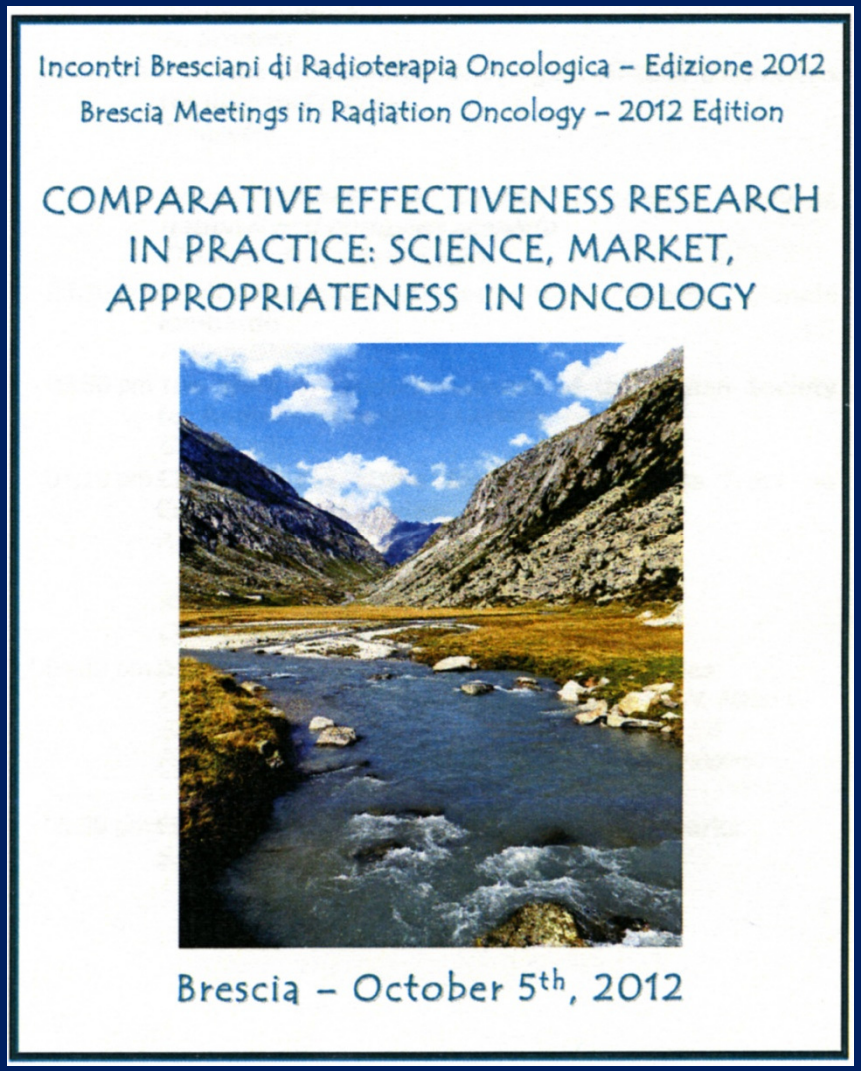
The role of Surgeon:

results of surgery and what surgeon asks for to other specialities

Clinica Chirurgica
Università degli Studi di Brescia

and



The “scenario” of liver cancer

Primary cancer

HCC

Intrahepatic cholangiocarcinoma

Metastatic cancer

Primary colorectal cancer

Other cancers

Chronic liver disease

Concomitant other sites metastasis

Clinical relevance of liver cancers

Incidence and prevalence ? *(power of diagnostic tools)*

Evolution in culture and attitude

Multiple therapeutic approaches

Liver cancers: evolution in the standards of care

A more confident and aggressive attitude

Primary liver cancer

Hepatocarcinoma in Brescia

in the five-year period '86 –'90

349 patients

- **10 hepatic resections**
- **21 PEI**
- **7 TAE**

Collaborazione: Prof. F. Donato, Cattedra di Igiene ed Epidemiologia, Università di Brescia

Hepatocarcinoma in Brescia

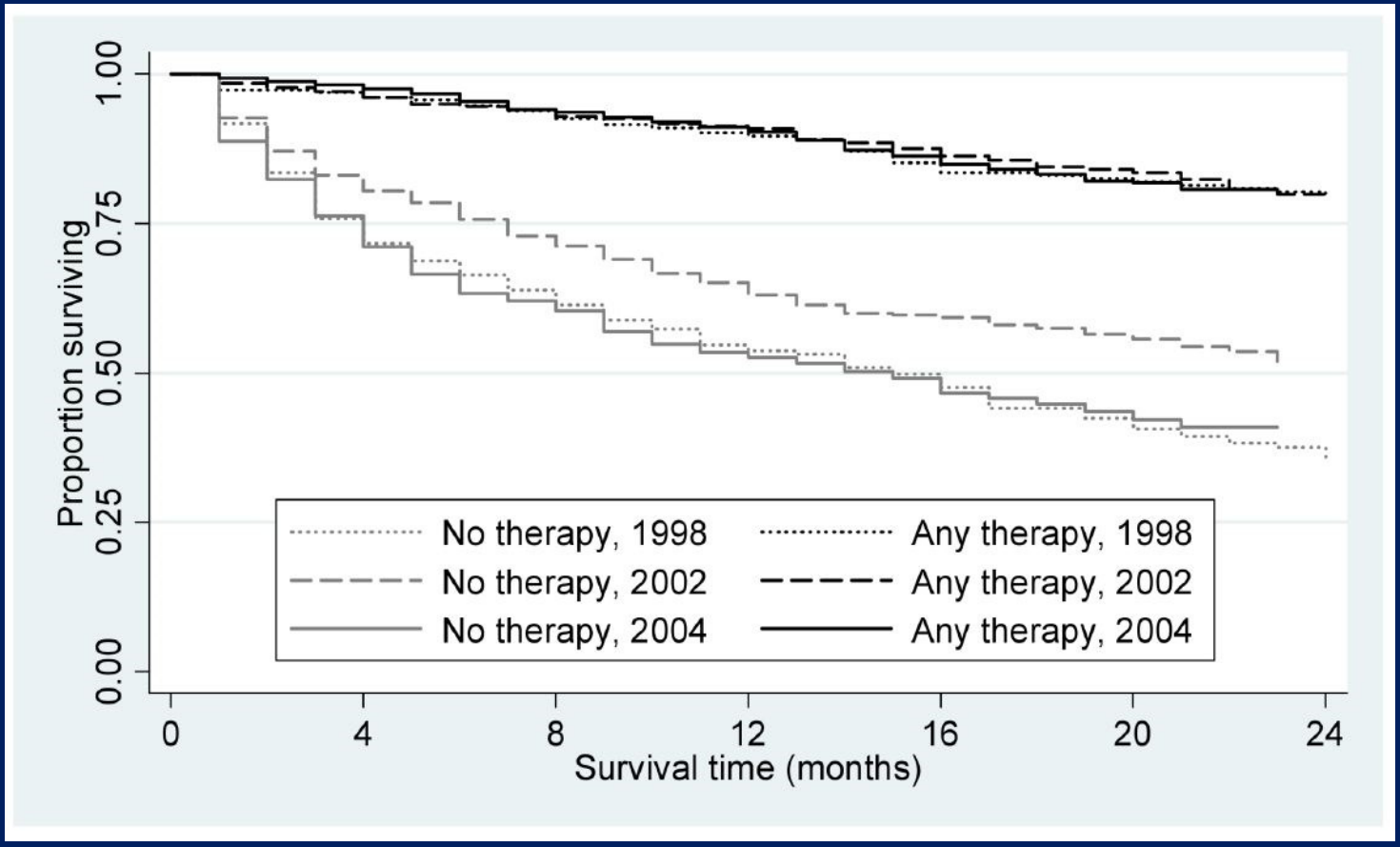
in the five-year period '07 –'11

210 hepatic resections

perioperative mortality 1.9%

Is liver cancer a "surgical pathology"?

