



Università degli Studi di Verona
Dipartimento di Chirurgia
Chirurgia Generale ed Epatobiliare
Policlinico G.B. Rossi



Patient Journey
Approccio personalizzato al
paziente e esperienze a
confronto:
Epatocarcinoma e
Colangiocarcinoma

01 Febbraio 2024
VERONA
CROWNE PLAZA
Via Belgio, 16

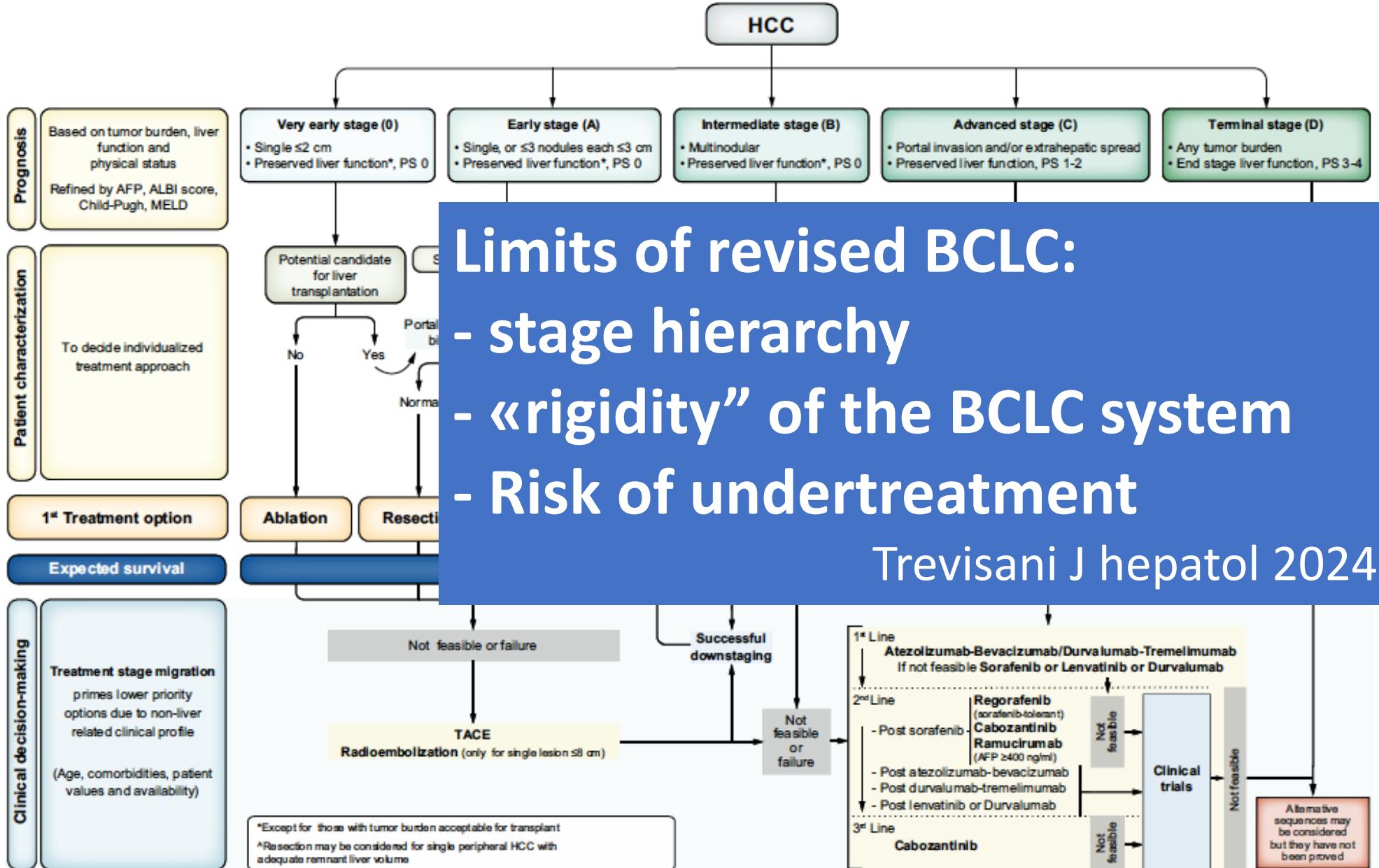


Ruolo del chirurgo nell'epatocarcinoma

Andrea Ruzzenente

Verona, 1 febbraio 2024

TRATTAMENTO DELL'EPATOCARCINOMA



Personalised management of patients with hepatocellular carcinoma: a multiparametric therapeutic hierarchy concept

