COLORECTAL LIVER METASTASES – SYNCHRONOUS

1st Maastricht E-AHPBA Post-Graduate Course

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COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Detected in 15-25% of colorectal cancer cases
- Presumed to represent more aggressive disease

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 1:
  - Is there any evidence that these patients do worse after liver resection?

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Recent reviews:
  - Adam R et al
    Managing synchronous liver metastases from colorectal cancer: a multidisciplinary international consensus.
    Cancer Treat Rev 2015; 41: 729-41
  - Siriwardena AK et al
    Management of colorectal cancer presenting with synchronous liver metastases.
    Nature Reviews Clinical Oncology 2014; 11: 46-459

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Conclusion 1:
  - Although recommendations have been made for systemic chemotherapy before consideration of surgery, there is no hard evidence that patients with synchronous metastases do worse.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 2:
  - Should these patients have concurrent or staged liver resection?

YOKOHAMA EXPERIENCE

- 39 consecutive patients
- 39 concurrent – multivariate analysis for safety and success rate
- Risk factor for morbidity – volume of resected liver
  - 350g vs 150g ($p<0.05$)
- Poor overall survival with poorly differentiated and mucinous adenocarcinomas ($p<0.05$)

- Conclusion: 1 stage resection desirable except in patients over 70 years of age and those with poorly differentiated and mucinous adenocarcinomas

Tanaka K et al. Surgery 2004; 136: 650-9.

TOKYO EXPERIENCE

- 187 consecutive patients, 1980-2002
- 142 concurrent, 27 staged resections
- 21 clinicopathological factors analysed

- Prognosis affected by
  - multiple liver metastases
  - 4 or more lymph node metastases around the primary tumour

- Conclusion: Simultaneous resection in patients with 3 or less colorectal lymph node metastases only

Minigawa M et al (Makuuchi). Arch Surg 2006; 141: 1006-12.

STRASBOURG EXPERIENCE

- 97 consecutive patients (1987-2000)
- 35 concurrent vs 62 staged
- Concurrent resection if <4 unilobar metastases
- Morbidity 23% vs 32%
- Location of primary did not influence morbidity
- Overall survival:
  - 1yr 94% vs 92%
  - 3 yr 45% vs 45%
  - 5 yr 21% vs 22%

- Conclusion: Synchronous resection does not increase morbidity or mortality rates

Weber JC et al. (Jaeck) Br J Surg 2003; 90: 956-62.

BERLIN EXPERIENCE

- 219 consecutive patients (1988-2005)
- 40 concurrent vs 179 staged
- Concurrent resection if colon primary (p=0.004) and less extensive liver resection (p<0.001)
- Morbidity similar
- Mortality higher in concurrent group (p=0.012)
- Mortality in concurrent group (n=4) after major hepatectomy and age >70 yrs
- No significant difference in long-term survival

- Conclusion: decision should be based on age and extent of liver resection

Thelen A et al. (Neuhaus) Int J Colorectal Dis 2007; Feb 21 (Epub ahead of print).

MAYO CLINIC EXPERIENCE

- 96 consecutive patients (1986-1999)
- 64 concurrent vs 32 staged
- Perioperative morbidity 53% vs 41%
- Disease free survival 13 vs 13 months
- Overall survival 27 vs 34 months (p=0.52)

- Hospitalisation 11 vs 22 day (p<0.001)

Chua et al (Nagorney). Dis Colon Rectum 2004; 47: 1310-6

MSKCC EXPERIENCE

- 240 consecutive patients (1984-2001)
- 134 concurrent vs 106 staged
- Concurrent resection: more right colon primaries ($p<0.001$), smaller ($p<0.001$) and fewer ($p<0.001$) liver metastases, and less extensive liver resection ($p<0.001$)
- Complications: 49% vs 67% ($p<0.003$)
- Median 10 vs 18 days in hospital ($p<0.001$)
- Mortality n=3 vs n=3

- Conclusion: Simultaneous resection safe and efficient, with reduced morbidity and shorter treatment time

Martin R et al. (Blumgart) J Am Coll Surg 2003; 197: 233-42.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Conclusion 2:
  - Concurrent resection is preferable if safe and logistically possible.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 3:
  - If the liver metastases are borderline for surgery, is it reasonable to deal with them first?

‘Liver First’ Approach in the Treatment of Colorectal Cancer with Synchronous Liver Metastases

Gilles Mentha[a] Arnaud D. Roth[b] Sylvain Terraz[c] Emiliano Giostra[d]
Pascal Gervaz[a] Axel Andres[a] Philippe Morel[a] Laura Rubbia-Brandt[e]
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Departments of [a]Surgery, [b]Oncology, [c]Radiology, [d]Hepato-Gastroenterology, and [e]Pathology, University Hospitals of Geneva, Geneva, Switzerland

Dig Surg 2008;25:430–435

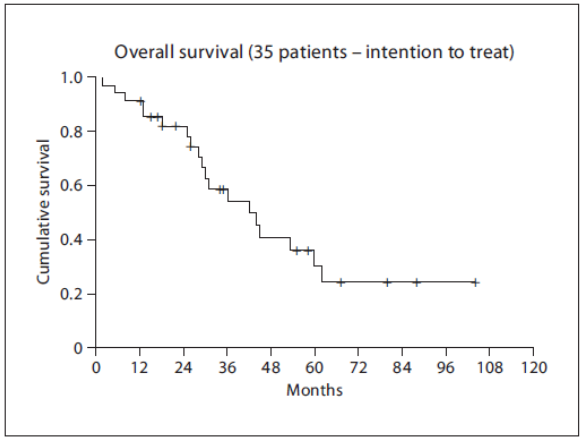

Fig. 1. Overall survival of all patients treated with the reverse strategy (intention to treat).

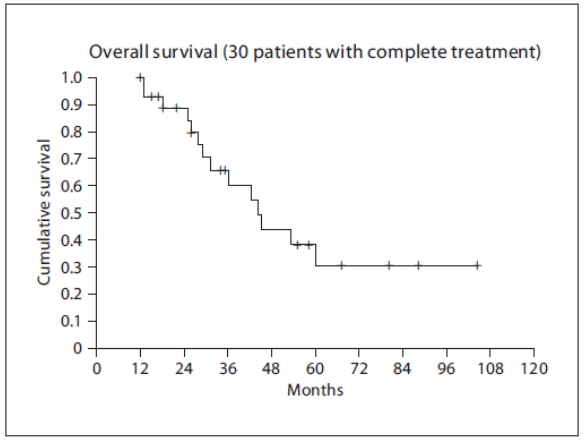

Fig. 2. Overall survival of the 30 patients who completed the treatment.

A Survival Analysis of the Liver-First Reversed Management of Advanced Simultaneous Colorectal Liver Metastases

A LiverMetSurvey-Based Study

Axel Andres, MD, Christian Toso, MD, PhD,* Rene Adam, MD, PhD,† Eduardo Barroso, MD,‡ Catherine Hubert, MD,§ Lorenzo Capussotti, MD,|| Eric Gerstel, MD,* Arnaud Roth, MD,* Pietro E. Majno, MD,* and Gilles Mentha, MD**

(*Ann Surg* 2012;256: 772–779)

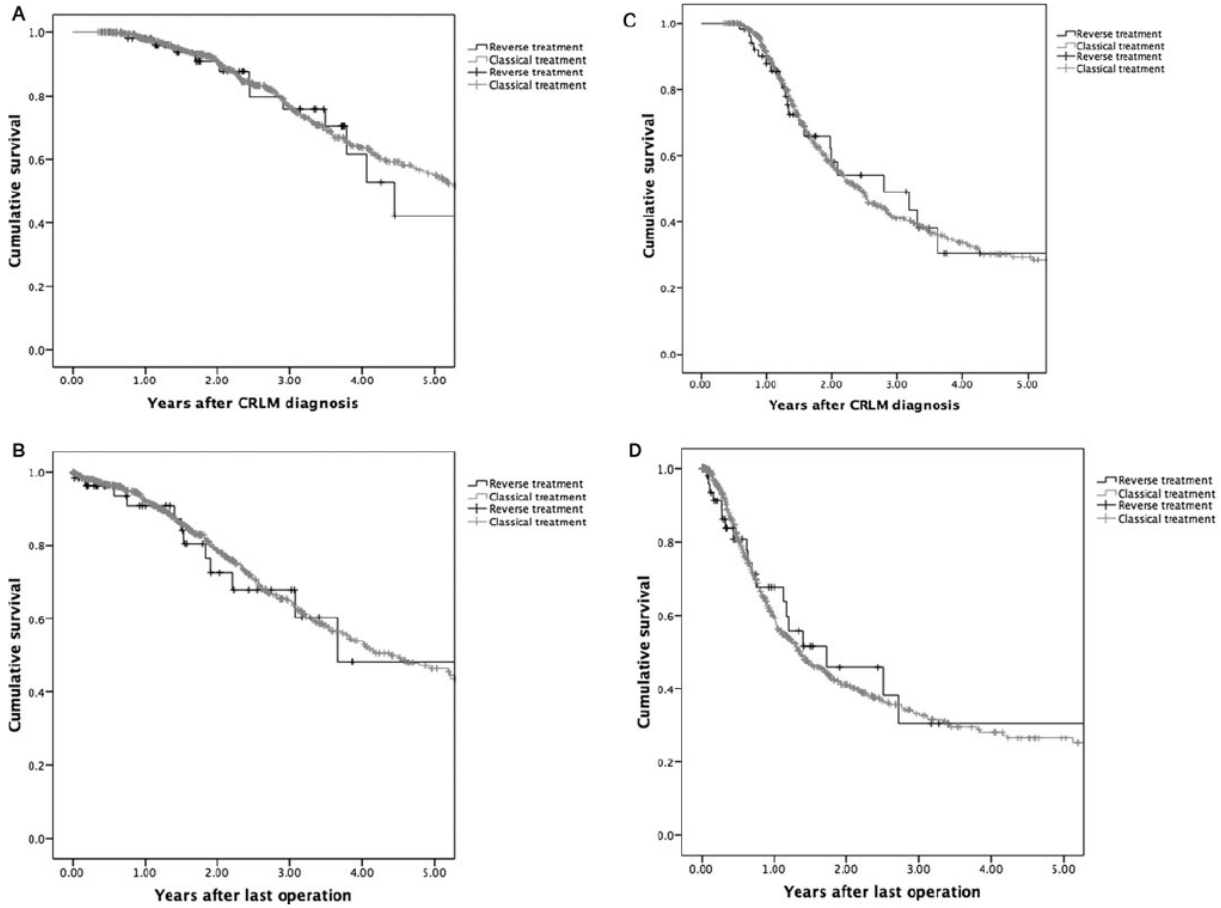

FIGURE 2. Kaplan-Meier survival curves depending on reversed or classical treatment groups. A, Overall survival after CRLM diagnosis, $P = 0.960$. B, Overall survival after the last operation, $P = 0.965$. C, Disease-free survival after CRLM diagnosis, $P = 0.992$. D, Disease-free survival after the last operation, $P = 0.839$.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Conclusion 3:
  - The results of the liver first approach are equivalent to the classical primary first approach.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 4:
  - Does the extent of resection needed influence outcomes?

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ANNALS OF SURGERY

A Monthly Review of Surgical Science and Practice Since 1885

Left Hepatic Trisectionectomy for Hepatobiliary Malignancy

Results and an Appraisal of Its Current Role

Hideki Nishio, MD, PhD, Ernest Hidalgo, MD, PhD, Zaed Z. R. Hamady, MRCS, Kadiyala V Ravindra, MCh, Anil Kotru, FRCS, Dowmitra Dasgupta, FRCS, Ahmed Al-Mukhtar, FRCS, K. Rajendra Prasad, MCh, FRCS, Giles J. Toogood, DM, FRCS, and J. Peter A. Lodge, MD, FRCS

Objective: To analyze results of 70 patients undergoing left hepatic trisectionectomy and to clarify its current role.

Summary Background Data: Left hepatic trisectionectomy remains a complicated hepatectomy, and few reports have described the long-term results of the procedure.

Methods: Short-term and long-term outcomes of 70 consecutive patients who underwent left hepatic trisectionectomy from January 1993 to February 2004 were analyzed.

Results: Of the 70 patients, 36 had colorectal liver metastasis, 24 had cholangiocarcinoma, 4 had hepatocellular carcinoma, and the remaining 6 had other tumors. Overall morbidity, 30-day and 90-day mortality rates were 46%, 7%, and 9%, respectively. Multivariate analysis disclosed that preoperative jaundice and intraoperative blood transfusion were positive independent predictors for postoperative morbidity; however, there were no independent predictors for postoperative mortality. Postoperative morbidity (87% versus 35%, $P < 0.001$) and mortality (20% versus 5%, $P = 0.108$) were observed more frequently in patients with preoperative obstructive jaundice than in those without jaundice. Each survival according to tumor type was acceptable compared with reported survivals. Survival for patients with colorectal liver metastasis undergoing left hepatic trisectionectomy with concomitant partial resection of the remnant liver was similar to those without this concomitant procedure. This concomitant procedure was not associated with postoperative morbidity and mortality.

Conclusions: Left hepatic trisectionectomy remains a challenging procedure. Preoperative obstructive jaundice considerably increases perioperative risk. Concomitant partial resection of the remaining liver appears to be safe and offers the potential for cure in patients with colorectal metastasis affecting all liver segments.

(*Ann Surg* 2005;242: 267–275)

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Left hepatic trisectionectomy (resection of hepatic segments 2, 3, 4, 5, and 8 ± 1) was first described in detail by Starzl as left hepatic trisegmentectomy in 1982[1] and has recently been renamed.[2] This procedure has enabled the resection of advanced tumors with curative intent. Despite advances in surgical technique and perioperative management,[3–7] it remains the most challenging of the major anatomic hepatectomies with higher complication rates than other hepatic resection,[8,9] and worldwide experience remains small. Although several authors have focused on this complicated hepatectomy,[3,4,10–13] few reports have described the results of large series[14] and long-term follow-up has rarely been considered.[13] In this study, we analyze perioperative features and long-term outcome of 70 consecutive patients undergoing left hepatic trisectionectomy in our hepatobiliary unit.

This is the largest series reported to date, and we consider predictive factors for morbidity and mortality, follow-up data, and present an appraisal of the current role of this difficult procedure.

MATERIALS AND METHODS

From January 1993 to February 2004, 756 hepatectomies (right-sided hepatectomy, $n = 362$; left-sided hepatectomy, $n = 126$; central hepatectomy, $n = 3$; sectionectomy or less, $n = 265$) have been performed in the HPB and Transplant Unit at St. James's University Hospital in Leeds, UK. Of the 756 patients, 70 (9%) underwent left hepatic trisectionectomy and were enrolled in this study; 69 of the 70 patients were operated on by the senior author (J.P.A.L.). There were 41 male and 29 female patients with a mean age of 57 years, ranging from 30 to 76 years. One of the 70 patients underwent the left hepatic trisectionectomy using the ante-situm technique[15] and the remaining 69 patients underwent resection in standard fashion.

Inevitably, operative techniques have developed with increasing experience. Currently, our technique is as follows,

Right Hepatic Trisectionectomy for Hepatobiliary Diseases

Results and an Appraisal of Its Current Role

Kartim J. Halazun, MRCS, Ahmed Al-Mukhtar, FRCS, Amer Aldouri, MRCS, Hassan Z. Malik, MD, FRCS, Magdy S. Attia, MD, MS, FRCS, K. Rajendra Prasad, MS, FRCS, Giles J. Toogood, DM, FRCS, and J. Peter A. Lodge, MD, FRCS

Objective: To assess the results of 275 patients undergoing right hepatic trisectionectomy and to clarify its current role.

Summary Background Data: Right hepatic trisectionectomy is considered one of the most extensive liver resections, and few reports have described the long-term results of the procedure.

Methods: Short- and long-term outcomes of 275 consecutive patients who underwent right hepatic trisectionectomy from January 1993 to January 2006 were analyzed.

Results: Of the 275 patients, 160 had colorectal metastases, 49 had biliary tract cancers, 20 had hepatocellular carcinomas, 20 had other metastatic tumors, and 12 had benign diseases. Fourteen of the 275 patients underwent right hepatic trisectionectomy as part of auxiliary liver transplantation for acute liver failure and were excluded. Concomitant procedures were carried out in 192 patients: caudate lobectomy in 45 patients, resection of tumors from the liver remnant in 57 patients, resection of the extrahepatic biliary tree in 45 patients, and lymphadenectomy in 45 patients. One-, 3-, 5-, and 10-year survivals were 74%, 54%, 43%, and 36%, respectively. Overall hospital morbidity and 30-day and in-hospital mortalities were 41%, 7%, and 8%, respectively. Survivals for individual tumor types were acceptable, with 5-year survivals for colorectal metastasis and cholangiocarcinoma being 38% and 32%, respectively. Multivariate analysis disclosed the amount of intraoperative blood transfusion to be the sole independent predictor for the development of hospital morbidity. Age over 70 years, preoperative bilirubin levels, and the development of postoperative renal failure were found to be independent predictors of long-term survival.

Conclusion: Right hepatic trisectionectomy remains a challenging procedure. The outcome is not influenced by additional concomitant resection of tumors from the planned liver remnant. Caution must be taken when considering patients older than 70 years for such resections.