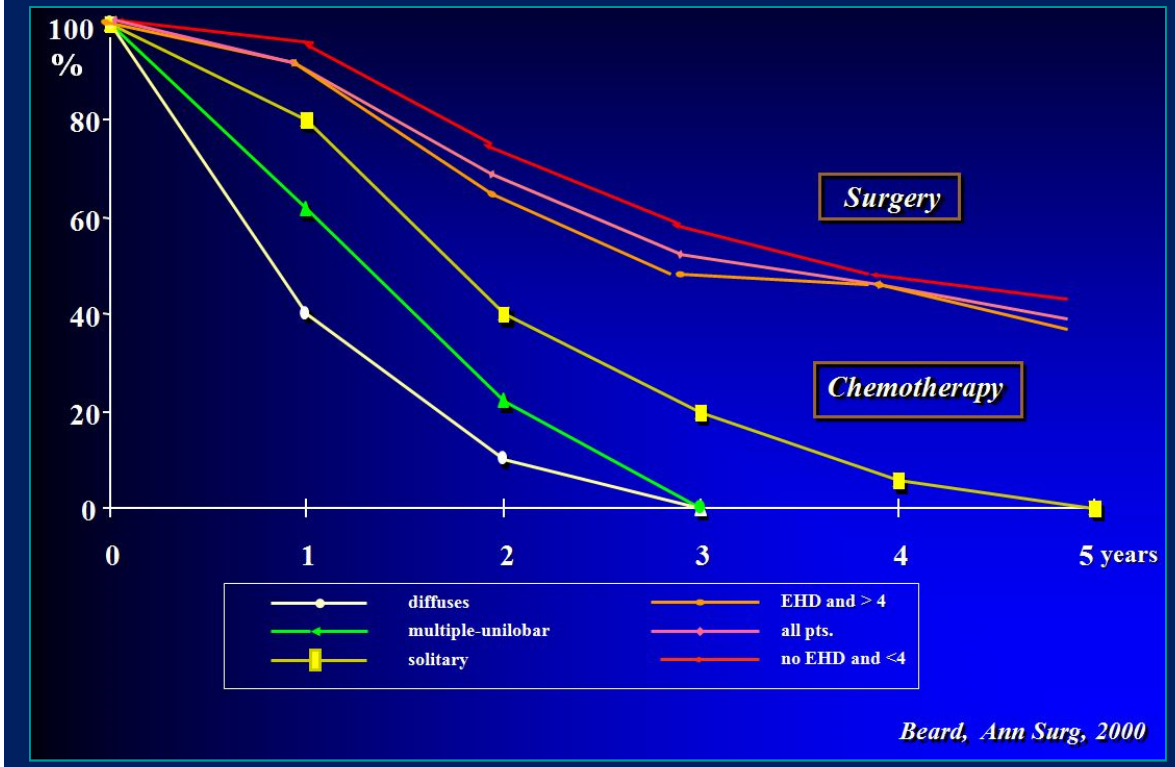
Primary liver cancer



Massarweh, 2010

Is liver cancer a “surgical pathology”?

Metastatic cancer



Liver resection

Surgery is the mainstay treatment

Sugihara, 2012

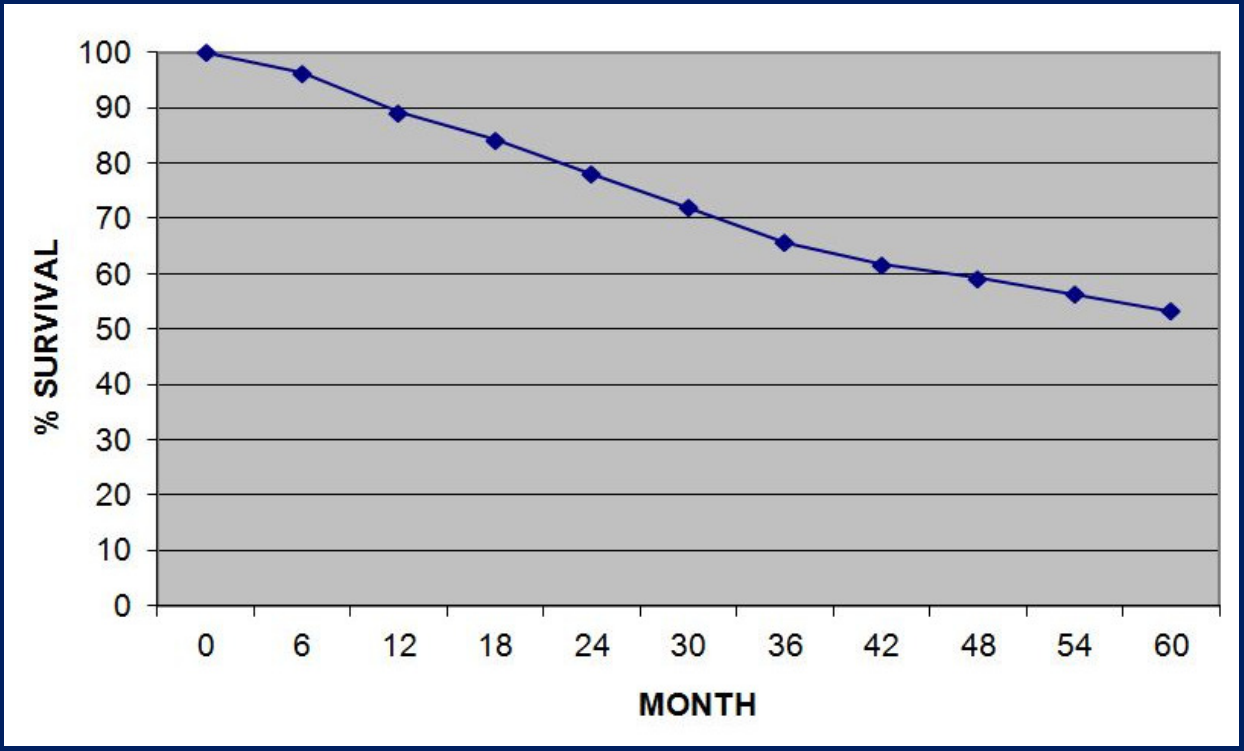
liver metastasis as a marker of a locoregional diffusion

Is surgery the definitive cure of liver cancer?

