Imperial College London

Metastatic disease…

Is Surgery The Answer?

Piers Boshier

Post Doctoral Fellow Francis Crick Institute
Honorary Clinical Lecture, Imperial College London
prb03@ic.ac.uk

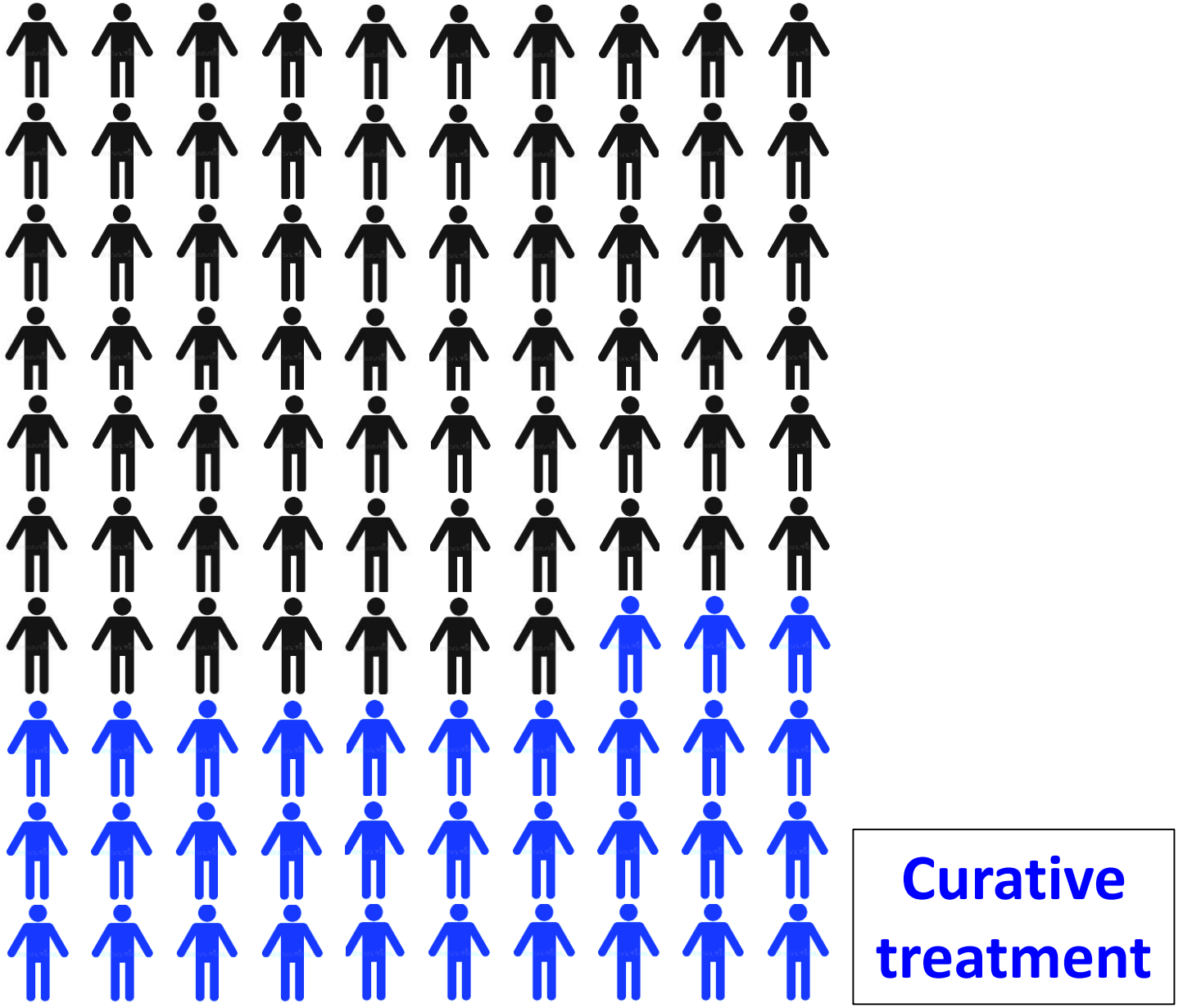
Disclosures

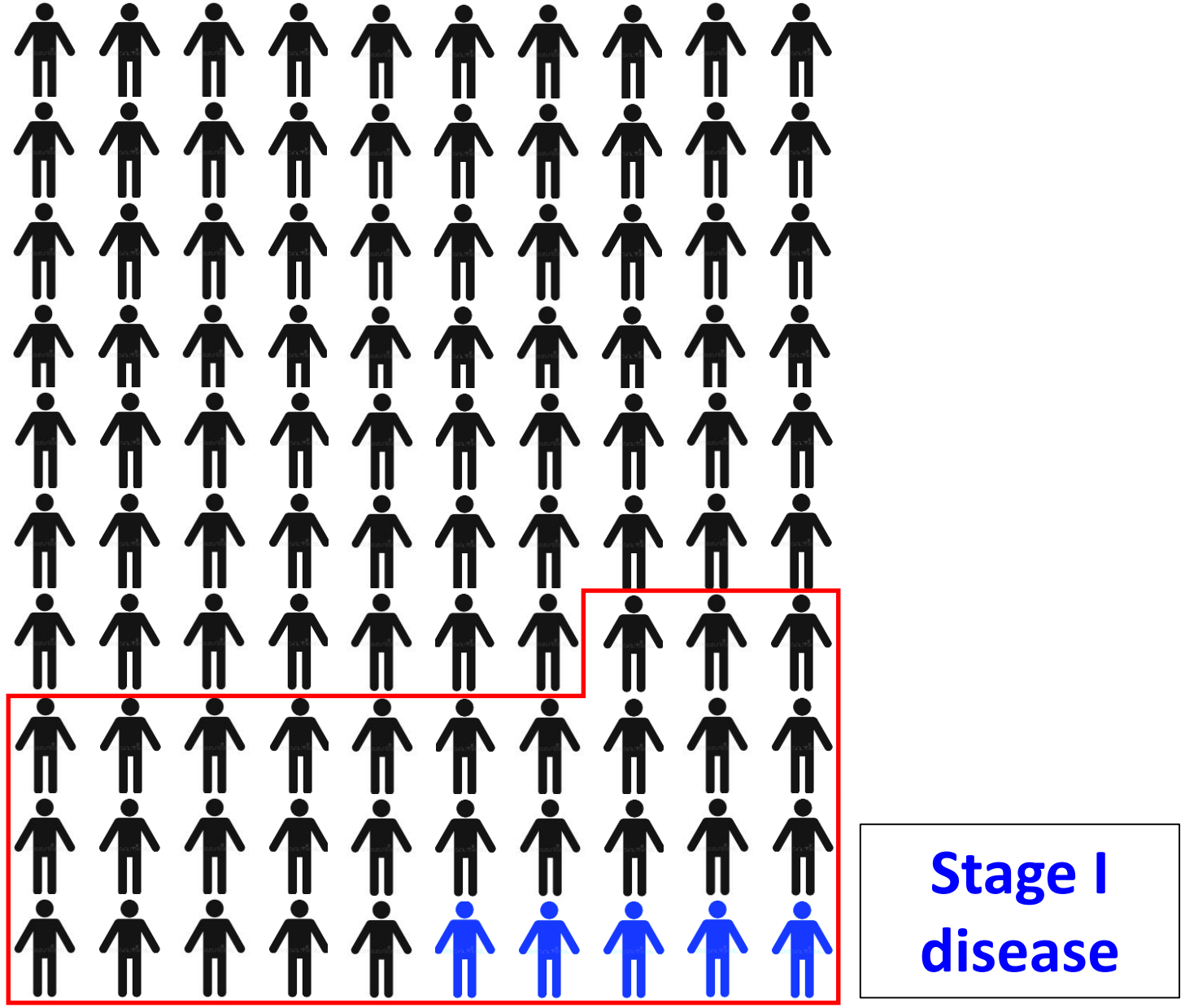
Gastroesophageal cancer

- **Gastric cancer**: **1.16** million people diagnosed and **0.83** million deaths annually
- **Oesophageal cancer**: **0.6** million people diagnosed and **0.55** million deaths annually

- Poor survival largely reflects **delayed diagnosis**

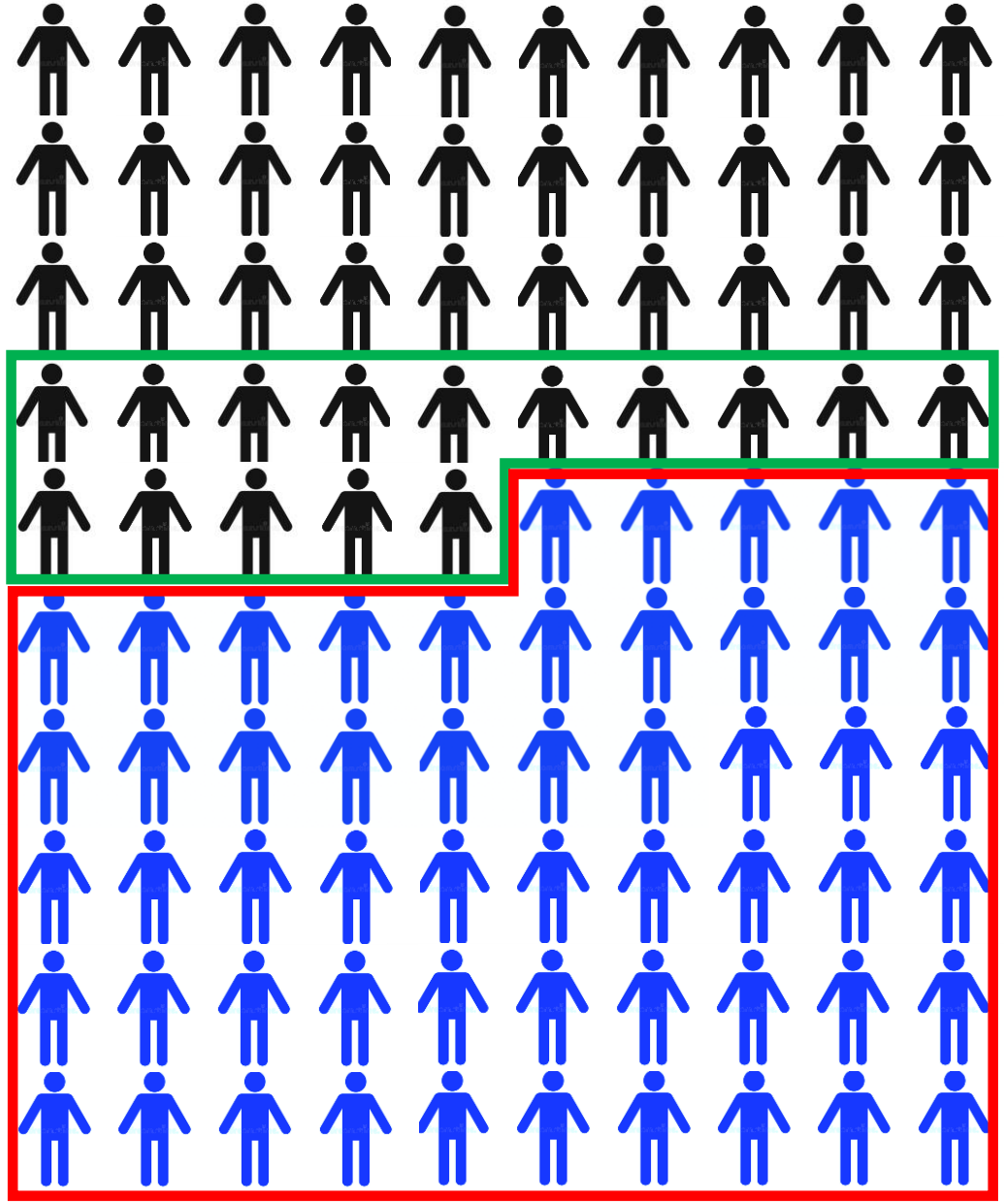
- In many patients disease has spread beyond the standard field of surgical resection