(*Ann Surg* 2007;246: 1065–1074)

From the HPB and Transplant Unit, St. James's University Hospital, Leeds, United Kingdom.

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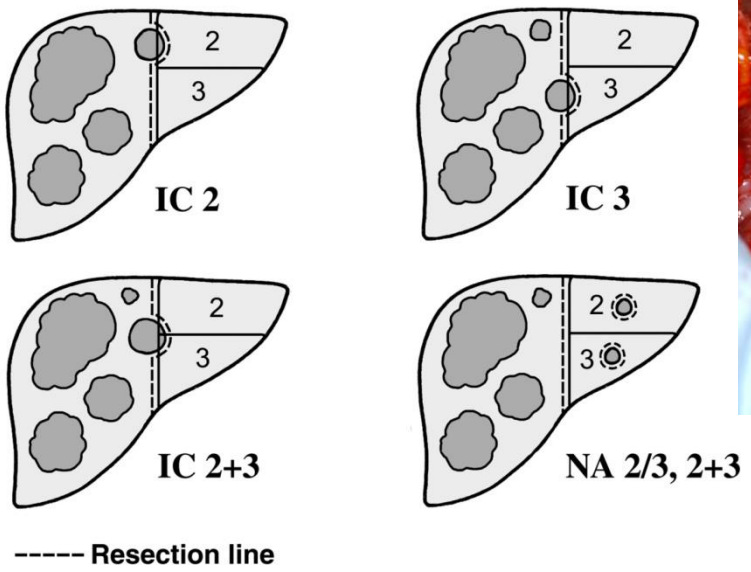
DOI: 10.1097/SLA.0b013e3181492795

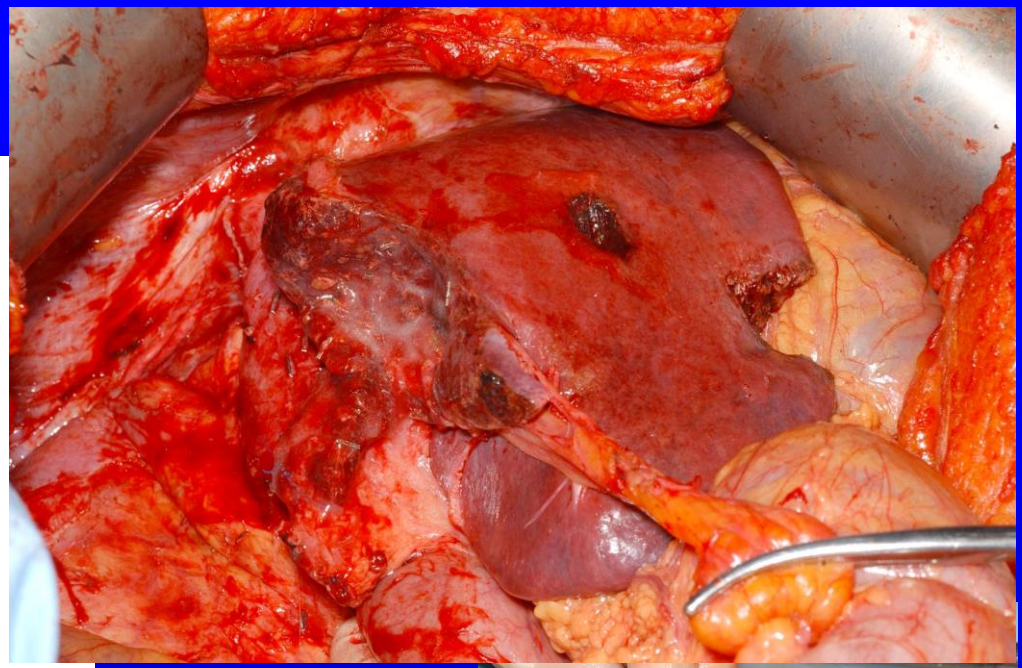
Liver resection remains the mainstay of treatment for neoplastic disease of the liver. The safety and long-term survival results being reported in the literature for hepatic resections are continually improving,[1–6] mainly as a result of improved surgical techniques and pre-, intra-, and postoperative critical care management of patients. As such, an increasing number of centers are taking more aggressive approaches toward the treatment of patients with primary and secondary hepatic malignancies. Right hepatic trisectionectomy (resection of segments 4, 5, 6, 7, 8 ± 1) was first described by Lortat-Jacob et al as right hepatic lobectomy in 1952,[7] and in detail by Starzl et al as right trisegmentectomy in 1980.[8] The procedure has recently been renamed because of international confusion in nomenclature: terms such as extended right hepatectomy have become ill-defined.[9] It remains a procedure used in few highly specialized units primarily for the treatment of extensive and advanced hepatic or biliary disease. Despite the advances in surgical and anesthetic techniques made in recent years, this procedure is still thought to be associated with higher rates of morbidity and mortality than other resections. This is mainly attributable to the aggressive nature of the (usually malignant) disease being treated, but may also be related to the extent of liver volume being resected, estimated at approximately 80% by several authors.[8–11] There are, however, no large series that report on the overall and long-term outcomes after right hepatic trisectionectomy, making it extremely difficult to accurately determine the efficacy and safety of this procedure. The objective of this study was therefore to analyze the results of all right hepatic trisectionectomies performed at a single Hepato-Pancreato-Biliary (HPB) unit, and to describe the operative technique used by our surgeons. In addition to assessing long-term outcome, this study also investigates factors affecting morbidity and overall survival, and provides a critical appraisal for the role of right hepatic trisectionectomy in current clinical practice.

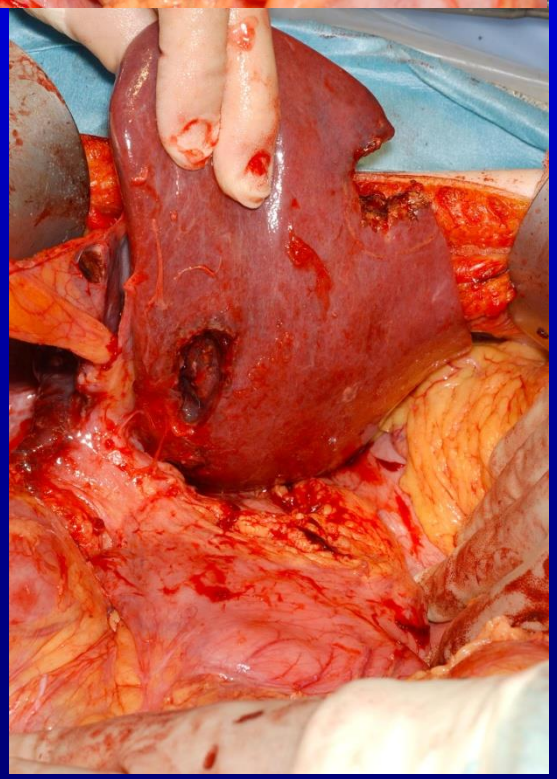
PATIENTS AND METHODS

Between January 1993 and January 2006, 997 liver resections, and 1288 liver transplants were performed in the HPB and Transplant Unit at St James's University Hospital in Leeds, United Kingdom. The resections were in summary: right-sided hepatectomy, n = 455; left-sided hepatectomy, n = 146; central

Figure 1







In-contiguity and non-anatomical extension of right hepatic trisectionectomy for liver metastases

J. P. A. Lodge, K. V. Menon, S. W. Fenwick, K. R. Prasad and G. J. Toogood

British Journal of Surgery 2005; **92**: 340–347

Right Hepatic Trisectionectomy for Hepatobiliary Diseases

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Annals of Surgery • Volume 246, Number 6, December 2007

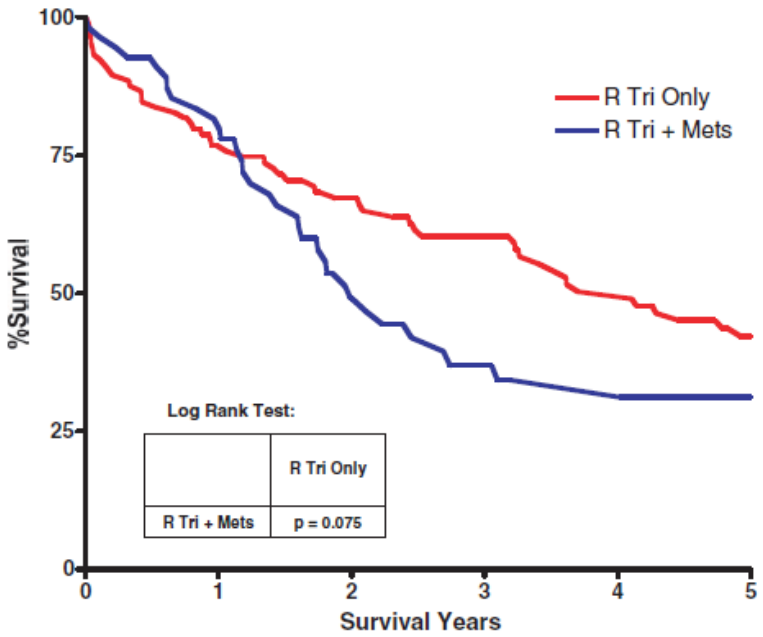
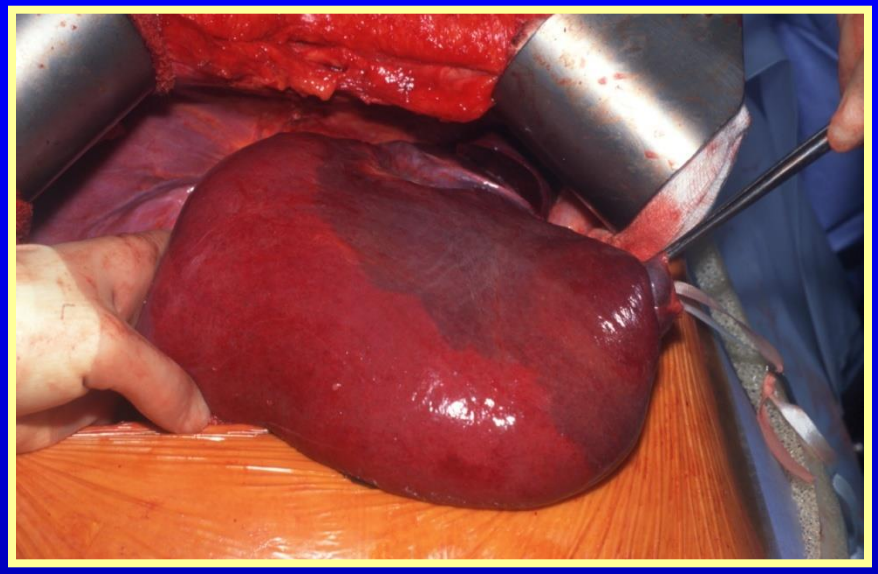
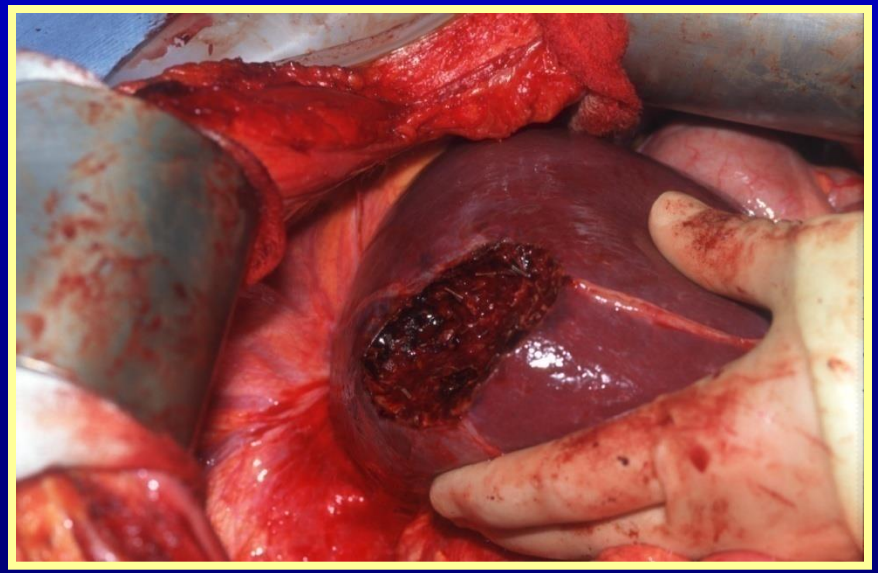
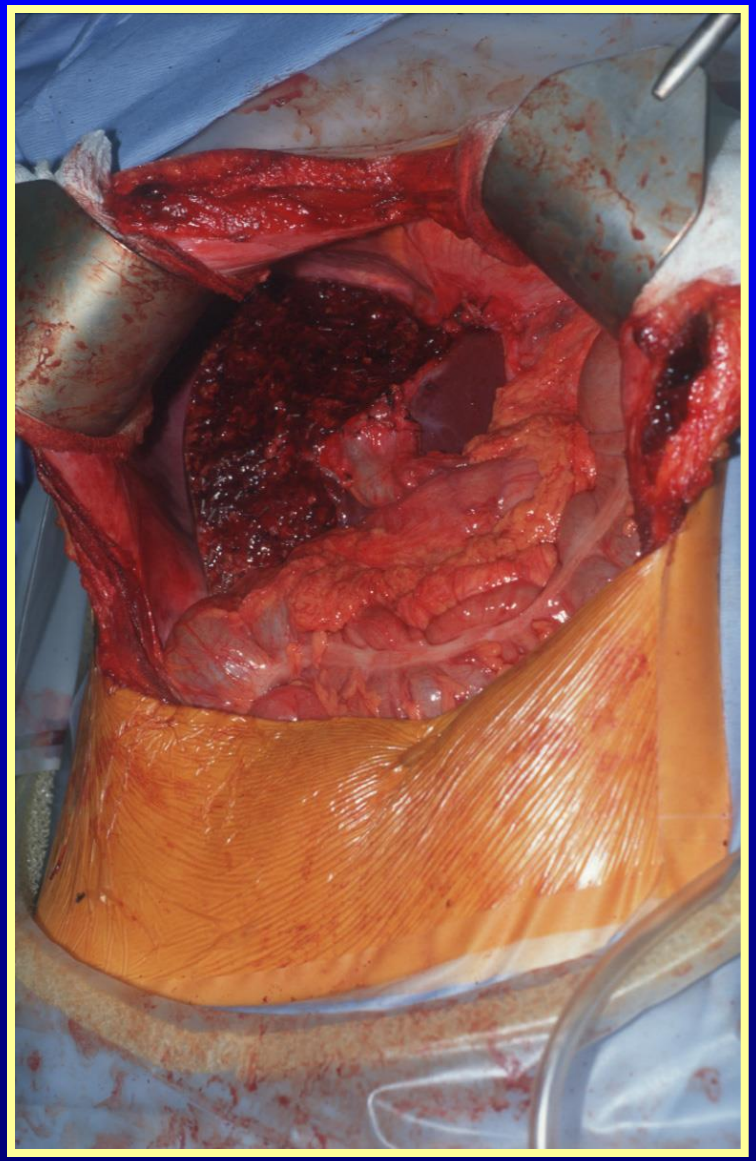


FIGURE 6. Kaplan-Meier survival curves for patients with colorectal liver metastases who underwent right hepatic trisectionectomy only (R Tri only) versus those who had a right hepatic trisectionectomy and metastasectomy from the liver remnant (R Tri + Mets).

