Saturday November 7 - Vancouver, BC

2015 SON Fall Update

GI Tract Cancers: From Top to Bottom

BC Surgical Oncology Network

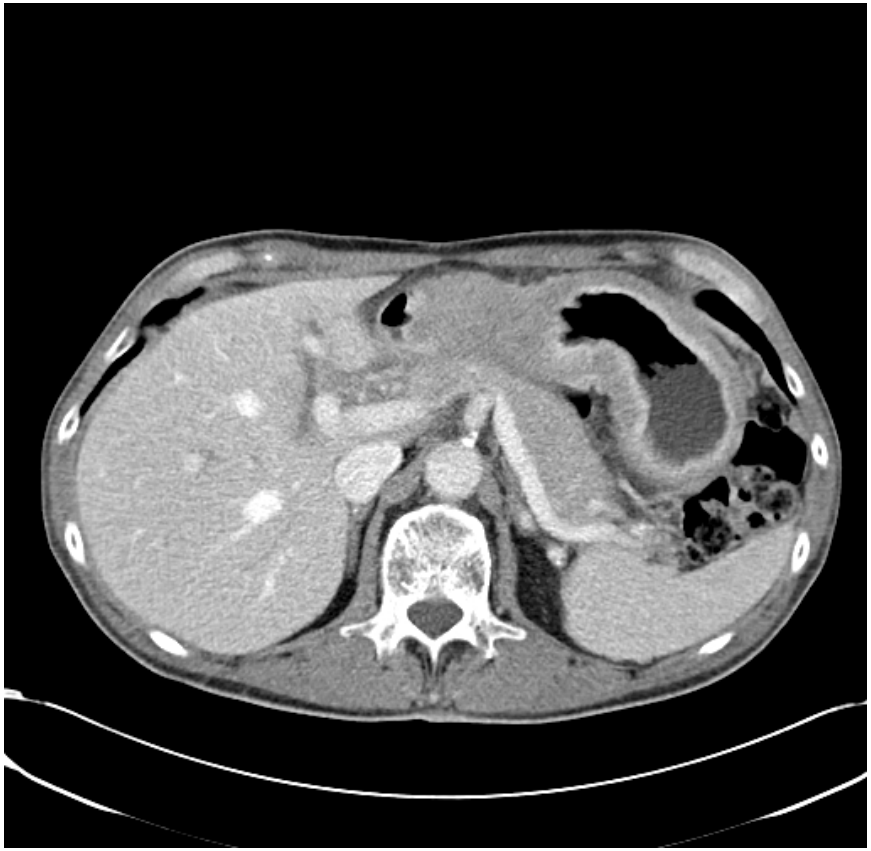
BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

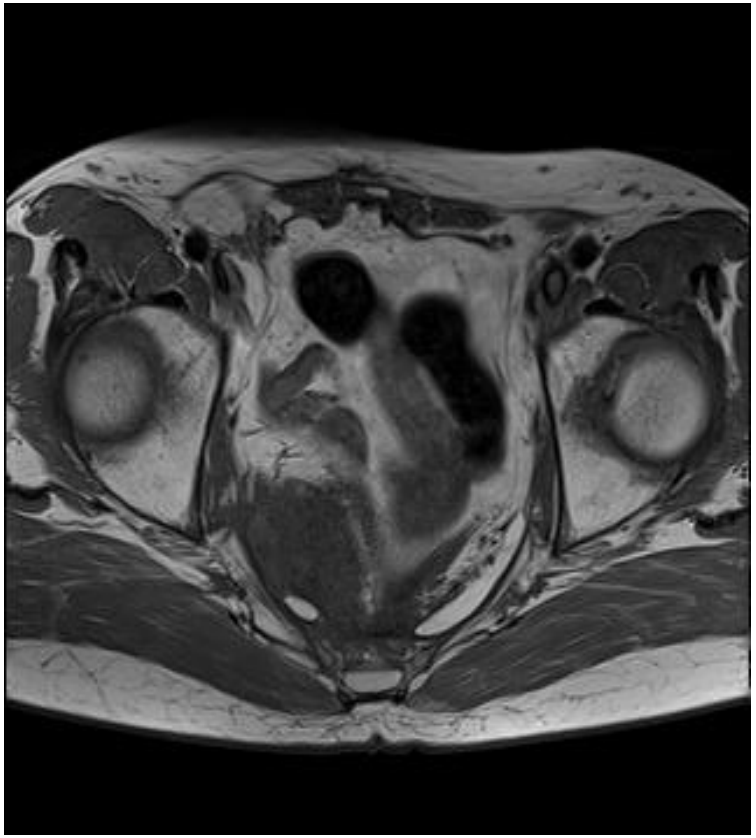
Management of Recurrent and Advanced Tumours: When are Tumours Resectable, and Multidisciplinary Management

