Mesenteric approach during pancreaticoduodenectomy for pancreatic ductal adenocarcinoma

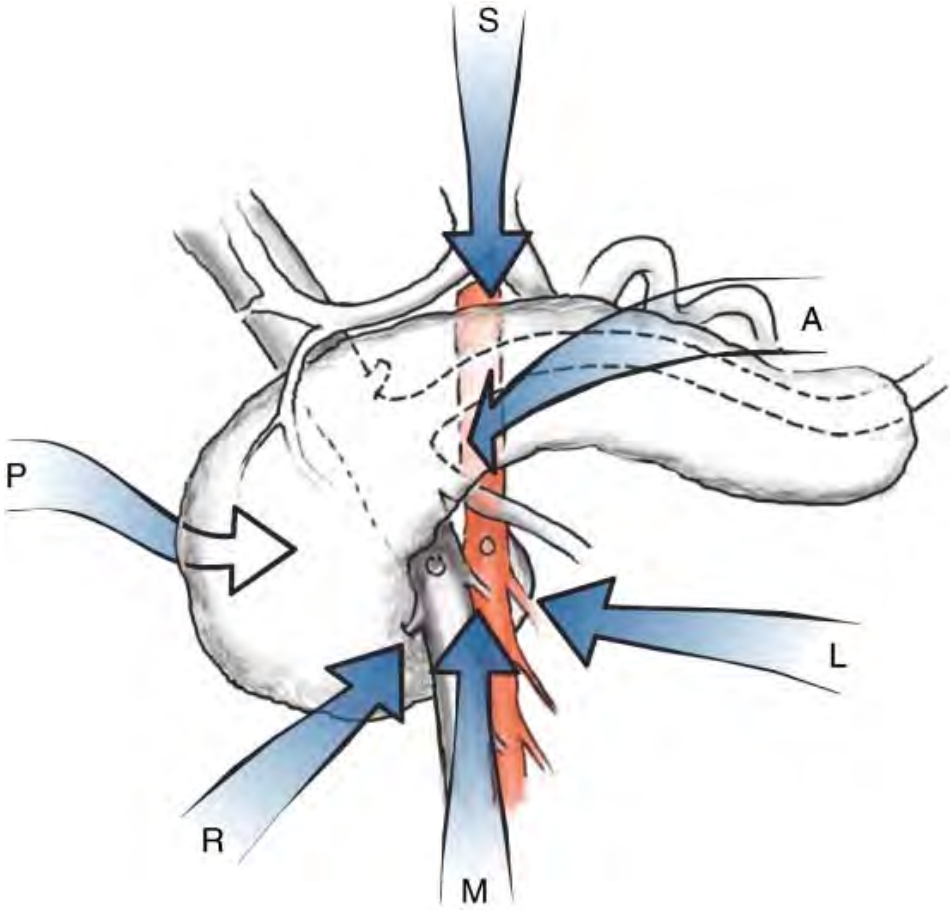
MAPLE-PD trial

Department of Surgery, Wakayama Medical University

Hiroki Yamaue

Wakayama Medical University

Artery-First Approach in Whipple's Operation



(1) Posterior approach
Ohigashi et al. ***Hepatogastroenterology 2004***
Pessaux et al. ***J Gastrointest Surg 2006***

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'Artery-first' approaches to pancreatoduodenecotmy.
Sanjay et al. ***Br J Surg 2012;99:1027-1935***

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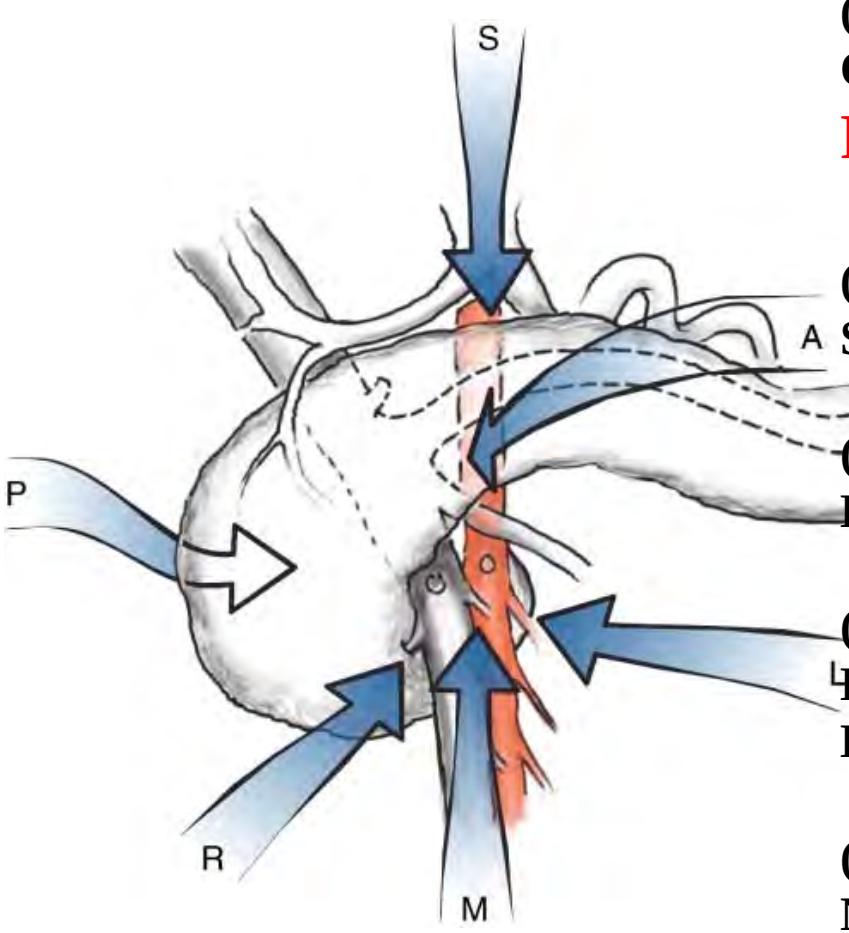

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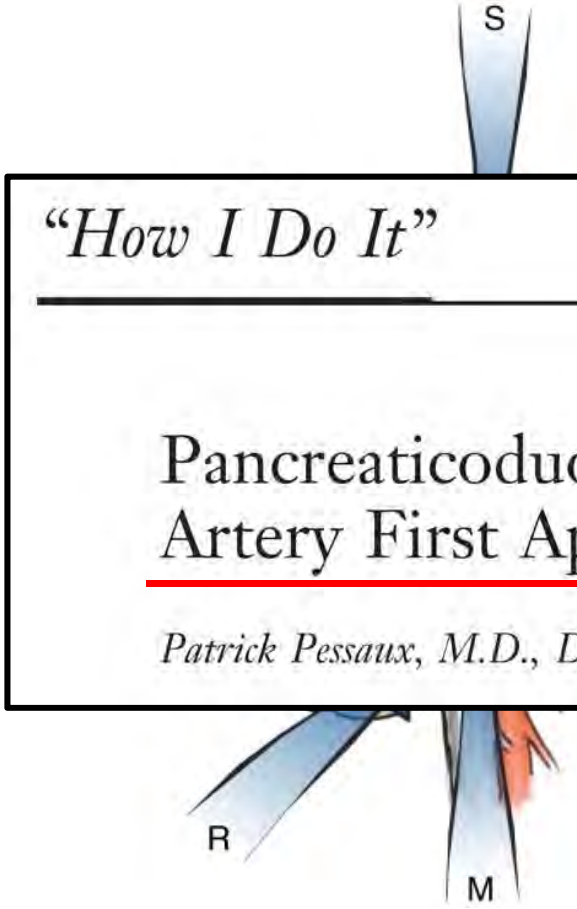

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Ohigashi et al. ***Hepatogastroenterology 2004***
Pessaux et al. ***J Gastrointest Surg 2006***

"How I Do It"

Pancreaticoduodenectomy: Superior Mesenteric Artery First Approach

Patrick Pessaux, M.D., Deepak Varma, M.D., Jean-Pierre Arnaud, M.D.

Kurosaki et al. ***JOP 2011***

(5) Mesenteric approach
Nakao et al. ***Hepatogastroenterology 1993***
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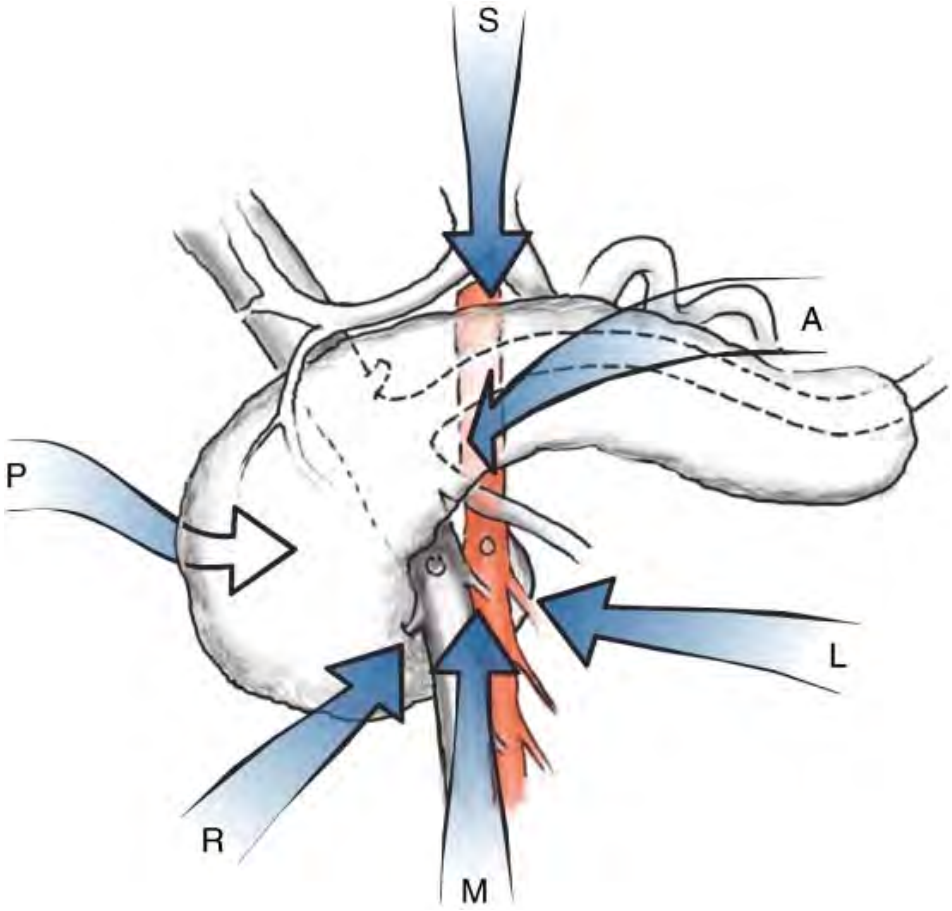