Curative
treatment


Stage I
disease

Earlier diagnosis
Therapeutic advancement

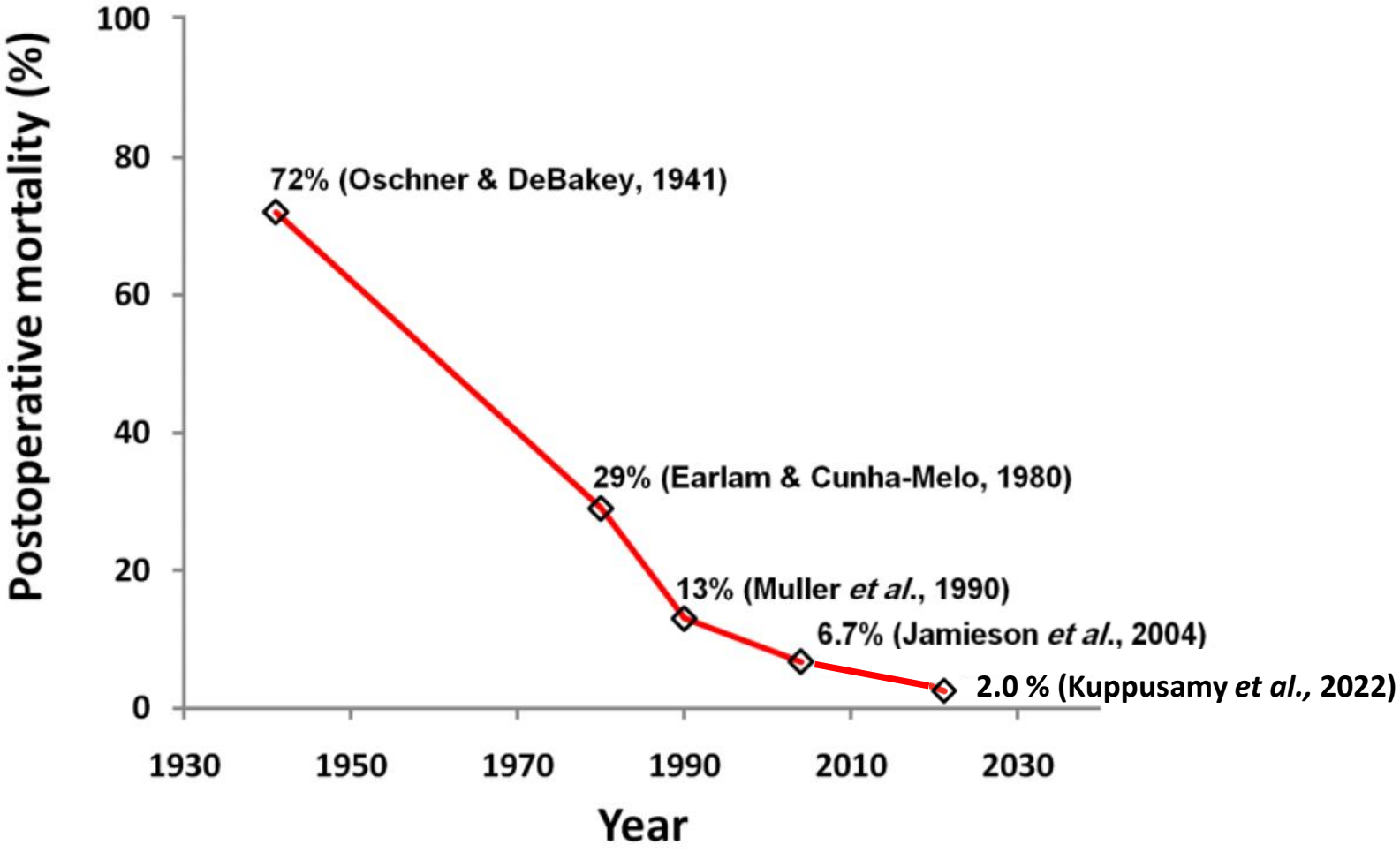
More radical resection
Therapeutic advancement



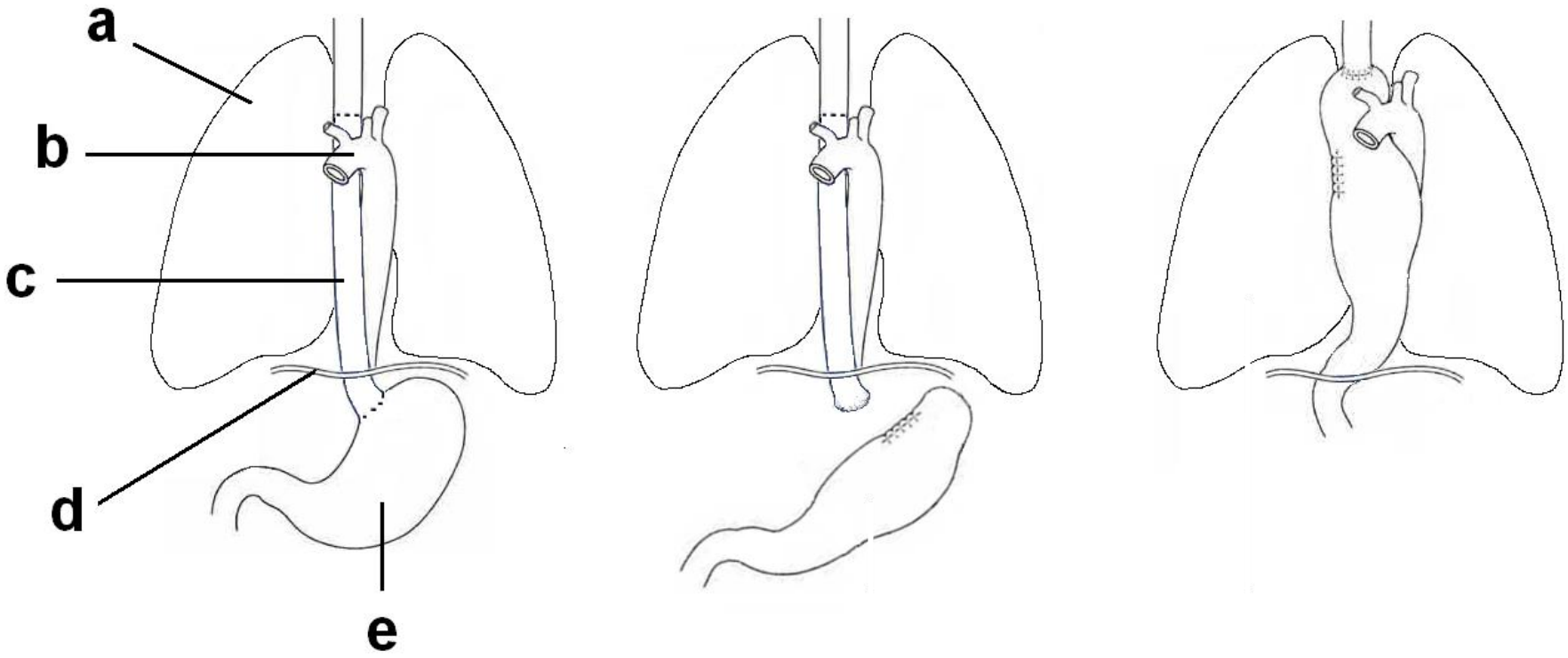
Is Surgery The Answer?

1881

1913

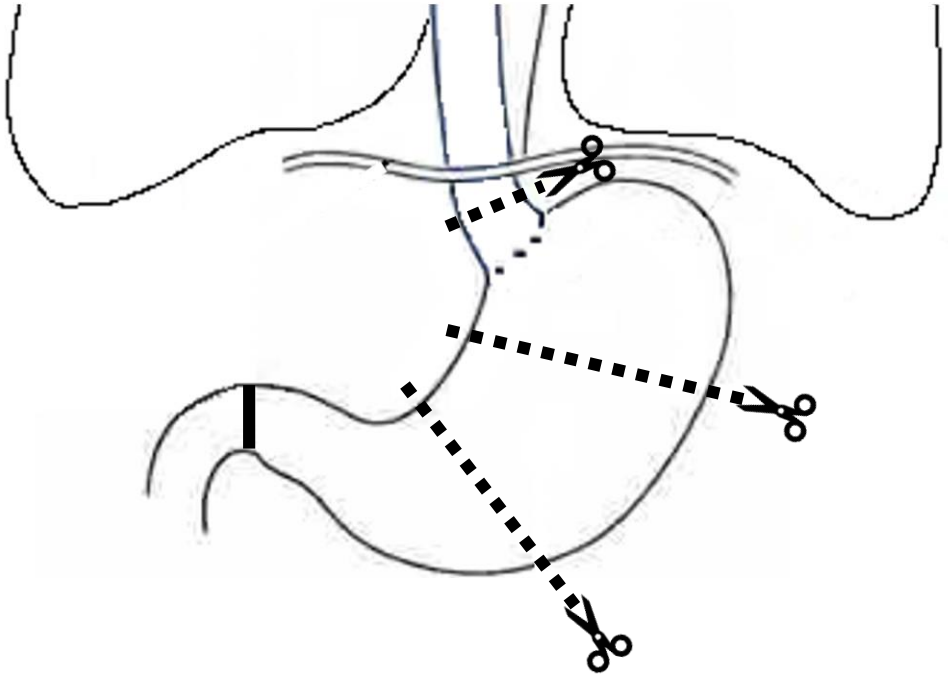

Postoperative mortality (%)
100
80
60
40
20
0
1930
1950
1970
1990
2010
2030
Year
72% (Oschner & DeBakey, 1941)
29% (Earlam & Cunha-Melo, 1980)
13% (Muller *et al.*, 1990)
6.7% (Jamieson *et al.*, 2004)
2.0 % (Kuppusamy *et al.*, 2022)