Dr. Andrew McFadden

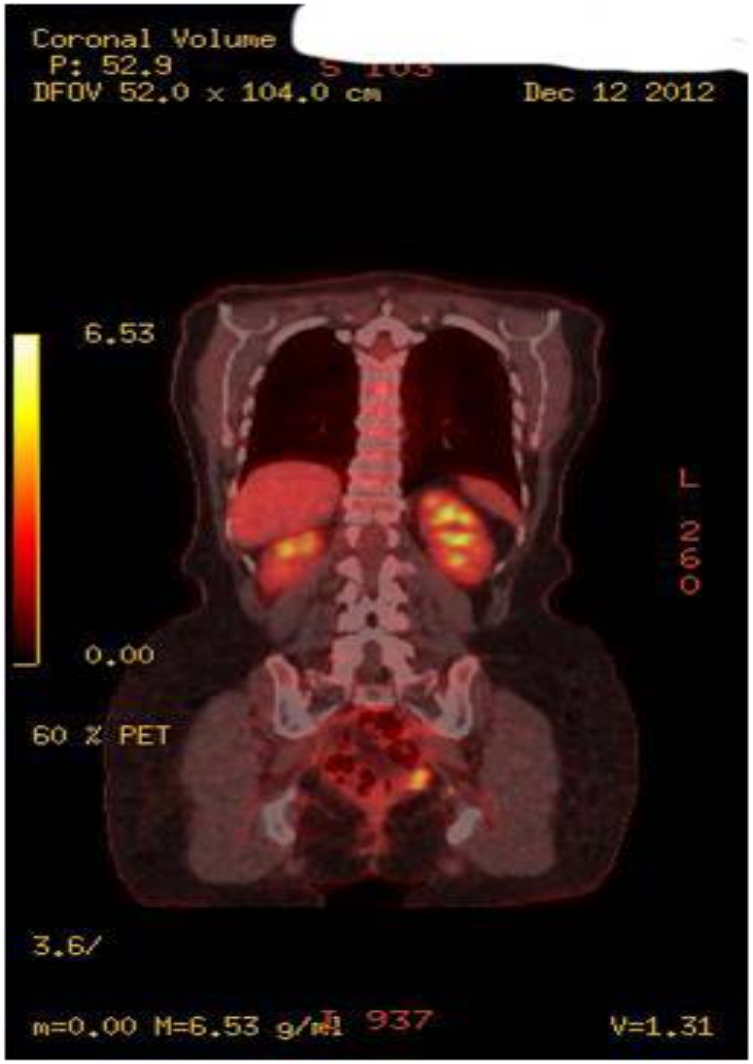
Surgical Oncology

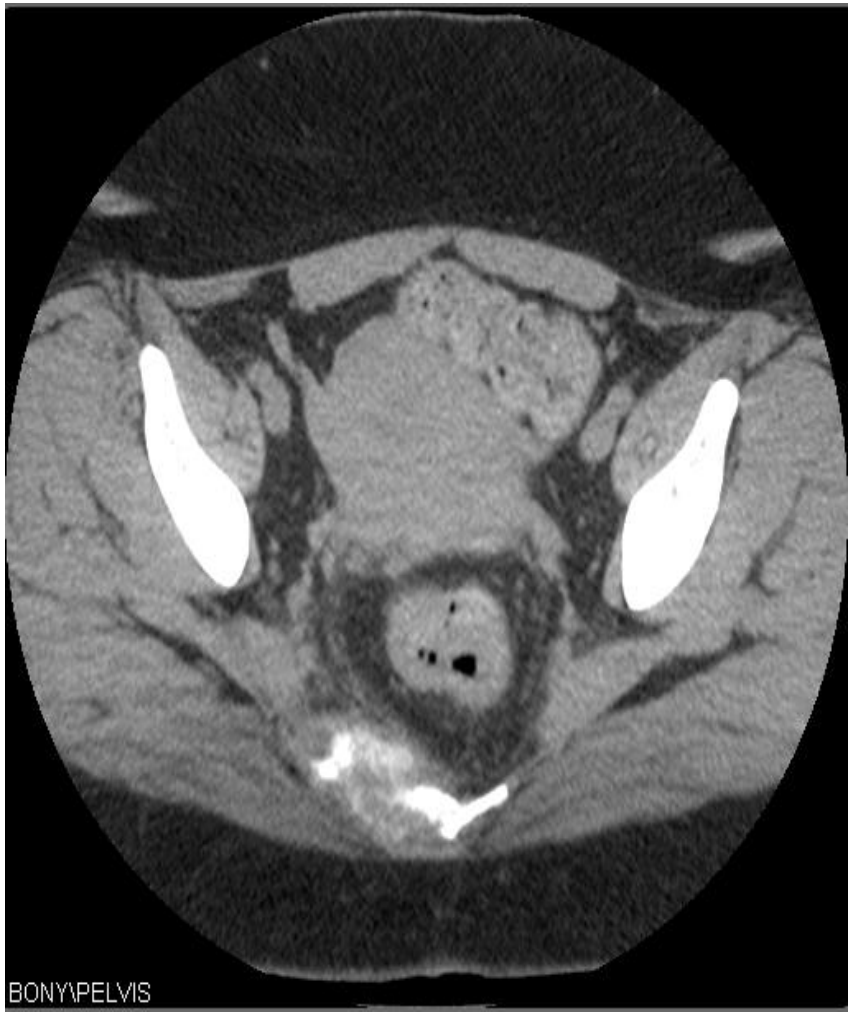
Management of Recurrent and Advanced Tumours: When are Tumours Resectable, and Multidisciplinary Management





