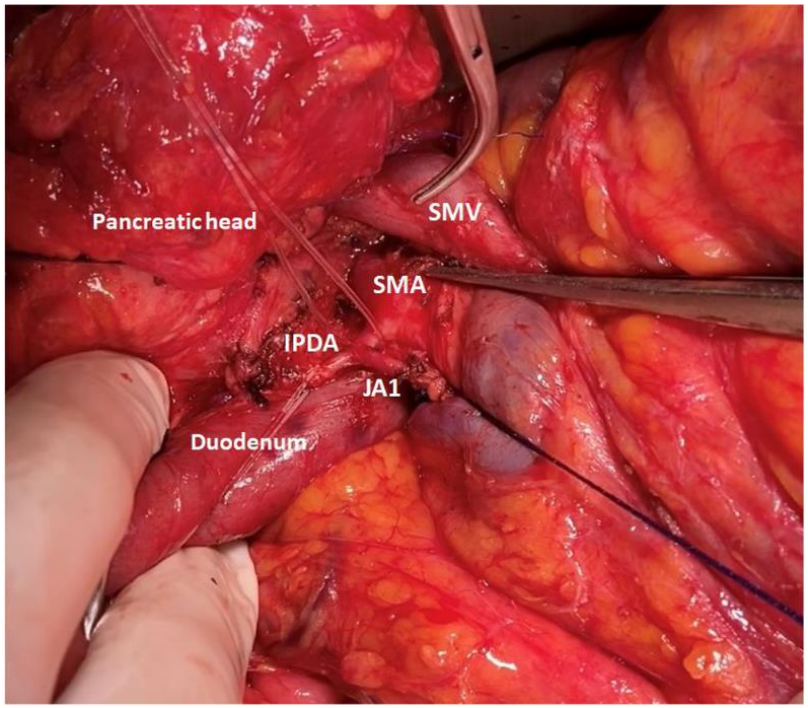
Early assessment of non-resectability (SMA involvement)

Better delineation of SMA – abnormalities

Easier “en block” resection and
”NO touch” PV-SMV reconstruction

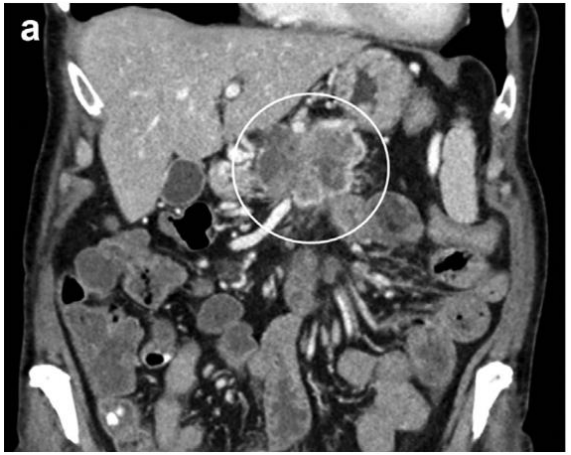
Reduced need for graft substitution

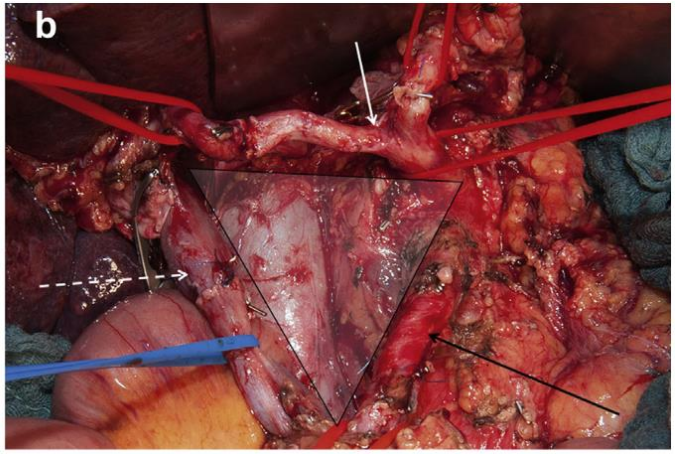
Reduced operative time and reduced blood loss (early ligation of IPDA/JA1)