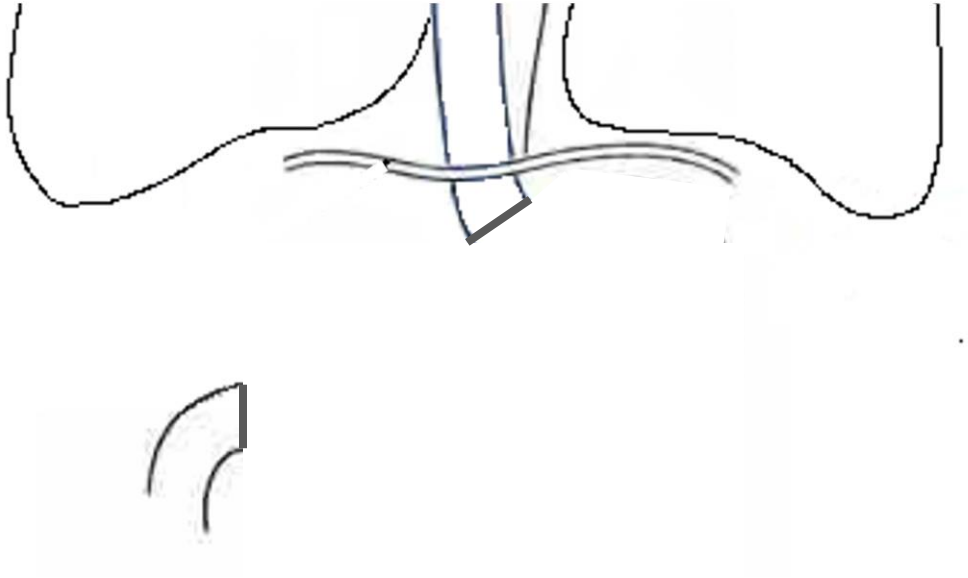
Oesophagectomy

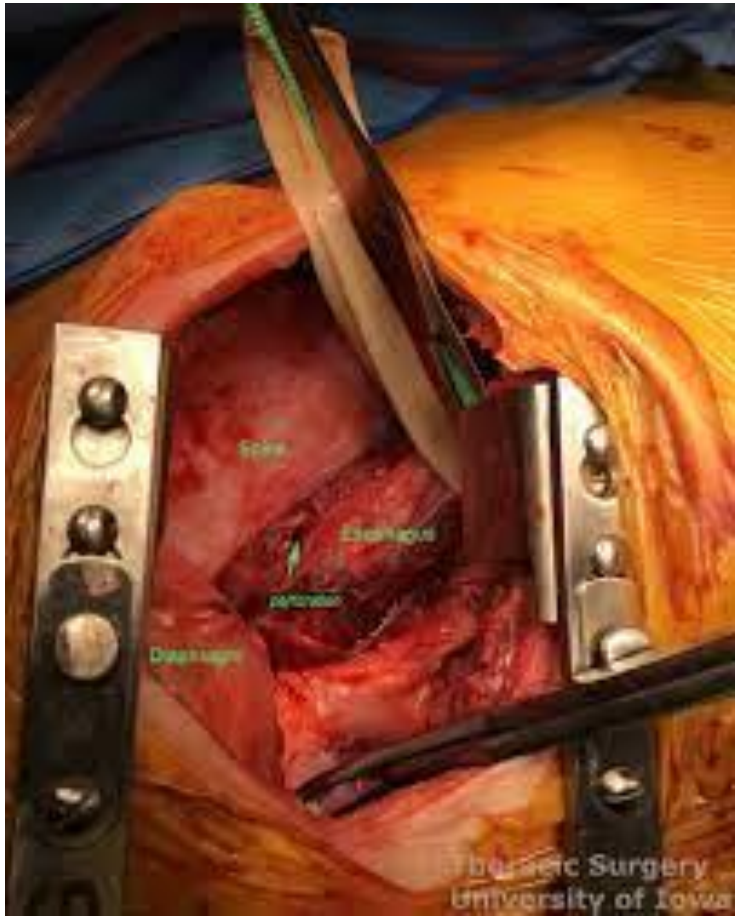


(a) right lung
(b) aortic arch
(c) thoracic oesophagus
(d) thoracic diaphragm
(e) (e) stomach

Gastrectomy

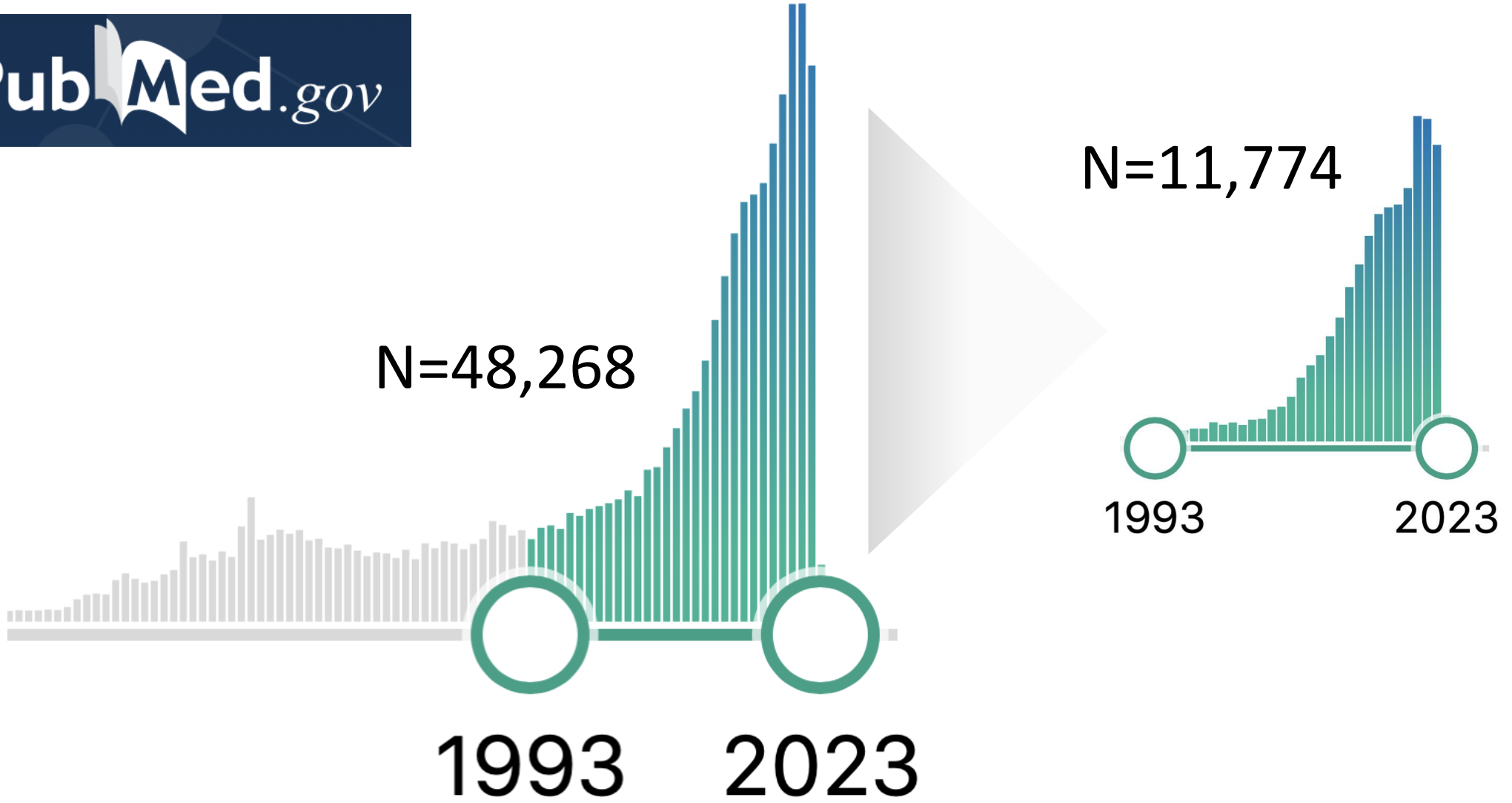





Spleen
Esophagus
pericardium
Diaphragm
Surgery
University of Iowa

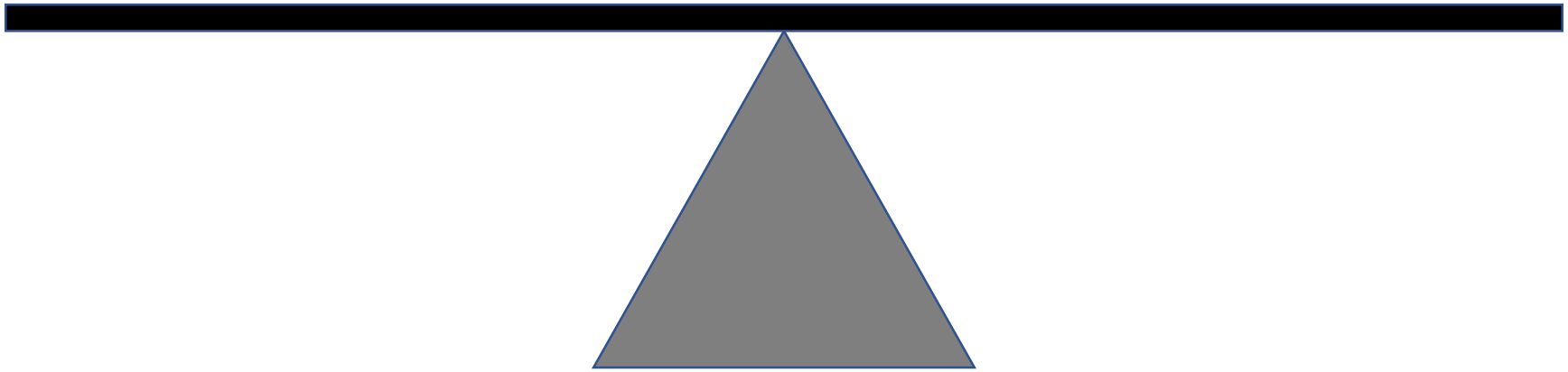
VS.

PubMed.gov



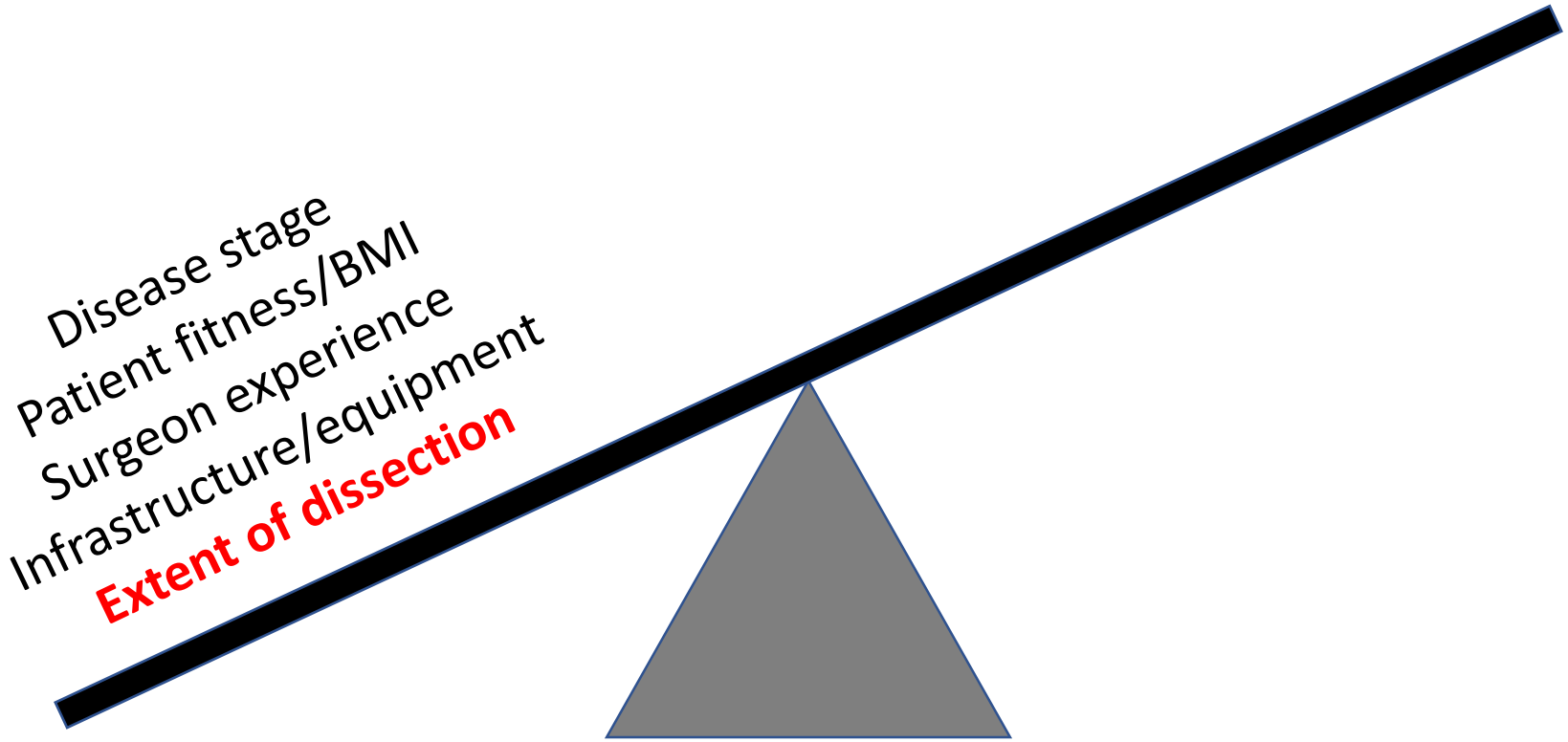
(esophagectomy OR gastrectomy)