LEFT TRISECTIONECTOMY WITH METASTASECTOMY







Left Hepatic Trisectionectomy for Hepatobiliary Malignancy

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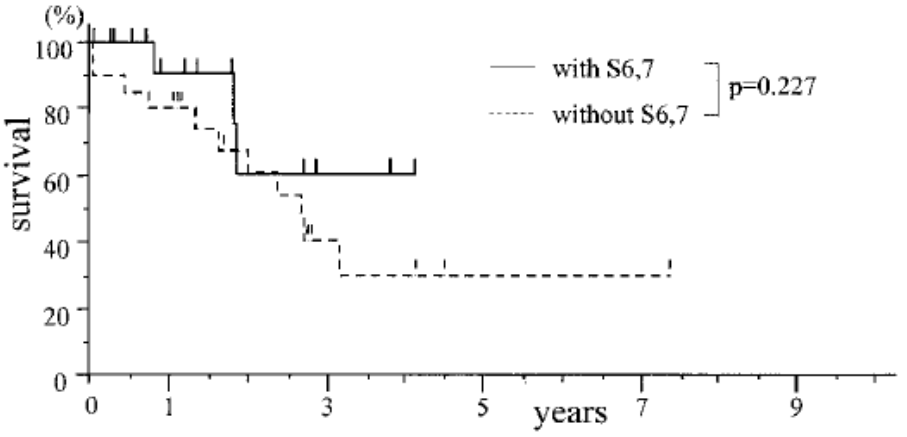
(*Ann Surg* 2005;242: 267–275)

B

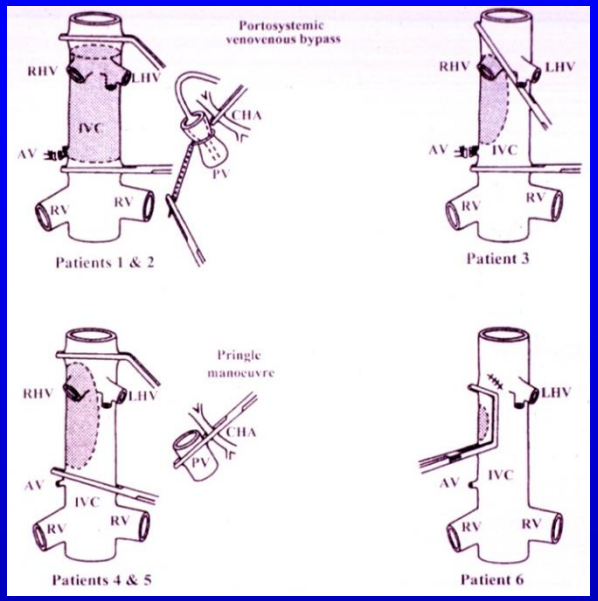


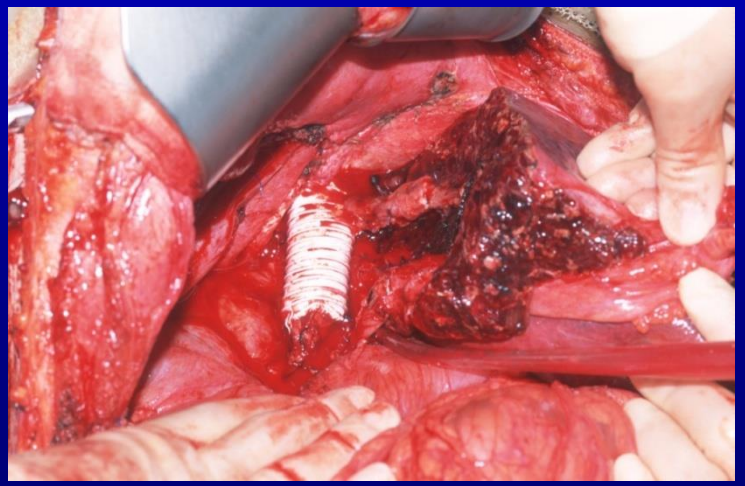
No. at risk (survival rate)					*Median survival (months)*
with S6,7	16	9 (91%)	2 (61%)		-
without S6,7	20	16 (80%)	4 (41%)	1 (31%)	32

HEPATIC RESECTION

Hepatic ischaemia techniques

- Pringle manoeuvre
  - Intermittent
  - Continuous
- Hepatic vascular exclusion
- In situ hypothermic perfusion
- Ante situm procedure
- Ex vivo hepatic resection

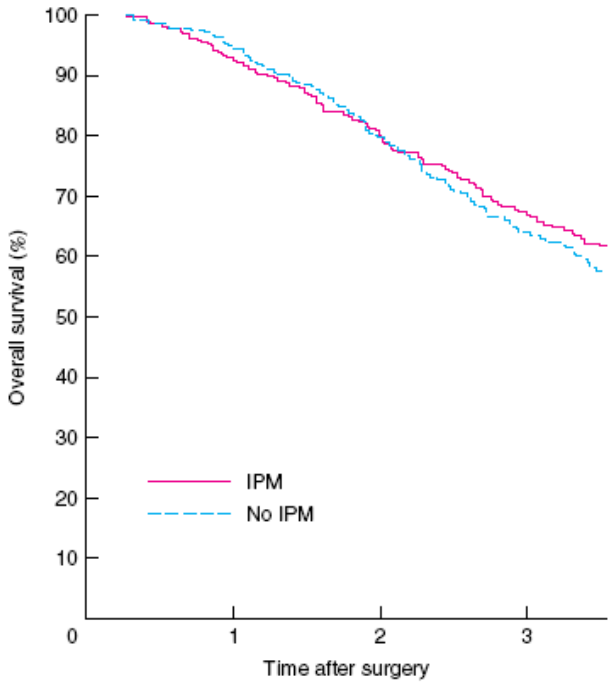




Intermittent Pringle manoeuvre is not associated with adverse long-term prognosis after resection for colorectal liver metastases

K. H. V. Wong, Z. Z. R. Hamady, H. Z. Malik, R. Prasad, J. P. A. Lodge and G. J. Toogood

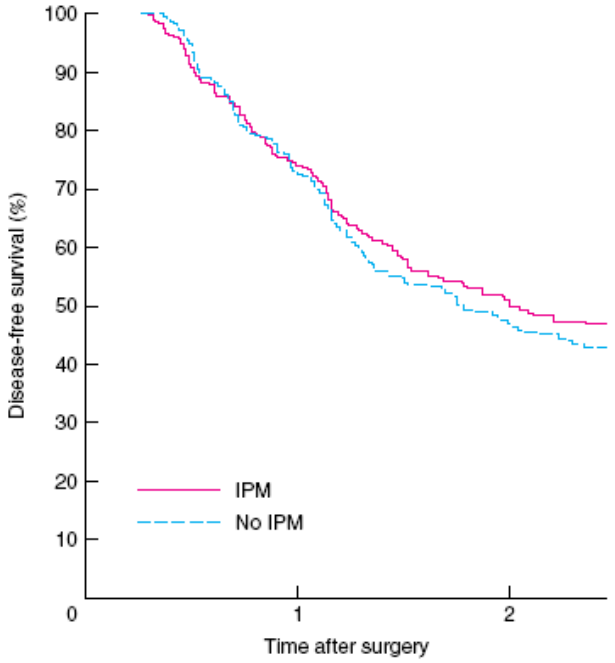
British Journal of Surgery 2008; **95**: 985–989



No. at risk

IPM	289	227	165	120
No IPM	274	234	180	124

Fig. 1 Overall survival in patients who had an intermittent Pringle manoeuvre (IPM) and those who did not ($P = 0{\cdot}406$, log rank test)



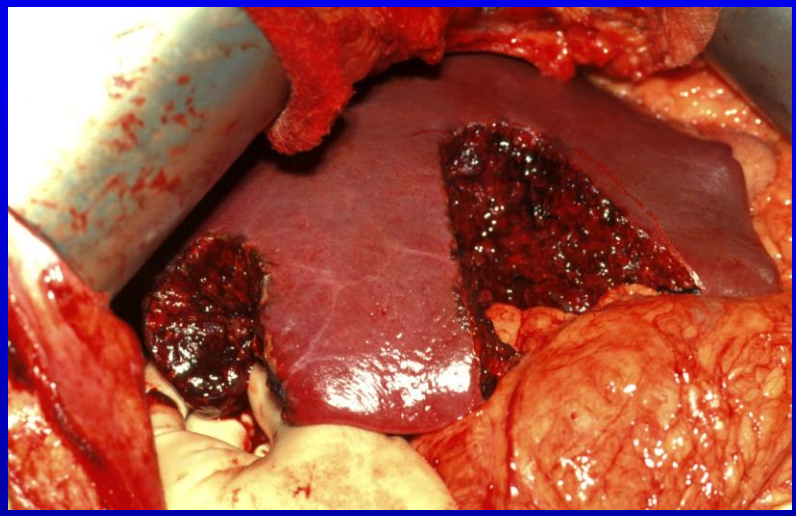
No. at risk

IPM	289	156	84
No IPM	274	153	84

Fig. 2 Disease-free survival in patients who had an intermittent Pringle manoeuvre (IPM) and those who did not ($P = 0{\cdot}199$, log rank test)

Surgical strategy for liver

- New developments
  - Extending resection outside accepted anatomical boundaries
  - Multi-stage hepatic resection
  - Redefining operability



Effect of type of resection on outcome of hepatic resection for colorectal metastases

R. J. B. Finch, H. Z. Malik, Z. Z. R. Hamady, A. Al-Mukhtar, R. Adair, K. R. Prasad, J. P. A. Lodge and G. J. Toogood

Hepatobiliary and Transplant Unit, St James's University Hospital, Beckett Street, Leeds LS9 7TF, UK
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British Journal of Surgery 2007; 94: 1242–1248

LEEDS DATA

January 1993-December 2003

494 consecutive patients - assessed in January 2006

Actuarial survival:	1 year	82%
	3 years	58%
	5 years	44%
	10 years	36%

- New data – the 1 cm clearance rule needs to be reappraised: If clearance is achieved, the resection margin alone has no influence on survival or recurrence rate: 1mm is enough

Hamady et al (Lodge) Eur J Surg Oncol 2006; 32: 557-563

One-Millimeter Cancer-Free Margin Is Curative for Colorectal Liver Metastases

A Propensity Score Case-Match Approach

Zaed Z. R. Hamady, PhD, FRCS,† J. Peter A. Lodge, MD, FRCS,† Fenella K. Welsh, FRCS,* Giles J. Toogood, DM, FRCS,† Alan White, MRCS,† Timothy John, FRCS,* and Myrddin Rees, FRCS**

(*Ann Surg* 2014;259:543–548)

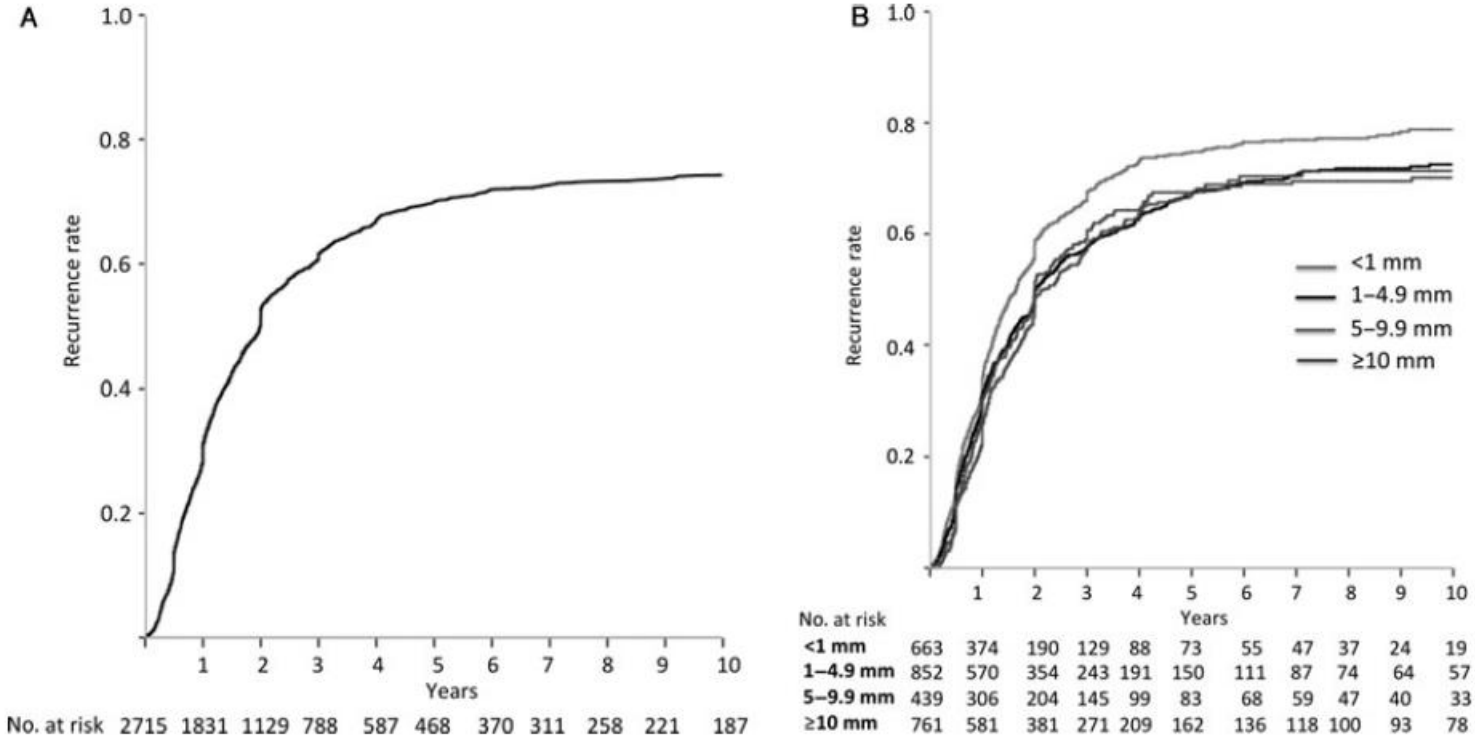


FIGURE 1. A, Kaplan-Meier curve of overall disease recurrence rates for 2715 patients after potentially curative resection for colorectal liver metastases. B, Kaplan-Meier curve of overall disease recurrence for 2715 patients after resection of colorectal liver metastases stratified by resection margin clearance status. The wider-margin groups showed similar trend of disease recurrence, which is significantly less than the narrow-margin group.

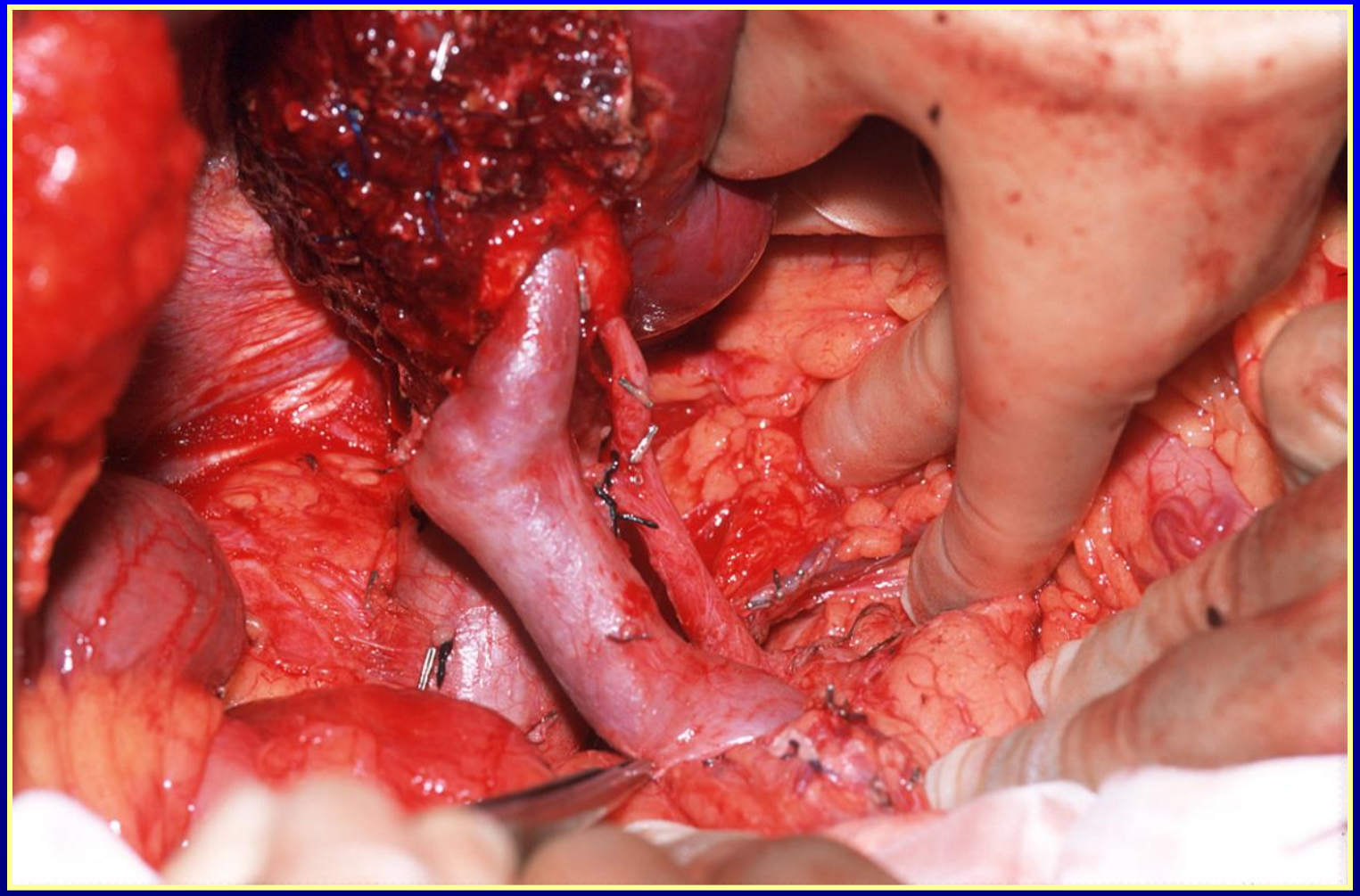
COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Conclusion 4:
  - The extent of resection needed has not significantly influenced outcomes as long as negative margins were achieved.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 5:
  - What should we do if lymph nodes are involved?