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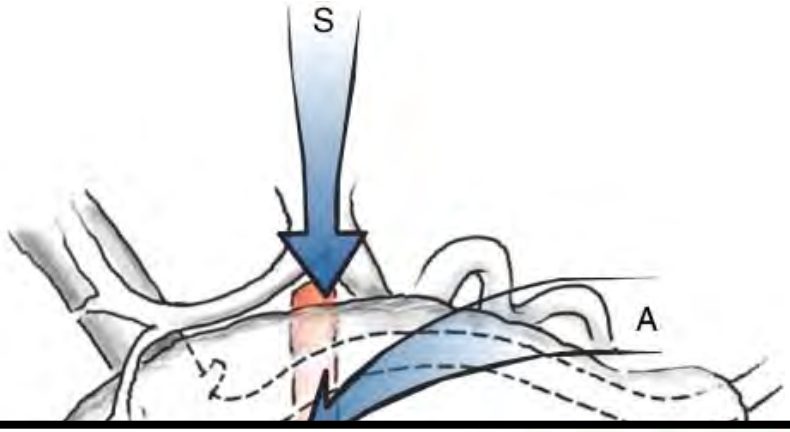

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(2) Medical unicinate approach
Shukla et al. *Hepatogastroenterology 2007*

(3) CLIP method

SURGEON AT WORK

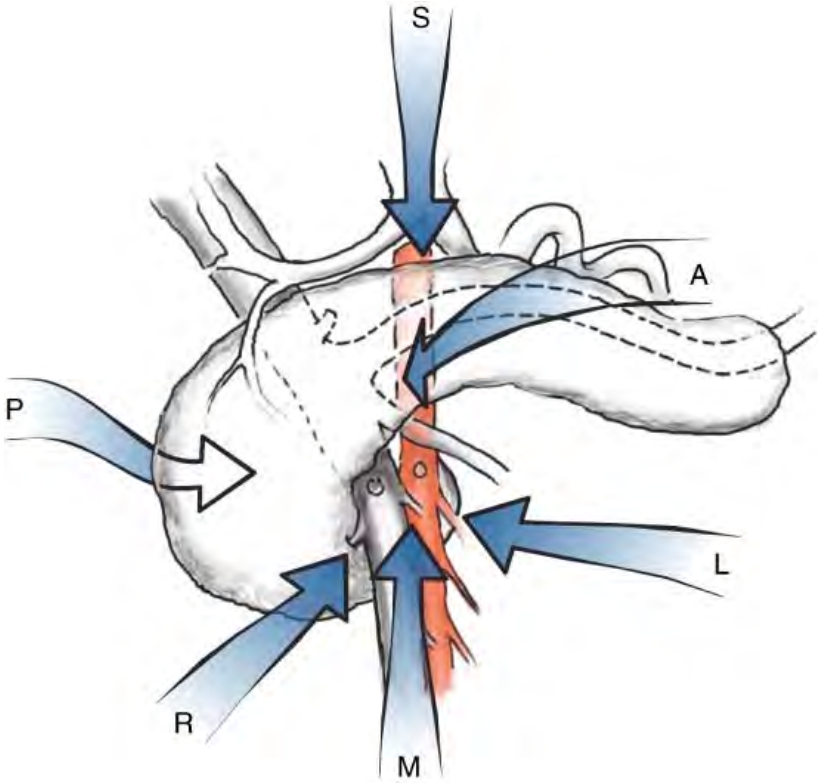
The "Artery First" Approach for Resection of Pancreatic Head Cancer

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

Weitz et al. *J Am Coll Surg 2010*

'Artery-first' approaches to pancreatoduodenecotmy.
Sanjay et al. *Br J Surg 2012;99:1027-1935*

Artery-First Approach in Whipple's Operation



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Hepatogastroenterology

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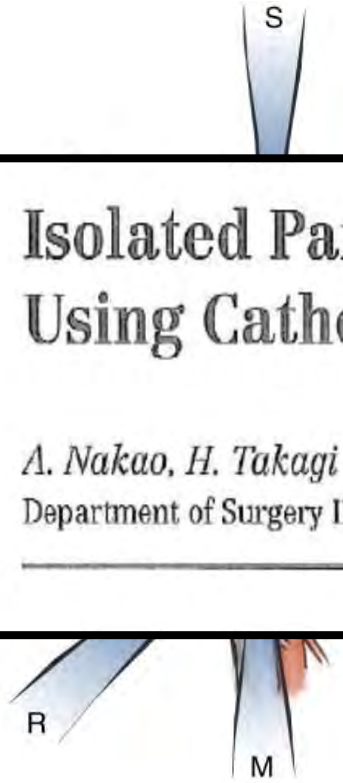


Isolated Pancreatectomy for Pancreatic Head Carcinoma Using Catheter Bypass of the Portal Vein

A. Nakao, H. Takagi
Department of Surgery II, Nagoya University School of Medicine, Nagoya, Japan

(5) Mesenteric approach

Nakao et al.

Hepatogastroenterology

1993

Weitz et al. *J Am Coll Surg 2010*

Concept of artery-first approach during PD for PDAC

Artery-first approach

PD starts from dissection of connective tissues around the SMA and division of the inferior pancreaticoduodenal artery (IPDA)

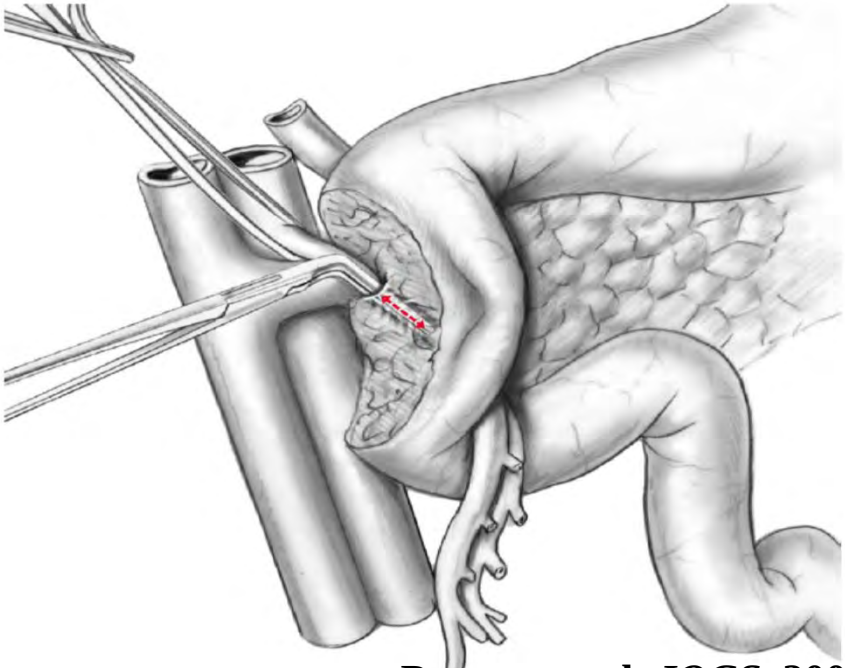
The aims of artery-first approach

- ✓ **Early determination of the resectability status for PDAC during PD**
- ✓ **Control of pancreatic head congestion by early division of the IPDA**
  → **Decrease of intraoperative blood loss volume**
- ✓ **Complete dissection around the SMA**
  → **Increase of the R0 rate**

Posterior approach as artery-first approach

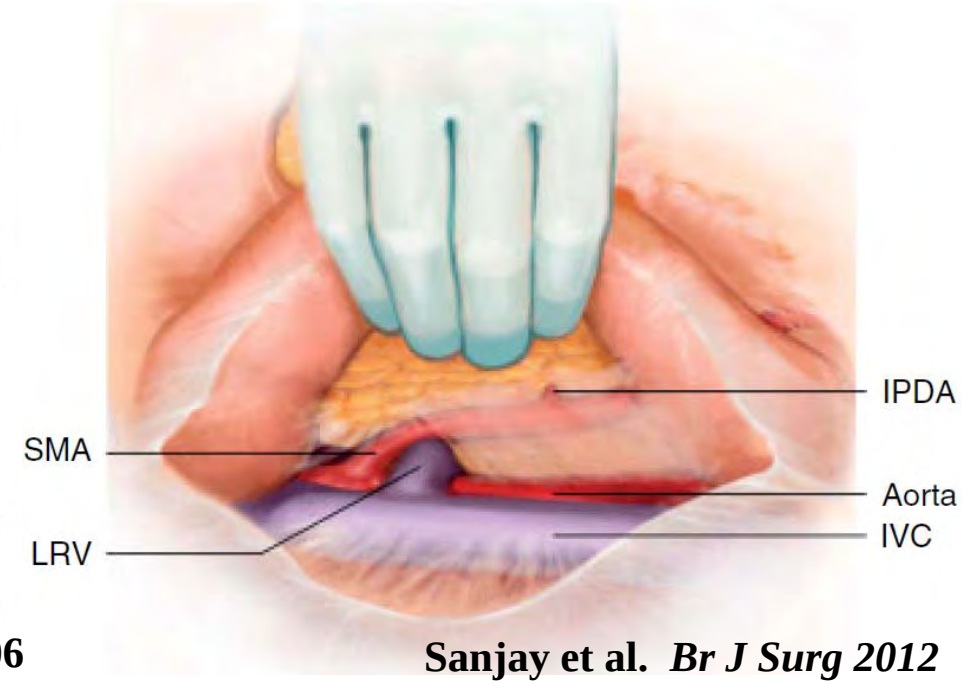
Posterior approach: exposing the origin of superior mesenteric artery (SMA) in front of the left renal vein after kocherization.

	author	publish	year	number	page
1	Ohigashi et al.	*Hepatogastroenterology*	2004	51	4-5
2	Pessaux et al.	*J Gastrointest Surg*	2006	10	921-926
3	Traian et al.	*Langenbecks Arch Surg*	2010	395	677-684



Pessaux et al. *JOGS*, 2006

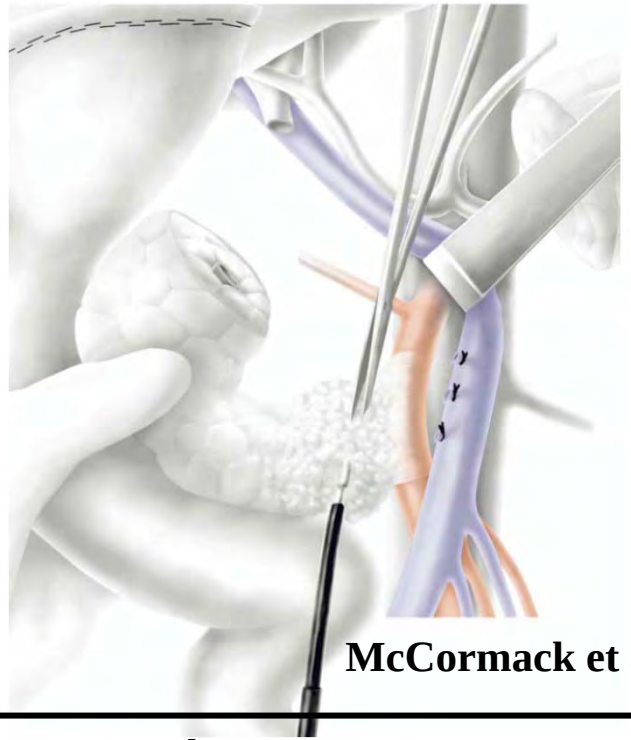
Fig. 1. Origin of superior mesenteric artery is taped and dissected distally along the vessel.