HARDLY EVER

(except for OLT for small HCC)

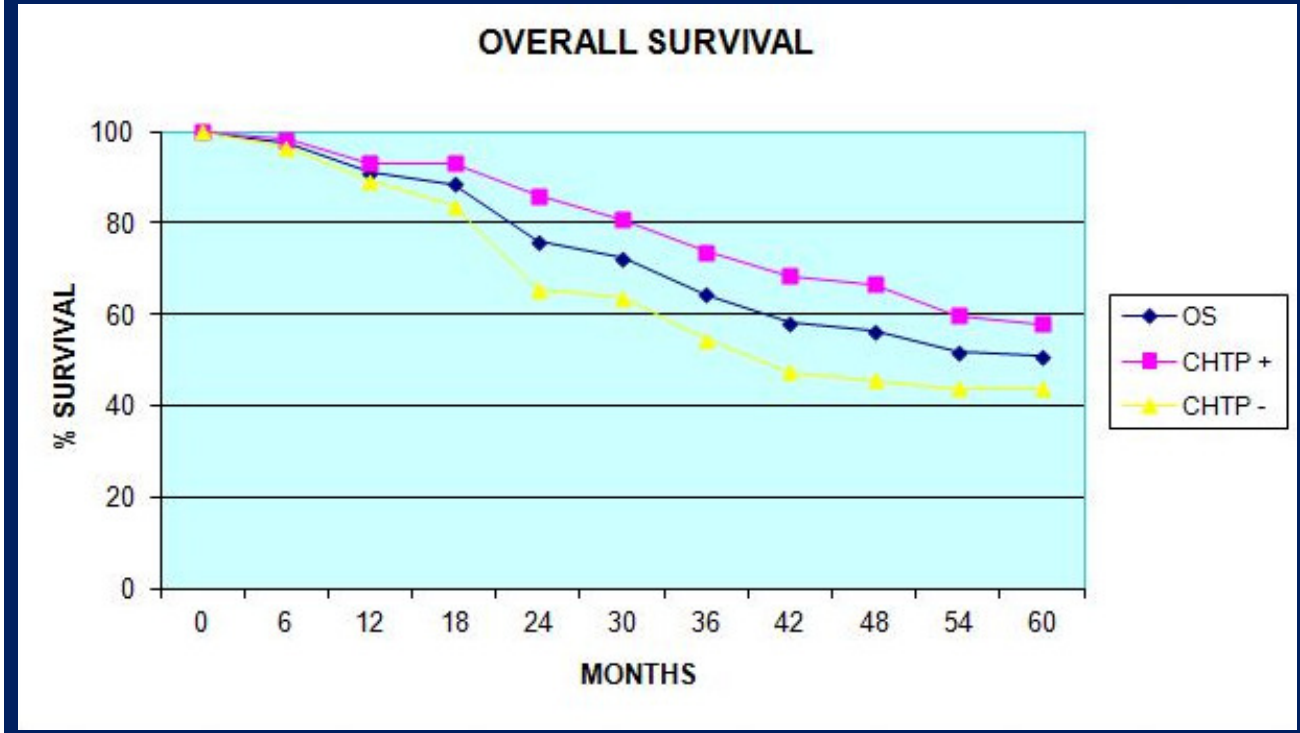
Liver resection for HCC *(1999-09):* **441** patients



*only **31%** of long term survivors were treated only by primary liver resection*

Is surgery the definitive cure of liver cancer?

Liver resection for metastasis *(2004-11):* **107** patients



*only **54** patients had not been treated with chemotherapy too*

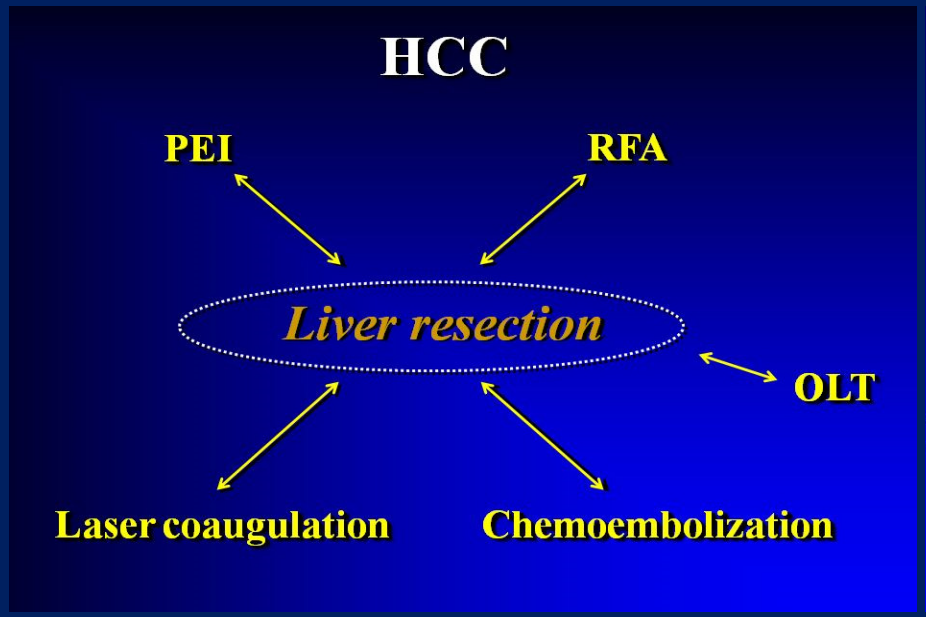
CHT +: medium age: 66.2

CHT - : medium age: 69.3

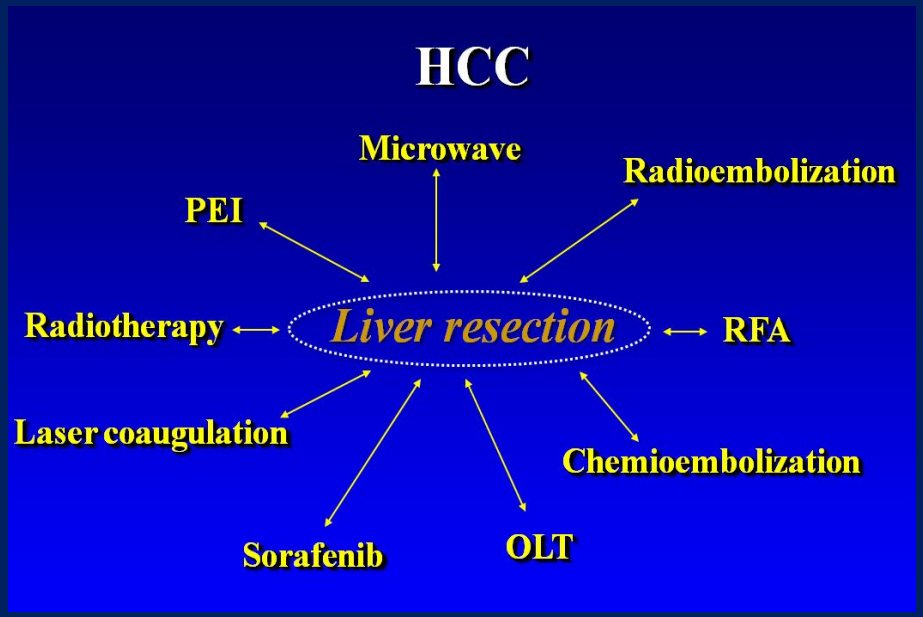
The concept of multidisciplinary approach is of paramount value in this field

A multidisciplinary approach to HCC

Venoock, 2000



Current treatments, 2012



The different therapies can be competitive *(above all for the small HCC)* but the best approach is toward a selective treatment *(the best therapy for the single patient)* or a combined one

Trends in the Utilization and Impact of Radiofrequency Ablation for Hepatocellular Carcinoma