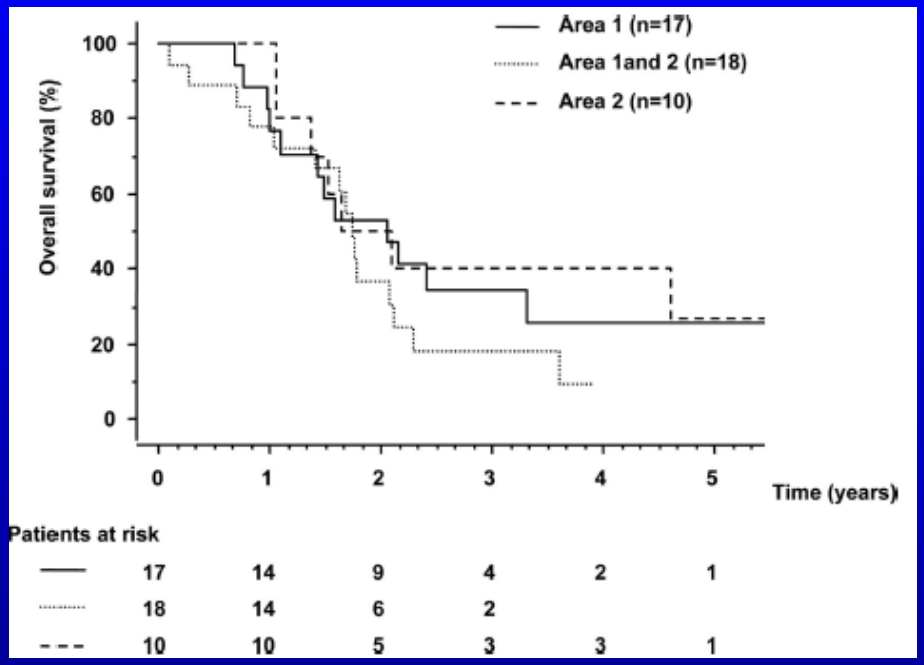
LYMPHADENECTOMY

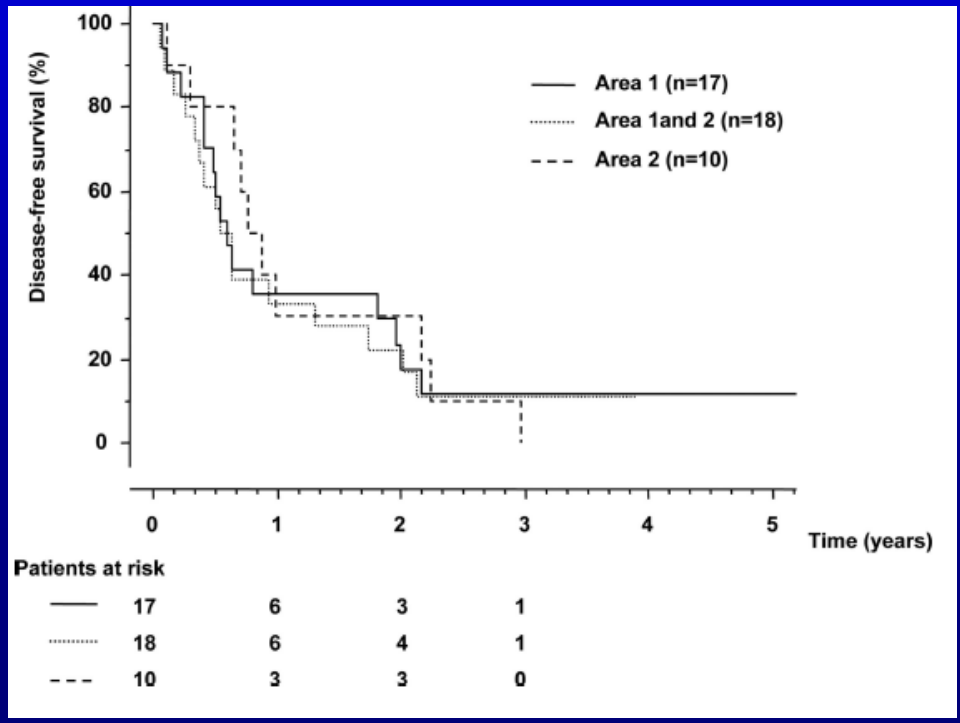


Long-Term Survival After Liver Resection for Colorectal Liver Metastases in Patients With Hepatic Pedicle Lymph Nodes Involvement in the Era of New Chemotherapy Regimens

Elie Oussoultzoglou, MD, Benoit Romain, MD, Fabrizio Panaro, MD, Edoardo Rosso, MD, Patrick Pessaux, MD, PhD, Philippe Bachellier, MD, and Daniel Jaeck, MD, PhD, FRCS

(*Ann Surg* 2009;249: 879–886)





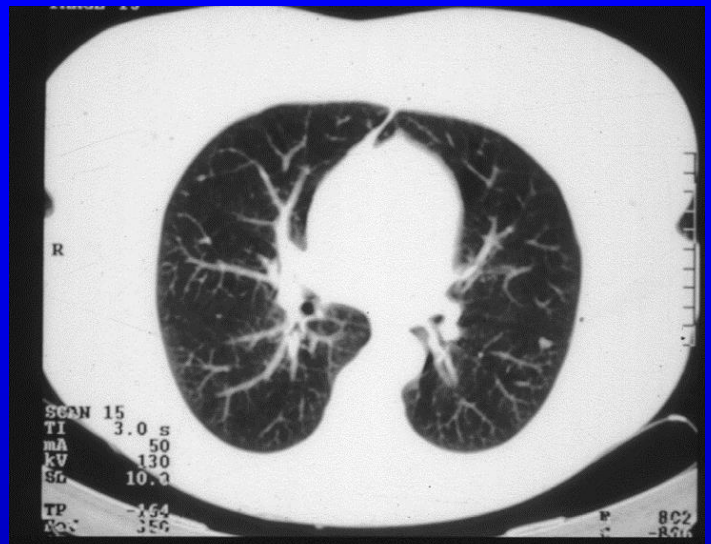
COLORECTAL LIVER METASTASES - SYNCHRONOUS

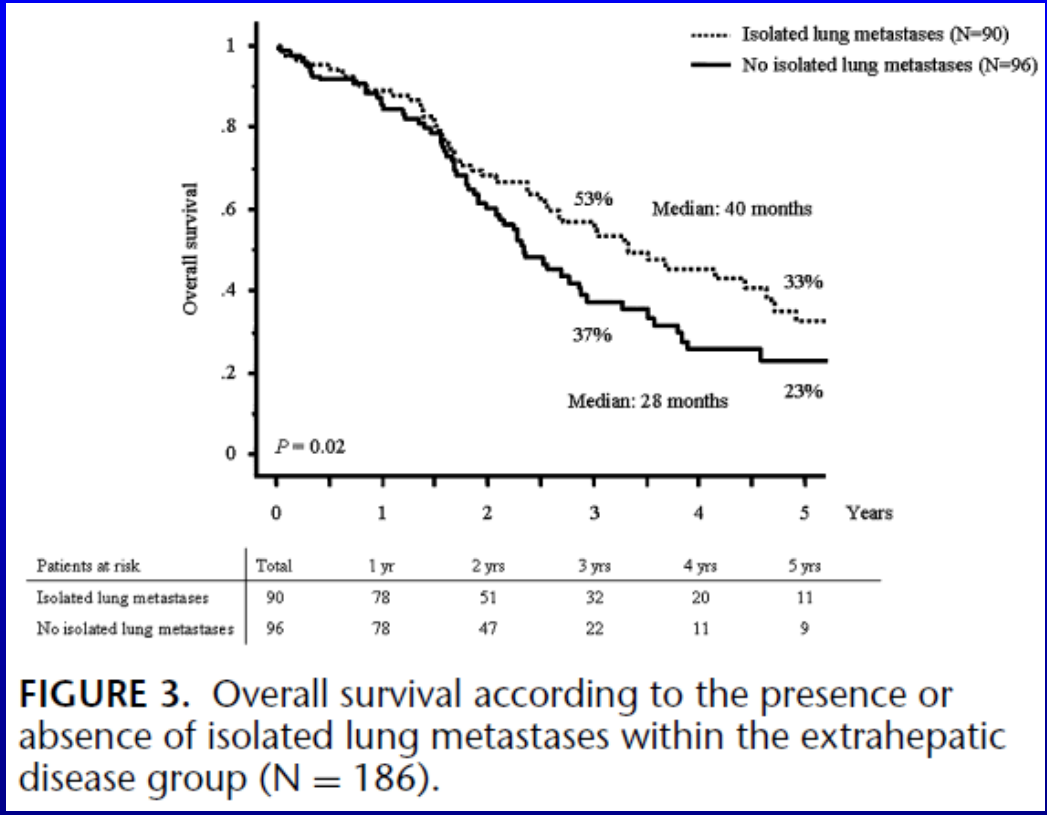
- Conclusion 5:
  - In selected cases, regional lymphadenectomy should be considered.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 6:
  - What should we do if there are simultaneous lung metastases?

LUNG METASTASES





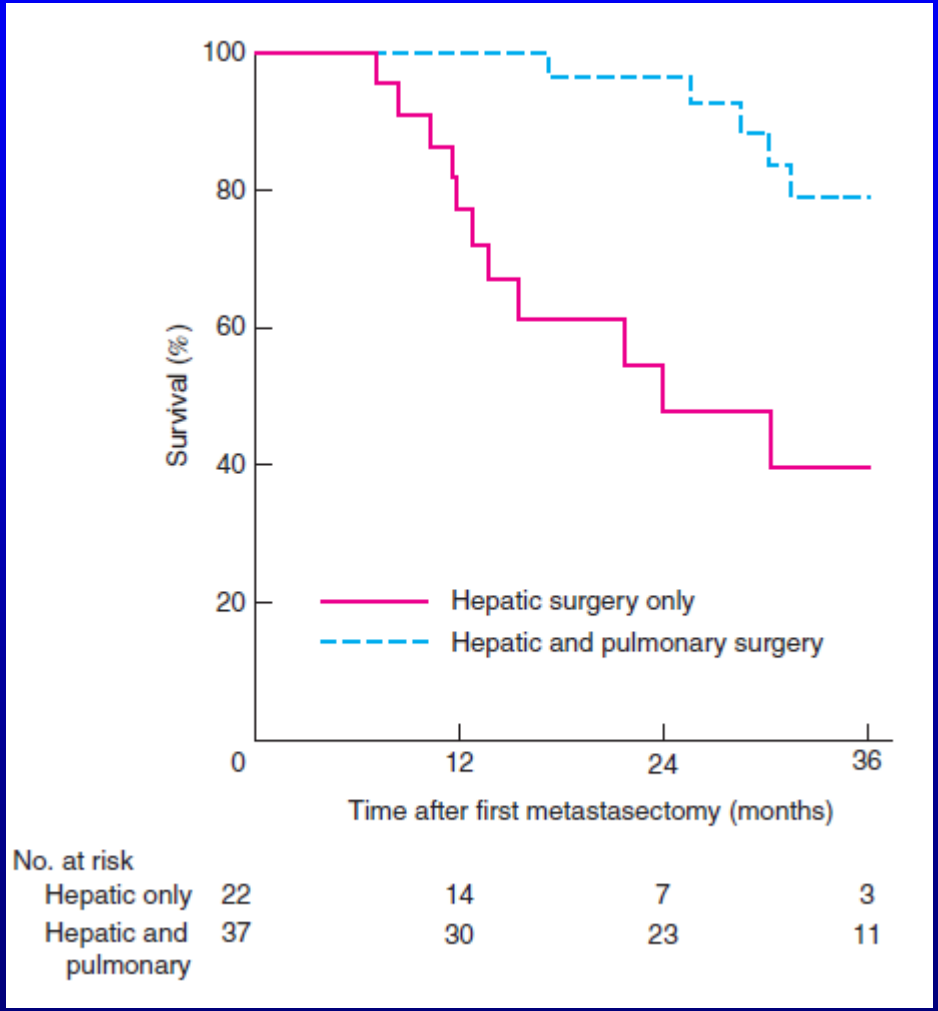
Patients at risk	Total	1 yr	2 yrs	3 yrs	4 yrs	5 yrs
Isolated lung metastases	90	78	51	32	20	11
No isolated lung metastases	96	78	47	22	11	9

FIGURE 3. Overall survival according to the presence or absence of isolated lung metastases within the extrahepatic disease group (N = 186).

Outcome after liver resection in patients presenting with simultaneous hepatopulmonary colorectal metastases

R. V. Dave[1], S. Pathak[1], A. D. White[1], E. Hidalgo[1], K. R. Prasad[1], J. P. A. Lodge[1], R. Milton[2] and G. J. Toogood[1]

BJS 2015; **102**: 261–268



COLORECTAL LIVER METASTASES - SYNCHRONOUS

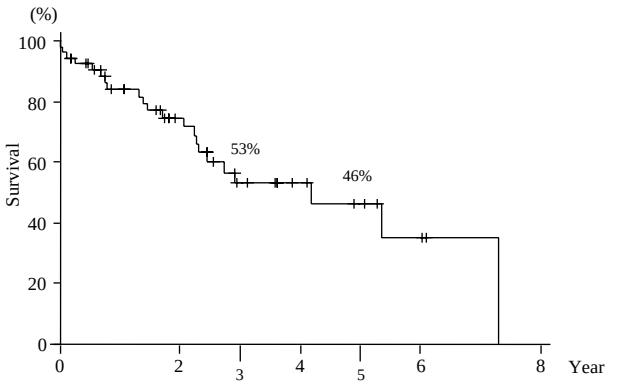
- Conclusion 6:
  - In selected cases, lung metastasectomy should be considered.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

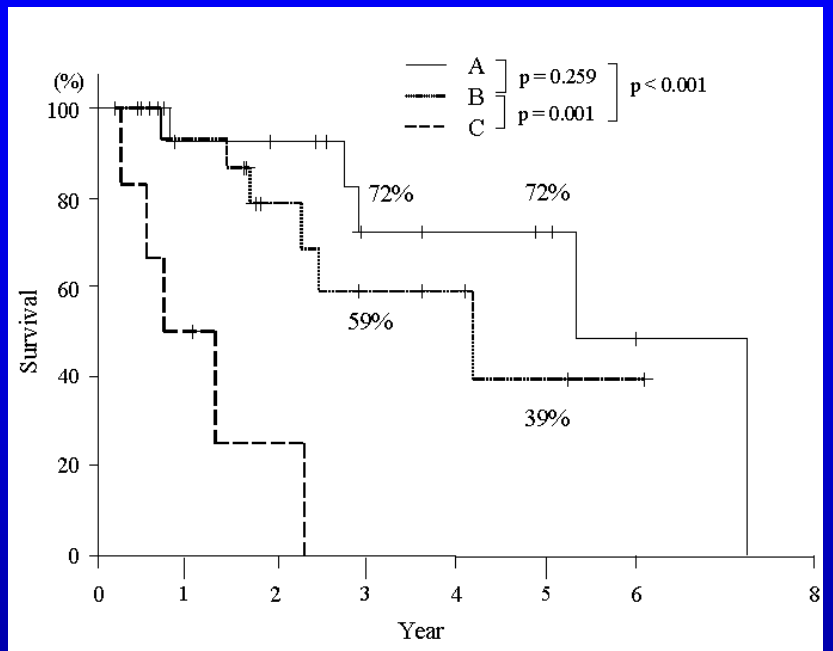
- Question 7:
  - What should we do for recurrent liver metastases?

COLORECTAL METASTASES

IMPACT OF REDO HEPATIC RESECTION



No. at risk (survival rate)			Median survival (months)
54	14	6	50



No. at risk				Median survival (year)
A 20	12	6	4	5.3
B 16	14	5	2	4.2
C 6	3	0	0	0.7

Figure 3

Nishio et al (Lodge) Eur J Surg Oncol 2007; 33: 729-734

Repeat hepatic resection for colorectal liver metastases

R. A. Adair, A. L. Young, A. J. Cockbain, D. Malde, K. R. Prasad, J. P. A. Lodge and G. J. Toogood

Department of Hepatobiliary and Transplant Surgery, St James's University Hospital, Beckett Street, Leeds LS9 7TF, UK
Correspondence to: Mr G. J. Toogood (e-mail: giles.toogood@leedsth.nhs.uk)

British Journal of Surgery 2012; **99**: 1278–1283

1993-2010

195 repeat hepatic resections
- 166 second resections
- 26 third resections
- 3 fourth resections

30 day mortality 1.5%

From redo resection:

1 year survival	91.4%
3 year survival	44.3%
5 year survival	29.4%
10 year survival	11.7%

Median survival 25 months (range 0-186)

Tumour size >5cm only predictor of poor survival

Table 4 Univariable analysis of factors associated with survival

	*P**
Sex	0·996
Age	0·951
Node-positive primary	0·254
Synchronous disease	0·798
Anatomical resection	0·295
Major resection	0·054
Bilobar disease	0·376
CEA level	0·372
Postoperative complication	0·141
Intraoperative blood transfusion	0·391
Multiple hepatic tumours	0·609
Clear resection margin 1 mm	0·102
Clear resection margin 10 mm	0·271
Tumour size	0·012
Adjuvant chemotherapy for primary tumour	0·702
Neoadjuvant chemotherapy	0·250

CEA, carcinoembryonic antigen. *Proportional hazards model.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Conclusion 7:
  - In selected cases, redo liver resection should be considered.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 8:
  - Can we predict who should do well?