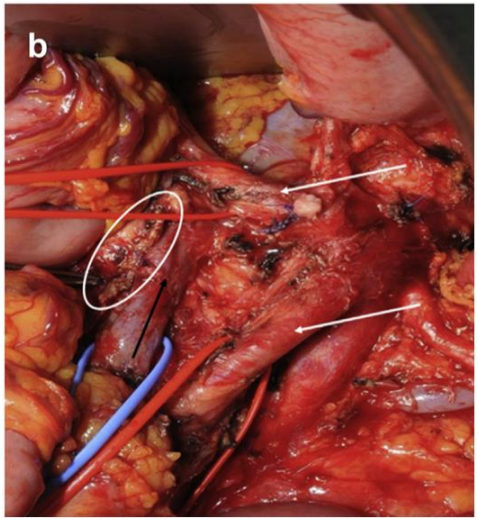


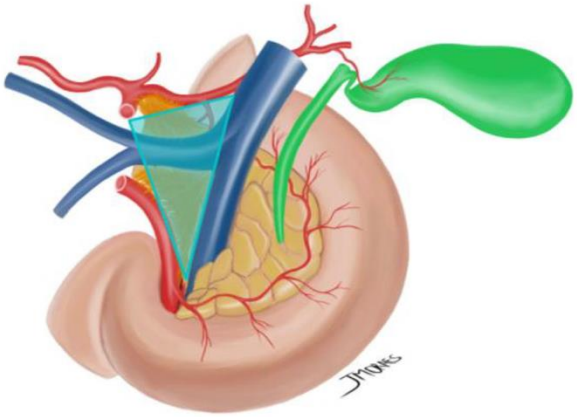
J Pancreatobil Pancr Sci 2017

TRIANGLE Operation – Vascular Oriented technique



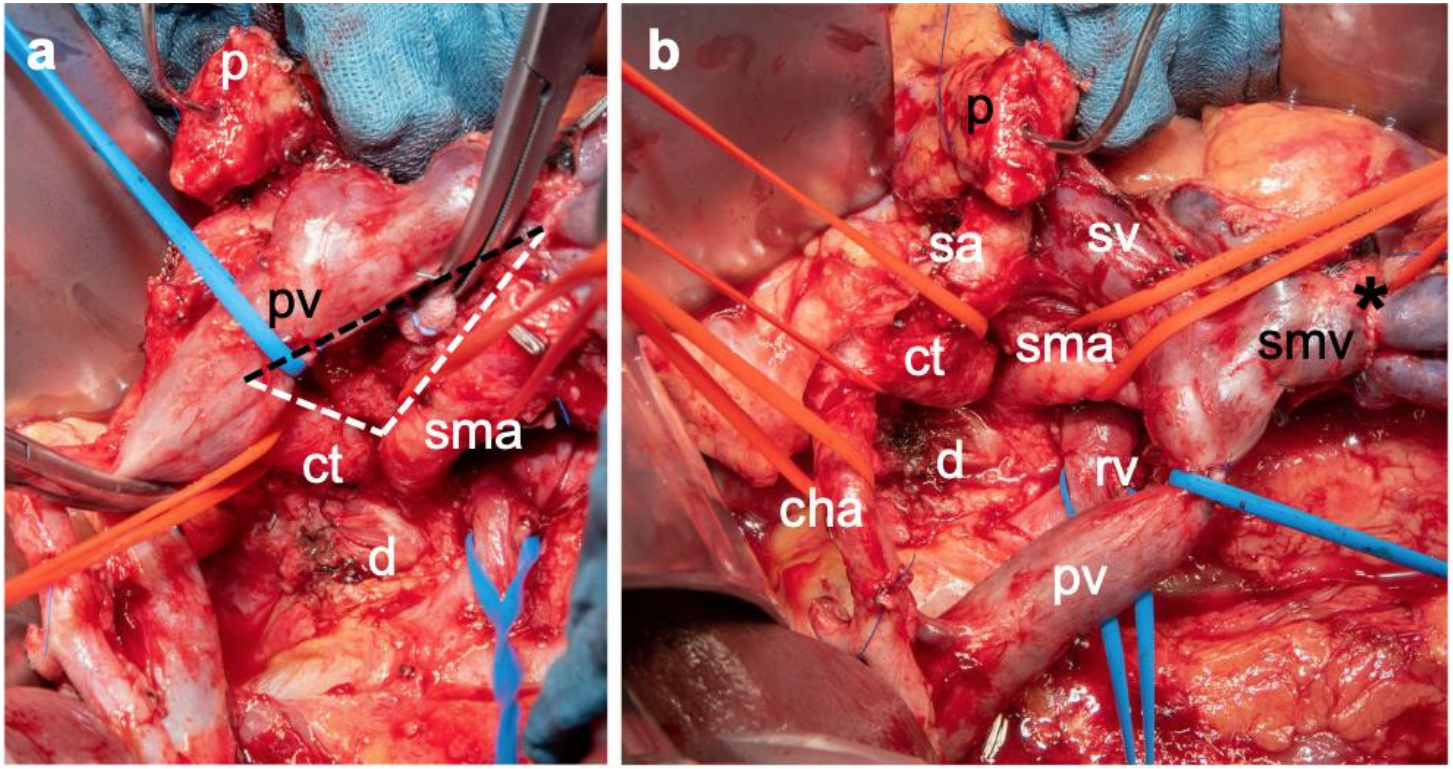






HPB 2017

TMPE – Surgical Technique

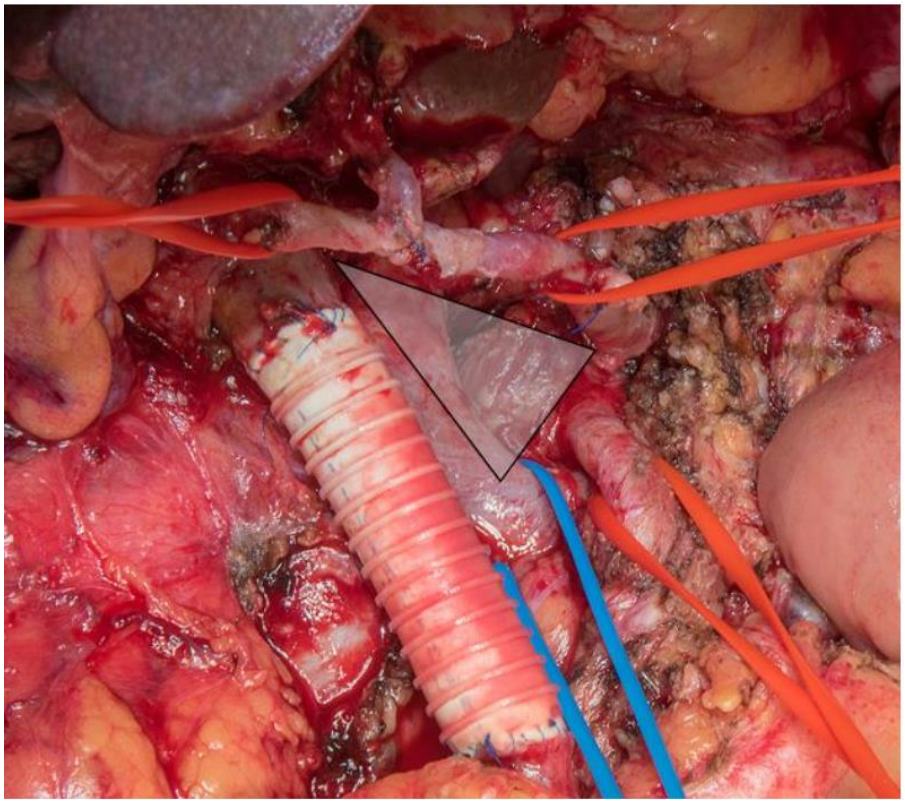


Langenbeck's Arch Surg 2019

The TRIANGLE operation for pancreatic head and body cancers: early postoperative outcomes

Rosa Klotz[1,2], Thilo Hackert[1], Patrick Heger[1,2], Pascal Probst[1,2], Ulf Hinz[1], Martin Loos[1], Christoph Berchtold[1], Arianeb Mehrabi[1], Martin Schneider[1], Beat P. Müller-Stich[1], Oliver Strobel[1], Markus K. Diener[1,2], André L. Mihaljevic[1,2,*] & Markus W. Büchler[1*]