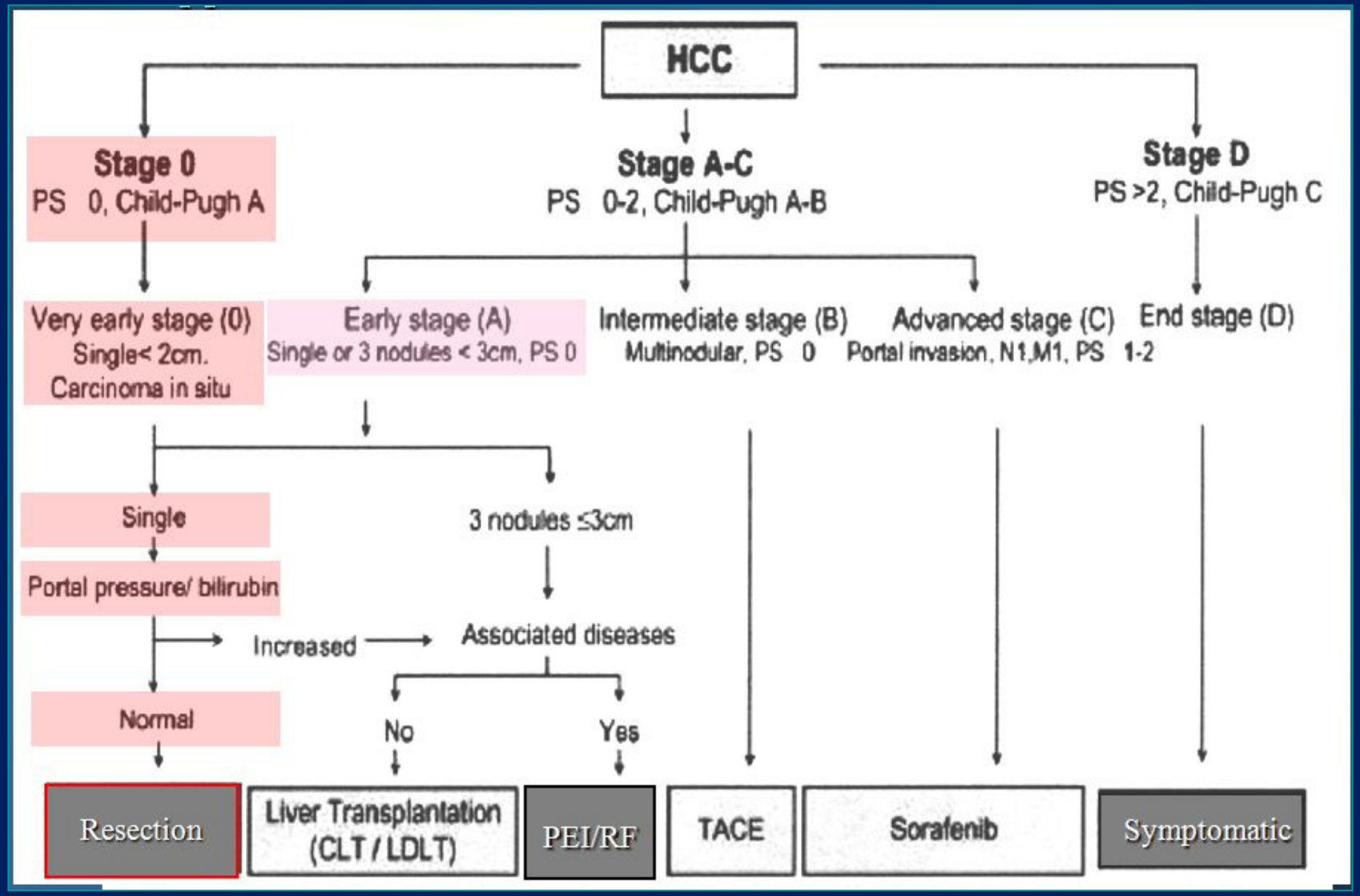
Nader N Massarweh, MD, James O Park, MD, Farhood Farjah, MD, MPH, Raymond SW Yeung, MD, FACS, Rebecca Gaston Symons, MPH, Thomas L Vaughan, MD, MPH, FACS, Laura-Mae Baldwin, MD, MPH, David R Flum, MD, MPH, FACS

Table 1. Temporal Changes in the Rate of Utilization of Surgical Therapy (per 100 Hepatocellular Carcinoma Patients)

Therapy	1998, % (n =1,373)	1999, % (n =1,465)	2000, % (n =2,682)	2001, % (n =2,967)	2002, % (n = 3,042)	2003, % (n = 3,326)	2004, % (n = 3,527)	2005, % (n = 3,721)	p Value*
Any intervention	14.9	16.2	17.7	18.6	22.1	24.2	26.1	28.4	<0.001
Any ablation	3.2	3.6	4.9	6.0	7.7	9.5	10.5	12.1	<0.001
RFA	0.4	0.3	1.0	1.8	3.2	5.6	5.8	6.2	<0.001
Other ablation	2.8	3.3	3.8	4.3	4.5	3.9	4.8	6.0	<0.001
Resection	8.5	9.2	9.2	8.3	7.8	7.6	7.7	9.1	0.37
Transplant	3.1	3.3	3.6	4.3	6.5	6.4	6.9	6.3	<0.001
Resection/ablation	0	0	0	0	0	0.7	0.9	0.9	<0.001

CONCLUSIONS: Use of interventions for the treatment of HCC, and specifically RFA, have markedly increased over time. Because increased use of RFA among patients with potentially resectable disease is likely to occur, and because of a lack of high-level evidence supporting expanded indications, continued evaluation of the indications for RFA and subsequent outcomes among US patients is warranted.
(J Am Coll Surg 2010;210:441–448.

The role of surgery for the treatment of HCC



HCC: *resection "beyond the guidelines"*

Large HCC (> 5 cm)

Authors	Nations	n° pts	major res. %	oper. mort. %	% survival at 5 years large HCC	% survival at 5 years small HCC	% vasc.inf.
LIAU 2005*	USA	**82**	**-**	**2.0**	**33**	**38**	**-**
PAVLIK 2005*	Multic.	**300**	**63**	**5.0**	**26.9**	**ND**	**69.3**
CHO 2007	JAPAN	**61**	**-**	**1.6**	**52.9**	**59**	**-**
SHAH 2007*	CANADA	**24**	**50**	**-**	**54**	**53**	**-**
PANDEY 2008	SING.	**166**	**48.2**	**3.0**	**28.6**	**ND**	**-**
YANG 2009	CINA	**260**	**-**	**2.3**	**38.2**	**45**	**55**
DELIS 2009	GRECIA	**66**	**100**	**0**	**32**	**ND**	**40**
GIULINI 2010	ITALIA	**120**	**45**	**3.3**	**32.3**	**50.4**	**44.5**

* *HCC > 10 cm*

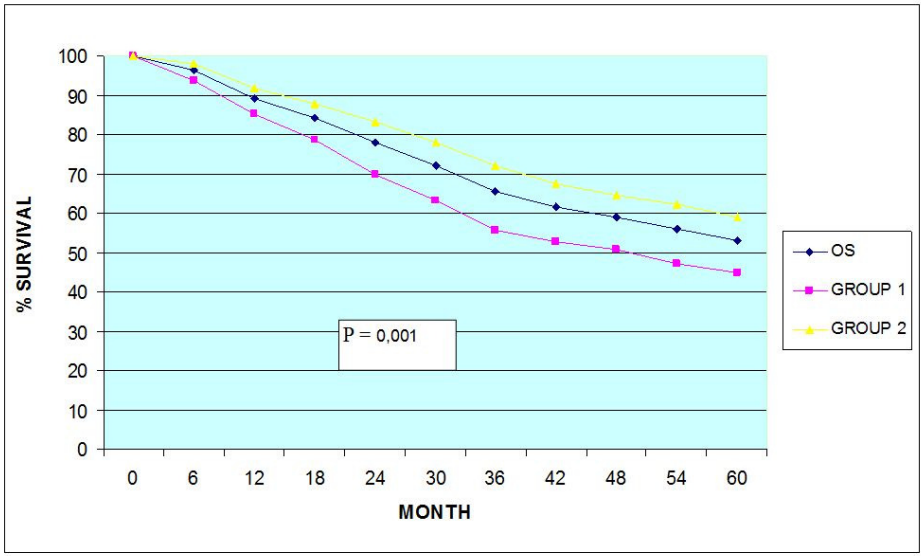
HCC: *resection "beyond the guidelines"*