Management of Recurrent and Advanced Tumours: When are Tumours Resectable, and Multidisciplinary Management





Turcotte jury faces gruesome evidence

Concordia student pleads guilty to assaulting ex-girlfriend

More sexual assault accusations against Catholic Brother

Doctor suspended three months

Police raid drug-selling locations

Six arrests in Montreal North shooting

PQ boycotts lieutenant governor's swearing-in

Former CAQ president Anglade to run for Liberals in byelection

What I used to know !

Resectability – Gastric

1. positive cytology
2. surgical palliation
3. multiorgan resection

NCCN Comprehensive Cancer Network®

NCCN Guidelines Version 3.2015 Staging Gastric Cancer

NCCN Guidelines Index
Gastric Cancer Table of Contents
Discussion

Table 1

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Carcinoma of the Stomach
(7th ed., 2010)

Primary Tumor (T)
- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria
- T1 Tumor invades lamina propria, muscularis mucosae or submucosa
- T1a Tumor invades lamina propria or muscularis mucosae
- T1b Tumor invades submucosa
- T2 Tumor invades muscularis propria*
- T3 Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures**,***
- T4 Tumor invades serosa (visceral peritoneum) or adjacent structures**,***
- T4a Tumor invades serosa (visceral peritoneum)
- T4b Tumor invades adjacent structures

Regional Lymph Nodes (N)
- NX Regional lymph node(s) cannot be assessed
- N0 No regional lymph node metastasis§
- N1 Metastasis in 1 - 2 regional lymph nodes
- N2 Metastasis in 3 - 6 regional lymph nodes
- N3 Metastasis in seven or more regional lymph nodes
- N3a Metastasis in 7 - 15 regional lymph nodes
- N3b Metastasis in 16 or more regional lymph nodes

Distant Metastasis (M)
- M0 No distant metastasis
- M1 Distant metastasis

Histologic Grade (G)
- GX Grade cannot be assessed
- G1 Well differentiated
- G2 Moderately differentiated
- G3 Poorly differentiated
- G4 Undifferentiated

*Note: A tumor may penetrate the muscularis propria with extension into the gastrocolic or gastrohepatic ligaments, or into the greater or lesser omentum, without perforation of the visceral peritoneum covering these structures. In this case, the tumor is classified T3. If there is perforation of the visceral peritoneum covering the gastric ligaments or the omentum, the tumor should be classified T4.

**The adjacent structures of the stomach include the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum.

***Intramural extension to the duodenum or esophagus is classified by the depth of the greatest invasion in any of these sites, including the stomach.

§A designation of pN0 should be used if all examined lymph nodes are negative, regardless of the total number removed and examined.

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2015 Staging Gastric Cancer

Table 1 - Continued

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Carcinoma of the Stomach
(7th ed., 2010)

Anatomic Stage/Prognostic Groups

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
	T1	N1	M0
Stage IIA	T3	N0	M0
	T2	N1	M0
	T1	N2	M0
Stage IIB	T4a	N0	M0
	T3	N1	M0
	T2	N2	M0
	T1	N3	M0
Stage IIIA	T4a	N1	M0
	T3	N2	M0
	T2	N3	M0
Stage IIIB	T4b	N0	M0
	T4b	N1	M0
	T4a	N2	M0
	T3	N3	M0
Stage IIIC	T4b	N2	M0
	T4b	N3	M0
	T4a	N3	M0
Stage IV	Any T	Any N	M1

Stage	5 year observed survival
Stage IA	71%
Stage IB	57%
Stage IIA	46%
Stage IIB	33%
Stage IIIA	20%
Stage IIIB	14%
Stage IIIC	9%
Stage IV	4%

The overall 5-year *relative* survival rate of all people

What I used to know !