HPB 2022

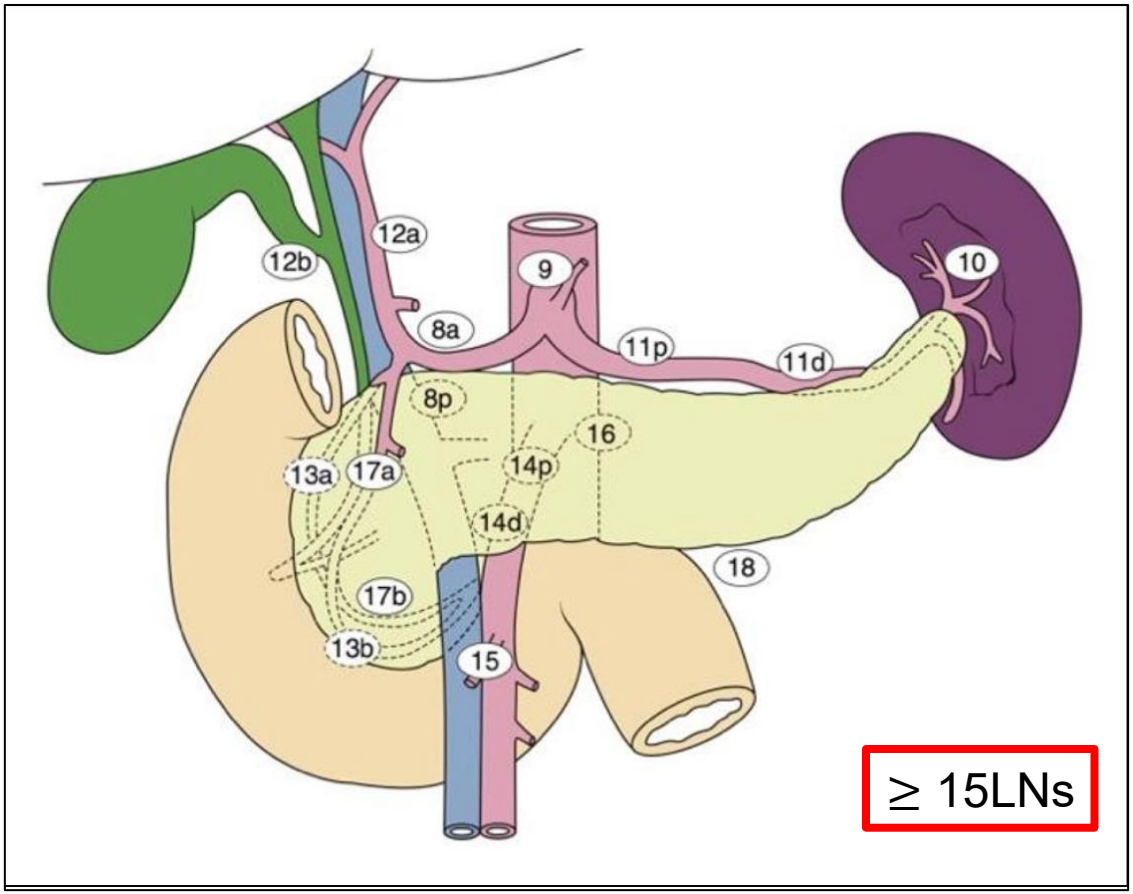


TMPE – Sharp dissection – Frozen sections
Arterial Skeletonization – Avoid arterial resection / reconstruction
No increase in Mortality / Morbidity
Increase RLNs – R0 rate

Consensus

Definition of a standard lymphadenectomy in surgery for pancreatic ductal adenocarcinoma: A consensus statement by the International Study Group on Pancreatic Surgery (ISGPS)

Standard Lymphadenectomy in Pancreatoduodenectomy



Supra and infra pyloric (stations 5/6)
Anterior-superior group along the CHA (station 8a)
Along the bile duct/cystic duct (stations 12b/12c)
Posterior aspect of the superior/Inferior aspect of the head of pancreas (13a/13b)
Right lateral side of the SMA (stations 14a/14b)
Anterior surface of superior/inferior aspect of head (stations 17a/17b)