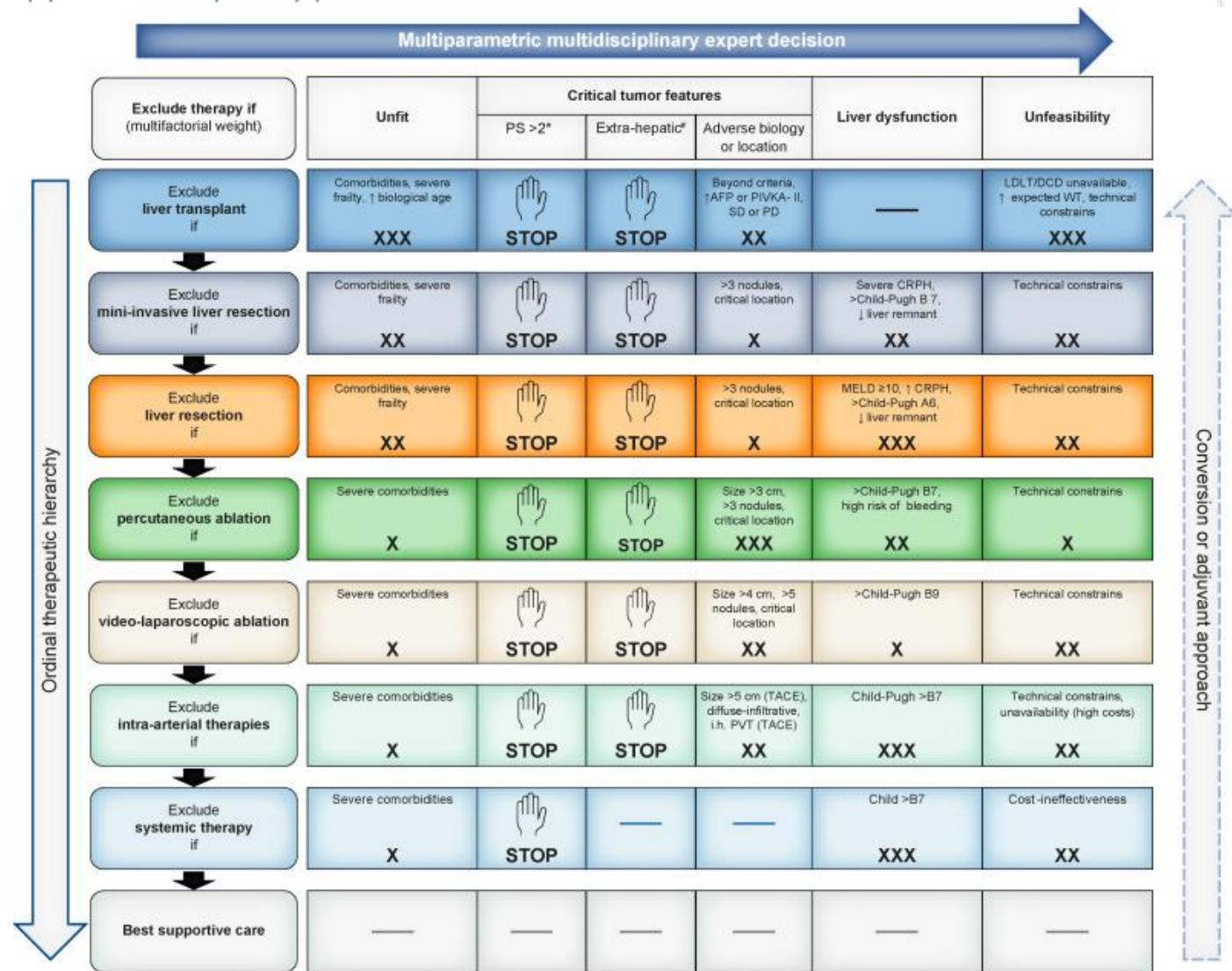
Alessandro Vitale, Giuseppe Cabibbo, Massimo Iavarone, Luca Viganò, David J Pinato, Francesca Romana Ponziani, Quirino Lai, Andrea Casadei-Gardini, Ciro Celsa, Giovanni Galati, Martina Gambato, Laura Crocetti, Matteo Renzulli, Edoardo G Giannini, Fabio Farinati, Franco Trevisani, Umberto Cillo, on behalf of the HCC Special Interest Group of the Italian Association for the Study of the Liver*



Personalised management of patients with hepatocellular carcinoma: a multiparametric therapeutic hierarchy concept



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EXPLORE THE TREATMENT WITH
THE BEST SURVIVAL BENEFIT
according to