Resectability –Colon and rectal

1. retroperitoneal lymph node recurrences
2. Involvement of pelvic side wall & sacrum
3. Lung mets/ lung mets and liver mets
4. Unresectable
5. Peritoneal seeding

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NCCN Guidelines Version 1.2016 Staging Colon Cancer

NCCN Guidelines Index
Colon Cancer Table of Contents
Discussion

Table 1. Definitions for T, N, M

Primary Tumor (T)

TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Tis Carcinoma in situ: intraepithelial or invasion of lamina propria[a]
T1 Tumor invades submucosa
T2 Tumor invades muscularis propria
T3 Tumor invades through the muscularis propria into the pericolorectal tissues
T4a Tumor penetrates to the surface of the visceral peritoneum[b]
T4b Tumor directly invades or is adherent to other organs or structures[b,c]

Regional Lymph Nodes (N)

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in 1-3 regional lymph nodes
N1a Metastasis in one regional lymph node
N1b Metastasis in 2-3 regional lymph nodes
N1c Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
N2 Metastasis in four or more regional lymph nodes
N2a Metastasis in 4-6 regional lymph nodes
N2b Metastasis in seven or more regional lymph nodes

Distant Metastasis (M)

M0 No distant metastasis
M1 Distant metastasis
M1a Metastasis confined to one organ or site (eg, liver, lung, ovary, nonregional node)
M1b Metastases in more than one organ/site or the peritoneum

Table 2. Anatomic Stage/Prognostic Groups

Stage	T	N	M	Dukes*	MAC*
0	Tis	N0	M0	-	-
I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
IIA	T3	N0	M0	B	B2
IIB	T4a	N0	M0	B	B2
IIC	T4b	N0	M0	B	B3
IIIA	T1-T2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3-T4a	N1/N1c	M0	C	C2
	T2-T3	N2a	M0	C	C1/C2
	T1-T2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3-T4a	N2b	M0	C	C2
	T4b	N1-N2	M0	C	C3
IVA	Any T	Any N	M1a	-	-
IVB	Any T	Any N	M1b	-	-

Note: cTNM is the clinical classification, pTNM is the pathologic classification. The y prefix is used for those cancers that are classified after neoadjuvant pretreatment (eg, ypTNM). Patients who have a complete pathologic response are ypT0N0cM0 that may be similar to Stage Group 0 or I. The r prefix is to be used for those cancers that have recurred after a disease-free interval (rTNM).

*Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (Any TN1 M0 and Any T N2 M0). MAC is the modified Astler-Coller classification.

The numbers below come from the National Cancer Institute's SEER database, looking at people diagnosed with colon cancer between 2004 and 2010.

Stage	5-year Relative Survival Rate
I	92%
IIA	87%
IIB	63%*
IIIA	89%*
IIIB	69%
IIIC	53%
IV	11%

*These numbers are correct : patients with stage IIIA or IIIB cancers have better survival than those with stage IIB cancers.

These statistics are based on a previous version of the staging system. In that version, there was no stage IIC (those cancers were grouped considered stage IIB). Also, some cancers that are now considered stage IIIC were classified as stage IIIB, while some other cancers that are now considered stage IIIB were classified as stage IIIC.

Survival rates for rectal cancer, by stage

The numbers below come from the National Cancer Institute's SEER database, looking at people diagnosed with rectal cancer between 2004 and 2010.

Stage	5-year Relative Survival Rate
I	87%
IIA	80*%
IIB	49*%
IIIA	84%
IIIB	71%
IIIC	58%
IV	12%

*These numbers are correct; survival was better for some stage III cancers than for some stage II cancers.

Recurrent and Metastatic Disease: outcomes

- Patients to receive nonsurgical treatment do not survive 5 years
- 30% 1 year
  - 8% 2 years
    - 1% 4 years

Recurrent and Metastatic Disease :outcomes

- Surgery only form of treatment that is potentially curative (R0 resection)
- 50% patients with local recurrence have mets
- Demanding surgery

Surgery for nodal recurrences

After curative resection for CRC:

20% develop locoregional recurrence

10% will have disease in retroperitoneum

1-2% isolated nodal recurrence

1. Surgery for nodal recurrences

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EJSO
the Journal of Cancer Surgery

EJSO 40 (2014) 739–746

www.ejso.com

CrossMark

Long-term outcomes following resection of retroperitoneal recurrence of colorectal cancer

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Accepted 9 October 2013
Available online 1 November 2013

1. Surgery for nodal recurrences

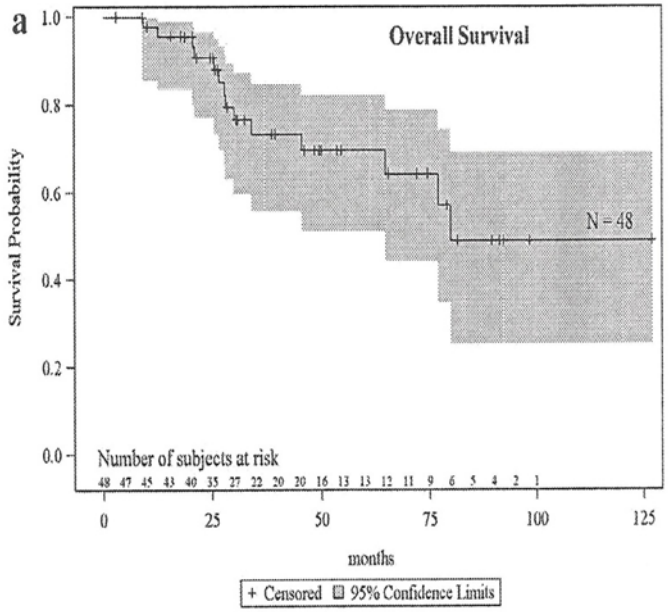

Figure 2a. Overall survival of the whole cohort ($n = 48$).