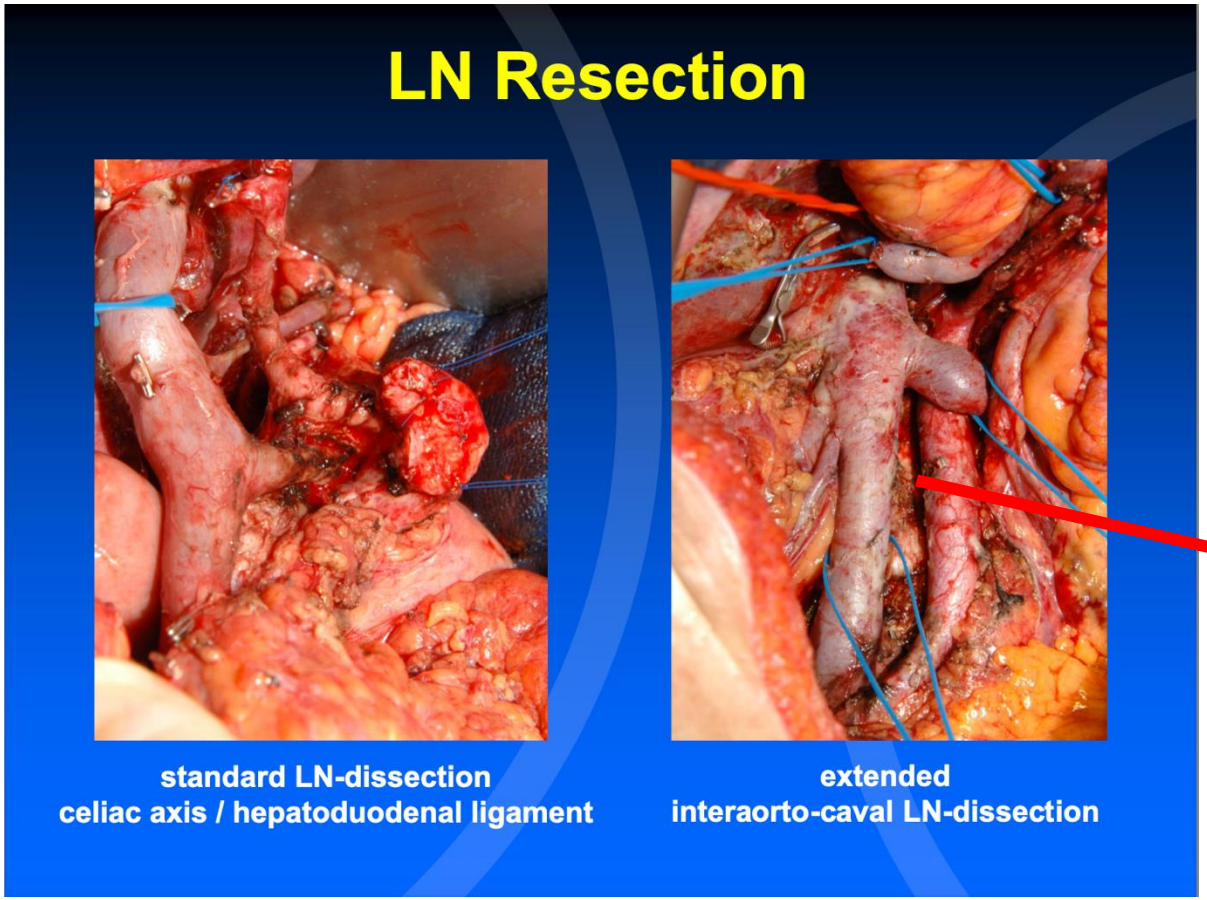
Surgery 2015

Standard vs Extended Lymphadenectomy

RCTs

Author	Year	Country	Number of Cases	Standard Dissection	Extended Dissection	Standard Dissection	Extended Dissection	Prognosis
				Lymph Node Dissection *		SMA Nerve Plexus Dissection		
Pedrazzoli S et al. [1]	1998	Italy	81	5, 6, 12b, 13, 17	5, 6, 9, 12b, 13, 14, 17, 16a2, 16b1	Not described N+!!!		MST Standard: 335 days Extended: 500 days
Yeo C et al. [2]	2002	United States	299	12b2, 12c, 13, 14b, 14v, 17	3, 4, 5, 6, 9, 12b2, 12c, 13, 14b, 14v, 16a2, 16b1, 17	Not described		5-year survival rate Standard: 23% Extended: 29%
Farnell M et al. [3]	2005	United States	132	3, 4, 6, 8a, 12b1, 12b2, 12c, 13a, 13b, 14a, 14b, 17a, 17b	3, 4, 6, 8a, 8p, 9, 12a1, 12a2, 12b1, 12b2, 12p1, 12p2, 12c, 13a, 13b, 14a, 14b, 14c, 14d, 14v, 16a2, 16b, 17a, 17b	Not described		5-year survival rate Standard: 17% Extended: 16%
Nimura Y et al. [4]	2012	Japan	112	13a, 13b, 17a, 17b	8a, 8p, 9, 14p, 1416a2, 16b112a, 12b, 12p	None	full circumference dissection	5-year survival rate Standard: 15.7% Extended: 6.0%
Jang JY et al. [5]	2014	Korea	244	12c, 13, 17	9, 12, 13, 14, 16, 17	None	right half-circumferential dissection	5-year survival rate Standard: 44.5% Extended: 35.7%

Cancers 2023



Increase No of harvested LNs but NOT increase No of (+) LNs/LNR
Offers NO advantage in OS/DFS in RCTs
↑↑Morbidity: DGE
Intractable diarrhea
Ascites
POPF

Langenbeck's Archives of Surgery 2020

Prognostic Value of LN & Grading

ORIGINAL ARTICLE

Pancreatic Adenocarcinoma

Number of Positive Nodes Allows to Distinguish Several N Categories

Oliver Strobel, MD, Ulf Hinz, MSc,*† Alexander Gluth, MD,*§ Thomas Hank, MD,* Thilo Hackert, MD,* Frank Bergmann, MD,‡ Jens Werner, MD,*§ and Markus W. Büchler, MD**