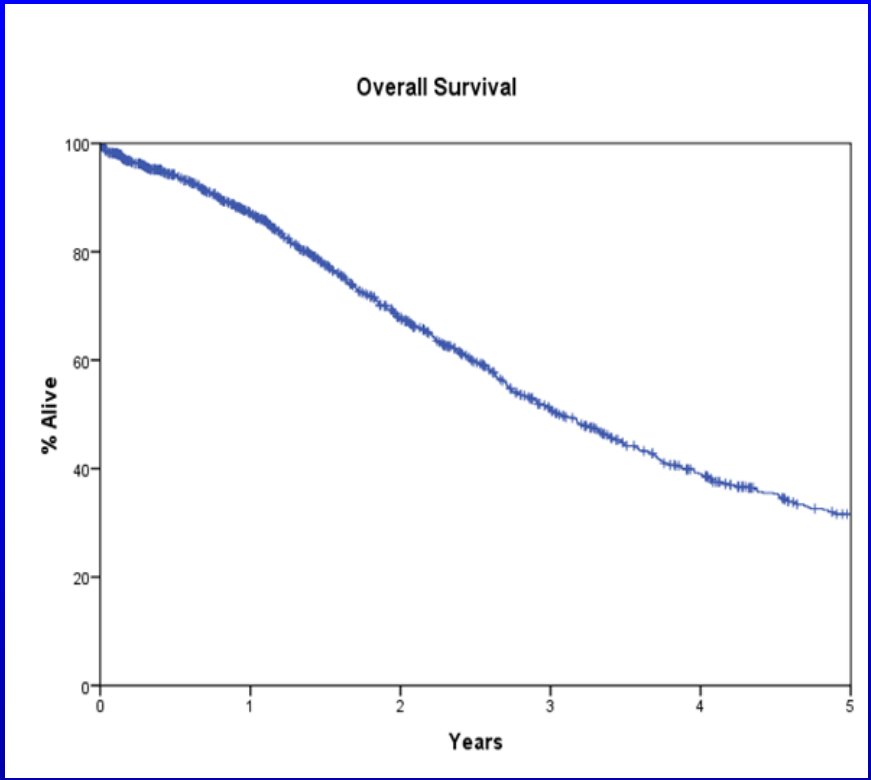
Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer - analysis of 1001 consecutive cases

Fong et al, Annals of Surgery 1999; 230: 309

- Nodal status of primary
- Disease-free interval from primary to discovery of the liver metastases of < 12 months
- Number of tumours > 1
- Preoperative CEA level > 200 ng/ml
- Size of largest tumour > 5 cm

- Overall actuarial survival 37% at 5 years, 22% at 10 years
- Clinical Risk Score (CRS) predictive of long term outcome ($p<0.0001$)
- Actuarial survival 60% if CRS =1, 14% if CRS = 5

LEEDS RESULTS - COLORECTAL METASTASES



- 1281 patients 1992-2009
- 393 (31%) were > 70years old
- 205 (16%) had neo-adjuvant chemotherapy
- Mortality rate (30 day) 2.6%

Survival

1 year	87%
3 years	52%
5 years	32%
10 years	21%

Multivariate Analysis

Primary Node Positive	p= < 0.0001
CEA >200	p= 0.145
Size >5cm	p= 0.038
Disease free interval from primary < 1year	p= 0.950
Number of Metastases >5	p= 0.072

Performance of prognostic scores in predicting long-term outcome following resection of colorectal liver metastases

K. J. Roberts[2], A. White[1], A. Cockbain[1], J. Hodson[3], E. Hidalgo[1], G. J. Toogood[1] and J. P. A. Lodge[1]

BJS 2014; **101**: 856–866

286 consecutive CRLM resection patients 10 year survivors 1992-2001

8 prognostic scoring systems analysed

Actual disease free survival at	1 year	86.6%
	3 years	58.3%
	5 years	39.5%
	10 years	24.5%

70 patients underwent 105 further resections

Conclusion: Although available risk scores can predict DFS and DSS, none does so with sufficient discriminatory accuracy to identify all episodes of recurrent disease. A non-negligible proportion of patients develop recurrent disease beyond 5 years of follow-up and so surveillance beyond this point may be advantageous.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

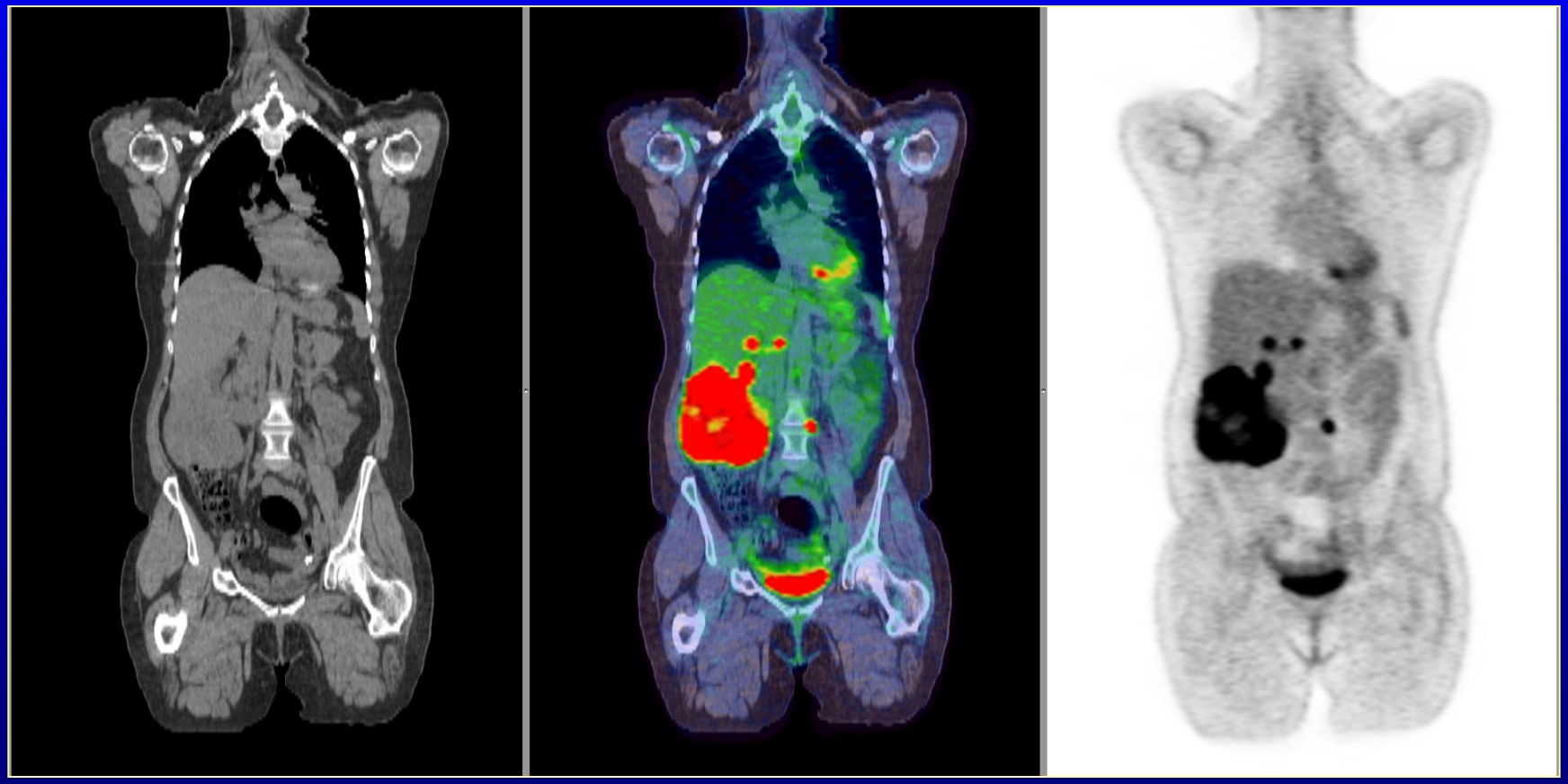
- Conclusion 8:
  - Patients should not be denied surgery based on pre-operative prognostic scoring systems.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 9:
  - Can we improve outcomes with pre-operative imaging ?

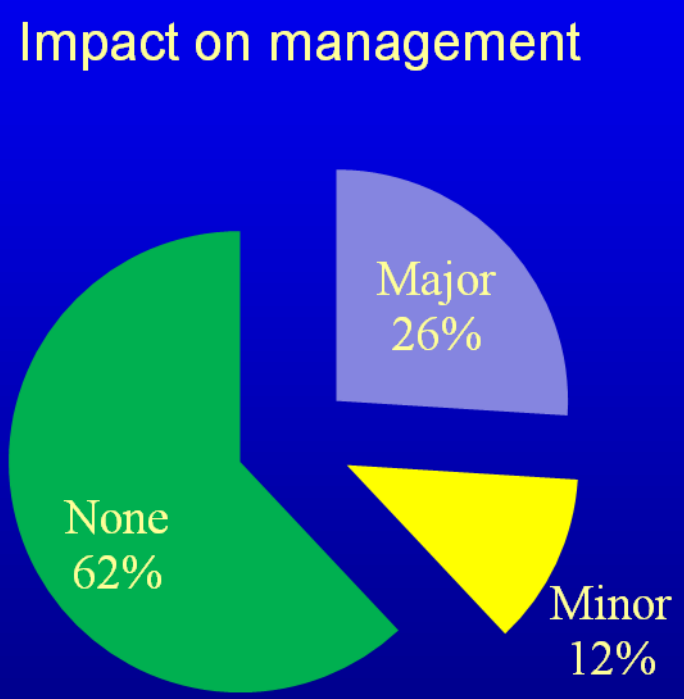
HEPATIC RESECTION
IMPROVING RESULTS

- PET-CT
  - Improved results



HEPATIC RESECTION
IMPROVING RESULTS

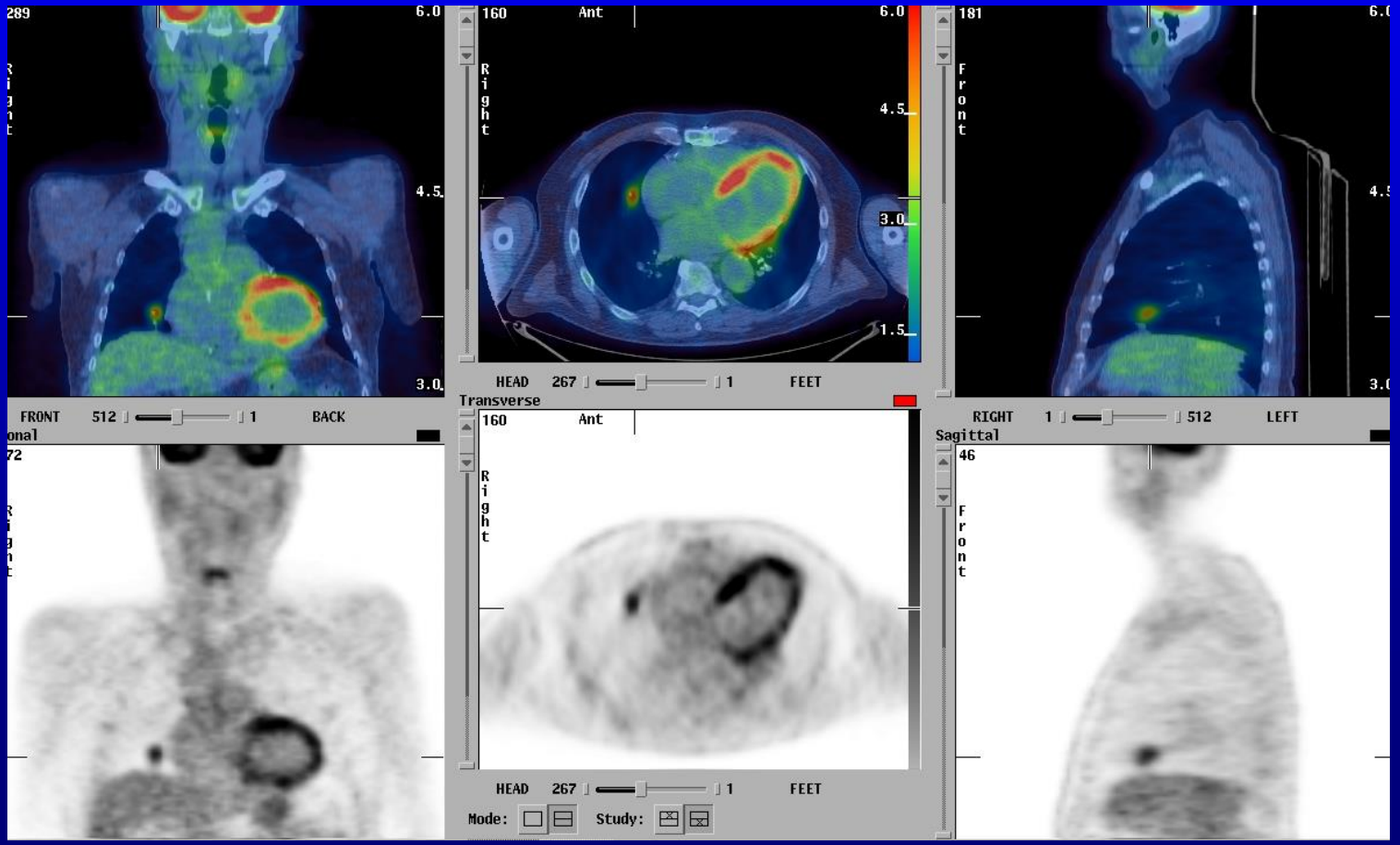
- PET-CT
  - Improved results



Occult metastastic disease
Unsuspected lymph nodes
Confirmed inoperability

HEPATIC RESECTION
IMPROVING RESULTS

- PET-CT
  - Improved results?
  - Should we aim for cure or “additional patient years”?



COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Conclusion 9:
  - Patients may be disadvantaged by complex pre-operative imaging if surgery is then denied: a measured judgment is important for appropriate patient care.

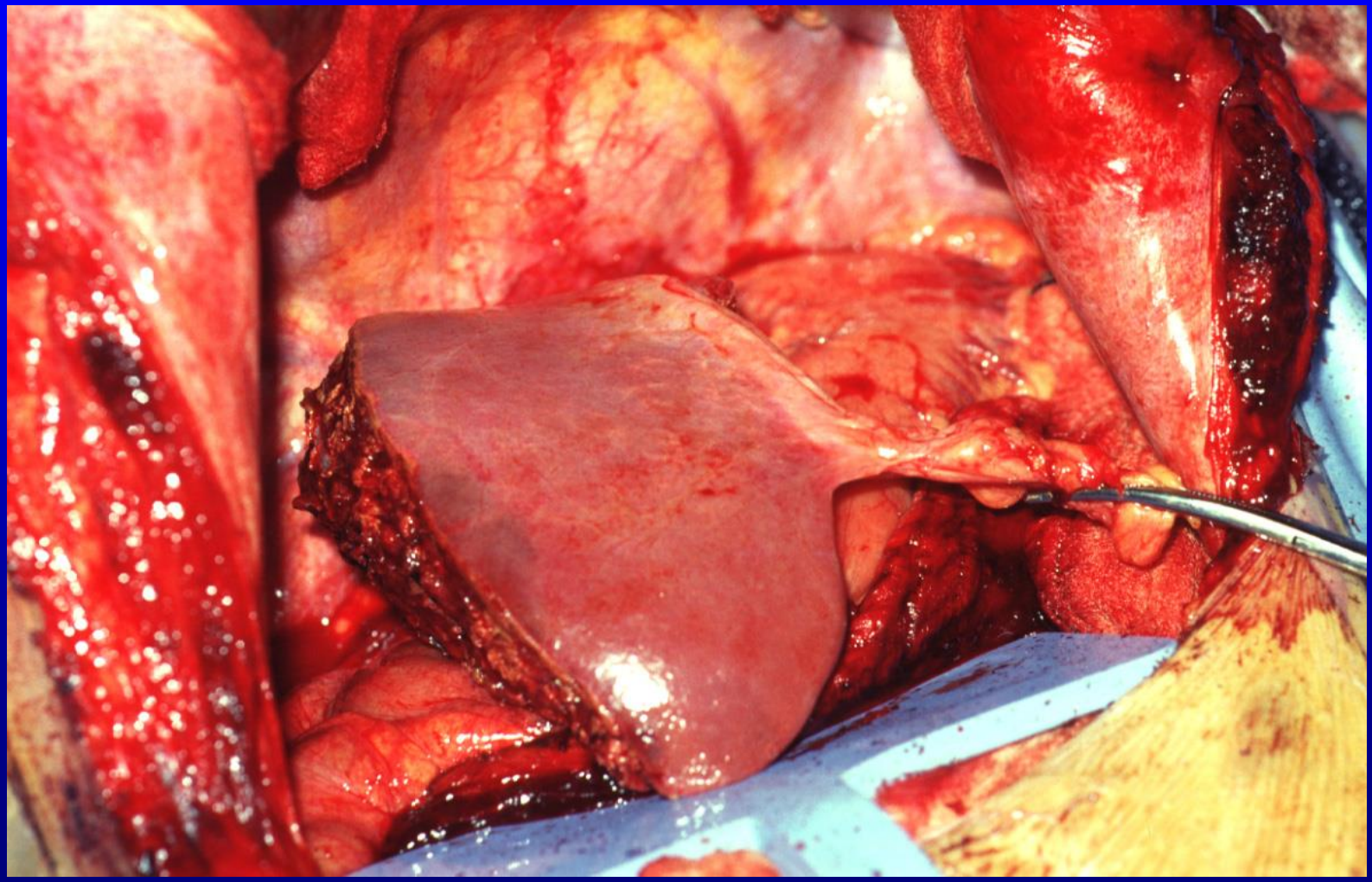
COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 10:
  - What about chemotherapy?