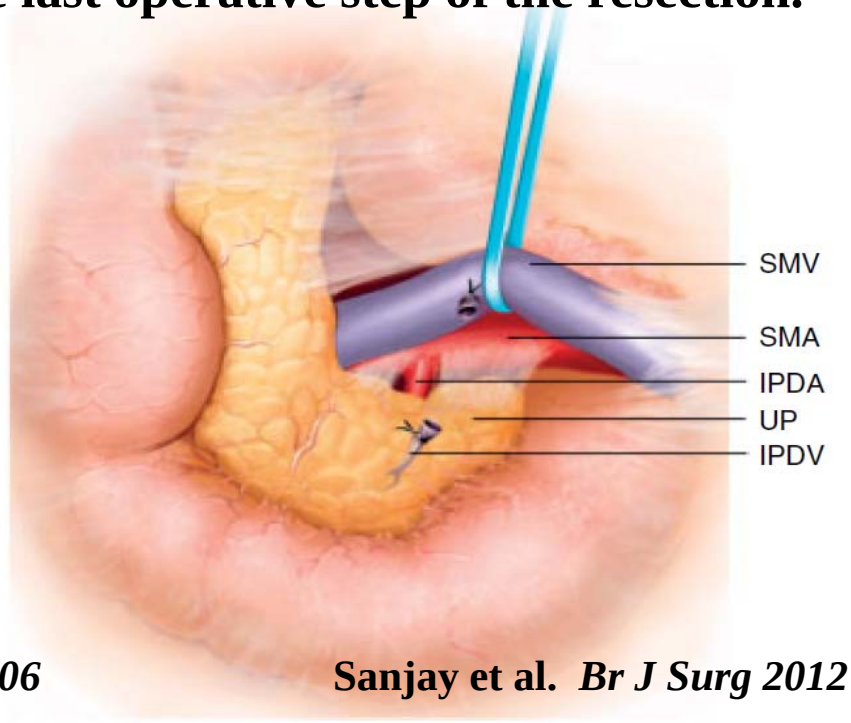
Sanjay et al. *Br J Surg 2012*

Medial uncinate approach as artery-first approach

Medial uncinate approach: Retrograde resection of the pancreatic head is performed starting with the uncinate process after division of the first jejunal loop and transection of the pancreas as the last operative step of the resection.



McCormack et al. *JACS 2006*



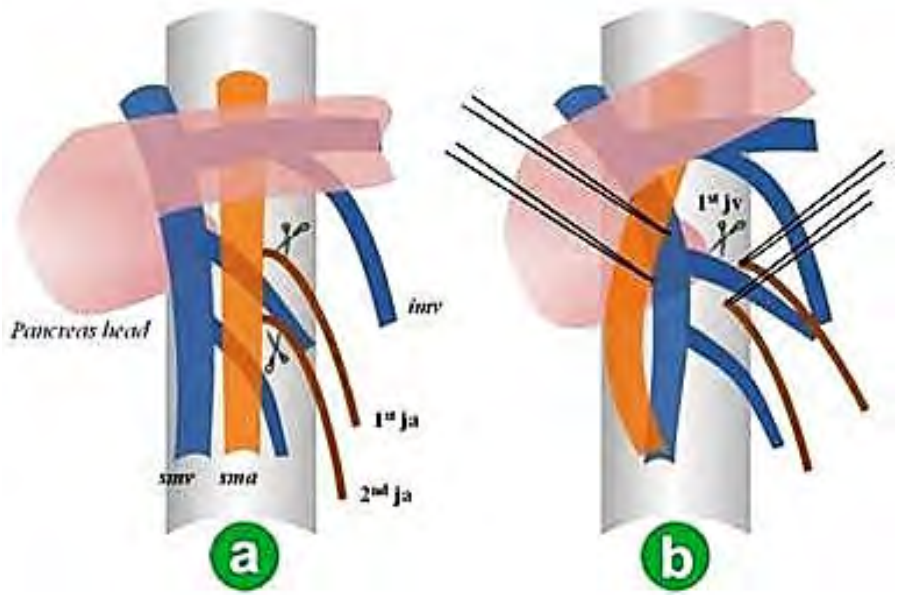
Sanjay et al. *Br J Surg 2012*

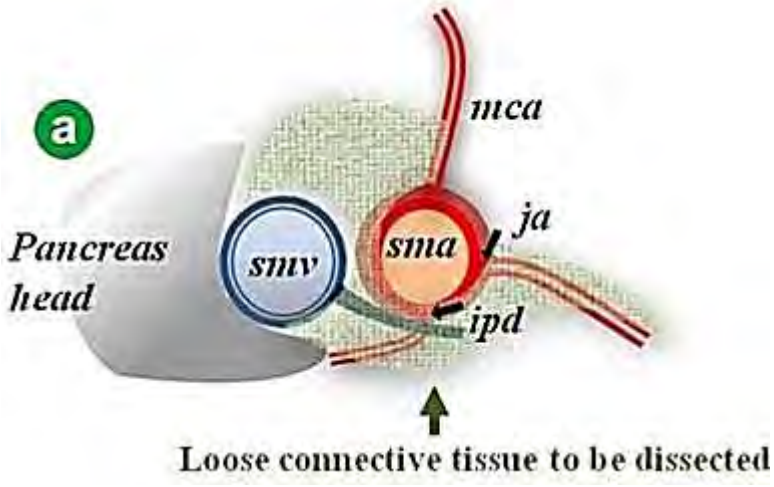
	author	publish	year	number	page
1	**Shukla et al.**	***Hepatogastroenterology***	**2007**	**54**	**1728-1730**
2	**Hackert et al.**	***Langenbecks Arch Surg***	**2010**	**395**	**1161-1164**
3	**Shrikhande et al.**	***Langenbecks Arch Surg***	**2011**	**396**	**1205-1212**

Left posterior approach as artery-first approach

Left posterior approach: exposing J1 and J2 arteries at their origin on the SMA in the transverse mesocolon. As next step, division of the IPDA arising from the posterior surface of the SMA.

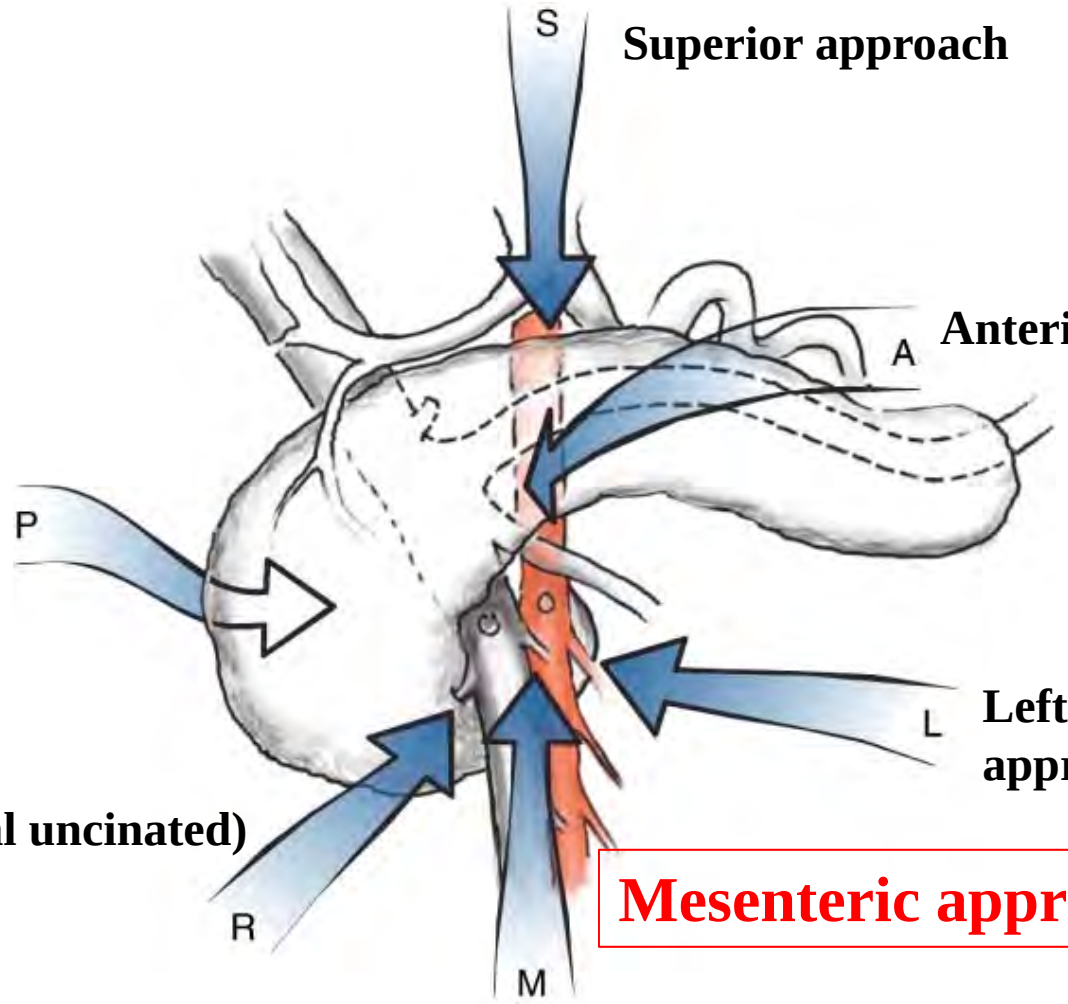
	author	publish	year	number	page
1	**Horiguchi et al.**	***JHBPS***	**2007**	**14**	**575-578**
2	**Kurosaki et al.**	***JOP***	**2011**	**12**	**220-229**