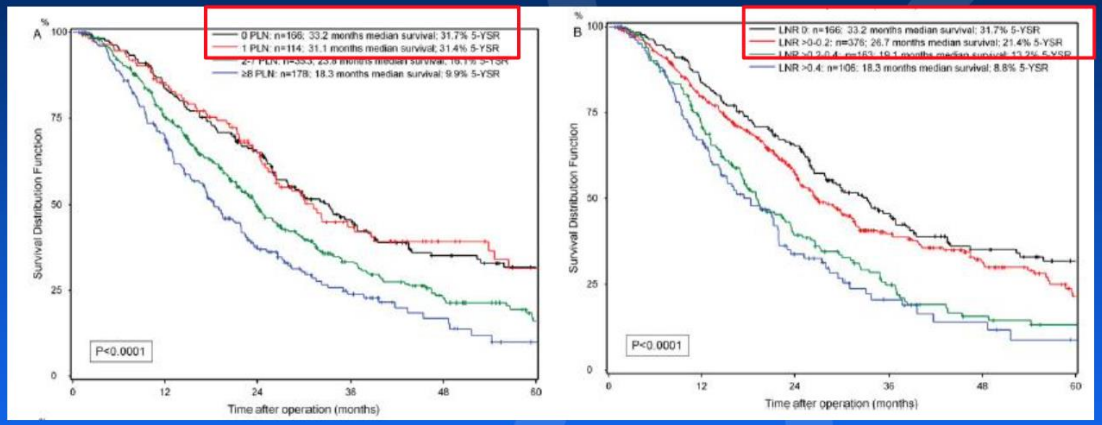
811 resected PDAC patients

prognostic impact of LN status & grading

multivariate analysis of survival parameters

Strobel et al., Ann Surg 2014

Prognostic Value of LN & Grading

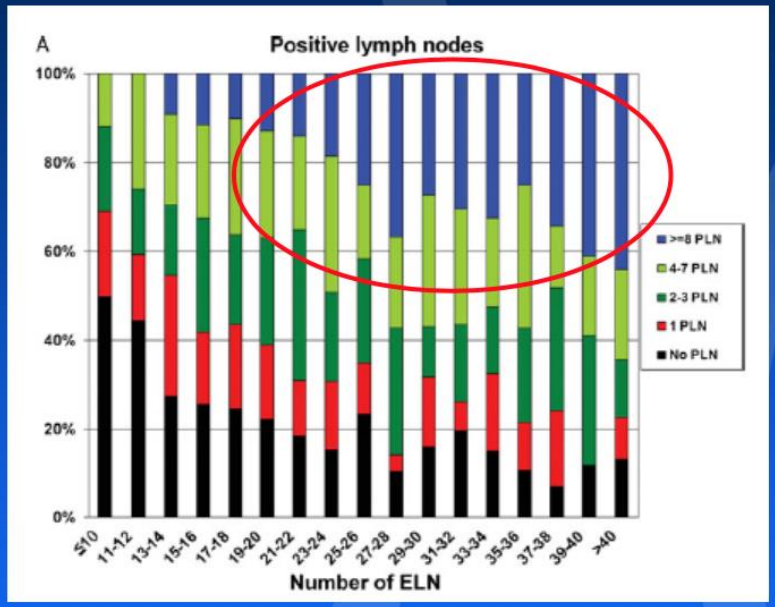


survival highly dependent on no. of positive LN and LNR

Strobel et al., Ann Surg 2014

Positive LNs	OS (months)	LNR	MS(months)	5-YRS
1	31.1	0	33.2	31.7%
2-3	26.1	>0-0.2	26.7	21.4%
4-7	21.9	>0.2-0.4	19.1	13.2%
≥ 8	18.3	>0.4	18.3	8.8%

Prognostic Value of LN & Grading



but both parameters only valid if adequate no. of LN is examined (>24 LN)

Strobel et al., Ann Surg 2014

N0/N1, PNL, or LNR? The Effect of Lymph Node Number on Accurate Survival Prediction in Pancreatic Ductal Adenocarcinoma

J Gastrointest Surg 2015

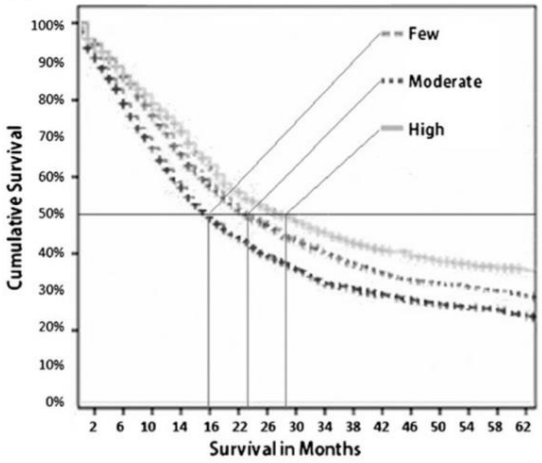
N0 patients

No LNs	OS
≥13	28
≤5	18
	(p<0.05)

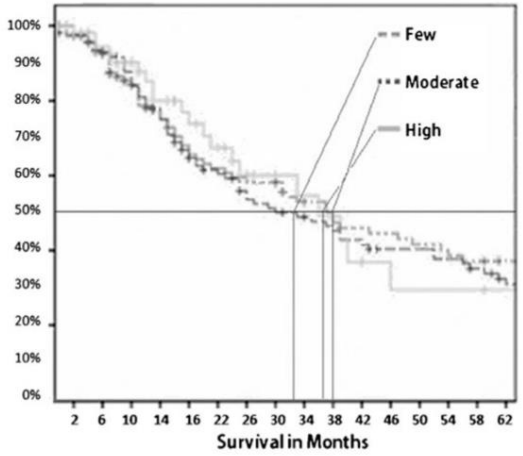
N1 patients

No LNs	OS
≥13	16
≤5	11
	(p<0.001)