AND ("minimally invasive" Or robotic OR laparoscopic)



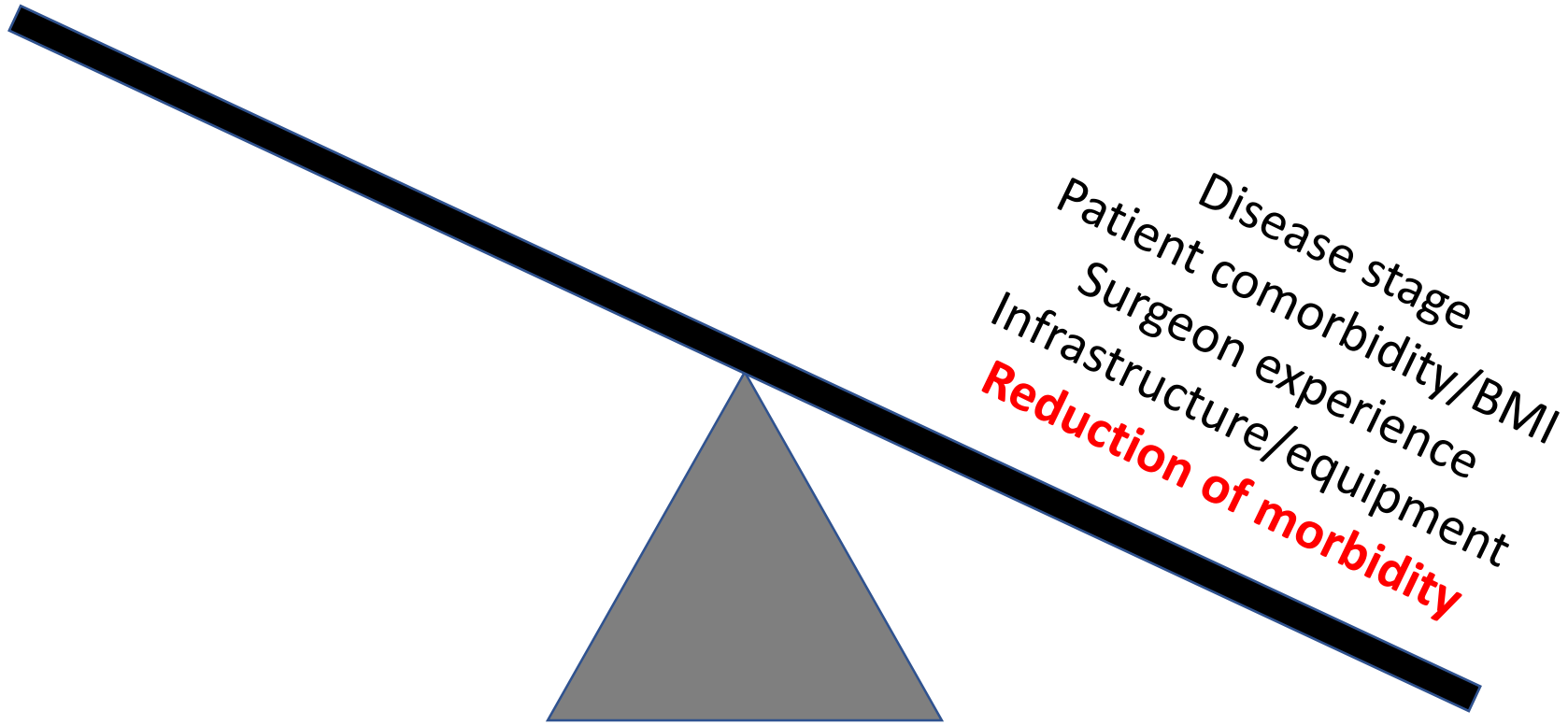
Open

Minimally invasive



Open

Minimally invasive



Open

Minimally invasive

Open vs. MI Oesophagectomy

Meta-analysis of randomized controlled trials and individual patient data comparing minimally invasive with open oesophagectomy for cancer

B. P. Müller-Stich[1,*], P. Probst[1,2], H. Nienhüser[1], S. Fazeli[1], J. Senft[1], E. Kalkum[2], P. Heger[1,2], R. Warschkow[3], F. Nickel[1],

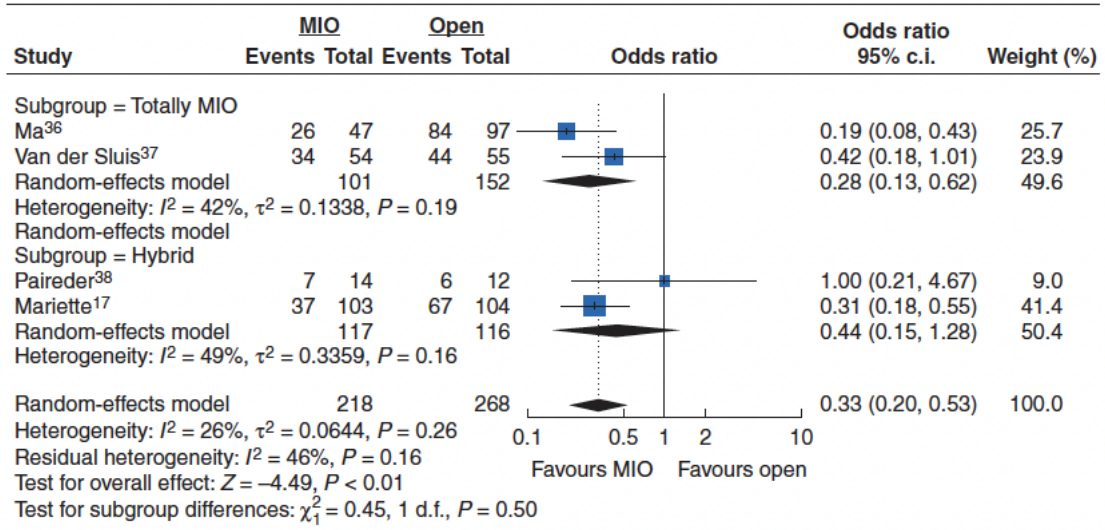
BJS

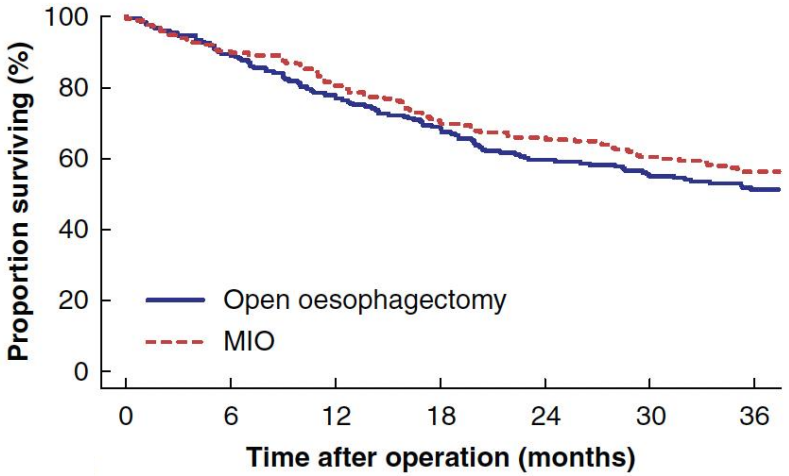
BJS, 2021, **108**, 1026–1033

Table 1 Summary and characteristics of included trials

Study/year	Procedures	Anastomosis	*n*	Tumour types		
				AEG	SCC	Other
TIME trial 2012[9,33,34]	Totally minimally invasive	Cervical (64%) Thoracic (29%)	59	35	24	0
	Open	Cervical (66%) Thoracic (27%)	56	36	19	1
Guo *et al.* 2013[35]	Totally minimally invasive	Cervical	111	nr	nr	nr
	Open	Cervical	110	nr	nr	nr
Ma *et al.* 2018[36]	Totally minimally invasive	Thoracic	47	43	0	4
	Open	Thoracic	97	91	2	4
van der Sluis *et al.* 2019[37]	Totally minimally invasive (robot-assisted)	Cervical	54	41	13	0
	Open	Cervical	55	43	12	0
Paireder *et al.* 2018[38]	Hybrid (abdominal part laparoscopic)	Thoracic	14	10	4	0
	Open	Thoracic	12	11	1	0
Mariette *et al.* 2019[17]	Hybrid (abdominal part laparoscopic)	Thoracic	103	57	46	0
	Open	Thoracic	104	66	38	0

AEG, adenocarcinoma of oesophagogastric junction; SSC, squamous cell carcinoma; nr, not recorded.





Open vs. MI Gastrectomy

Basic characteristics of included studies.