Kurosaki et al. *JOP* 2011; 12: 220-229

The methods of artery-first approaches



Superior approach

Anterior approach

Posterior approach

Left posterior approach

Right (Medial uncinated) approach

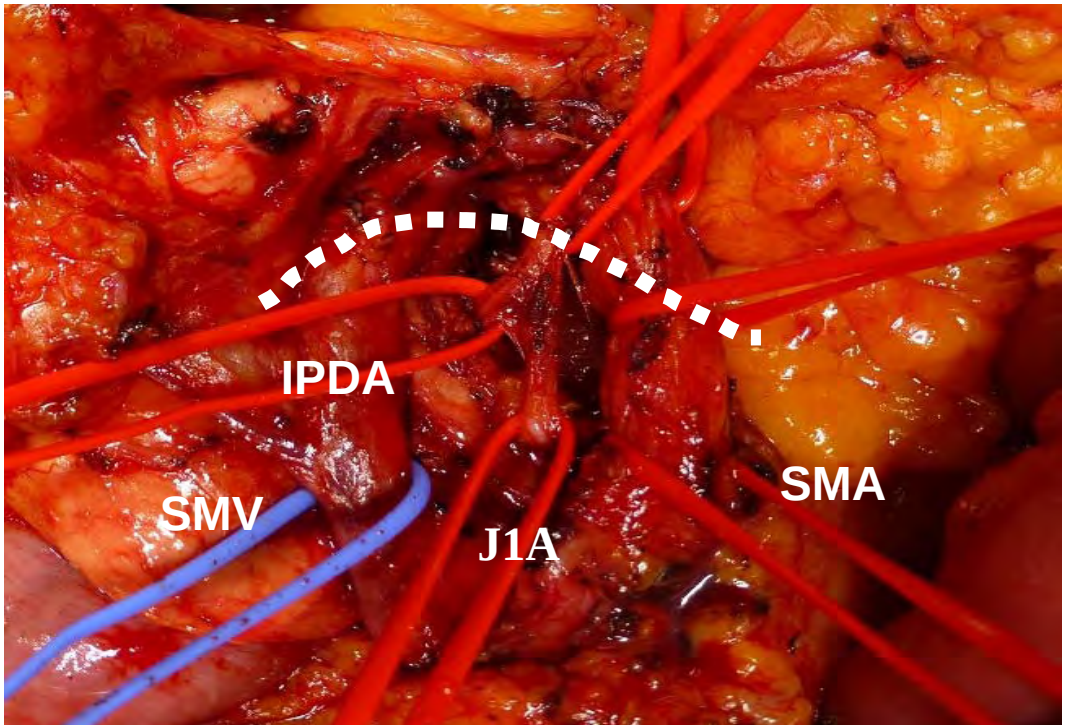
Mesenteric approach

***Br J Surg*, 2012**

Mesenteric approach as artery-first approach

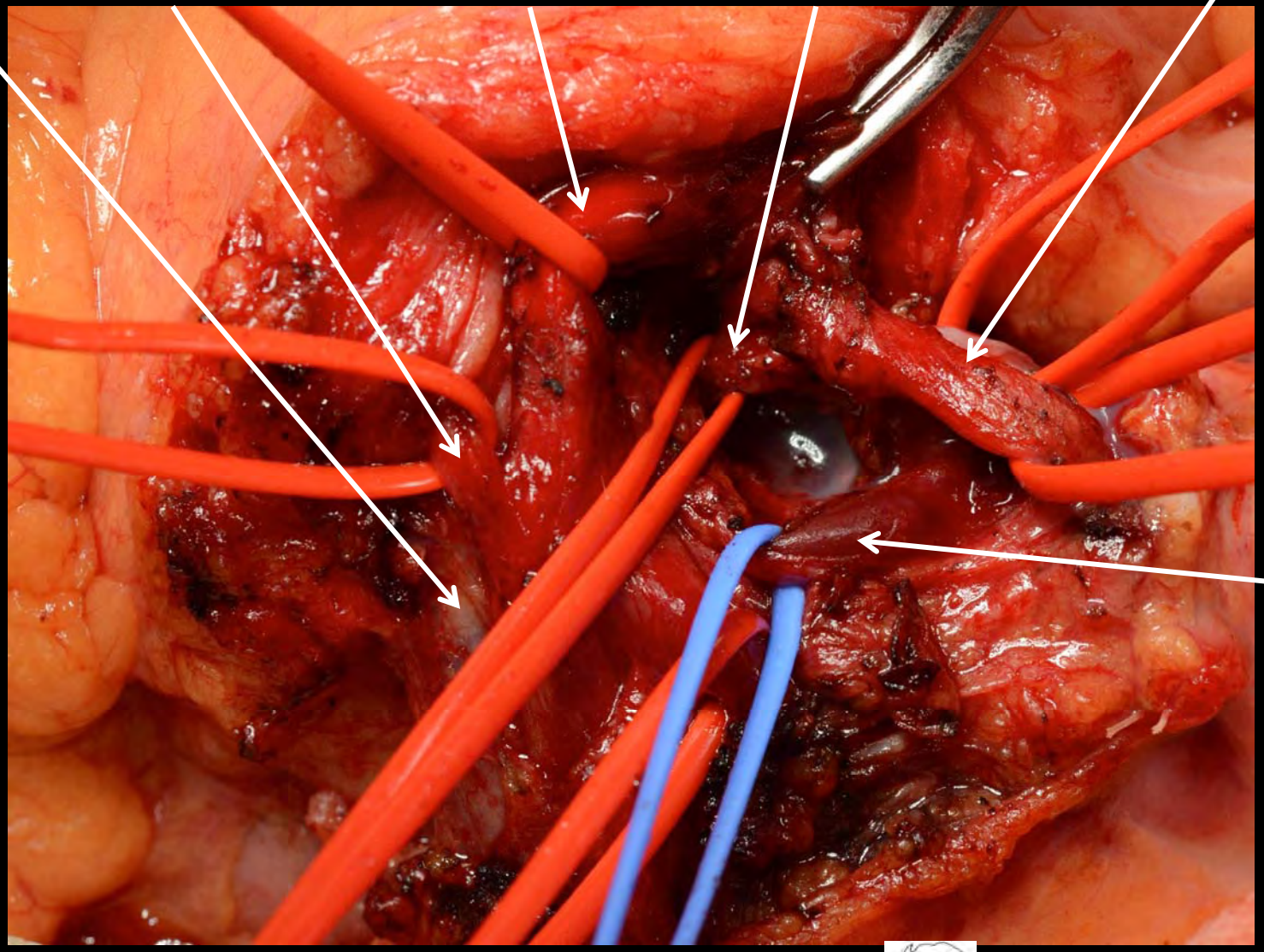
First, exposing the SMA-SMV at the base of the transverse mesocolon

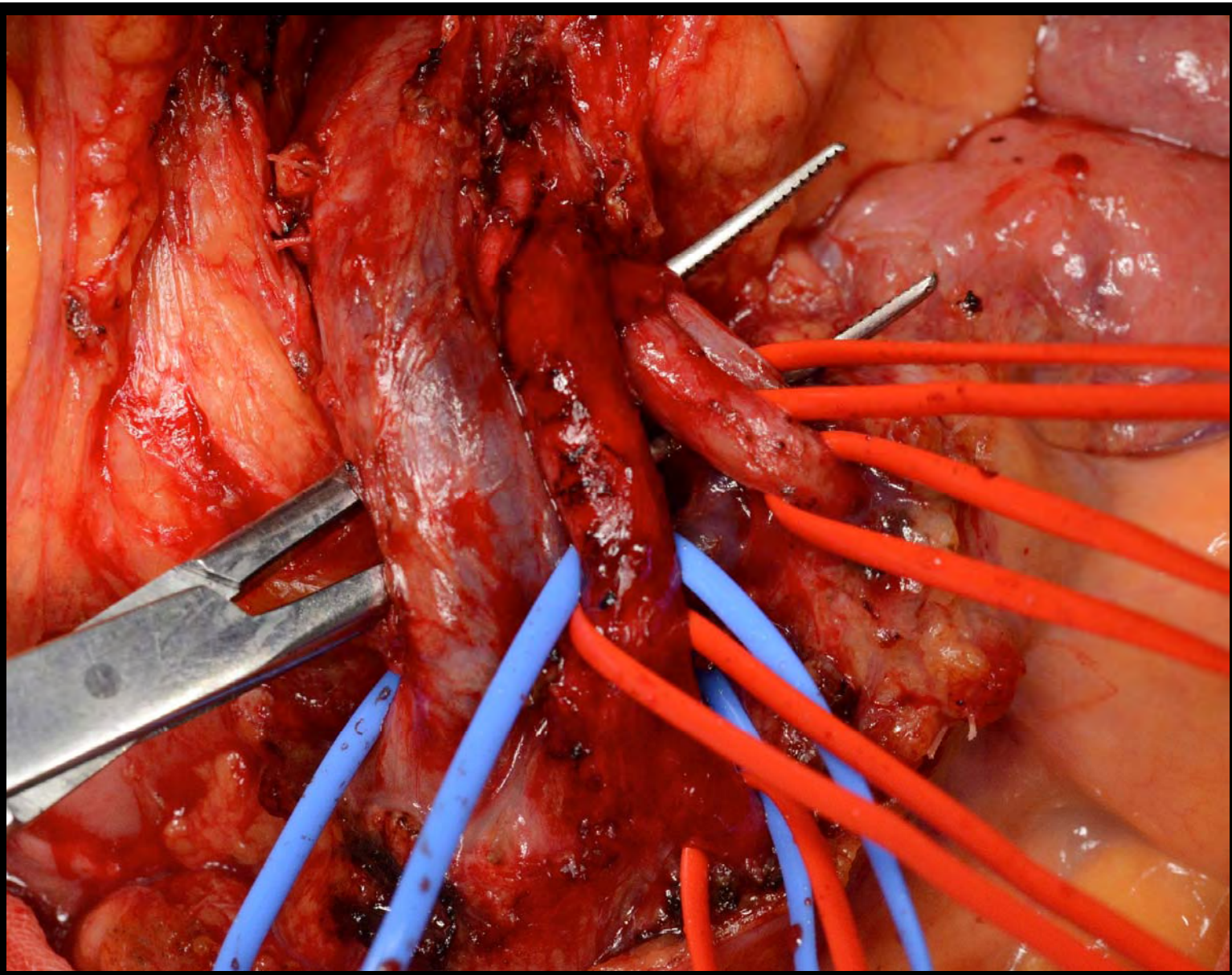
	author	publish	year	number	page
1	Nakao et al.	*Hepatogastroenterology*	1993	40	426-429
2	Weitz et al.	*J Am Coll Surg*	2010	210	e1-e4
3	Nakao et al.	*Dig Surg*	2016	33	308-13
4	Hirono et al.	*Ann Gastroenterol Surg*	2017	*in press*	



Area of incision of the peritoneum at duodenojejunal flexure (dotted line).