Multifocal HCC

Authors	Nations	n° pts.	oper. mort.	% survival at 5 years		predictive value number of nodules	
				O.S.	D.F.S.	O.S.	D.F.S.
UTSUNOMIYA 2000	JAPAN	**34**	**-**	**38**	**25**	NO	NO
ITAMOTO 2005	JAPAN	**25**	**2,9**	**46**	**18**	NO	NO
ISHIZAKA 2008	JAPAN	**126**	**0**	**58**	**25**	NO	P 0.001
GIULINI 2010	ITALIA	**82**	**5,3**	**35**	**22**	NO	NO

Liver resection for HCC with *(group 1)* and without *(group 2)* microvascular infiltration

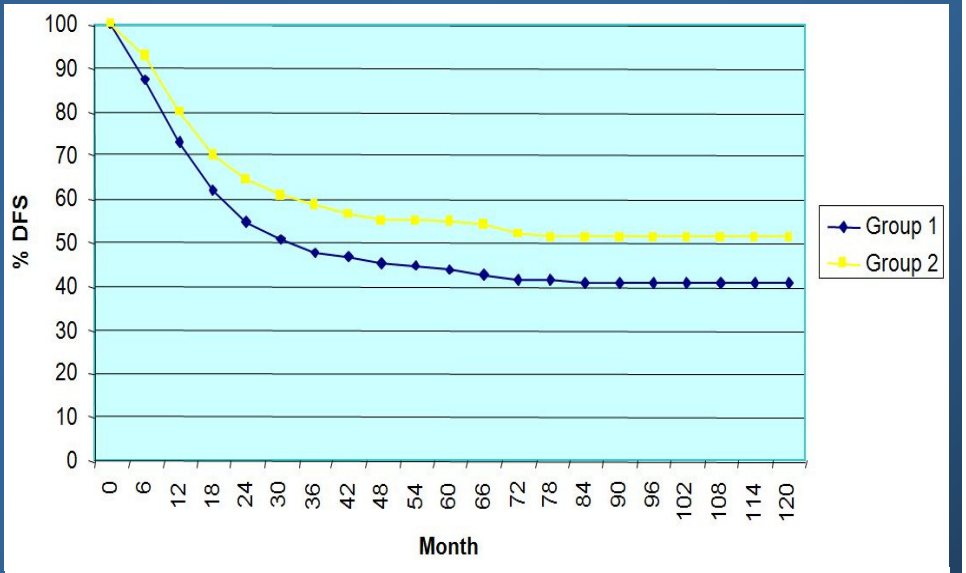
Overall survival



Patients at risk

GROUP 1	163	153	139	128	114	103	91	86	83	77	73
GROUP 2	241	236	221	212	201	188	174	163	156	150	142
MONTH	0	6	12	18	24	30	36	42	48	54	60

Disease free survival



Patients at risk

GROUP 1	189	165	138	117	103	96	90	88	85	84	83	80	78	78	77	77	77	77	77	77	77	
GROUP 2	252	234	201	176	162	153	147	142	138	138	137	136	130	129	129	129	129	129	129	129	129	
MONTH	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84	90	96	102	108	114	120	

Early and Late Recurrence After Liver Resection for Hepatocellular Carcinoma

Prognostic and Therapeutic Implications

Nazario Portolani, MD, Arianna Coniglio, MD,* Sara Ghidoni, MD,* Mara Giovanelli, MD,* Anna Benetti, MD,† Guido Alberto Massimo Tiberio, MD,* and Stefano Maria Giulini, MD**

Annals of Surgery, 2006

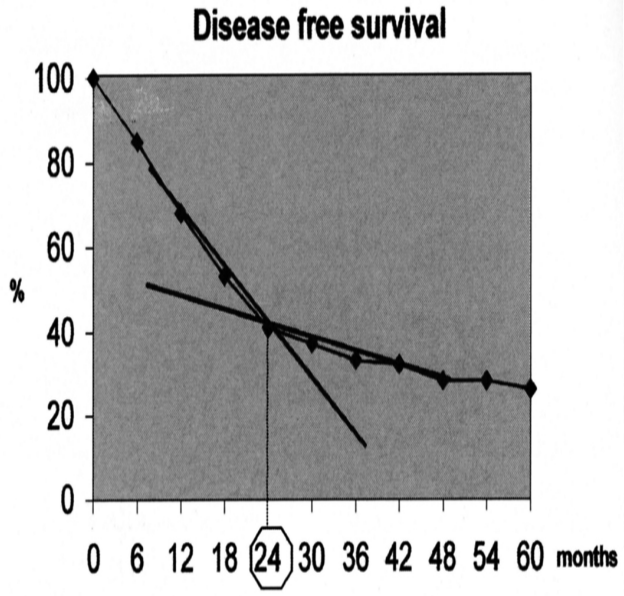


FIGURE 1. Hepatic resection for HCC. Distribution in time of intrahepatic recurrences (disease free survival) and classification of early and late recurrences.

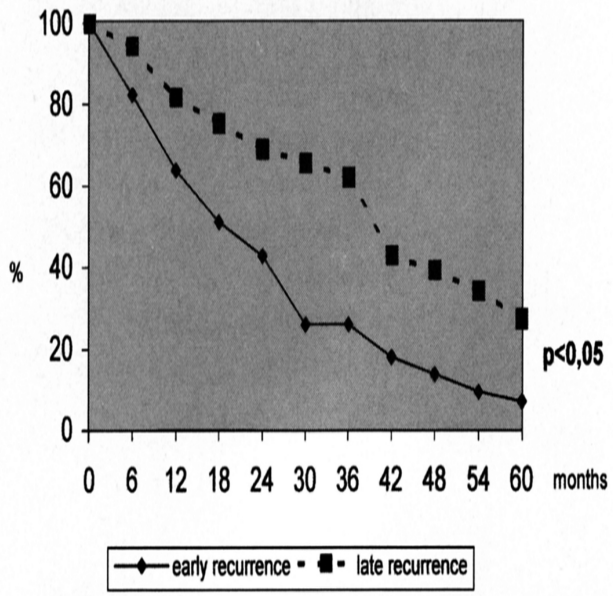


FIGURE 2. Long-term survival from the diagnosis of intrahepatic recurrence according to time of presentation (earlier or later than 24 months).

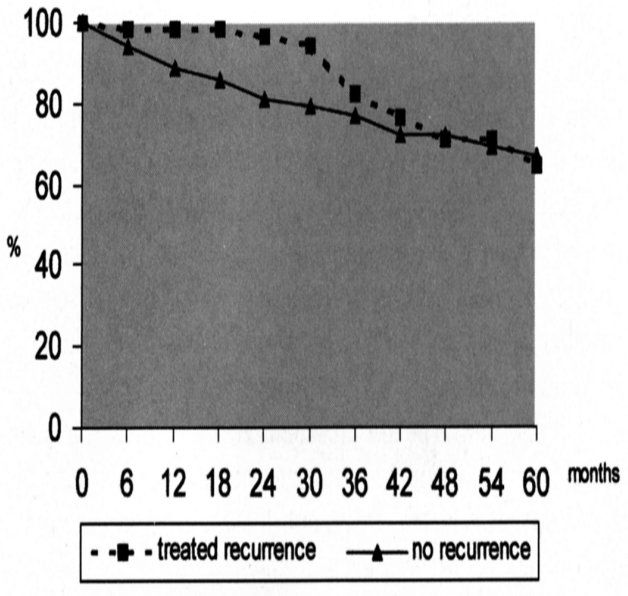


FIGURE 3. Survival from the primary resection of the patients without recurrence and of the patients with intrahepatic recurrence treated with radical purpose.