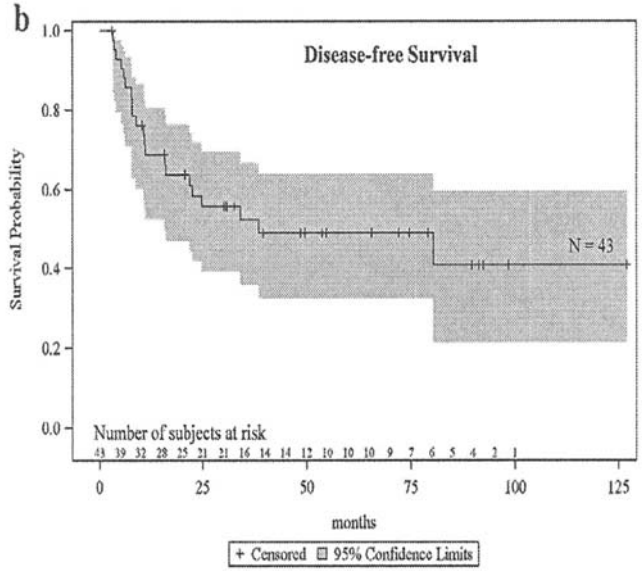

Figure 2b. Disease-free survival of patients without gross residual disease after RPR surgery ($n = 43$).

1. Surgery for nodal recurrences

Systematic review HO,Mack,Temple 2011

110 patients : series from 1993-2010

median survival 34-44 months'
median DFS 17-21 months

Too heterogeneous for prime time

2. Local recurrence & locally advanced disease

Radiological criteria[a]	Compartment[b]	Median value[c]	Mean	SD	Importance value 1–3, %
Anterior tumor involving the uterus	Ant	1.0	1.2	0.60	100
Ovary or fallopian tube involvement	Ax	1.0	1.2	0.48	100
Anterior tumor involving the bladder	Ant	1.0	1.2	0.61	100
Anal canal involvement	Ax	1.0	1.2	0.56	100
Central tumor involving the anastomosis	Ax	1.0	1.3	0.84	97.0
Small-bowel involvement	Others	1.0	1.3	0.53	100
Anterior tumor involving the seminal vesicles	Ant	1.0	1.4	0.90	97.0
Involvement of the perineum	Ant	1.0	1.5	0.71	100
Anterior tumor involving the vagina	Ant	1.0	1.6	1.20	90.9
Levator ani involvement	Ant/Ax/Post	1.0	1.6	1.09	93.9
Anterior tumor involving the prostate	Ant	1.0	1.6	0.90	97.0
Single site of disease in the pelvis	Others	1.0	1.6	0.97	97.0
Posterior tumor involving the sacrum S3 and below	Post	1.0	1.8	1.09	90.9
Single-site pelvic disease with increased activity on PET	Others	1.0	1.9	1.48	84.8
Involvement of the urethra	Ant	2.0	2.0	1.19	87.9
Lateral tumor involving the pelvic ureter	Lat	2.0	2.1	1.57	90.9
Posterior tumor involving the presacral fascia	Post	2.0	2.4	1.73	81.8
Central tumor with nodal recurrence	Ax	2.0	2.6	1.98	78.8
Diagnostic quality of the MRI	Others	2.0	2.6	2.06	72.7
Internal iliac node involvement	Lat	3.0	3.1	1.84	69.7
Lateral tumor involving the internal iliac artery	Lat	3.0	3.1	1.68	63.6
Pelvic disease without increased activity on PET	Others	3.0	3.1	2.18	63.6
Lateral tumor involving the internal iliac vein causing thrombosis	Lat	3.0	3.4	1.93	60.6
Common iliac node involvement	Lat	3.0	3.4	2.14	63.6
Size/bulk of disease in pelvis	Others	3.0	3.8	2.19	54.5
Posterior tumor involving the sacrum S2 and below	Post	3.0	3.8	2.55	57.6
External iliac node involvement	Lat	3.0	3.8	2.39	57.6
Lateral tumor involving the obturator internus muscle	Lat	3.0	3.9	1.63	51.5
Lateral tumor involving the piriformis muscle	Lat	3.0	4.1	1.85	51.5
Anterior tumor involving the symphysis pubis or pubic rami	Ant	4.0	4.2	2.36	45.5
Greater than 1 site of disease in the pelvis	Others	4.0	4.5	2.45	48.5
Lateral tumor involving the ileum	Lat	4.0	4.7	2.88	42.4
Lateral tumor involving the external iliac artery	Lat	5.0	4.8	2.46	33.3
Inguinal node involvement	Others	5.0	4.9	2.75	39.4
Lateral tumor involving the external iliac vein causing thrombosis	Lat	5.0	5.1	2.66	39.4
Lateral tumor involving the ischium	Lat	5.0	5.1	2.45	30.3
Posterior tumor involving the sacral nerves	Post	5.0	5.5	2.81	30.3
Multifocal pelvic disease with increased activity on PET	Others	5.0	5.7	2.36	21.2
Posterior tumor involving the sacrum S1 and below	Post	7.0	6.1	2.80	24.2
Metastatic disease with increased activity on PET	Others	5.0	6.3	2.23	6.1
Lateral tumor involving the sciatic nerve or nerve roots	Lat	6.0	6.3	2.46	15.2