Mesenteric approach



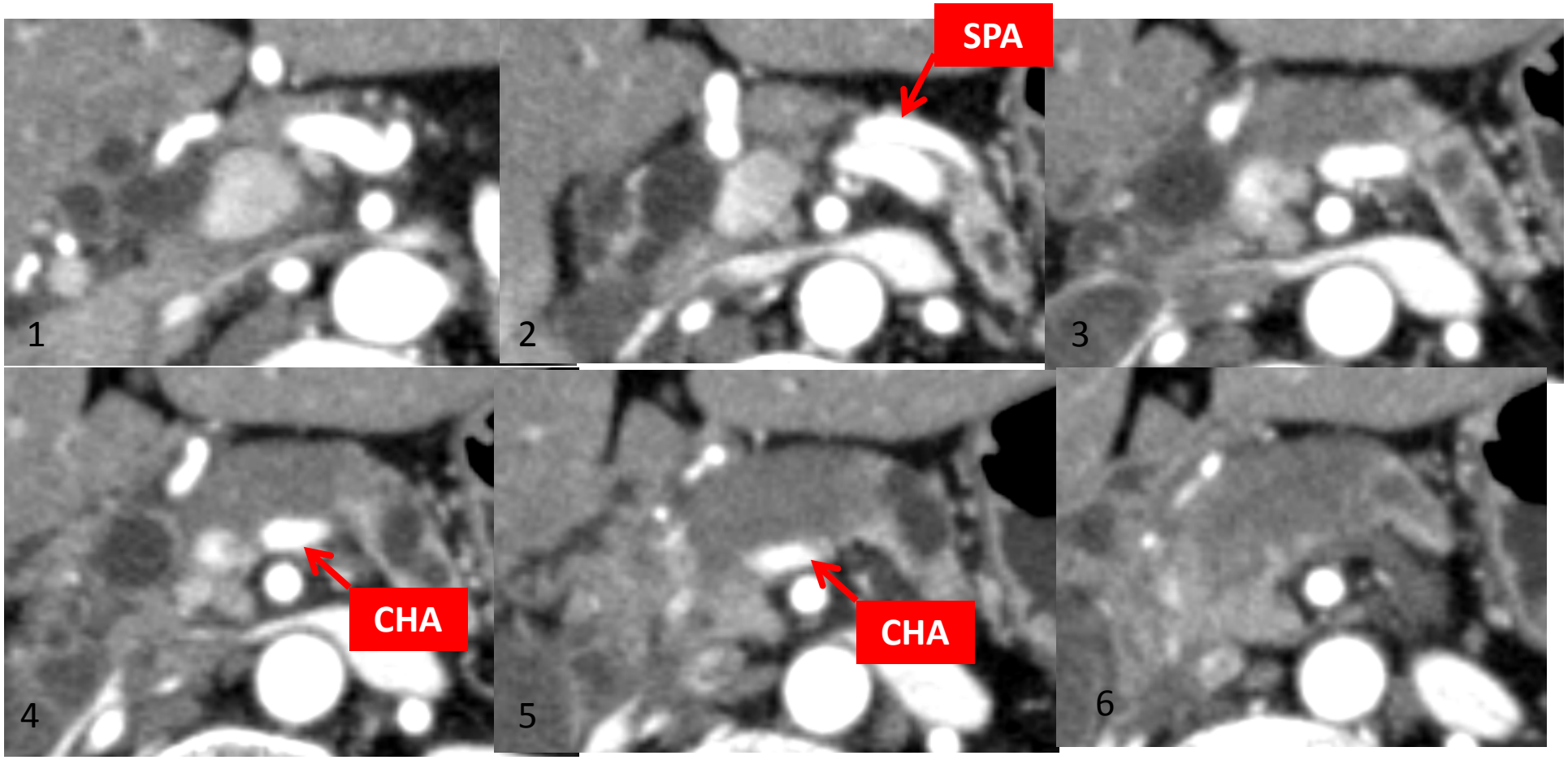


Mesentric approach can facilitate dissection of posterior soft tissues of SMA and SMV, so called mesoduodenum and mesopancreas, at the first step of Whipple's operation.

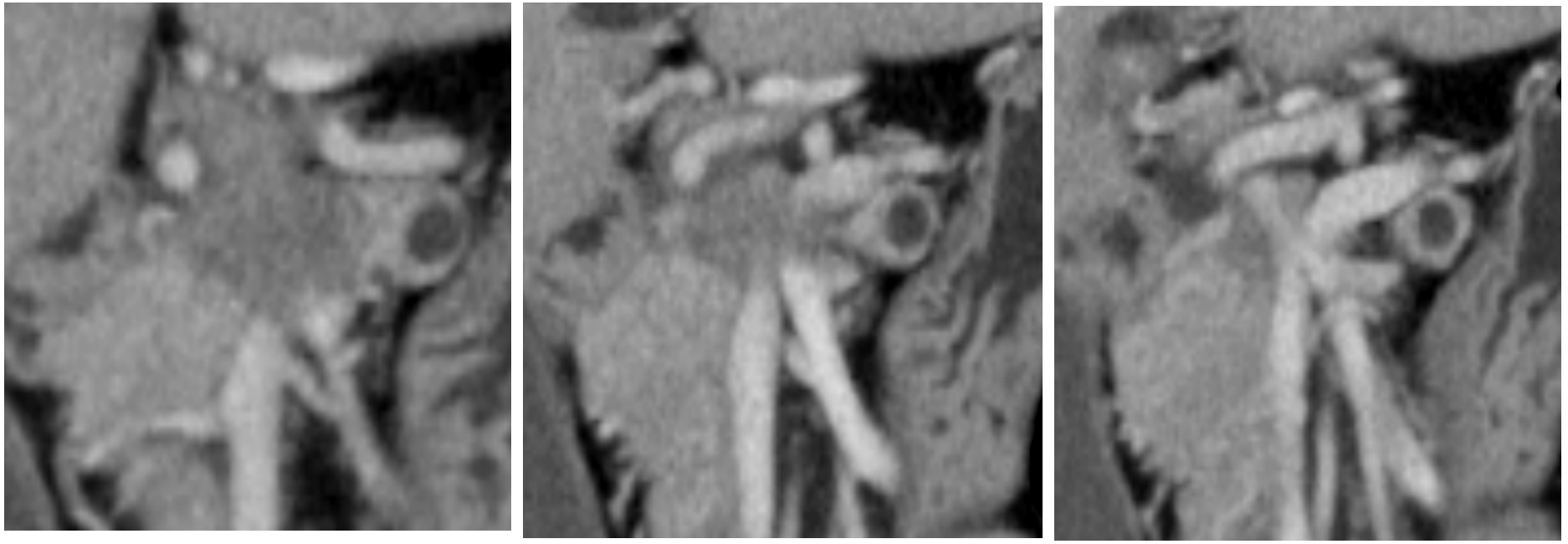
Pancreaticoduodenectomy with CHA resection (PD-CHAR)

Patient;	50-y, female
Diagnosis;	Pancreas Neck ～ Body Cancer with common hepatic artery and portal vein invasion
NAC;	GEM + nab-paclitaxel 2 courses → NAC-GA trial (NCT02926183, UMIN000024154)
Effects of NAC;	Tumor diameter 30mm → 30mm (SD) PET-CT SUVmax3.38 → 2.07 CA19-9 88.9 → 66.0 U/ml, CEA 1.3 → 1.7 ng/ml
Operation;	PD-CHAR
Operation time;	8hr 27min, Bleeding 585 ml, No blood tranfusion
Pathology;	CH(+) DU(-) S(+) RP(+) PV(+) Ach(+) Plcha(+) OO(-) n(+:8a) T4（PV,A） N1 M0 StageⅣa

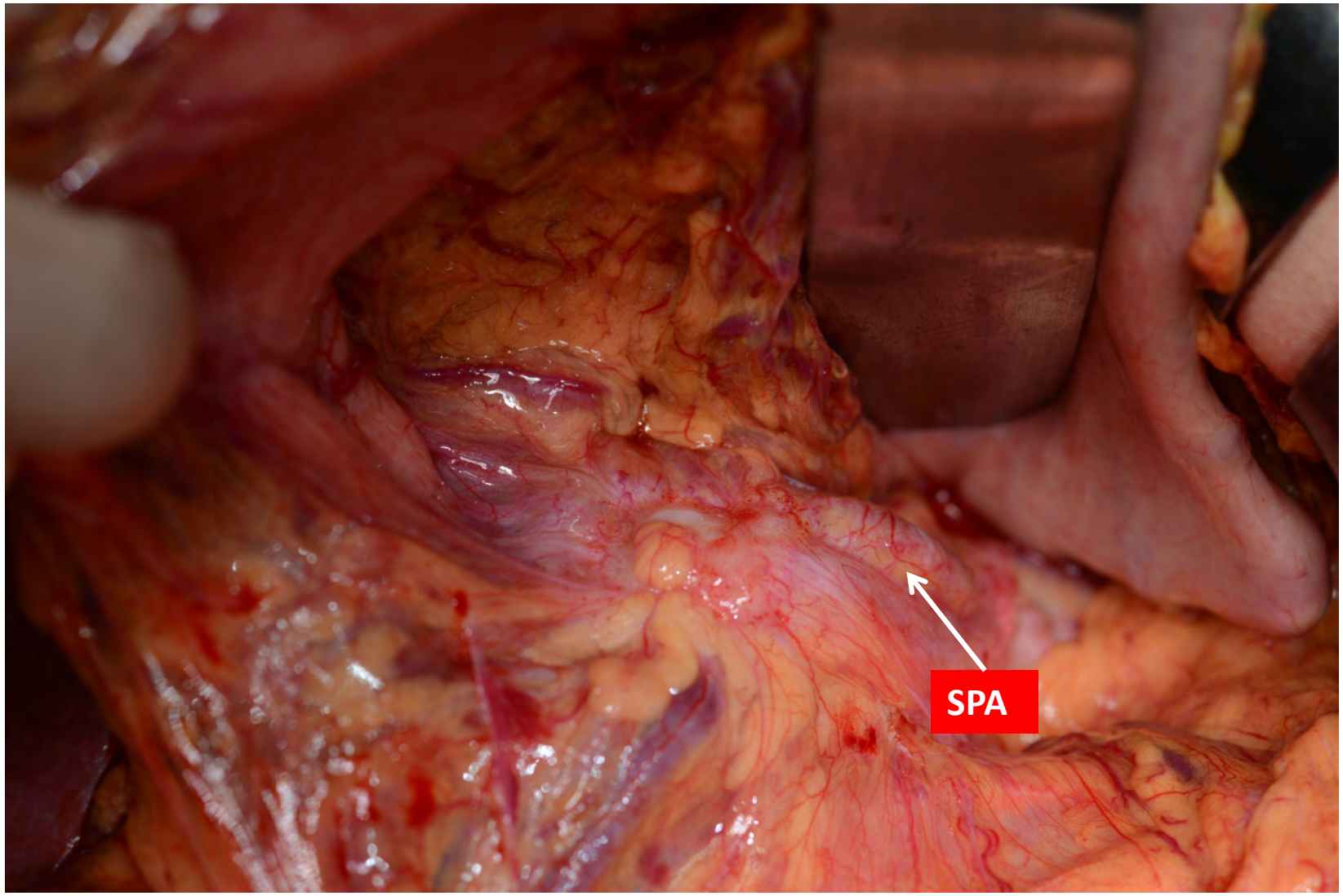
Preoperative MD-CT findings; CHA invasion