Transplant

MILS Resection

Open resection

Percutaneous ablation

MILS Ablation

Intra-arterial therapies

Systemic

BSC

Multiparametric Evaluation

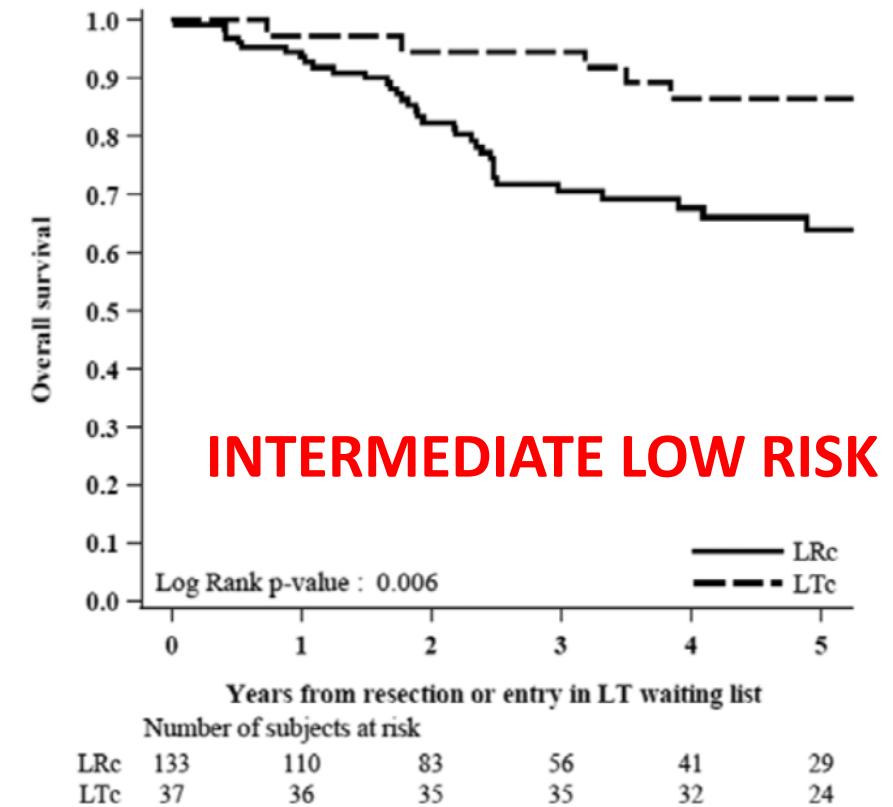
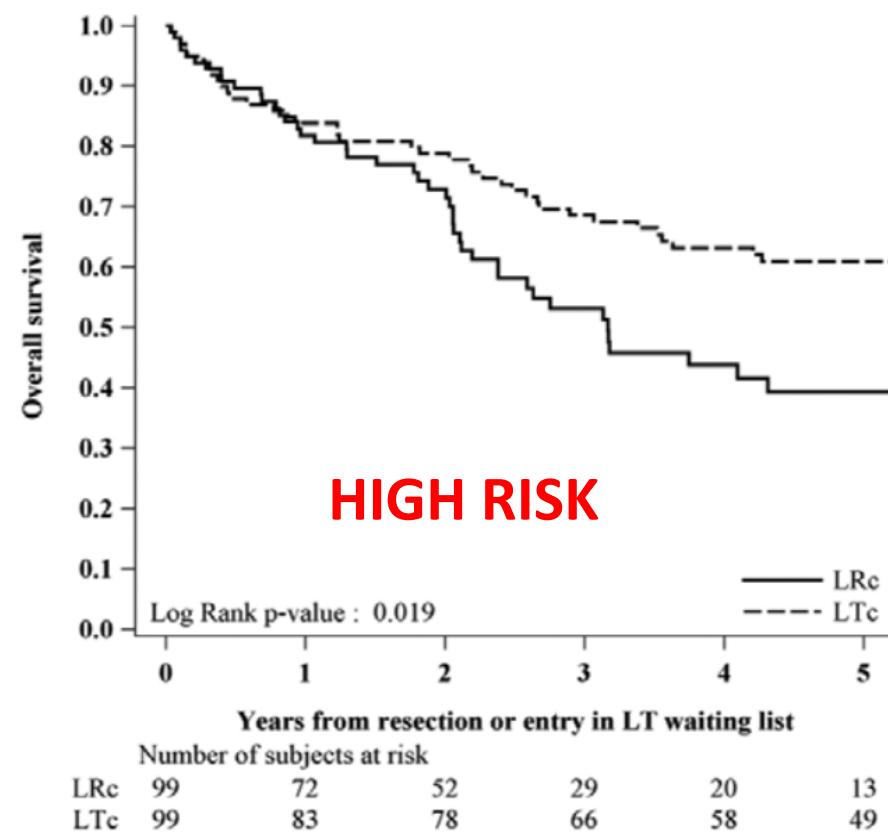
- Oncological Staging
- Patient's PS and frailty
- Comorbidities
- Tumor Location
- Liver Function (not only CHILD...)
- Specific technical contraindications
- Resource availability

Surgical Treatment of Hepatocellular Carcinoma: Multicenter Competing-risk Analysis of Tumor-related Death Following Liver Resection and Transplantation Under an Intention-to-treat Perspective