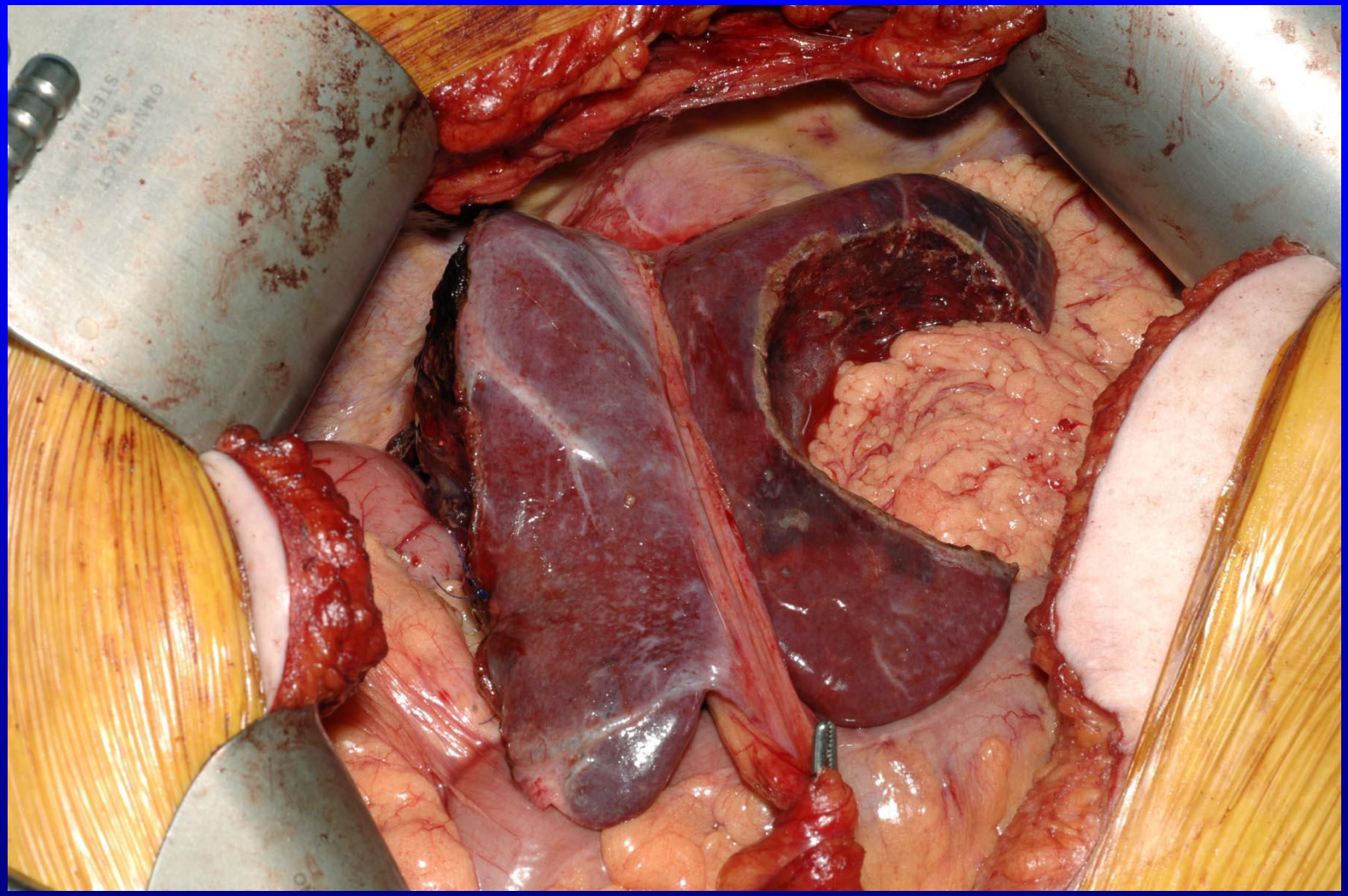
HEPATIC RESECTION
IMPROVING RESULTS

- Neoadjuvant therapies
  - What is the evidence?
  - What is the role of biological agents?
  - Could we miss the window of opportunity for surgery?
  - Could it make liver resection more risky?

RIGHT HEMIHEPATECTOMY WITH LEFT LATERAL SECTIONECTOMY



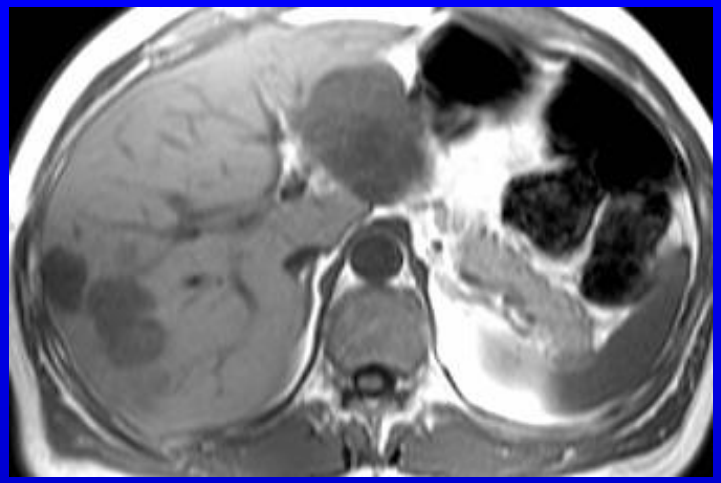
RIGHT HEMI-HEPATECTOMY WITH SEGMENT 2/3 METASTASECTOMY

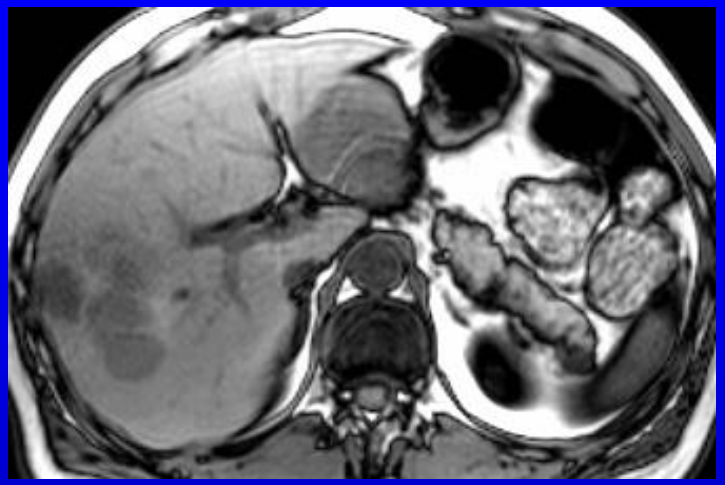


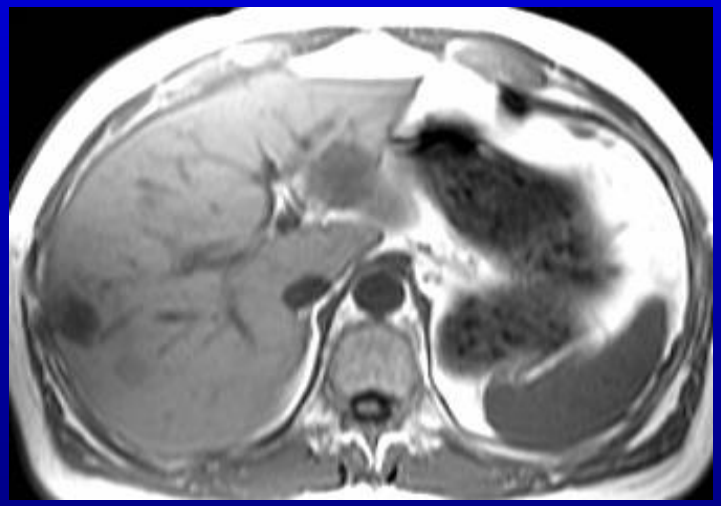
Is it safe after chemotherapy?
Should we consider 2 stage surgery and/or portal vein embolisation?

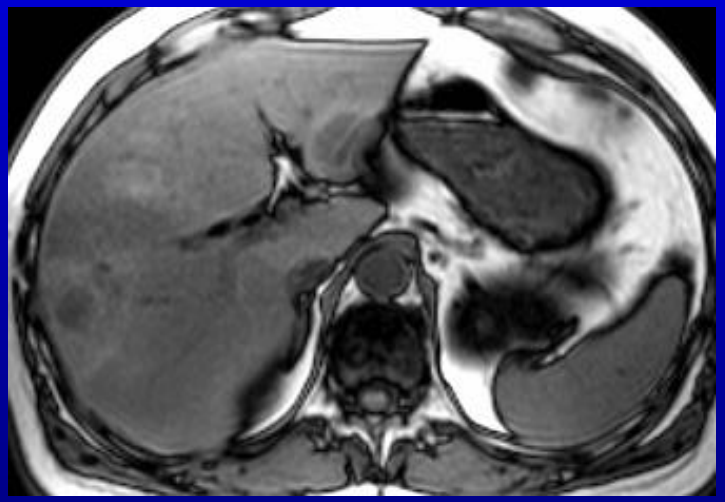
Steatosis

pre chemo





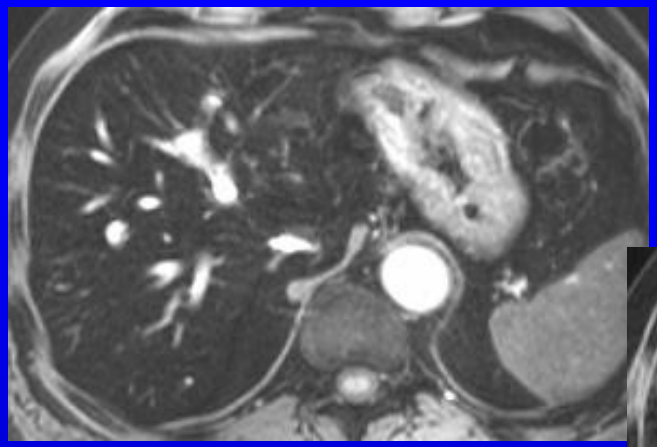




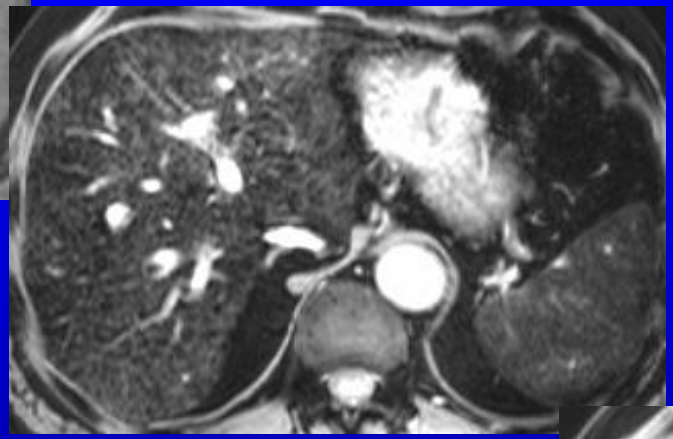
post chemo

Surgical plan: Wait 6 weeks, consider PVE

Sinusoidal Obstructive Syndrome (SOS)



05/04



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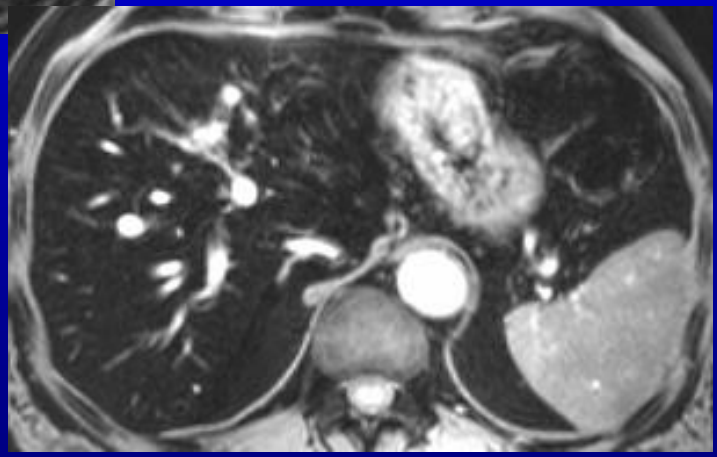


01/05

Problems:

Up to 4 months to resolve

Pressure from patient and family

Pressure from oncologist

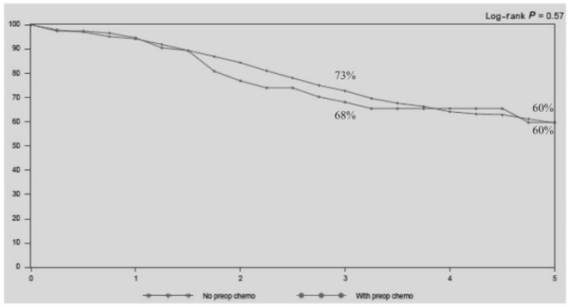
Risk of postoperative liver failure

Increased morbidity and mortality

Is Perioperative Chemotherapy Useful for Solitary, Metachronous, Colorectal Liver Metastases?

Rene Adam, MD, PhD, Prashant Bhangui, MS*, Graeme Poston, FRCS†, Darius Mirza, MS, FRCS‡, Gennaro Nuzzo, MD§, Eduardo Barroso, MD¶, Jan Ijzermans, MD, PhD**, Catherine Hubert, MD††, Theo Ruers, PhD‡‡, Lorenzo Capussotti, MD§§, Jean-Francois Ouellet, MD¶¶, Christophe Laurent, MD***, Esteban Cugat, MD†††, Pierre Emmanuel Colombo, MD‡‡‡, and Miroslav Milicevic, MD§§§*

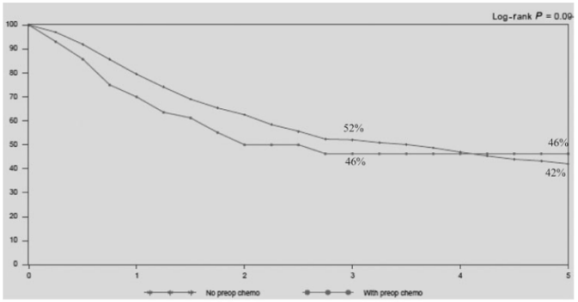
(*Ann Surg* 2010;252:774–787)



Number of exposed patients

	Total	1 yr	2 yr	3 yr	4 yr	5 yr
No preop chemo	1282	861	549	335	224	148
With preop chemo	168	95	56	28	13	8

A

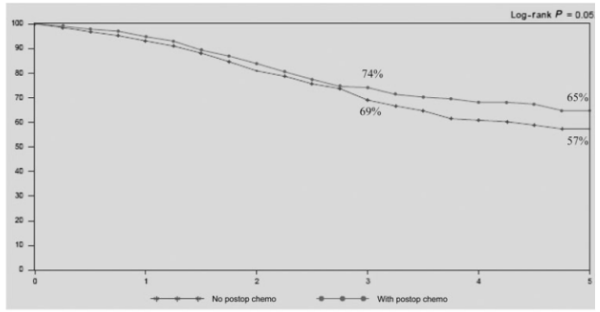


Number of exposed patients

	Total	1 yr	2 yr	3 yr	4 yr	5 yr
No preop chemo	1198	680	383	221	154	100
With preop chemo	157	68	39	20	10	6

B

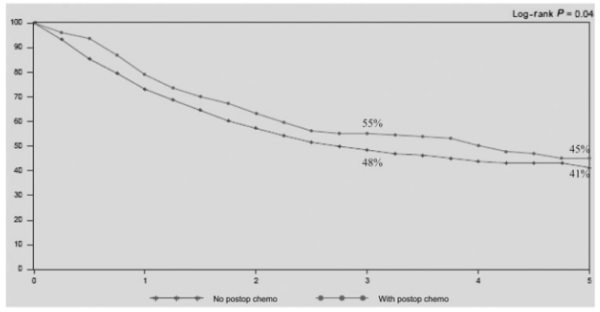
FIGURE 2. Overall survival (OS) (A) and disease-free survival (DFS) (B) for patients undergoing surgery upfront (group S) compared with group receiving preoperative chemotherapy followed by surgery (group CS). Preop indicates preoperative; chemo, chemotherapy.



Number of exposed patients

	Total	1 yr	2 yr	3 yr	4 yr	5 yr
No postop chemo	622	434	272	151	101	64
With postop chemo	441	322	211	144	94	63

A



Number of exposed patients

	Total	1 yr	2 yr	3 yr	4 yr	5 yr
No postop chemo	579	318	182	94	66	42
With postop chemo	393	243	146	97	65	44

B

FIGURE 3. Overall survival (OS) (A) and disease-free survival (DFS) (B) in patients with a minimum follow-up period of 2 months posthepatectomy receiving postoperative chemotherapy compared with the group not receiving postoperative chemotherapy. Postop indicates postoperative; chem, chemotherapy.