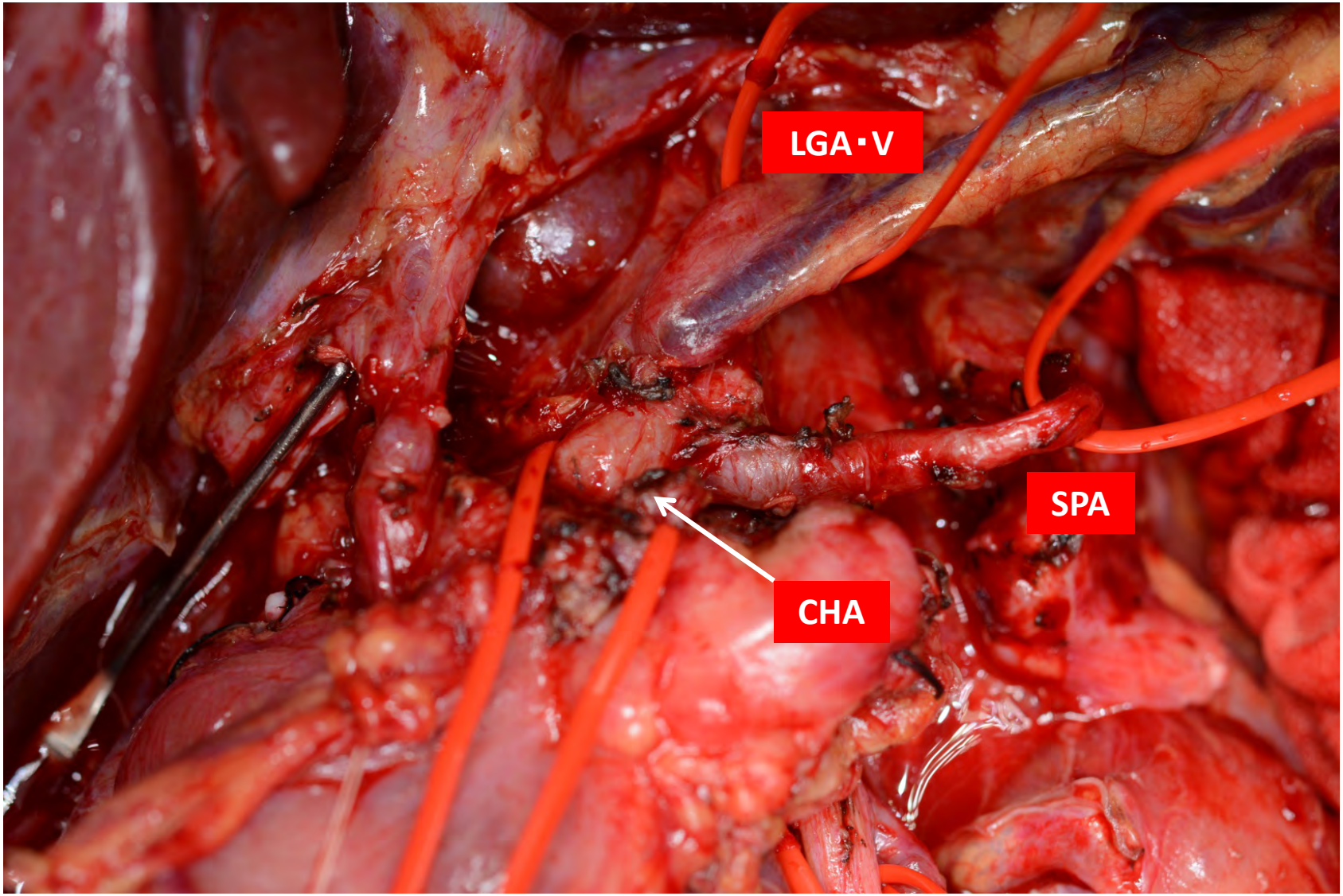
Preoperative MD-CT findings; SMV・Portal vein invasion