[a]All criteria are MRI criteria, unless otherwise stated as PET.
[b]Ant = anterior compartment: bladder, prostate, seminal vesicles, vas deferens, urethra, anterior half of vagina, pelvic bone (pubic symphysis, superior and inferior pubic rami), and anterior pelvic floor; Ax = central/axial compartment: posterior half of vagina, uterus, ovaries, fallopian tubes, rectum, anal canal and pelvic floor, lower sacrum (S4 down), coccyx, and pelvic floor muscle; Post = posterior compartment: pelvic bone (sacrum and coccyx) posterior pelvic floor, internal iliac vessel branches, piriformis muscle, and sacral nerves S1 to S4; Lat = lateral compartment: ureter, internal iliac vessels, external iliac vessels, ischium including tuberosity and spine, ischium muscles and ligamentous attachments, lumbosacral trunk, obturator nerve and vessels; Others = factors other than tumor involvement in the compartments listed above.
[c]Criteria were ranked on a scale of 1 to 9. A criterion considered "definitely important" was ranked with a value of 1, a criterion considered "undecided" was ranked with a value of 5, whereas a criterion considered "definitely not important" was ranked with a value of 9.

Clinical, MRI, and PET-CT Criteria Used by Surgeons to Determine Suitability for Pelvic Exenteration Surgery for Recurrent Rectal Cancers: A Delphi Study.

Chew, Min-Hoe; Brown, Wendy; Masya, Lindy; Harrison, James; Myers, Eddie; Solomon, Michael

Diseases of the Colon & Rectum. 56(6):717-725, June 2013.
DOI:

2. Local recurrence & locally advanced disease

Clinicopathological criteria	Characteristic	Median value*	Mean	SD	Importance value 1–3, %
Ascites	Clinical	1.0	1.41	0.83	97.3
Jaundice	Clinical	1.0	1.49	1.43	94.6
Portal hypertension	Clinical	1.0	1.5	0.93	91.2
Cognitive impairment	Social	1.0	1.8	0.99	97.1
Renal failure treated by hemodialysis	Clinical	1.0	1.8	1.42	88.2
Cachexia	Clinical	1.0	1.8	1.68	91.9
History of pain	Presenting symptom	1.0	1.9	1.58	88.2
History of leg swelling	Presenting symptom	1.0	1.9	1.51	88.2
Lateral pelvic recurrence	Clinical	1.0	2.0	2.08	91.2
Bilateral or unilateral leg weakness with sensory deficit	Presenting symptom	1.0	2.0	1.63	89.2
Unable to consent because of poor comprehension	Social	1.0	2.0	1.71	89.2
Pelvic bone pain (sacrum/coccyx/hip)	Presenting symptom	1.0	2.1	1.78	88.2
ASA grade	Clinical	2.0	2.1	1.54	91.9
Isolated localized recurrence after previous exenteration surgery	Clinical	1.0	2.2	1.93	85.3
Fixed tumor to pelvic bone	Clinical	1.0	2.3	2.47	79.4
Circumferential pelvic tumor	Clinical	1.0	2.3	2.53	82.4
Anorexia and weight loss	Presenting symptom	2.0	2.5	1.29	76.5
Evidence of deep vein thrombosis	Clinical	3.0	2.7	1.73	91.2
Physically disabled	Social	2.0	2.9	2.22	70.6
Patient lives in a nursing home	Social	2.0	3.0	2.77	73.5
Resectable lung metastasis	Clinical	2.0	3.2	2.26	70.6
Resectable liver metastasis	Clinical	2.0	3.3	2.34	70.6
Age	Clinical	3.0	3.4	1.96	79.4
Posterior pelvic recurrence	Clinical	2.0	3.5	3.17	67.6
Smokes >30 cigarettes/d	Social	3.0	3.6	2.20	64.7
Previous hepatectomy for colorectal metastasis	Clinical	3.0	4.0	2.00	52.9
Mild to moderate liver disease (eg, fatty liver, hepatitis)	Clinical	4.0	4.2	1.75	44.1
Previous lung metastasectomy	Clinical	4.0	4.2	1.88	47.1
Mild to moderate pulmonary disease	Clinical	4.0	4.3	1.76	29.4
Mild to moderate cardiovascular disease	Clinical	4.0	4.6	1.96	35.3
Large fungating tumor to perineum	Clinical	4.0	4.7	3.31	38.2
Lack of caregiver or supportive family	Social	4.0	4.9	2.84	38.2
Intestinal fistula	Clinical	5.0	5.0	2.54	26.5
Poorly differentiated histology of the recurrence	Clinical	5.0	5.1	2.63	38.2
Bowel obstruction	Clinical	6.0	5.3	2.99	32.4
Asymptomatic recurrence (recurrence detected on routine follow-up)	Presenting symptom	8.0	5.5	3.69	38.2
Past history of other cancer	Clinical	6.0	5.7	2.37	20.6
Antiplatelet or anticoagulant therapy	Clinical	6.5	5.9	2.69	23.5
Preoperative serum CEA >20 ng/mL	Clinical	7.0	6.5	2.54	20.6