Steatosis as a Risk Factor in Liver Surgery

Reeta Veteläinen, MD, Arlène van Vliet, PhD, Dirk J. Gouma, MD, and Thomas M. van Gulik, MD

(*Ann Surg* 2007;245: 20–30)

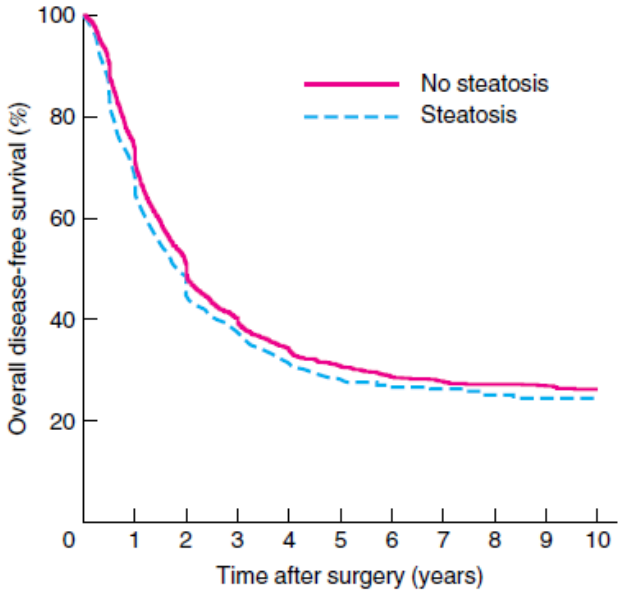
CONCLUSION

Steatosis plays an important role in hepatic surgery as it is a major risk factor in patient outcome after liver resection. This is due to lipid accumulation deranging hepatic energy homeostasis and inducing hepatocellular damage subsequently affecting hepatocellular recovery. Further research is needed to clarify the clinical relevance of the broad spectrum of all forms and severity grades of steatosis on patient outcome. Standardized grading and diagnostic modalities need to be applied in future clinical trials to be able to compare outcomes of different studies.

Fatty liver disease as a predictor of local recurrence following resection of colorectal liver metastases

Z. Z. R. Hamady[1,2], M. Rees[1], F. K. Welsh[1], G. J. Toogood[2], K. R. Prasad[2], T. K. John[1] and J. P. A. Lodge[2]

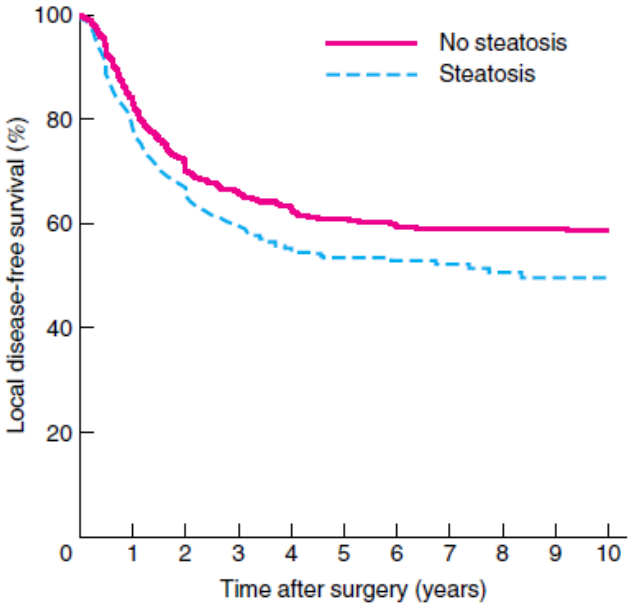
Br J Surg. 2013 May;100(6):820-6



No. at risk

No steatosis	1788	1233	791	575	444	374	299	256	215	189	163
Steatosis	927	598	338	213	143	94	71	55	43	32	24

Fig. 1 Kaplan–Meier cumulative overall disease-free survival curves for 2715 patients after resection of colorectal liver metastases, stratified by hepatic steatosis. $P = 0{\cdot}039$ (log rank test)



No. at risk

No steatosis	902	699	517	394	318	273	220	193	173	162	146
Steatosis	902	658	420	277	191	128	97	73	59	45	37

Fig. 2 Kaplan–Meier local (liver) disease-free survival curves for 1804 patients after resection of colorectal liver metastases, stratified by hepatic steatosis. The two groups were propensity score-matched. $P = 0{\cdot}002$ (log rank test)

Sinusoidal Injury Increases Morbidity After Major Hepatectomy in Patients With Colorectal Liver Metastases Receiving Preoperative Chemotherapy

Hiroshi Nakano, MD, PhD, Elie Oussoultzoglou, MD,* Edoardo Rosso, MD,* Selenia Casnedi, MD,† Marie-Pierre Chenard-Neu, MD, PhD,† Patrick Dufour, MD,‡ Philippe Bachellier, MD,* and Daniel Jaeck, MD, PhD, FRCS**

(*Ann Surg* 2008;247: 118–124)

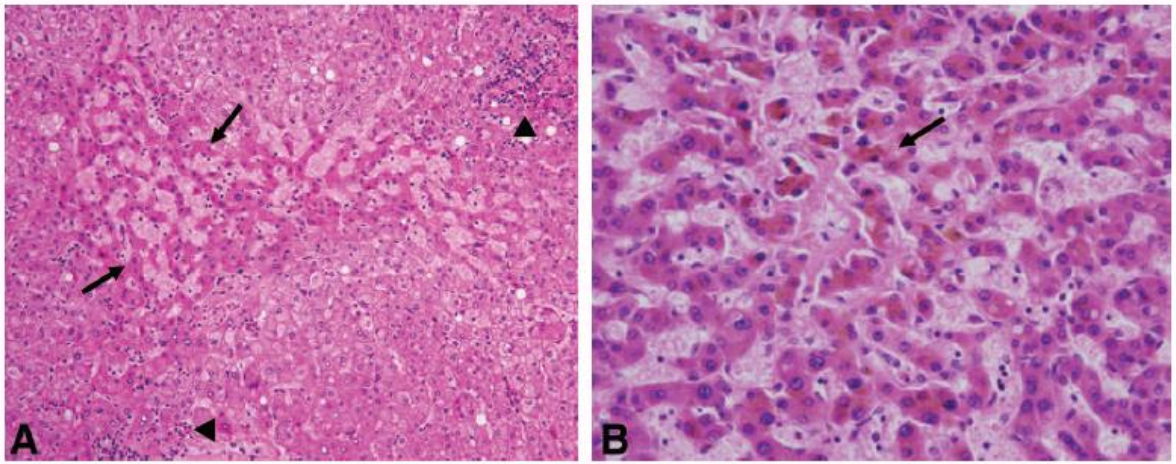
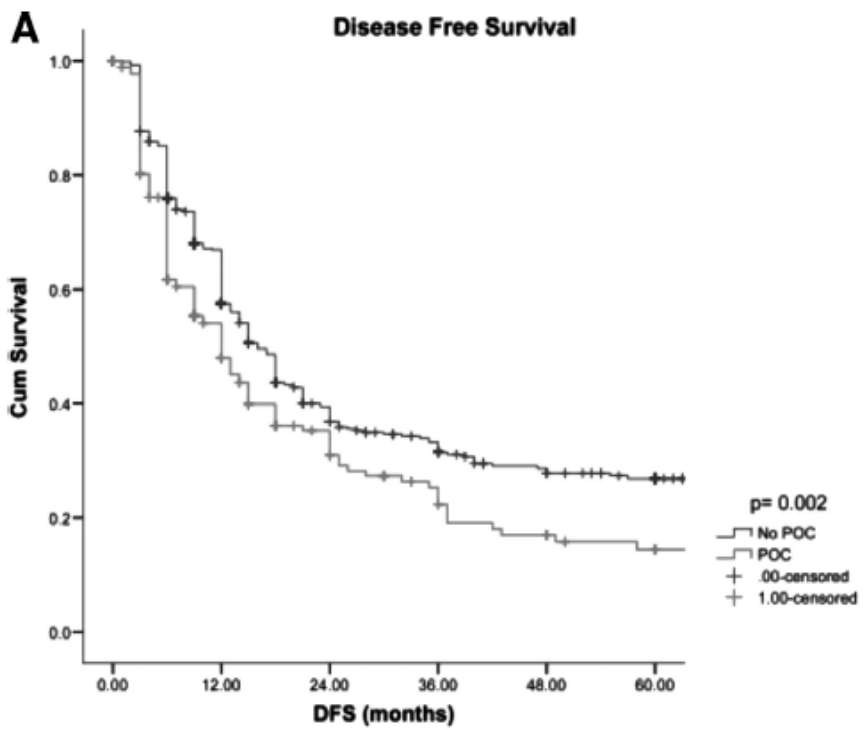


FIGURE 1. A, Marked sinusoidal dilatation and atrophic hepatocytes (arrows) with moderate lymphocytic infiltration are shown (arrowheads, magnification ×200, H & E stain). B, Sinusoidal dilatation and congestion, and prominent cholestasis in atrophic hepatocytes are shown (arrow, magnification ×400, H & E stain).

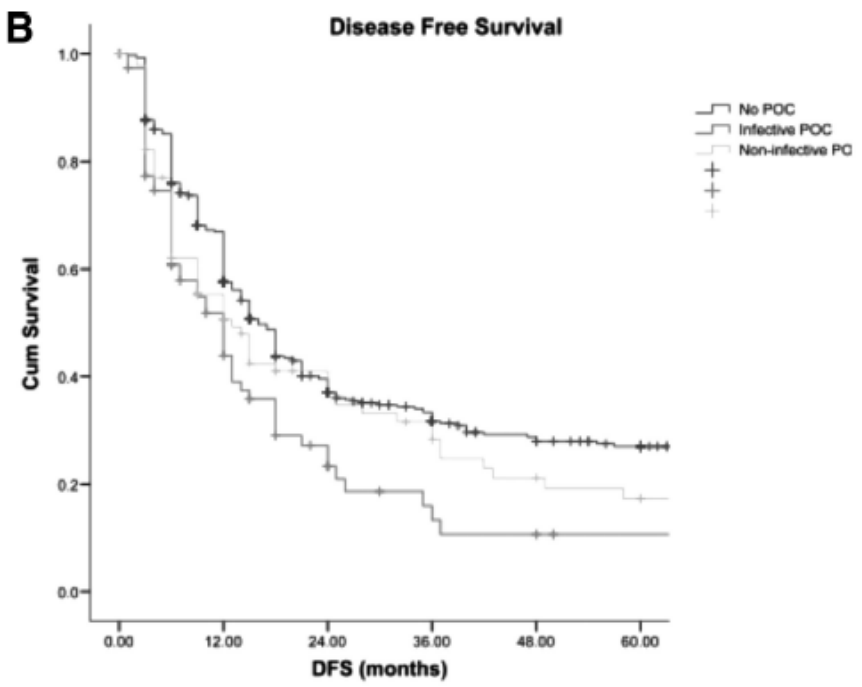
Correlation Between Postoperative Infective Complications and Long-Term Outcomes After Hepatic Resection for Colorectal Liver Metastasis

Shahid G. Farid, MRCS, Amer Aldouri, FRCS, Gareth Morris-Stiff, FRCS, Aamir Z. Khan, FRCS, Giles J. Toogood, FRCS, J. Peter A. Lodge, FRCS, and K. Rajendra Prasad, FRCS

(*Ann Surg* 2010;251: 91–100)



Numbers at risk (year)	0	1	2	3	4	5
No POC	504	297	137	97	66	56
POC	172	79	40	21	15	10



Numbers at risk(year)	0	1	2	3	4	5
No POC	508	300	138	97	67	55
Non infective POC	94	45	25	18	11	8
Infective POC	75	32	13	5	3	1

FIGURE 1. The Kaplan-Meier curves for DFS stratified by the presence and absence of POCs (A) and when subclassified as infective or noninfective POCs in (B).

Chemotherapy Before Liver Resection of Colorectal Metastases

Friend or Foe?

Kuno Lehmann, MD, Andreas Rickenbacher, MD,* Achim Weber, MD,† Bernhard C. Pestalozzi, MD,‡ and Pierre-Alain Clavien, MD, PhD, FACS**

(*Ann Surg* 2012;255:237–247)

CONCLUSION

Taken together, the data indicates that for unresectable liver metastases, downsizing chemotherapy may offer a chance for secondary resection in about a third of patients. Although the optimal regimen for this is still unclear, it seems reasonable to start with 2 cytotoxic drugs (5FU with either oxaliplatin or irinotecan). If this strategy fails, adding an antibody (cetuximab), or HAI may be an alternative in the absence of extrahepatic disease. In contrast, routine neoadjuvant chemotherapy cannot be recommended due to the increased risk of complications without clear benefit on survival. In patients with multiple, borderline resectable tumors, neoadjuvant therapy may identify good responders with favorable tumor biology and thus a better outcome.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Conclusion 10:
  - The view of the “experts” that patients with synchronous colorectal liver metastases should receive chemotherapy pre-operatively is not based on high level evidence.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 11:
  - What about ablation?

HEPATIC SURGERY
ABLATION TECHNOLOGY

- Radiofrequency ablation
  - What is the evidence?
  - For lesions up to 4 cm
  - Percutaneous, laparoscopic / open laparotomy
  - Targeting by US / CT / MRI
- Microwave ablation
  - Possibly more effective
  - Possibly more risky
- Consider for elderly, frail, small central tumour but only after appropriate MDT discussion

COLORECTAL LIVER METASTASES - SYNCHRONOUS

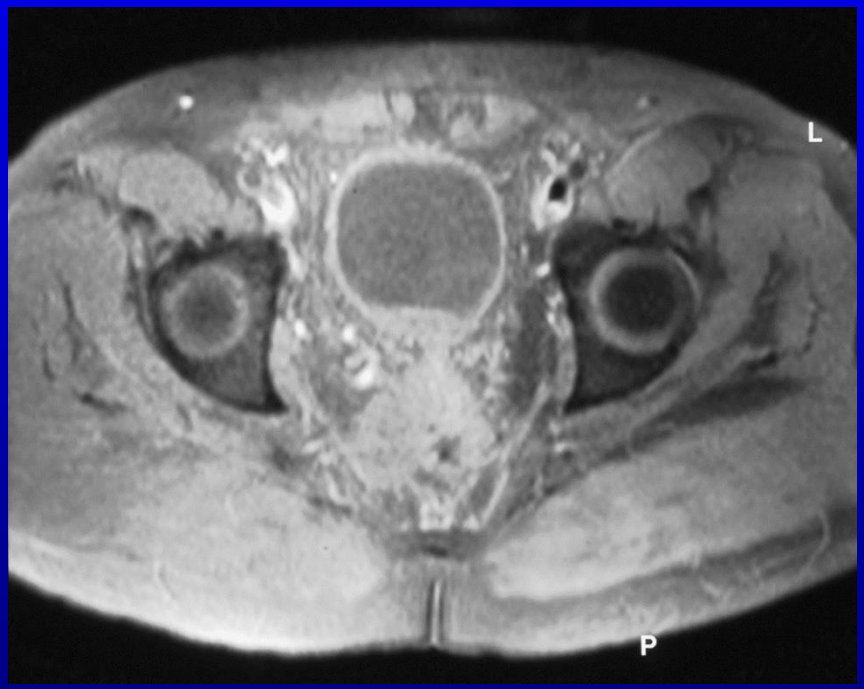
- Conclusion 11:
  - Ablation remains a “second best” therapy for colorectal liver metastases.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Question 12:
  - Is there anything else that's new?