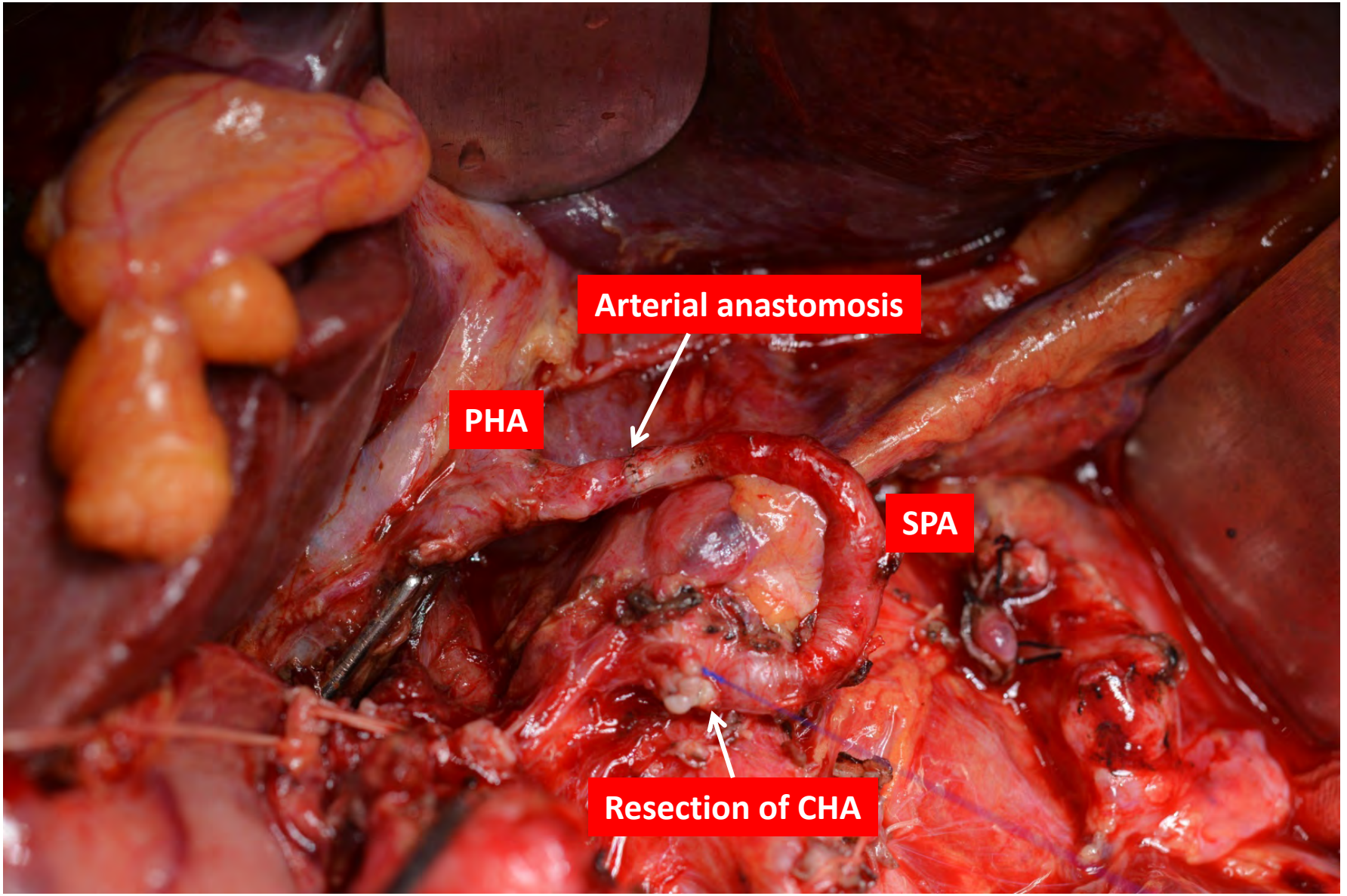
T4 pancreatic cancer in Neck and Body



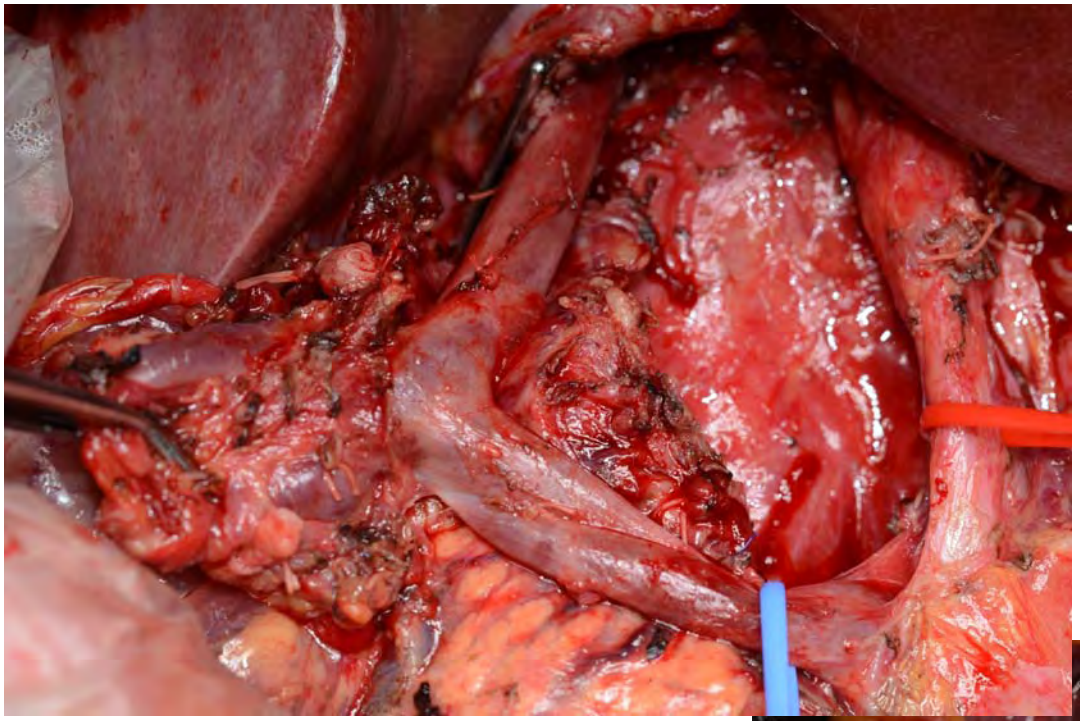
Splenic artery was removed 6cm
Taped the root of CHA

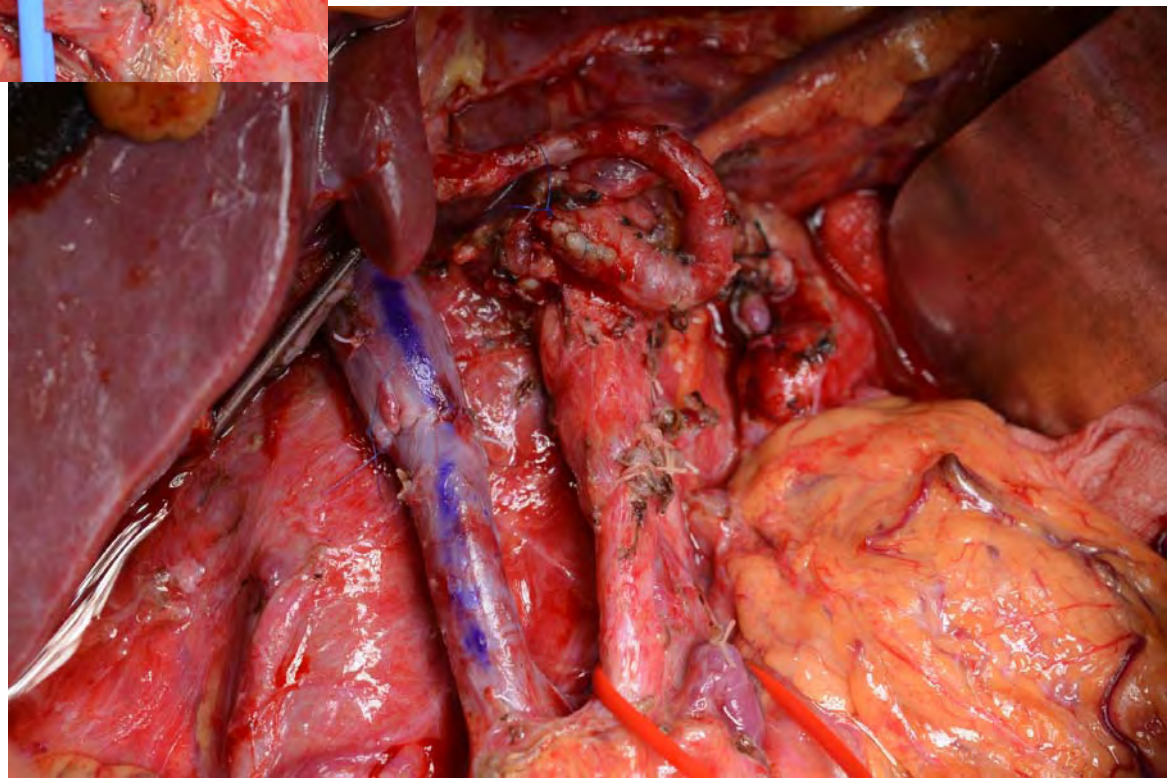


Splenic artery and PHA anastomosis

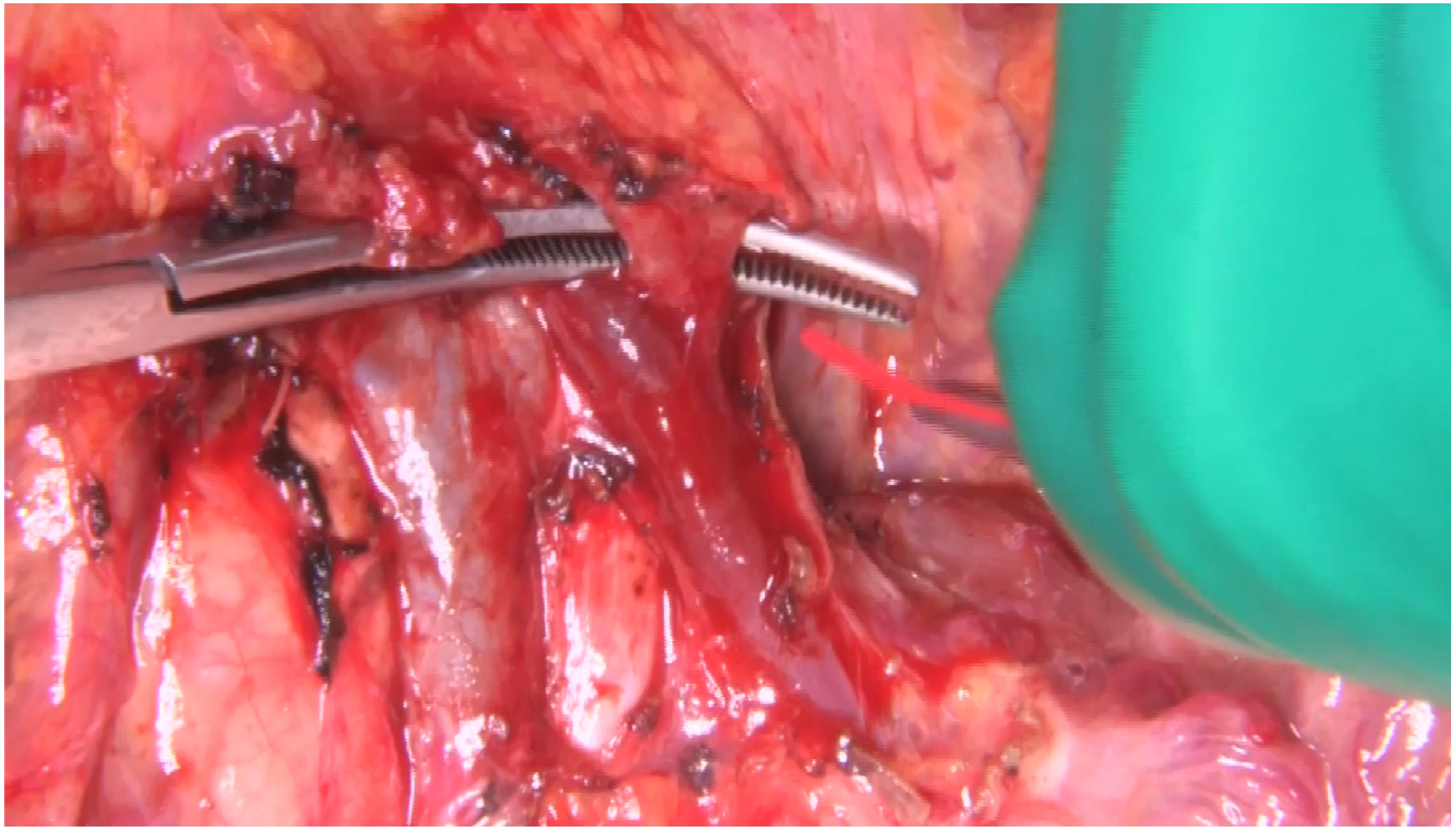


Reconstruction of portal vein





Pancreaticoduodenectomy with CHA resection



Operation; PD-CHAR, Arterial anastomosis under microscope
Op time; 8hr 27min
Bleeding; 585 ml

Clinical benefits of mesenteric approach

We evaluated the clinical benefits of mesenteric approach, especially survival benefits during pancreaticoduodenectomy (PD) for pancreatic ductal adenocarcinoma (PDAC) patients.

This is a first report regarding the long-term survival * of Mesenteric approach.

* Hirono S, Yamaue H, et al. Mesenteric approach during pancreaticoduodenectomy for pancreatic ductal adenocarcinoma.
Ann Gastroenterol Surg 2017, in press

Patients and methods

【Study design】 Retrospective cohort study

【Patients】 237 PD patients 2000 to 2015 at WMUH

- **Conventional approach group: 165 patients (2000～2011)**
- **Mesenteric approach group: 72 patients (2011～2015)**

【Surgical procedure】

Conventional approach：During resection procedure, after Kocher's maneuver at first step, regional lymph node dissection and resection of stomach, bile duct, and pancreas, and then, dissection of connective tissue around the SMA, including diving inferior pancreaticoduodenal artery (IPDA) at the final step.

Mesenteric approach: Dissection connected tissue around the SMA, including diving IPDA was performed at the first step.