*Criteria were ranked on a scale of 1 to 9. A criterion considered "definitely important" was ranked with a value of 1, a criterion considered "undecided" was ranked with a value of 5, whereas a criterion considered "definitely not important" was ranked with a value of 9.

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2. Local recurrence & locally advanced disease

Contraindications to surgery

1. Poor performance status/medically unfit
2. Bilateral sciatic nerve invovlement
3. Circumferential bone involvement

2. Local recurrence & locally advanced disease

Relative Contraindications to surgery

1. Extension of tumour thru sciatic notch
2. Encasement
3. Circumferential bone involvement
4. Lateral pelvic side wall involvement
5. High sacral involvement S1/S2

2. Local recurrence & locally advanced disease

What are we offering?

1. Mortality 0.6%-5%
2. Morbidity 25%-100%
3. 5 year survival 20-60%

3. VISCERAL METASTESES

I can't figure out who is eligible for a liver resection!

Basingstoke index:

3 hepatic mets

Node positive primary

Poorly differentiated primary

Extrahepatic disease

Tumour > 5 cm

Worst 0.7 years

Best 7.4 years

3. VISCERAL METASTESES

I can't figure out who is eligible for a liver resection!

Absolute CI:

1. Liver failure
2. Unresectable extrahepatic disease
3. >70% liver involvement
4. Medically unfit
5. Biliary and hepatic outflow preserved

3. VISCERAL METASTESES

. Lung mets should be considered potentially resectable with or without liver mets

. Liver mets with hepatic nodes don't do well

. Delphi study done in Ontario showed very poor agreement between HPB surgeons in 8 scenarios