Laparoscopic Ultrasound-Guided Radiofrequency Ablation as a Bridge to Liver Transplantation for Hepatocellular Carcinoma: Preliminary Results

F. Panaro, T. Piardi, M. Audet, F. Gheza, M.L. Woehl-Jaegle, N. Portolani, J. Cinqualbre, and P. Wolf

Transplant Proc, 2010

Radiofrequency Ablation of Small Hepatocellular Carcinoma in Cirrhotic Patients Awaiting Liver Transplantation

A Prospective Study

Vincenzo Mazzaferro, MD, Carlo Battiston, MD,* Stefano Perrone, MD,* Andrea Pulvirenti, MD,* Enrico Regalia, MD,* Raffaele Romito, MD,* Dario Sarli, MD,* Marcello Schiavo, MD,* Francesco Garbagnati, MD,† Alfonso Marchianò, MD,† Carlo Spreafico, MD,† Tiziana Camerini, PhD,‡ Luigi Mariani, MD,‡ Rosalba Miceli, MD,‡ and Salvatore Andreola, MD§*

Ann Surg, 2009

The Effect of Preoperative Transcatheter Hepatic Arterial Chemoembolization on Disease-Free Survival after Hepatectomy for Hepatocellular Carcinoma

Zhijian Zhang, M.D.[1]
Qi Liu, M.D.[2]
Jia He, Ph.D.[3]
Jiamei Yang, M.D.[1]
Guangshun Yang, M.D.[1]
Mengchao Wu, M.D.[1]

[1] Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, China.

Cancer, 2000

Effect of resection following downstaging of unresectable hepatocelluar carcinoma by transcatheter arterial chemoembolization

SHI Xian-jie, JIN Xin, WANG Mao-qiang, WEI Li-xin, YE Hui-yi, LIANG Yu-rong, LUO Ying and DONG Jia-hong

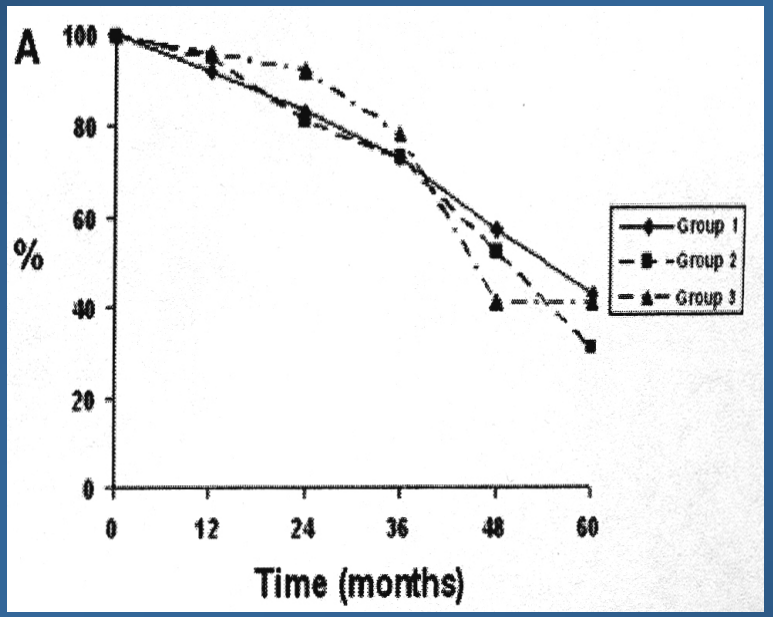
Chin Med J, 2012

Journal of Surgical Oncology 2009;100:580–584

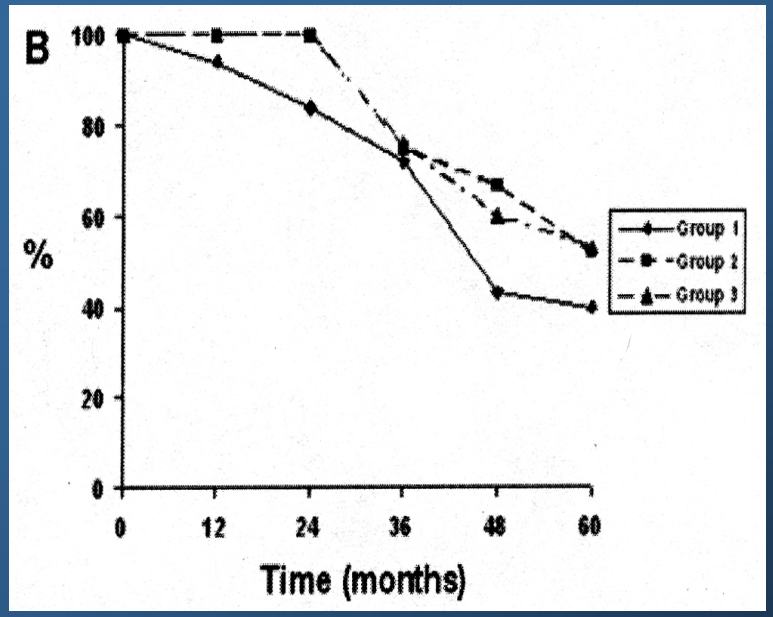
Sequential Multidisciplinary Treatment of Hepatocellular Carcinoma: The Role of Surgery as Rescue Therapy for Failure of Percutaneous Ablation Therapies

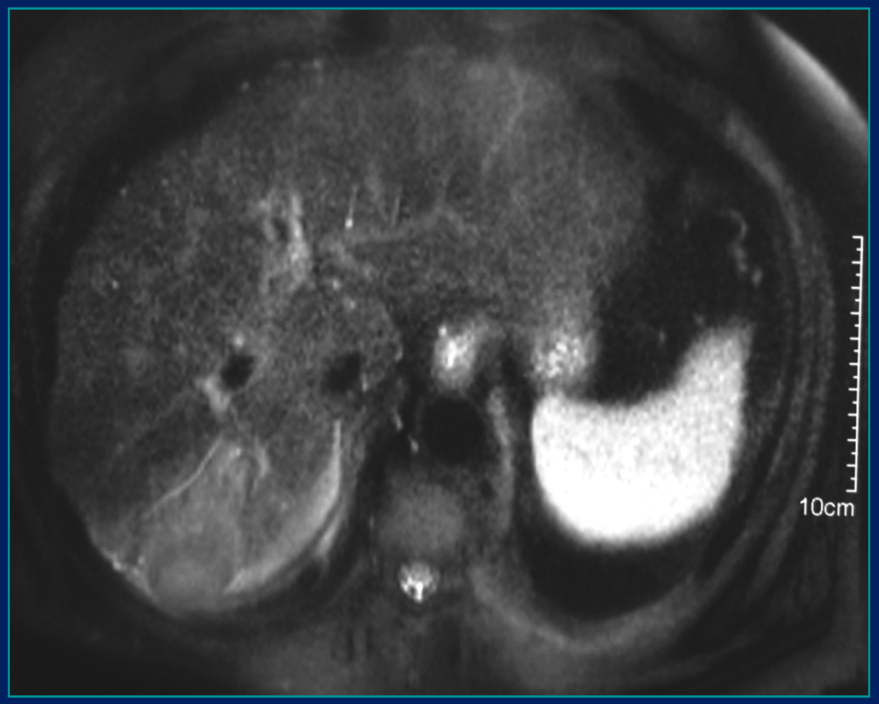
NAZARIO PORTOLANI, MD,[1] GIAN LUCA BAIOCCHI, MD,[1]* ARIANNA CONIGLIO, MD,[1]
LUIGI GRAZIOLI, MD,[2] ELEONORA FRASSI, MD,[1] FEDERICO GHEZA, MD,[1] AND STEFANO MARIA GIULINI, MD[1]
[1]*Department of Medical and Surgical Sciences, Surgical Clinic, Brescia University, Brescia, Italy*
[2]*1st Department of Radiology, Brescia Civil Hospital, Brescia, Italy*