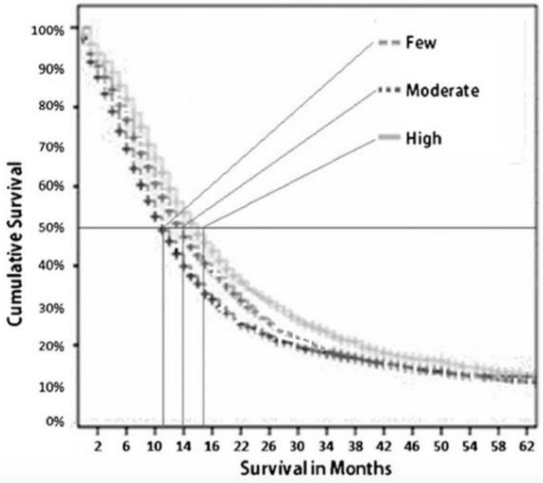
(a) SEER population, N0 patients



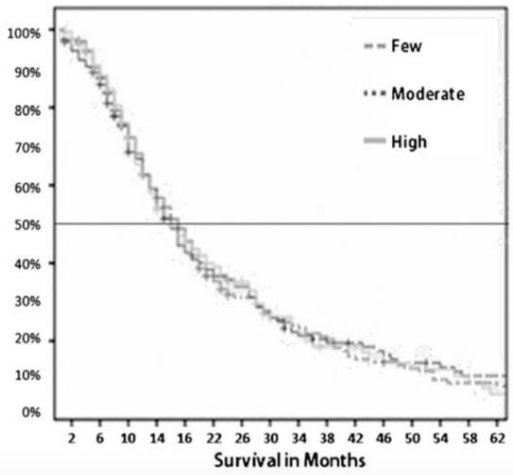
(b) Single institution population, N0 patients



(c) SEER population, N1 patients

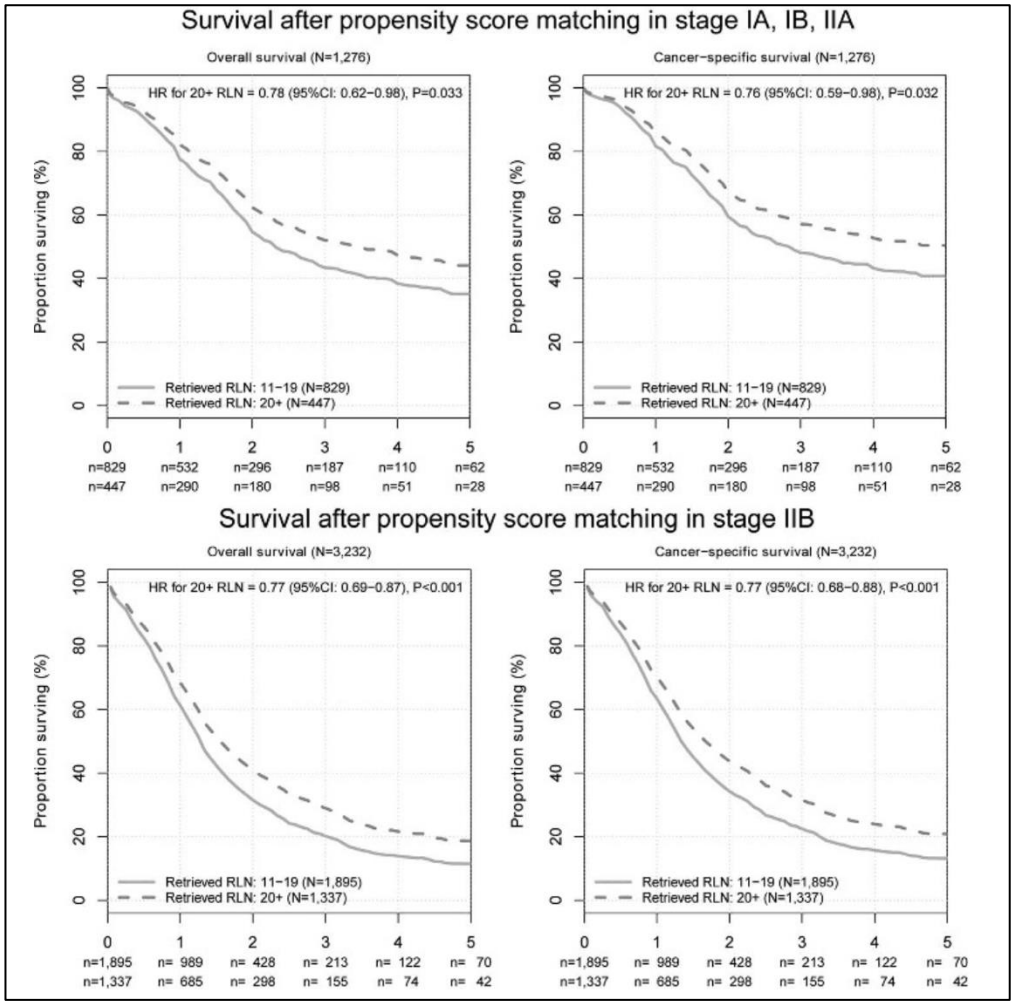


(d) Single institution population, N1 patients



The More the Better—Lower Rate of Stage Migration and Better Survival in Patients With Retrieval of 20 or More Regional Lymph Nodes in Pancreatic Cancer

A Population-Based Propensity Score Matched and Trend SEER Analysis



7685 stage I and II PDAC

3079 pts	1-10RLNs
2799	11-19
1807	20+

>RLNs increases R0 resection

>RLNs Decreases Recurrence

Significant Increase in OS when RLNs>20 BOTH in N+ and N- pts

Neoadjuvant chemo-radio???