Study	Country	Period	Cases	Female	Age	BMI
Kitano 2002	Japan	1998–2001	28	11	61.65	NR
Lee 2005	Korea	2001–2003	47	21	58.02	NR
Huscher 2005	European	1992–1996	59	20	63.40	NR
Hayashi 2005	Japan	1999–2001	28	6	59.00	22.75
Kim 2013	Korea	2003–2005	164	65	55.60	24.35
Cai 2011	China	2008–2009	96	20	60.22	22.43
Hu 2012	China	2009–2011	82	41	60.82	23.24
Yamashita 2016	Japan	2005–2008	63	21	59.52	22.60
Takiguchi 2013	Japan	2003–2006	40	15	61.82	23.21
Cui 2015	China	2010–2012	270	84	58.73	23.36
Hu 2015	China	2012–2013	66	21	62.25	NR
Kim 2019	Korea	2006–2010	1384	466	57.20	23.80
Liu 2016	China	2014–2015	84	42	68.98	21.70
Huang 2021	China	2012–2014	1039	313	56.15	22.70
Zhou 2017	China	2012–2015	200	100	53.17	NR
Luo 2017	China	2008–2012	124	39	64.00	21.53
Katai 2020	Japan	2010–2013	912	357	63.27	22.48
Park 2018	Korea	2010–2011	196	62	59.33	23.50
Guo 2018	China	2016–2017	222	73	57.22	22.70
Shi 2019	China	2010–2012	322	97	55.13	20.48
Li 2019	China	2015–2017	95	29	59.30	23.00
Hyung 2020	Korea	2011–2015	1011	295	59.70	23.60
Wang 2019	China	2014–2017	442	165	60.00	23.30
Liu 2020	China	2017–2018	214	59	59.59	23.79
Wielen 2021	European	2015–2018	96	36	60.63	25.84
Veen 2021	European	2015–2018	227	87	67.41	25.42
Sayed 2021	Egypt	2017–2019	36	12	52.50	NR
Luo 2021	China	2014–2018	96	30	70.00	21.51

Review

Laparoscopic versus open gastrectomy for gastric cancer: A systematic review and meta-analysis of randomized controlled trials

Shenghan Lou, Xin Yin, Yufei Wang, Yao Zhang, Yingwei Xue *

International Journal of Surgery 102 (2022) 106678

↓ **Total postoperative complications** (RR, 0.81; 95% CI, 0.73 to 0.91)

↓ **Wound complications** (RR, 0.67; 95% CI, 0.50 to 0.91)

↓ **Intra-abdominal fluid collection** (RR, 0.67; 95% CI, 0.46 to 0.97)

↔ **90-mortality**

↔ **Tumour recurrence**

↔ **Long-term survival**

Imperial College London

ORIGINAL ARTICLE

Development of a Reliable Surgical Quality Assurance System for 2-stage Esophagectomy in Randomized Controlled Trials

Alexander Harris, PhD, James Butterworth, MSc,* Piers R. Boshier, PhD,* Hugh MacKenzie, PhD,* Masanori Tokunaga, PhD,† Hideki Sunagawa, PhD,‡ Stella Mavroveli, PhD,* Melody Ni, PhD,* Sameh Mikhail, MD,§ Chi-Chuan Yeh, PhD,¶ Natalie S. Blencowe, PhD,||** Kerry N. L. Avery, PhD,** Richard Hardwick, MD,†† Arnulf Hoelscher, PhD,‡‡ Manuel Pera, PhD,§§ Giovanni Zaninotto, MD,* Simon Law, PhD,¶¶ Donald E. Low, MD,|||| Jan J. B. van Lanschot, PhD,*** Richard Berrisford, ChM,††† Christopher Paul Barham, MD,|| Jane M. Blazeby, MD,||** and George B. Hanna, PhD*✉*

TABLE 1. Essential Tasks for 2-stage Esophagectomy

Abdominal phase
Abdominal access
1. Confirm the absence of metastatic disease.
Diaphragmatic hiatus
2. Mobilize the gastroesophageal junction, resecting right and left paracardial lymph nodes (LN). (LN stations 1 and 2)
3. Resect a cuff of diaphragm and pleura to achieve a clear circumferential margin in advanced disease.
4. Dissect along the pre-aortic fascia.
Gastric mobilization
5. Mobilize the stomach based on the right gastroepiploic vessels
Celiac axis
6. Dissect LN tissue along the common hepatic artery, celiac artery, left gastric artery and proximal splenic artery. (LN stations 7, 8a, 9, 11p)
7. Ligate and divide the left gastric vein close to the portal vein and the left gastric artery at the celiac artery.
8. Dissect LN tissue from the left side of the celiac artery, to the left crus at the esophageal hiatus, and left side of Gerota's fascia.
9. Continue the dissection along the anterior surface of the proximal splenic artery towards the splenic hilum and ligate the posterior gastric vessels at their origin from the splenic artery.
Gastric tube
10. Create the gastric tube, removing tissue along the lesser curvature of the stomach. (LN stations 3a and 3b) This step may be done in the chest.

Thoracic phase
Thoracic access
1. Exclude metastatic disease in the chest.
Thoracic lymphadenectomy
2. Divide the inferior pulmonary ligament and ligate and divide the azygos arch.
3. Dissect along the pericardium until the left pulmonary vein is reached, including the left pleura in advanced disease.
4. Perform a sub-carinal lymphadenectomy (LN station 107) and clear both bronchi of LN tissue. (LN station 109)
5. Dissect the mediastinal pleura at the anterolateral border of the thoracic aorta and dissect along the pre-aortic fascia, from the proximal resection margin towards the diaphragm. (LN station 112)
6. Identify and ligate the thoracic duct at the proximal resection margin and above the diaphragm.
Specimen excision
7. Ensure that the thoracic part of the specimen is circumferentially free, from the previously completed diaphragmatic mobilization (performed during the abdominal phase) to at least the level of the aortic arch. (LN stations 108, 110, and 111)
8. Deliver the stomach into the right chest cavity, ensuring that the gastric tube can reach the site of anastomosis without tension or torsion.
9. Excise the specimen with suitable proximal and distal resection margins and send it to pathology as per the ROMIO trial protocol.
Anastomosis
10. Perform an esophago-gastrostomy using preferred technique.

LN indicates lymph nodes; ROMIO, randomized oesophagectomy – minimally invasive or open.

Instructions: *Please tick the appropriate description for the quality of the end product for each task.*

Key: **Complete** Anatomical structure is clearly demonstrated following complete dissection of all associated lymphatic (LN) tissue.
Incomplete Incomplete LN clearance of the anatomical structure (Quantify if incomplete).

Task 1 Diaphragmatic hiatus	**Complete**	**Incomplete**	**Not performed**	**Quantify if incomplete**
Right crus	☐	☐	☐	.....
Left crus	☐	☐	☐	.....
Aorta	☐	☐	☐	.....
Pericardium	☐	☐	☐	.....
Right lung	☐	☐	☐	.....
Left lung	☐	☐	☐	.....

Task 2 Abdominal lymphadenectomy	**Complete**	**Incomplete**	**Not performed**	**Quantify if incomplete**
Portal vein	☐	☐	☐	.....
Proper hepatic artery	☐	☐	☐	.....
Common hepatic artery	☐	☐	☐	.....
Celiac artery	☐	☐	☐	.....
Left gastric artery (stump)	☐	☐	☐	.....
Left gastric vein (stump)	☐	☐	☐	.....
Proximal splenic artery	☐	☐	☐	.....
Distal splenic artery	☐	☐	☐	.....
Splenic vein	☐	☐	☐	.....
Splenic hilum (if appropriate)	☐	☐	☐	.....

Task 3 Thoracic lymphadenectomy	**Complete**	**Incomplete**	**Not performed**	**Quantify if incomplete**
Carina	☐	☐	☐	.....
Right main bronchus	☐	☐	☐	.....
Left main bronchus	☐	☐	☐	.....
Right pulmonary veins	☐	☐	☐	.....
Left pulmonary veins	☐	☐	☐	.....
Pericardium	☐	☐	☐	.....
Aorta	☐	☐	☐	.....

Task 4 Reconstruction	**Yes**	**No**	**Borderline**	**Quantify if incomplete**
Viable color of gastric tube	☐	☐	☐	.....
Lesser curve cleared of LN tissue	☐	☐	☐	.....
Tension free anastomosis	☐	☐	☐	.....
Appropriate approximation of sutures	☐	☐	☐	.....

ROMIO ASSESSOR (Print):..... **SIGN:**..... **DATE:**.....

Imperial College London

Surgical Quality Assurance photographic assessment tool for (total or sub-total) Gastrectomy
Oncological resections up to and including pancreas and spleen preserving D2 lymphadenectomy

Case reference: .....

RESECTION

Key: **Please see overleaf for instructions on which lymph node stations are required to be cleared depending upon the type of gastrectomy performed and extent of the lymphadenectomy.**

1	**Complete**	Anatomical structure clearly visible and completely cleared of lymphatic (LN) tissue/ Vessel ligated at its origin or point of insertion.
2	**Incomplete**	Anatomical structure only partially visible as incompletely cleared of lymphatic tissue/ Vessel not ligated at its origin or insertion.
3	**Not performed**	Anatomical structure not visible as not cleared of lymphatic tissue/ Vessel not ligated, despite adequate view of structure from either photo or video file.
4	**Unable to rate**	Includes any/ all of the following reasons:
	N/A Not applicable	Anatomical structure/ lymph node station not applicable to the procedure performed.
	IE Insufficient evidence	Evidence submitted but unable to provide a rating e.g. blurred photo or obstructed field of view.
	A Absent data	No evidence submitted e.g. no photograph available.

Structures remaining	Rating						Comments
	1	2	3	N/A	IE	A	
Right crus							
Left crus				*Distal*			
Gastroesophageal junction				*Distal*			
Portal vein							
Hepatic artery proper							
Common hepatic artery							
Gastroduodenal artery							
Right gastroepiploic artery (stump)							
Gastrocolic trunk							
Right gastroepiploic vein (stump)							
Right gastric artery (stump)							
Right gastric vein (stump)							
Coeliac axis (trifurcation)							
Left gastric artery (stump)							
Left gastric vein (stump)							
Proximal splenic artery							
Distal splenic artery				*Distal*			
Splenic vein							
Splenic hilum							

RECONSTRUCTION

Key:

1	**Satisfactory**	**Anastomosis appears well perfused/ tension free/ tissue well aligned (e.g. orientation/ suture line).**
2	**Borderline**	**Anastomosis appears bruised/ concern regarding tension/ tissue alignment could be improved.**
3	**Unsatisfactory**	**Anastomosis does not appear viable/ tension apparent/ tissue poorly aligned (e.g. obvious kink/ gap in suture line).**
N/A	Not applicable	Anastomosis not applicable to the procedure performed.
IE	Insufficient evidence	Evidence submitted but unable to provide a rating e.g. blurred photo or obstructed field of view.
A	Absent data	No evidence submitted e.g. no photograph available.

Anastomosis	Element	Rating						Comments
		1	2	3	N/A	IE	A	
Oesophago/gastro-jejunostomy	**Viable colour**							
	Tension free							
	Appropriate alignment							
Jejunojejunostomy	**Viable colour**							
	Tension free							
	Appropriate alignment							

Assessor's interpretation of the procedure performed *(please delete as appropriate)*: Total/ Sub-total **D1/ D1+/ D2/ Other (expand)**.....

ASSESSOR (Print):..... **SIGN:**..... **DATE:**.....

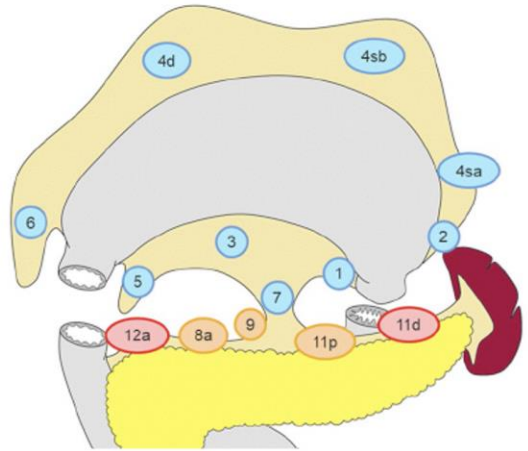
Lymphadenectomy

Adapted from JGCA Treatment Guidelines v4 2014 & v5 2020

Total gastrectomy

D1 LN stations 1-7 (Blue)
D1+ LN stations 1-7 plus 8a, 9 and 11p (Orange)
D2 LN stations 1-7 plus 8a, 9, 11p, 11d and 12a (Red)

Omentectomy is optional. Bursectomy is not required.