Overall survival



Disease free survival




10cm

From other specialities to surgery in diagnosis and therapy

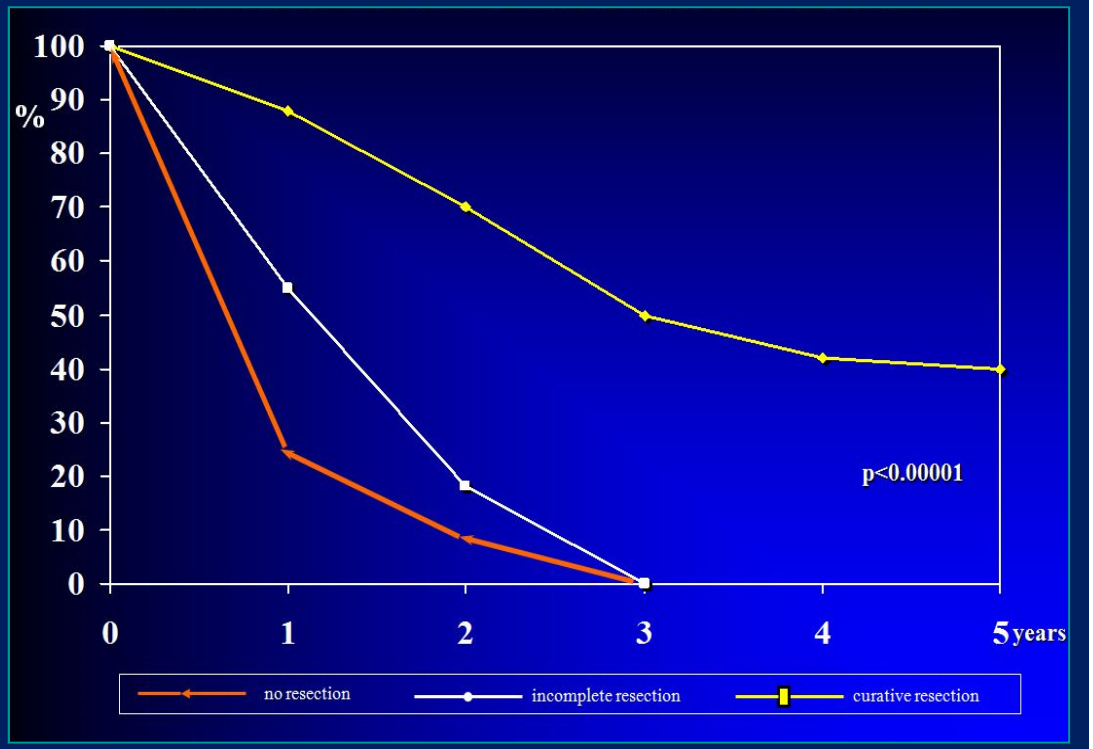
RADIOLOGY	A good preoperative stadiation	– *above all when OLT may be contemplated*
INTERVENTIONAL RADIOLOGY RADIOTHERAPY	Alternative treatments potentially curative or best palliation	– *treatment of small lesions in high risk patient* – *treatment of multi nodular cancer and recurrence* – *downstage of the tumor* – *a good "low risk" palliation*
PATHOLOGY	The identification of prognostic factor	– *above all when different treatments can be used*
ONCOLOGY HEPATOLOGY	Best medical treatment	– *as an adiuvant treatment* – *for the untreatable recurrence*

Surgery for liver metastasis

No more than 20-30% of patients
are fit for surgery

Ideally, the best indication is for

the patient:	*< 65 years-old*
	ASA ≤ 2
the tumour:	*< 5 cm size*
	≤ 4 nodules
the extrahepatic involvement:	*no node metastasis in the hepatic peduncle*
	no extrahepatic metastasis



Scheele, 1990

Surgery for liver metastasis

1990-2000

Focused on
cancer features

2000-2010

Focused on
remnant liver parenchima

Table 1 Indications for hepatectomy in the *Japanese Society of Cancer of the Colon and Rectum (JSCCR) guidelines 2010 for the treatment of colorectal cancer* [2]

1. The patient is capable of tolerating surgery
2. The primary tumor has been controlled or can be controlled
3. The metastatic liver tumor can be completely resected
4. There are no extrahepatic metastases or they can be controlled
5. The function of the remaining liver will be adequate

Surgery for liver metastasis

The limits of surgery for liver metastasis are progressively reducing

Technical inoperability

the remnant volume is judged as insufficient for liver function

↳ • *preoperative downstaging (TACE, RFA, RT, chemotherapy)*

• *increase of liver volume*

• *two stage surgery*

neoplastic residual tissue

↳ • *complementary therapies*

"Biological" inoperability

neoplastic aggressiveness
(vascular, lymphatic, nodal involvement, liver satellitosis)

↳ • *chemotherapy*

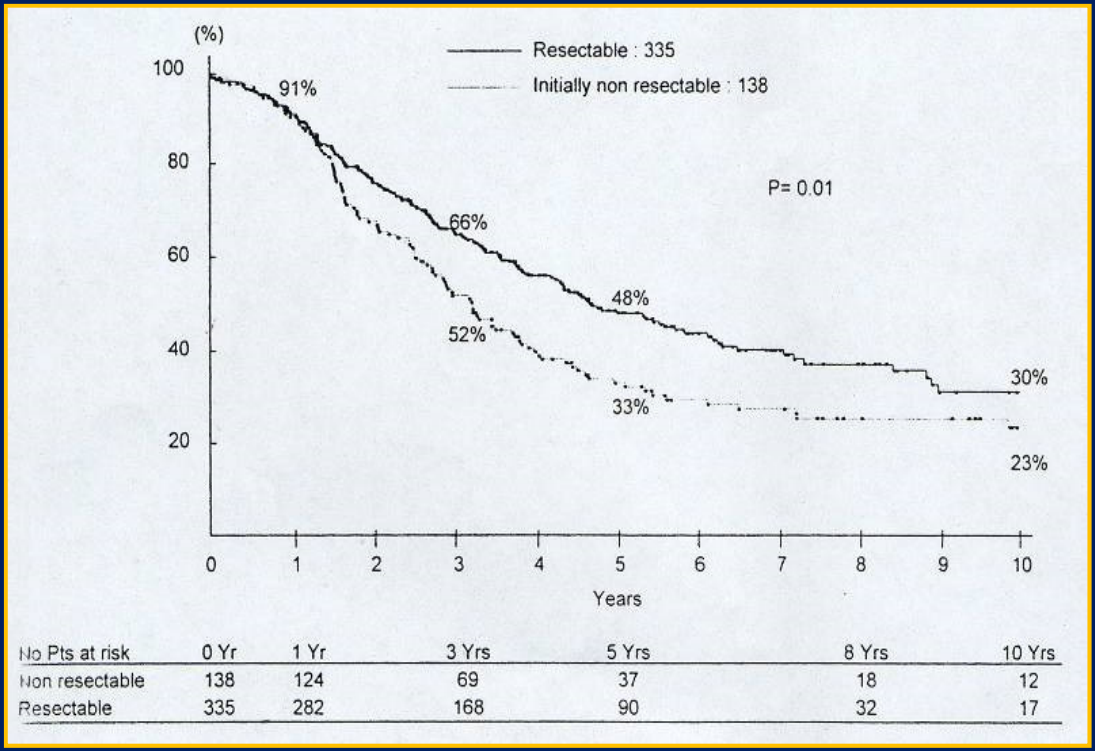
Conversion chemotherapy for unresectable liver metastasis