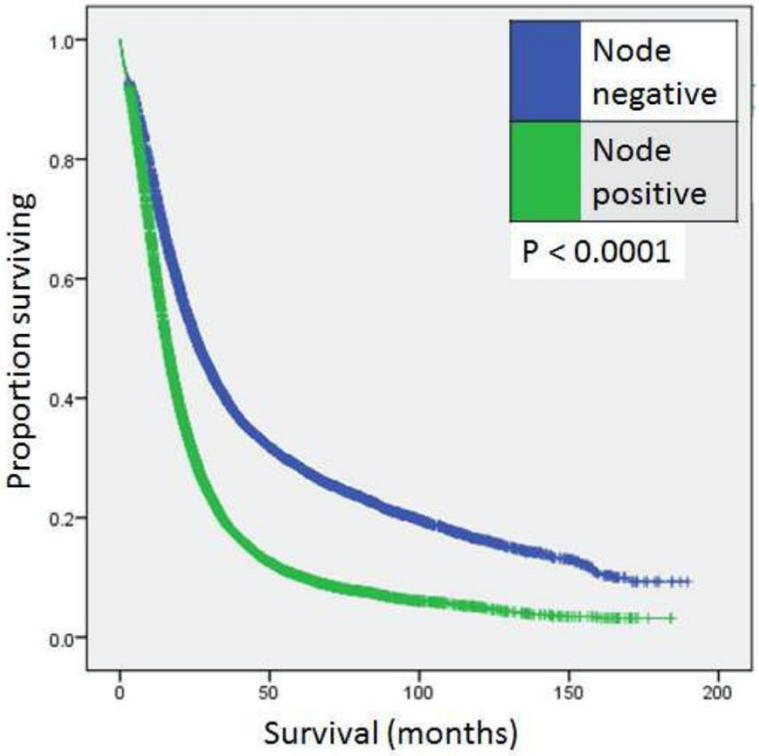
Pathological Assessment???

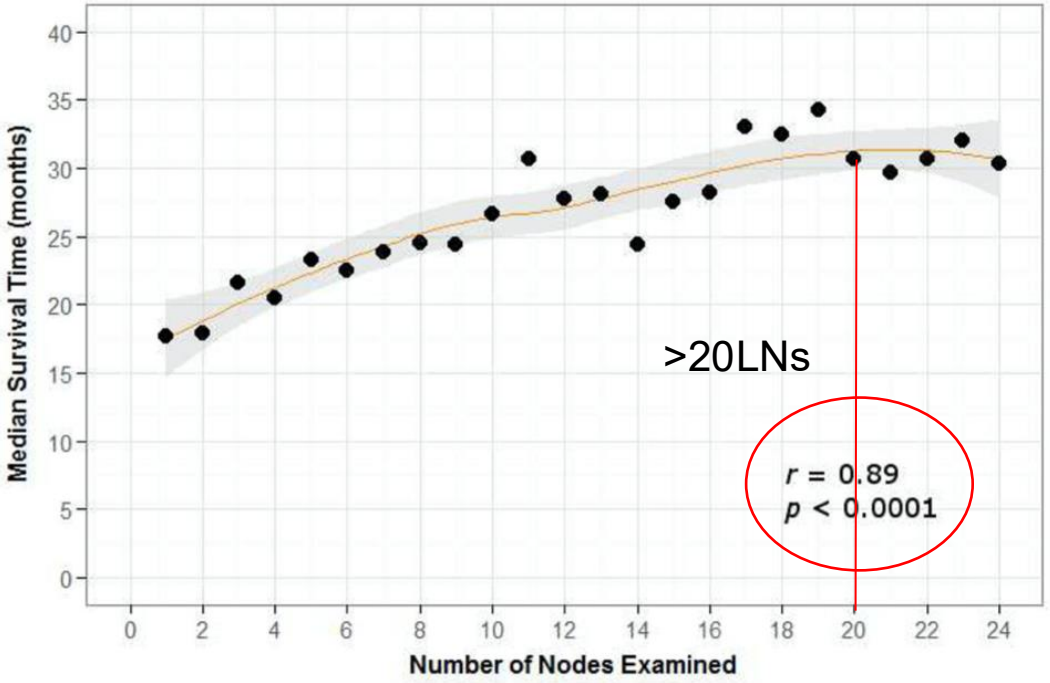
Pancreas 2017

Increased Pancreatic Cancer Survival with Greater Lymph Node Retrieval in the National Cancer Data Base

Carlo M. Contreras, MD[a], Chee Paul Lin, MA[b], Robert A. Oster, PhD[c], Sushanth Reddy, MD[a], Thomas Wang, MD, PhD[a], Selwyn Vickers, MD[a], and **Martin Heslin, MD, MSHA[a]**

Am J Surg 2017





27752 Whipples
1998-2011

↑No of RLNs → Independent Prognostic Factor → ↑↑↑ OS R0 resection

Conclusions

- Standardized right oncological pancreatectomy
- R0 resection
- TMPe as the standard approach in PD
- Artery – first
- Regional but not “extended” lymphadenectomy
- Increase RLNs improves R0 and Survival rates (>20LNs)
- Individualized treatment