Distal gastrectomy can omit LN stations 2 and 4sa.

For D1+ lymphadenectomy, can also omit 11p.

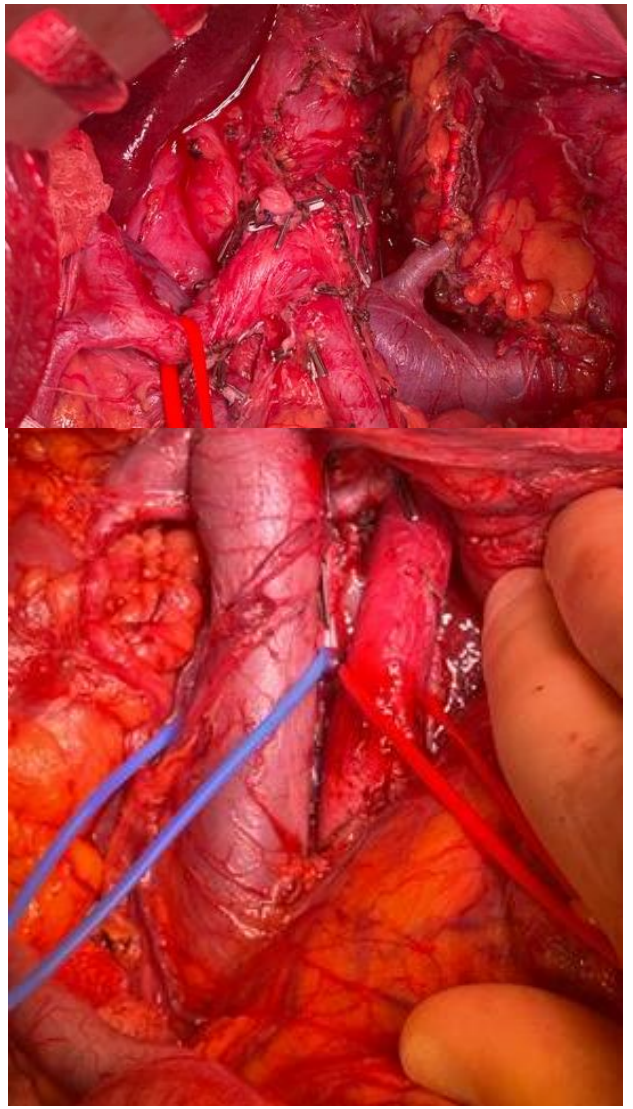
For D2 lymphadenectomy, 11p is required but 11d can be omitted.

1	Right paracardial LNs, including those along the first branch of the ascending limb of the left gastric artery.
2	Left paracardial LNs including those along the oesophagocardiac branch of the left subphrenic artery.
3a	Lesser curvature LNs along the branches of the left gastric artery.
3b	Lesser curvature LNs along the 2nd branch and distal part of the right gastric artery.
4sa	Left greater curvature LNs along the short gastric arteries (perigastric area).
4sb	Left greater curvature LNs along the left gastroepiploic artery (perigastric area).
4d	Rt. Greater curvature LNs along the 2nd branch and distal part of the right gastroepiploic artery.
5	Suprapyloric LNs along the 1st branch and proximal part of the right gastric artery.
6	Infrapyloric LNs along the first branch and proximal part of the right gastroepiploic artery down to the confluence of the right gastroepiploic vein and the anterior superior pancreatoduodenal vein.
7	LNs along the trunk of left gastric artery between its root and the origin of its ascending branch.
8a	Anterosuperior LNs along the common hepatic artery.
8p	Posterior LNs along the common hepatic artery.
9	Coeliac artery LNs.
10	Splenic hilar LNs including those adjacent to the splenic artery distal to the pancreatic tail, and those on the roots of the short gastric arteries and those along the left gastroepiploic artery proximal to its 1st gastric branch.
11p	Proximal splenic artery LNs from its origin to halfway between its origin and the pancreatic tail end.
11d	Distal splenic artery LNs from halfway between its origin and the pancreatic tail end to the end of the pancreatic tail.
12a	Hepatoduodenal ligament LNs along the proper hepatic artery, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas.
12b	Hepatoduodenal ligament LNs along the bile duct, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas.
12p	Hepatoduodenal ligament LNs along the portal vein in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas.
13	LNs on the posterior surface of the pancreatic head cranial to the duodenal papilla.
14v	LNs along the superior mesenteric vein.
15	LNs along the middle colic vessels.
16a1	Paraaortic LNs in the diaphragmatic aortic hiatus.
16a2	Paraaortic LNs between the upper margin of the origin of the coeliac artery and the lower border of the left renal vein.
16b1	Paraaortic LNs between the lower border of the left renal vein and the upper border of the origin of the inferior mesenteric artery.
16b2	Paraaortic LNs between the upper border of the origin of the inferior mesenteric artery and the aortic bifurcation.
17	LNs on the anterior surface of the pancreatic head beneath the pancreatic sheath.
18	LNs along the inferior border of the pancreatic body.
19	Infradiaphragmatic LNs predominantly along the subphrenic artery.
20	Paraesophageal LNs in the diaphragmatic oesophageal hiatus.
110	Paraesophageal LNs in the lower thorax.
111	Supradiaphragmatic LNs separate from the oesophagus.
112	Posterior mediastinal LNs separate from the oesophagus and the oesophageal hiatus.

Author	Trial	Cancer	Year
Bajetta	Surgery +/- adjuvant chemotherapy	G	2002
Nashimoto	Surgery +/- adjuvant chemo	G	2003
Xiao ZF	Surgery +/- Radiotherapy	O	2003
Chipponi	Surgery +/- adjuvant chemotherapy	G	2004
Bouche	Surgery +/- adjuvant chemotherapy	G	2005
Burmeister	Surgery +/- neoadjuvant chemoradiotherapy	O	2005
Yu	Gastrectomy +/- splenectomy	G	2006
Cunningham (MAGIC)	Surgery +/- perioperative chemotherapy	O + G	2006
Wu CW	Gastrectomy: D1 versus D3 nodal dissection	G	2006
De Vita	Surgery +/- adjuvant chemotherapy	G	2007
Kelsen	Surgery +/- neoadjuvant chemotherapy	O	2007
Omloo JM	Transthoracic versus transhiatal	O	2007
Di Costanzo	Surgery +/- adjuvant chemotherapy	G	2008
Sasako	D2 Gastrectomy +/- Para-aortic LN dissection	G	2008
Allum W (OEO2)	Surgery +/- neoadjuvant chemo	O	2009
Kulig	Surgery +/- adjuvant chemotherapy	G	2010
Songun (Dutch D1/D2)	D1 versus D2 Gastrectomy	G	2010
Miyashiro (JCOG9206-2)	Surgery +/- adjuvant chemotherapy	G	2011
Sasako	Surgery +/- adjuvant chemotherapy	G	2011
Smalley (SWOG 0116)	Surgery +/- adjuvant chemoradiotherapy	G	2012
Van Hagen P (CROSS)	Surgery +/- neoadjuvant chemoradiotherapy	O+ GOJ	2012
Bass GA	Surgery +/- neoadjuvant chemoradiotherapy	O	2014
Noh SH (CLASSIC)	D2 Gastrectomy +/- adjuvant chemotherapy	G	2014
Degiuli M	D1 versus D2 Gastrectomy	G	2014
Mariette C*	Surgery +/- neoadjuvant chemoradiotherapy	O	2014
Hirao M	Gastrectomy +/- bursectomy	G	2015
Yang Z Q	Open versus minimally invasive oesophagectomy	O	2016
Sano T	Gastrectomy +/- splenectomy	G	2017

Para-aortic lymphadenectomy

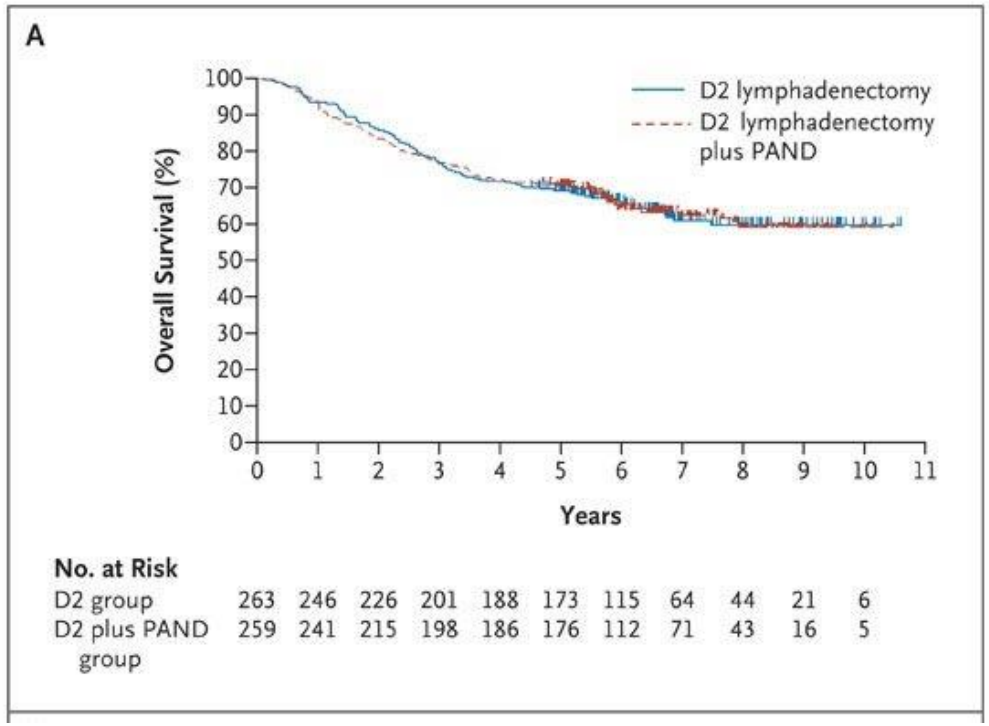
- Incidence 18-40% in advanced gastric cancer
- Associated with higher pN-stage (station 9)



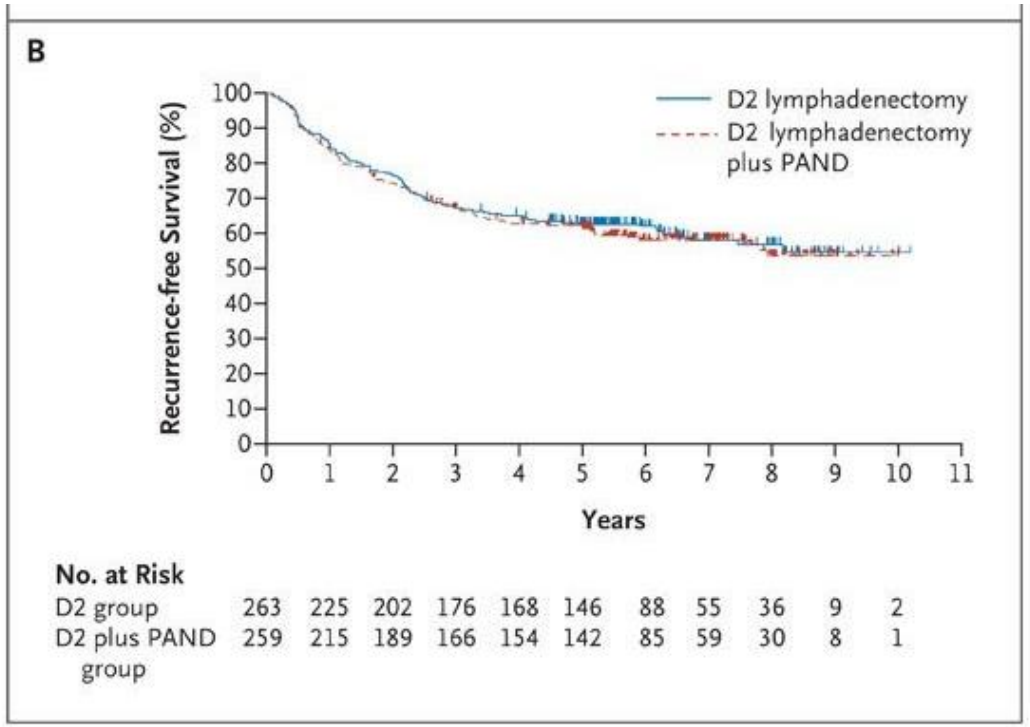
D2 Lymphadenectomy Alone or with Para-aortic Nodal Dissection for Gastric Cancer