Rescue Surgery for Unresectable Colorectal Liver Metastases Downstaged by Chemotherapy

A Model to Predict Long-term Survival

René Adam, MD, PhD, Valérie Delvart, Gérard Pascal, MD, Adrian Valeanu, MD, Denis Castaing, MD, Daniel Azoulay, MD, PhD, Sylvie Giacchetti, MD, Bernard Paule, MD, PhD, Francis Kunstlinger, MD, Odile Ghémard, MD, Francis Levi, MD, PhD, and Henri Bismuth, MD, FACS Hon

Ann Surg, 2004



No Pts at risk	0 Yr	1 Yr	3 Yrs	5 Yrs	8 Yrs	10 Yrs
Non resectable	138	124	69	37	18	12
Resectable	335	282	168	90	32	17

138/1104 patients (12.5%)

33% alive at 5 years
(median survival 39 m.)

10 cycles of chemotherapy on average

342 surgical interventions

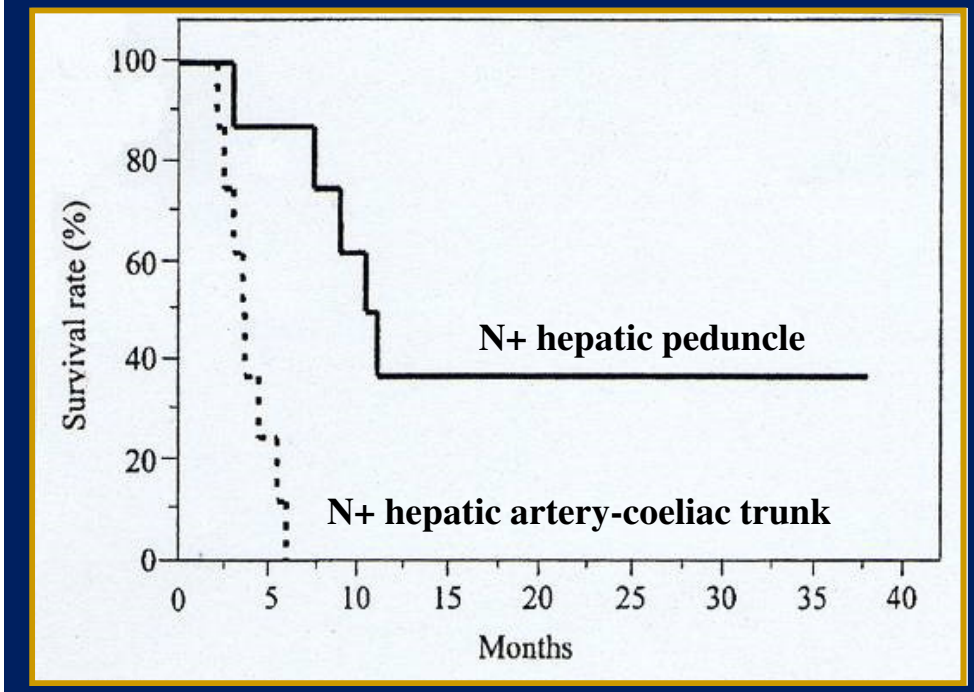
Liver resection for liver metastasis

Evolving strategy: chemotherapy has changed the indications of surgery

Significance of Hepatic Pedicle Lymph Node Involvement in Patients With Colorectal Liver Metastases: A Prospective Study

Daniel Jaeck, MD, PhD, Hiroshi Nakano, MD, PhD, Philippe Bachellier, MD, Keiichiro Inoue, MD, Jean-Christophe Weber, MD, Elie Oussoultzoglou, MD, Philippe Wolf, MD, PhD, and Marie-Pierre Chenard-Neu, MD, PhD

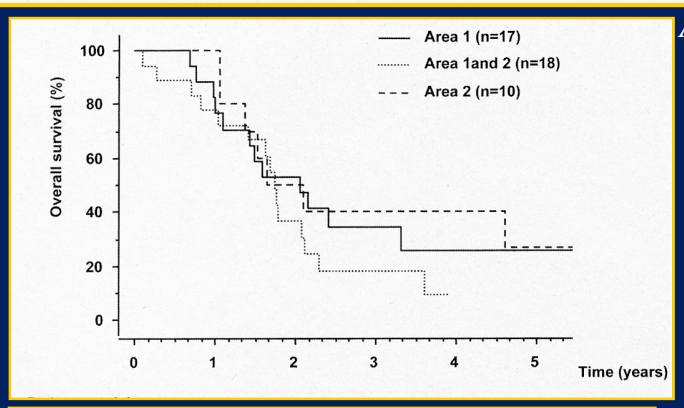
Ann Surg, 2002

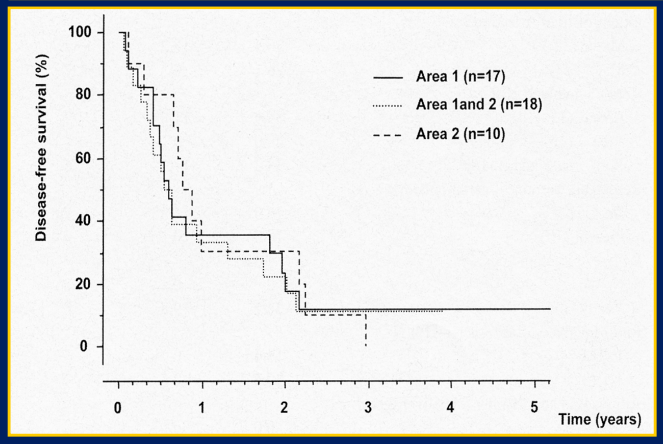


Long-Term Survival After Liver Resection for Colorectal Liver Metastases in Patients With Hepatic Pedicle Lymph Nodes Involvement in the Era of New Chemotherapy Regimens

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





REVIEW AND META-ANALYSIS

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: Preoperative standard chemotherapy can be recommended for downsizing unresectable liver metastases, but not for resectable lesions, for which adjuvant chemotherapy is preferred.

From other specialities to surgery in diagnosis and stadiation

RADIOLOGY	morphologic and topographic definition of the lesions and of the reminant liver	– *feasibility of R0 surgery*
NUCLEAR MEDICINE	better definition of suspect extrahepatic localizations	– *to guide feasible radical surgery* – *to avoid useless surgery*
BIOLOGY	a better knowledge of the cancer aggressiveness and genetic characterization	– *a tailored approach to medical therapy*
ONCOLOGY	A complessive therapeutic strategy	– *the best protocol of association among medical and surgical procedures*

From other specialities to surgery in the therapy

RADIOLOGY
RADIOTHERAPY
NUCLEAR MEDICINE

direct approach to residual or recurrent lesion

- Percutaneous ethanol ablation
- Radiofrequency ablation
- Radiotherapy
- Chemoembolization
- Radioembolization

BIOLOGY

a better knowledge of the cancer aggressiveness and genetic characterization

ONCOLOGY

tailored medical treatment

- *neoadiuvant*
- *adiuvant*

Chemotherapy

Brescia Meetings in Radiation Oncology - 2012