Statistical analysis

Matched-pairs analysis

: propensity score approach using a multiple logistic regression model with 4 covariates: age, sex, resectability status, and neoadjuvant therapy

- **Conventional approach: 58 patients**
- **Mesenteric approach: 58 patients**

(Resectable PDAC: 58 patients, BR PDAC: 58 patients)

Backgrounds: mesenteric vs. conventional

	Resectable PDAC		BR PDAC	
	Mesenteric (n=28)	Convention (n=30)	Mesenteric (n=30)	Convention (n=28)
Age, median	67(42-82)	69 (43-87)	70.5 (48-78)	70 (49-79)
Sex, male	18 (64%)	22 (73%)	15 (50%)	17 (61%)
Serum CA19-9 U/ml	135	140	525	349
Resectability（NCCN)				
Resectable	28 (100%)	30 (100%)	0	0
BR	0	0	30 (100%)	28 (100%)
BR-AV			10 (33%)	9 (32%)
BR-A			8 (27%)	9 (32%)
BR-V			12 (40%)	10 (36%)
Tumor size, mm	23.6	22.0	28.7	27.3
Neoadjuvant therapy	0	0	9 (30%)	9 (32%)
Follow-up (mo)	22.5	27.6	11.7	12.0

Surgical outcome for resectable PDAC
Mesenteric vs. conventional approach

	Mesenteric approach (n=28)	Conventional approach (n=30)	*P*
PV resection, n (%)	11 (39%)	6 (20%)	0.107
Operative time, min, median (range)	416 (314-535)	371 (254-520)	0.007
Blood loss volume, ml, median (range)	313 (40-1500)	502 (60-2230)	0.023
Transfusion, n (%)	1 (4%)	6 (20%)	0.055
Mobility, n (%)	5 (18%)	3 (10%)	0.386
Mortality, n (%)	0	1 (3%)	0.330
Hospital stay, day, median (range)	14 (10-36)	21 (11-65)	0.007

Surgical outcome for BR PDAC
Mesenteric vs. conventional approach

	Mesenteric approach (n=30)	Conventional approach (n=28)	*P*
PV resection, n (%)	24 (80%)	21 (75%)	0.648
Operative time, min, median (range)	459 (374-620)	452 (322-570)	0.210
Blood loss volume, ml, median (range)	507 (115-2225)	920 (115-3610)	0.003
Transfusion, n (%)	5 (17%)	13 (46%)	0.014
Mobility, n (%)	4 (13%)	5 (18%)	0.634
Mortality, n (%)	0	0	-
Hospital stay, day, median (range)	15 (9-59)	17.5 (10-42)	0.863

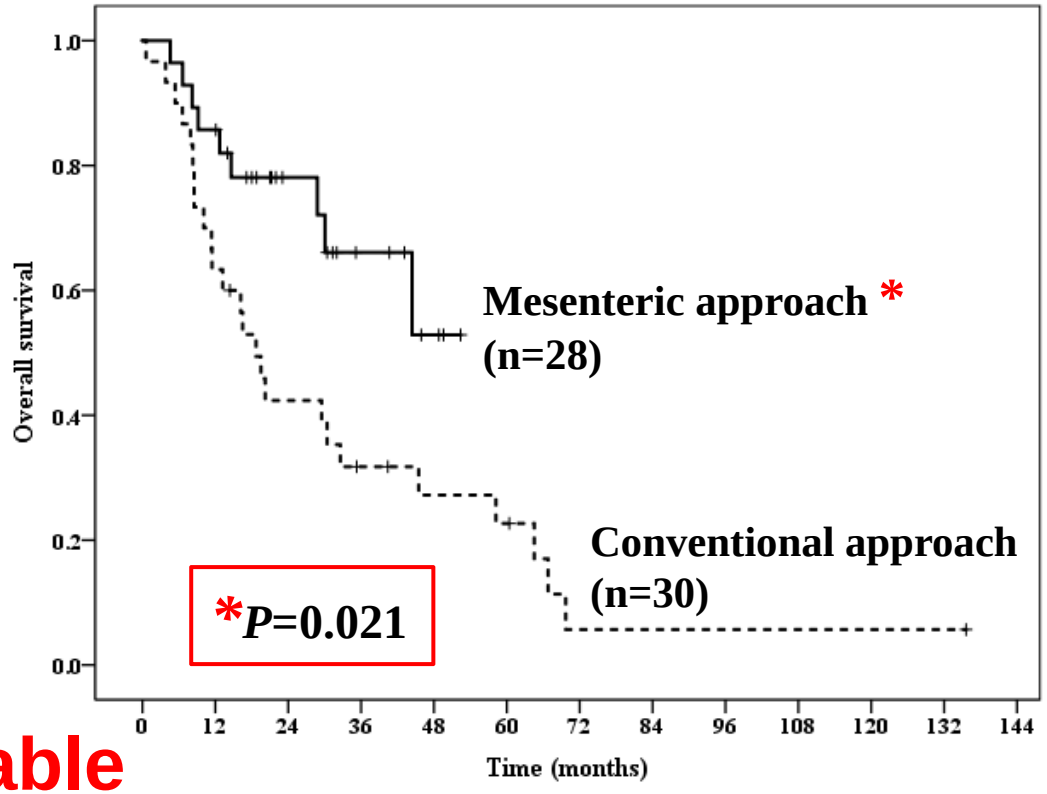
Pathological findings for resectable PDAC
Mesenteric vs. conventional approach

	Mesenteric approach (n=28)	Conventional approach (n=30)	*P*
Number of metastatic lymph nodes			0.229
0	7 (25%)	14 (47%)	
1-3	16 (57%)	12 (40%)	
≧4	5 (18%)	4 (13%)	
Number of harvested lymph nodes, n, median (range)	23 (11-53)	23.5 (11-48)	0.919
R0 rate	28 (100%)	26 (87%)	0.045
Adjuvant therapy within 8 weeks after surgery, n (%)	19 (68%)	17 (57%)	0.380
Completion of planned postoperative adjuvant therapy	20 (71%)	16 (53%)	0.156

Pathological findings for BR PDAC
Mesenteric vs. conventional approach

	Mesenteric approach (n=30)	Conventional approach (n=28)	*P*
Number of metastatic lymph nodes			0.114
0	6 (20%)	6 (21%)	
1-3	9 (30%)	15 (54%)	
≧4	15 (50%)	7 (25%)	
Number of harvested lymph nodes, n, median (range)	26.5 (10-53)	26 (9-49)	0.668
R0 rate	24 (80%)	24 (86%)	0.565
Adjuvant therapy within 8 weeks after surgery, n (%)	18 (60%)	14 (50%)	0.444
Completion of planned postoperative adjuvant therapy	12 (40%)	10 (36%)	0.737

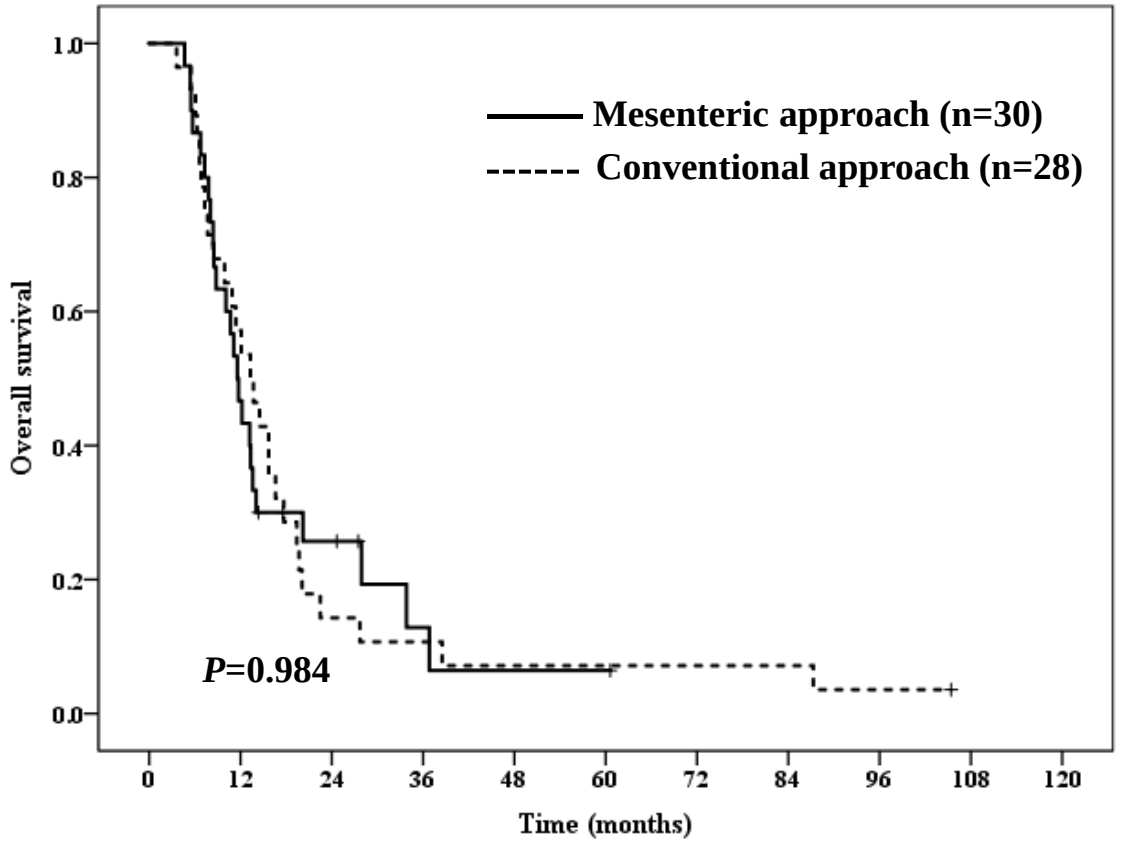
Overall survival for resectable PDAC
Mesenteric vs. conventional approach



Resectable

	MST
Mesenteric	(-)
Conventional	18.7 m

Overall survival for BR PDAC
Mesenteric vs. conventional approach



BR

	MST
Mesenteric approach	11.6 m
Conventional approach	13.3 m

Summary and conclusion

- ✓ **The blood loss volume and transfusion frequency were significantly lower in mesenteric approach group than in conventional approach group for both resectable PDAC and BR PDAC.**

- ✓ **The R0 rate was significantly higher in mesenteric approach group than in conventional approach group for resectable PDAC.**

→ **Mesenteric approach has survival benefits for resectable PC.**

- ✓ **There were no significant differences of R0 rate and overall survival between mesenteric and conventional approach groups for BR PDAC.**

→ **Mesenteric approach might not have oncological benefit for BR PDAC, and multidisciplinary treatments are essential to improve the survival for BR PDAC patients.**

Hirono S, Nakao A, Yamaue H, et al. *Ann Gastroenterol Surg* 2017

MAPLE-PD trial

Mesenteric APproach vs. conventionaL approach for pancrEatic cancer during PD

Multicenter Randomized Clinical Trial:

Primary endpoint: **Overall survival**

Secondary endpoints: **Operative time, Blood loss, Transfusion, Complications, R0 rate, Disease-free survival**

Accompanying research:

Circulating tumor DNA in portal vein blood during operation

We plan to start this RCT on August 2017!