Mitsuru Sasako, M.D., Takeshi Sano, M.D., Seiichiro Yamamoto, Ph.D., Yukinori Kurokawa, M.D., Atsushi Nashimoto, M.D., Akira Kurita, M.D., Masahiro Hiratsuka, M.D., Toshimasa Tsujinaka, M.D., Taira Kinoshita, M.D., Kuniyoshi Arai, M.D., Yoshitaka Yamamura, M.D., and Kunio Okajima, M.D. for the Japan Clinical Oncology Group

JCOG 9501



Overall survival



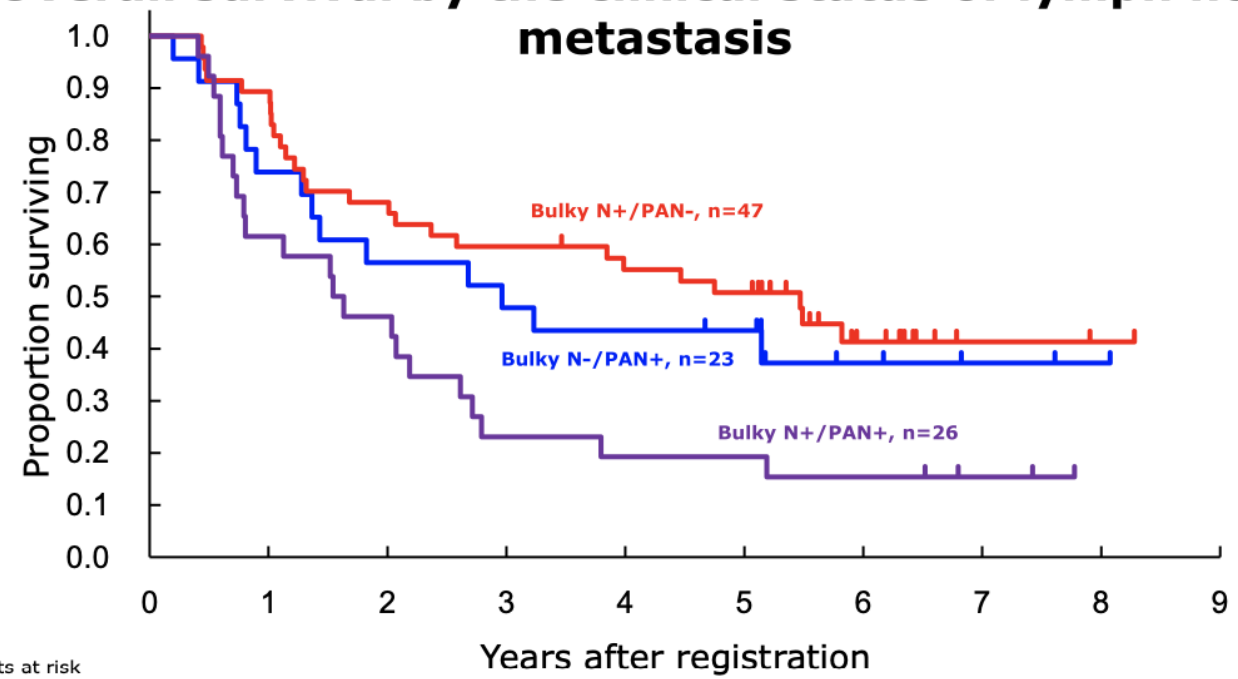
Disease free survival

SHORT COMMUNICATION

An integrated analysis of two phase II trials (JCOG0001 and JCOG0405) of preoperative chemotherapy followed by D3 gastrectomy for gastric cancer with extensive lymph node metastasis

Hiroshi Katayama[1] · Akira Tsuburaya[2] · Junki Mizusawa[1] · Kenichi Nakamura[1] · Hitoshi Katai[3] · Hiroshi Imamura[4] · Atsushi Nashimoto[5] · Norimasa Fukushima[6] · Takeshi Sano[7] · Mitsuru Sasako[8]

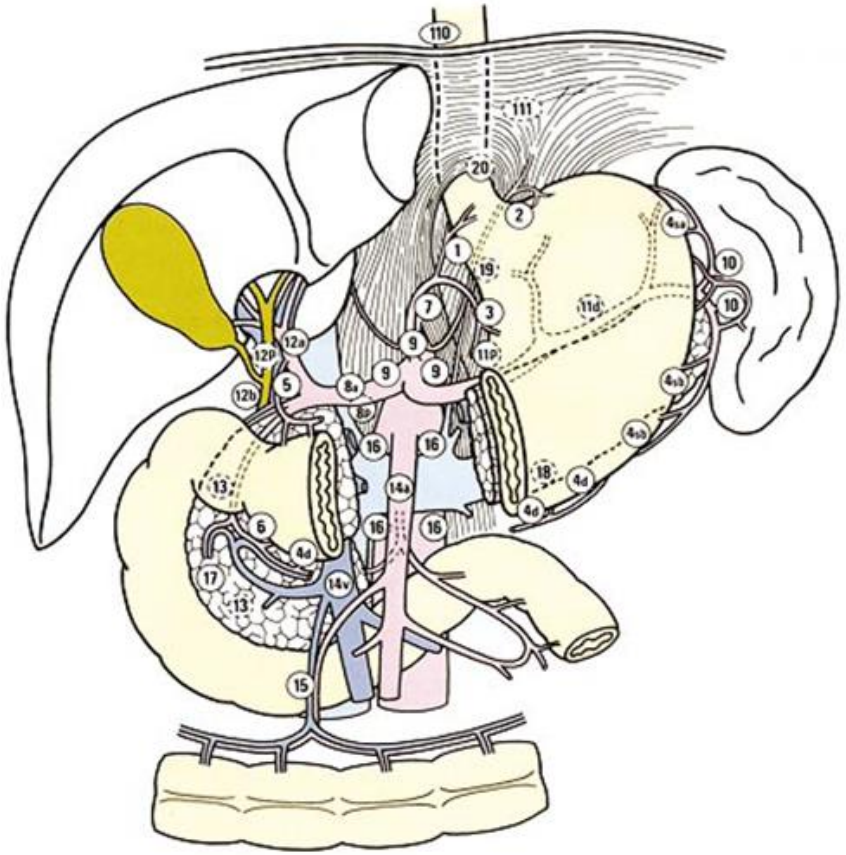
a Overall survival by the clinical status of lymph node metastasis



Patients at risk										
Bulky N+/PAN-	47	42	32	28	25	23	10	2	1	0
Bulky N-/PAN+	23	17	13	11	10	9	4	2	1	0
Bulky N+/PAN+	26	16	12	6	5	5	4	2	0	0

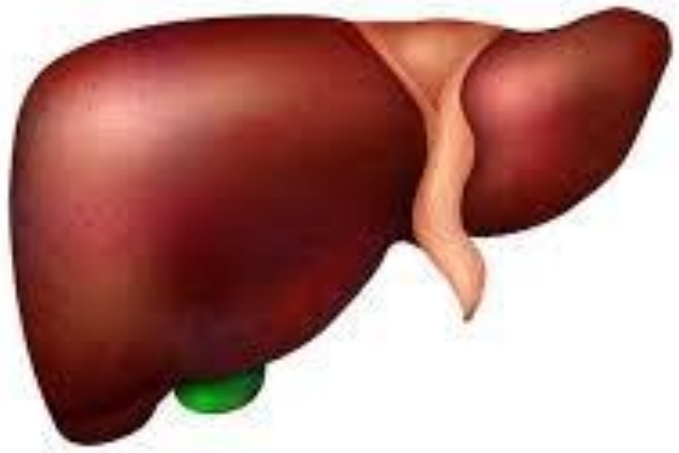
Multivisceral resection

- Colon
- Small bowel
- Liver
- Pancreas
- Spleen
- Adrenal



Liver metastasis

- Incidence 4-14% of patients presenting with gastric cancer
  - Synchronous 5–10%
  - Metachronous 37%



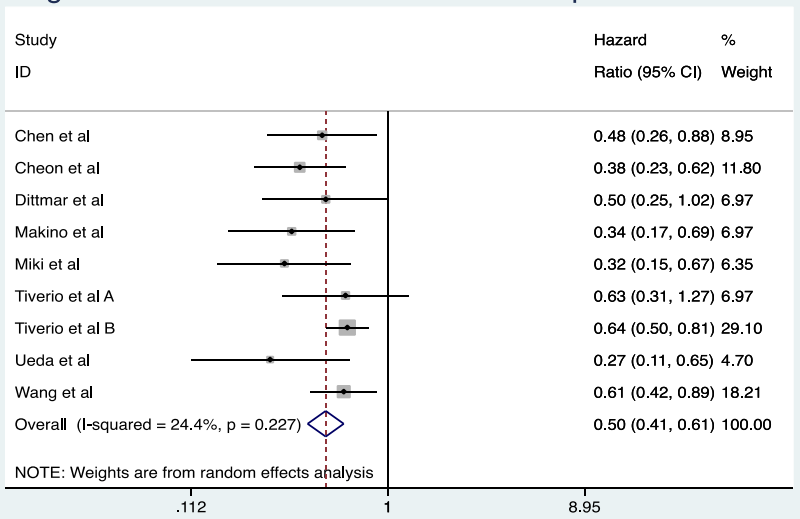
META-ANALYSIS

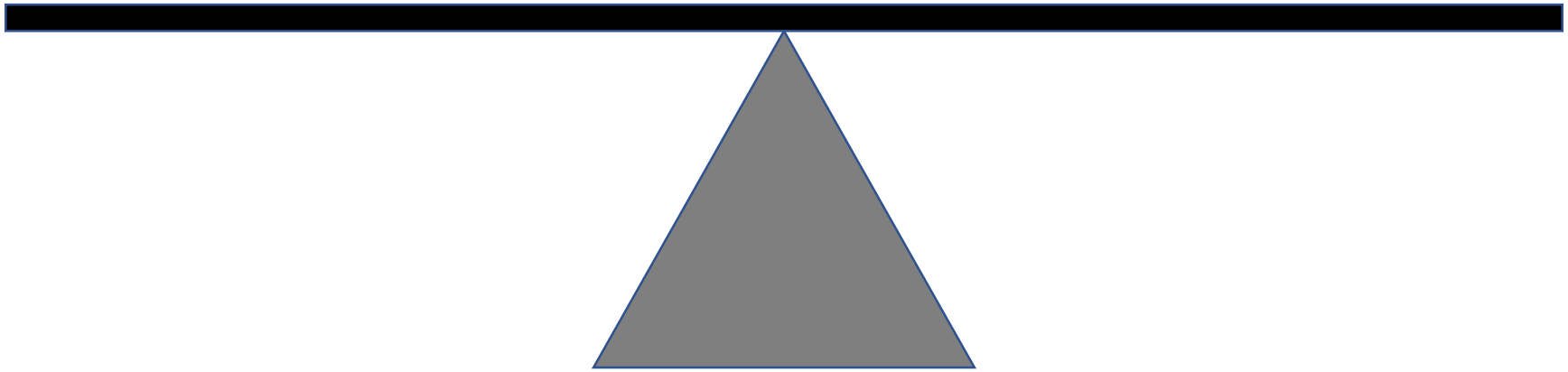
Influence of Surgical Resection of Hepatic Metastases From Gastric Adenocarcinoma on Long-term Survival: Systematic Review and Pooled Analysis