Pelvic recurrence

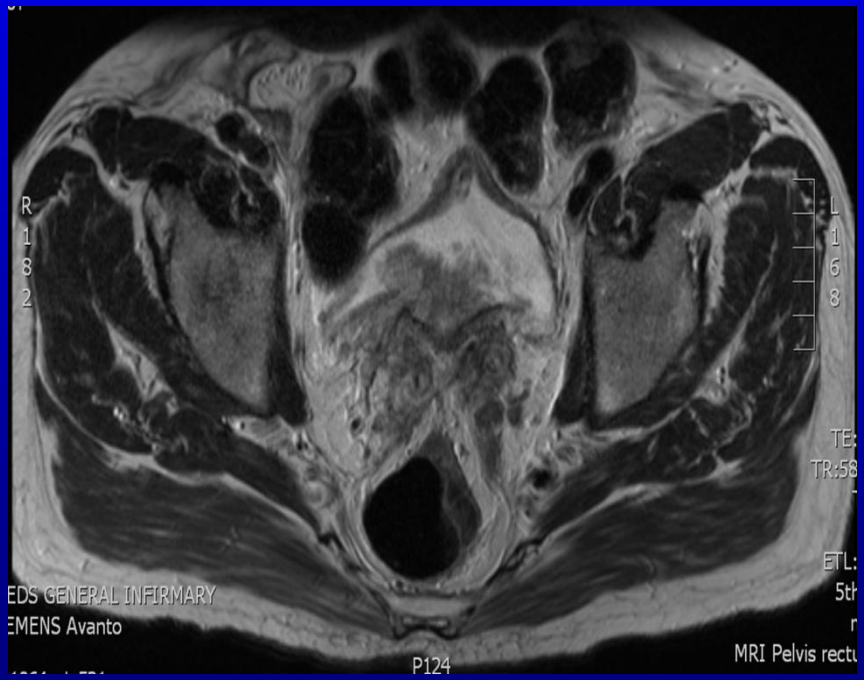
Central recurrence



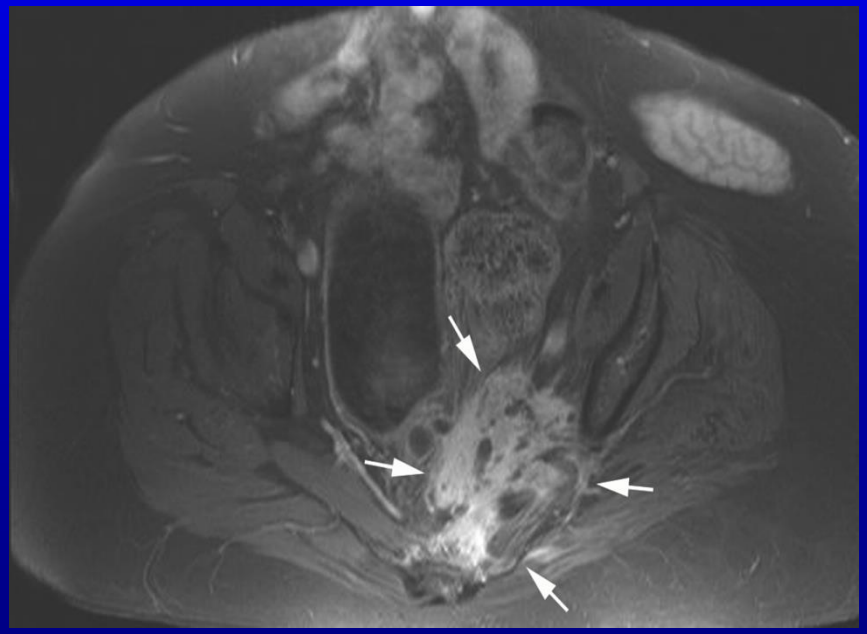
Posterior recurrence

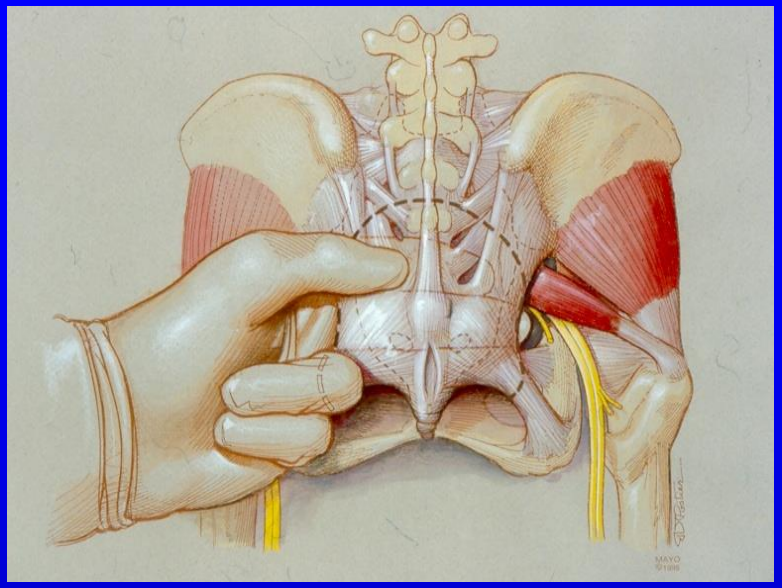
Pelvic recurrence

Bladder involvement

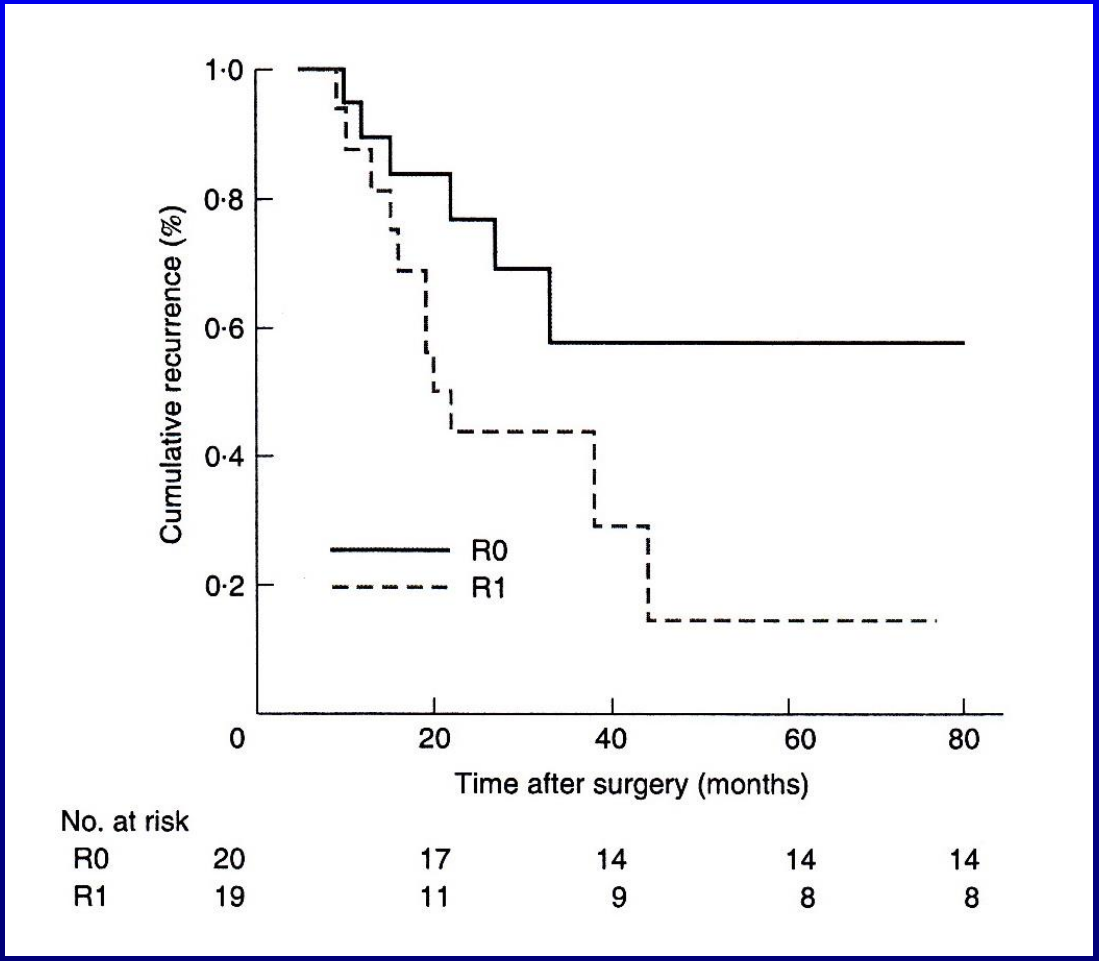


Pelvic side wall involvement



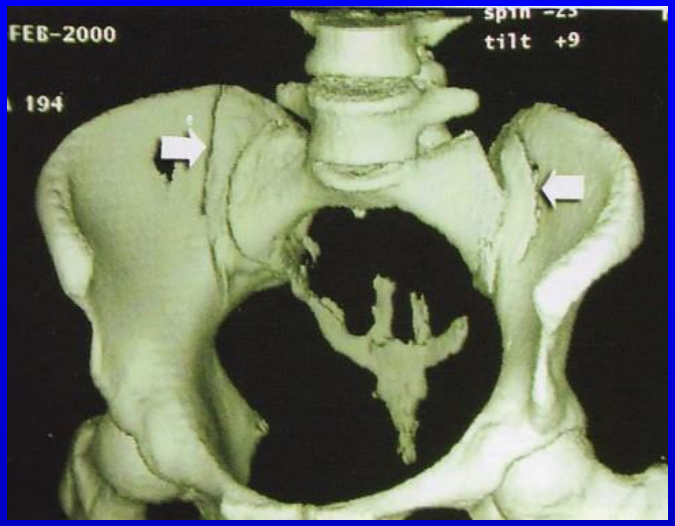


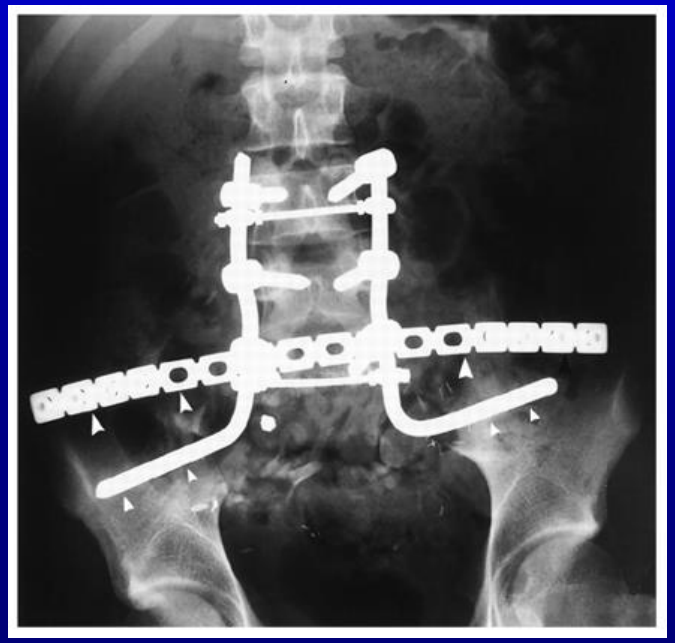
Disease-free survival R0 vs R1 resection



High sacrectomy

- Above 3rd sacral body
- Technically challenging
- Sacro-pelvic stability

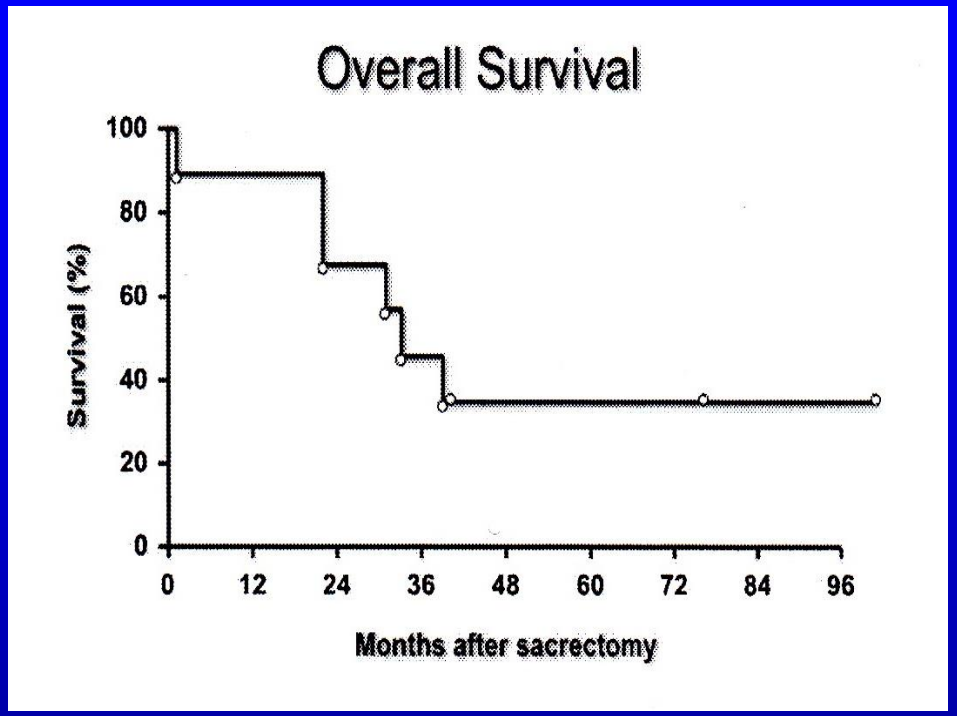




High sacrectomy

TABLE II. Re-Operative Characteristics

Variable	Number of patients
Procedure performed	
APR	3
Multi-visceral en bloc resection	3
Hartmann's procedure	2
Hemipelvectomy	1
Sacrectomy level	
Through S2	6
Through S1	2
Through L5-S1	1
Additional procedures	
TRAM flap	6
Cystoprostatectomy, ileal conduit	3
Thigh fillet flap	1



Dozois et al JSO 2011; 103: 105-9

One third will live five years

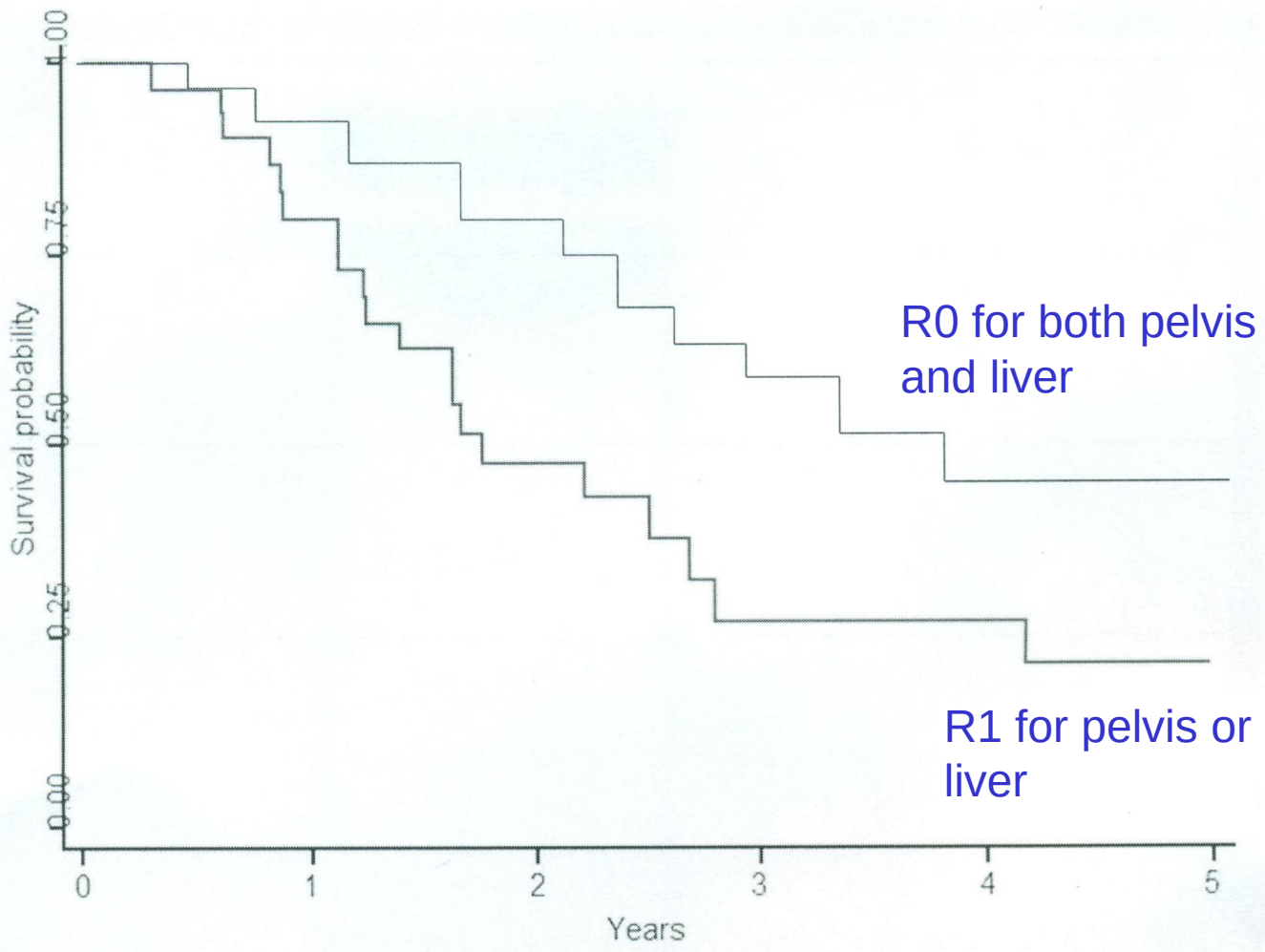
One third will recur locally (?re-operate)

One third will die of disseminated disease

Results when combined with liver resection

- 2002-2014, Leeds Teaching Hospitals
- 36 patients, 22 men, age 62 yrs (40-78)
- Resection of liver metastases
  - Before pelvic recurrence surgery (n=12)
  - At time of pelvic recurrence surgery (n=16)
  - After pelvic recurrence surgery (n=8)

Survival:
R0 vs R1 resection



COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Conclusion 12:
  - Diagnosis of pelvic recurrence is not a contraindication for liver metastases resection if pelvic surgery is possible.

COLORECTAL LIVER METASTASES - SYNCHRONOUS

- Summary:
  - Patients with synchronous colorectal liver metastases should be considered for surgical resection in the same way as patients with metachronous metastases.
  - The major management questions relate to timing of liver surgery in relation to the primary cancer resection and appropriate use of chemotherapy.