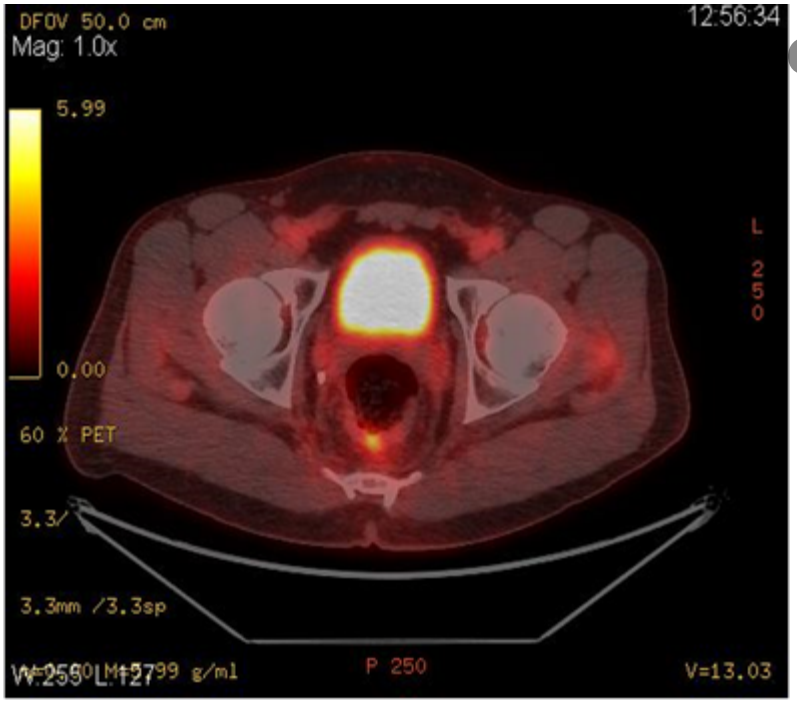
4. Advanced and Unresectable Disease

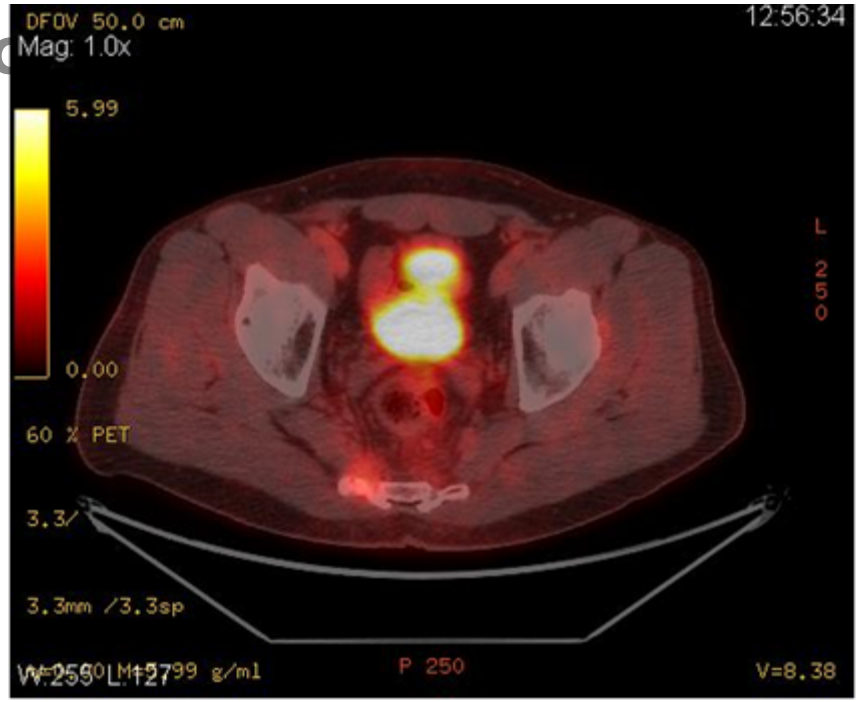
Neoadjuvant chemotherapy:

Who?

Neoadjuvant or adjuvant
Resectable or unresectable

4. Advanced and Unresectable Disease





4. Advanced and Unresectable Disease

Neoadjuvant chemotherapy:

Why?

- Micro metastases
- Evaluate chemo responsiveness
- Shrink tumour

4. Advanced and Unresectable Disease

IS chemo beneficial for patients with initially resectable liver mets?

Many studies no survival benefit
EORTC 40983 benefit

4. Advanced and Unresectable Disease

Can chemo convert unresectable to resectable?

50% potentially resectable become resectable with irinotecan or oxaliplatin based regimens

32% unresectable become resectable with FOLFIRI (16% with FOLFOX)

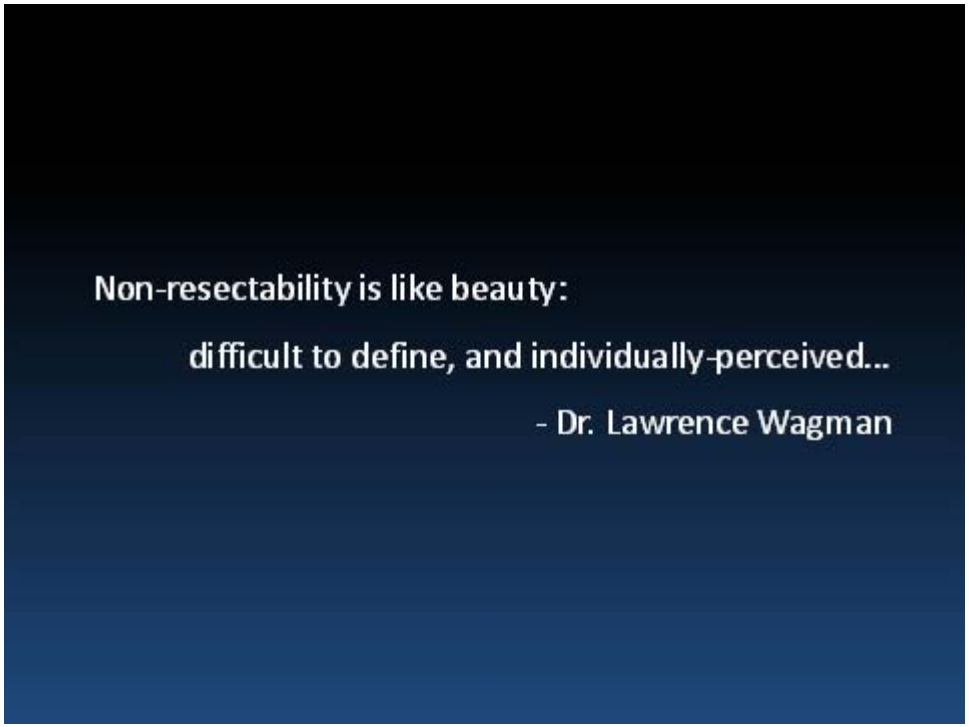
4. Advanced and Unresectable Disease

Role of biologics uncertain:

FOLFOXIRI : 28% histopathologic response

FOLOXIRI & bev: 63%

Management of Recurrent and Advanced Tumours: When are Tumours Resectable, and Multidisciplinary Management



Management of Recurrent and Advanced Tumours: When are Tumours Resectable, and Multidisciplinary Management

1. Advanced, recurrent and metastatic disease can be cured
2. Indications keep changing
3. Teams necessary
4. Few standard protocols
5. MDT conferences mainstay
6. Resource intense
7. M & M must be acceptable