Sheraz R. Markar, MRCS, MSc, MA, Sameh Mikhail, FRCS,*† George Malietzis, MRCS,* Thanos Athanasiou, PhD, FRCS,* Christophe Mariette, PhD, MD,‡ Mitsuru Sasako, PhD, MD,§ and George B. Hanna, PhD, FRCS**

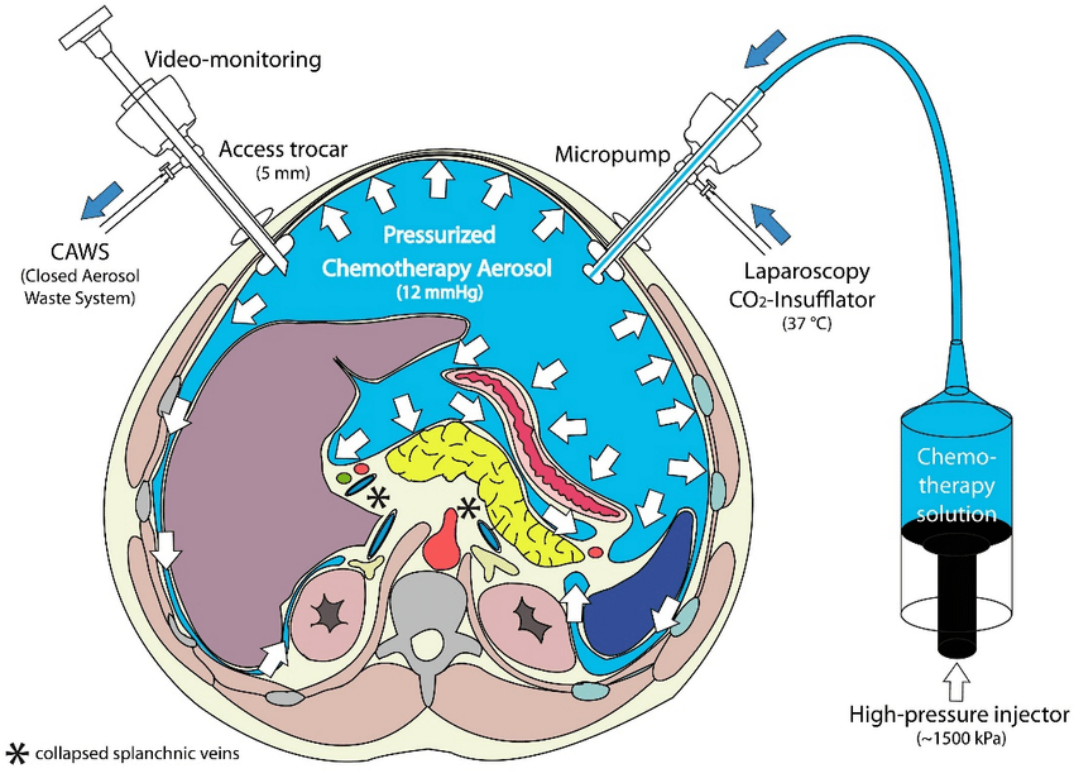
- 39 studies (991 patients)
- 9 studies in West (254 patients)
- 1, 3, 5-year survival 68%, 31% and 27% respectively
- Median survival of 21 months
- Solitary unilobar metastases had the best prognosis
- Majority of studies included up to 3 metastasis in one lobe

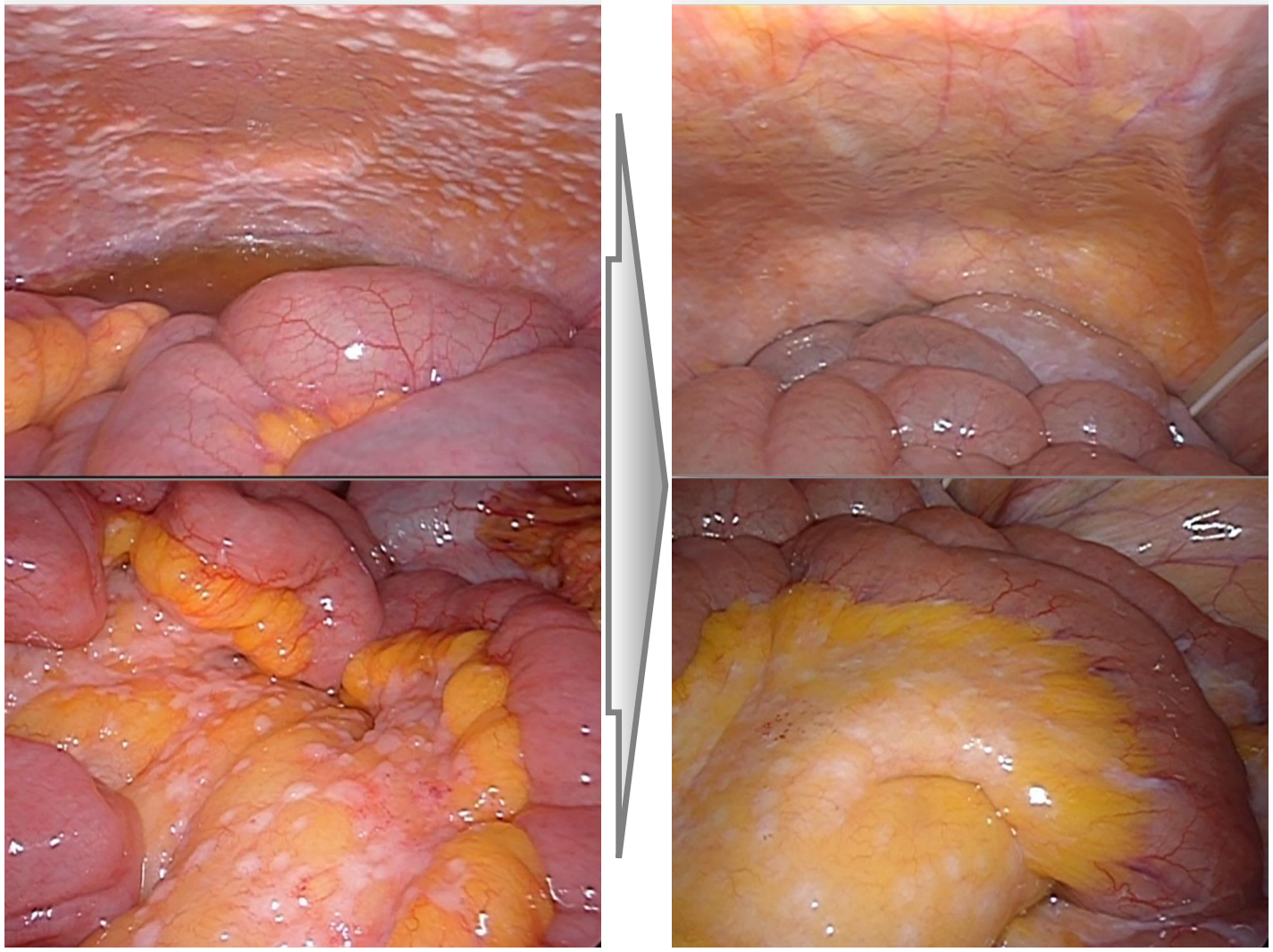
Surgical Resection vs. No Resection of Hepatic Metastases





Local and systemic therapies
Endoscopic and minimally invasive
Open/MI surgery



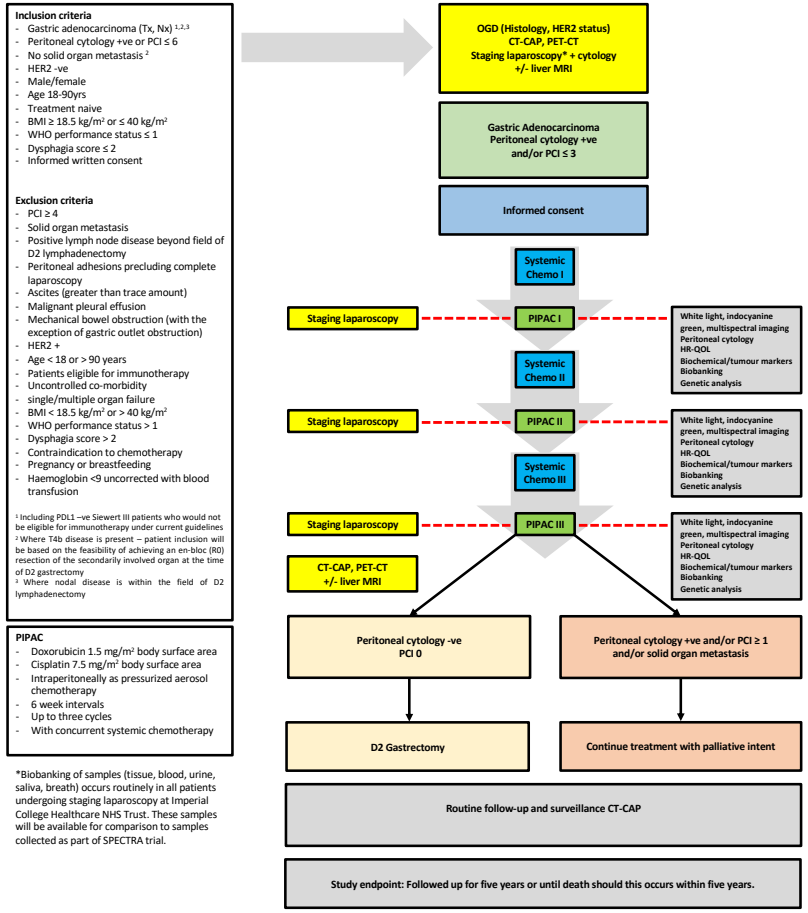


Kitayama etal. Ann Gastro Surg 2018

Imperial College London

SPECTRA

Neoadjuvant Systemic and PEritoneal ChemoTherapy for Regionally Advanced Gastric Cancer with Minimal Peritoneal Disease



Aims

Primary: To evaluate response – rate of peritoneal disease regression

Secondary:

i. To establish the feasibility and safety
ii. To assess treatment associated patient morbidity
iii. To establish a comprehensive bioresource

With thanks to our sponsors

Thank you for attending our first UKIOG Annual Meeting

If you haven't already joined our distribution list for information on our virtual monthly OG national MDT's please contact carly.biscoe@wales.nhs.uk to register.

Further information can be found on our website- www.ukiog.co.uk