Stefano Di Sandro, MD, PhD,¹ Carlo Sposito, MD,^{2,3} Matteo Ravaioli, MD, PhD,^{4,5} Andrea Lauterio, MD,^{6,7} Paolo Magistri, MD,¹ Marco Bongini, MD,² Federica Odaldi, MD,⁴ Riccardo De Carlis, MD,^{6,8} Francesca Botta, PhD,⁹ Leonardo Centonze, MD,^{6,10} Lorenzo Maroni, MD,⁴ Davide Citterio, MD,² Cristiano Guidetti, MD,¹ Vincenzo Bagnardi, PhD,⁹ Luciano De Carlis, MD,^{6,7} Matteo Cescon, MD, PhD,^{4,5} Vincenzo Mazzaferro, MD,^{2,3} and Fabrizio Di Benedetto, MD, PhD¹; HV-HCC-MRT-group*

RISK SCORE

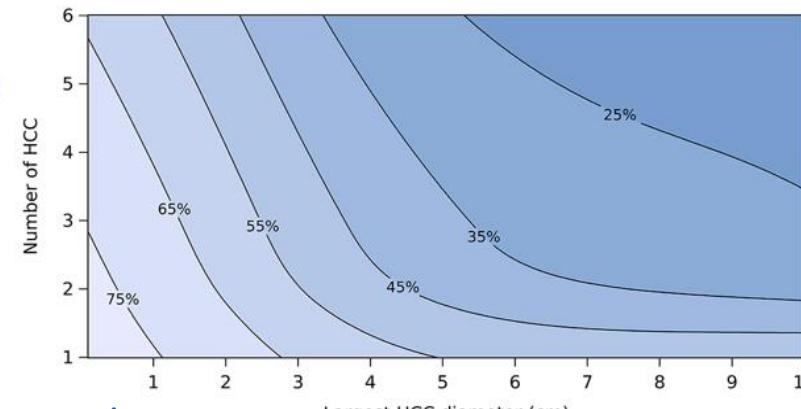
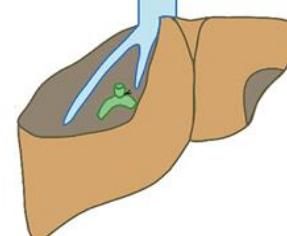
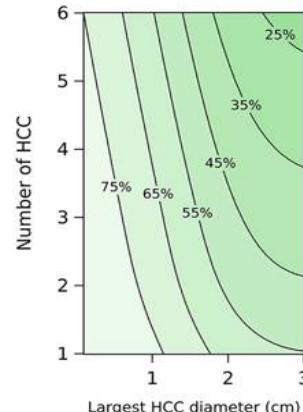
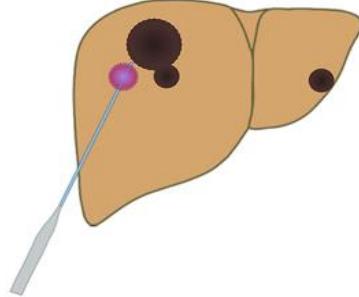
- liver cirrhosis
- aspartate transaminase (AST)
- MELD score
- alpha-feto- protein (α -FP)
- number of HCC nodules
- diameter of the largest nodule



Effect of Diameter and Number of Hepatocellular Carcinomas on Survival After Resection, Transarterial Chemoembolization, and Ablation

Kawaguchi, Yoshikuni MD, PhD^{1,*}; Hasegawa, Kiyoshi MD, PhD^{1,*}; Hagiwara, Yasuhiro PhD^{2,*}; De Bellis, Mario MD³; Famularo, Simone MD^{4,5}; Panettieri, Elena MD⁶; Matsuyama, Yutaka PhD^{2,*}; Tateishi, Ryosuke MD, PhD^{7,*}; Ichikawa, Tomoaki MD, PhD^{8,*}; Kokudo, Takashi MD, PhD^{1,*}; Izumi, Namiki MD, PhD^{9,*}; Kubo, Shoji MD, PhD^{10,*}; Sakamoto, Michiee MD, PhD^{11,*}; Shiina, Shuichiro MD, PhD^{12,*}; Takayama, Tadatoshi MD, PhD^{13,*}; Nakashima, Osamu MD, PhD^{14,*}; Murakami, Takamichi MD, PhD^{15,*}; Vauthey, Jean-Nicolas MD¹⁶; Giulianetti, Felice MD⁶; De Carlis, Luciano MD^{4,17}; Romano, Fabrizio MD^{4,5}; Ruzzene, Andrea MD, PhD³; Guglielmi, Alfredo MD³; Kudo, Masatoshi MD, PhD^{18,*}; Kokudo, Norihiro MD, PhD^{19,*}

◆Ablation



Am J Gastroenterol 2021

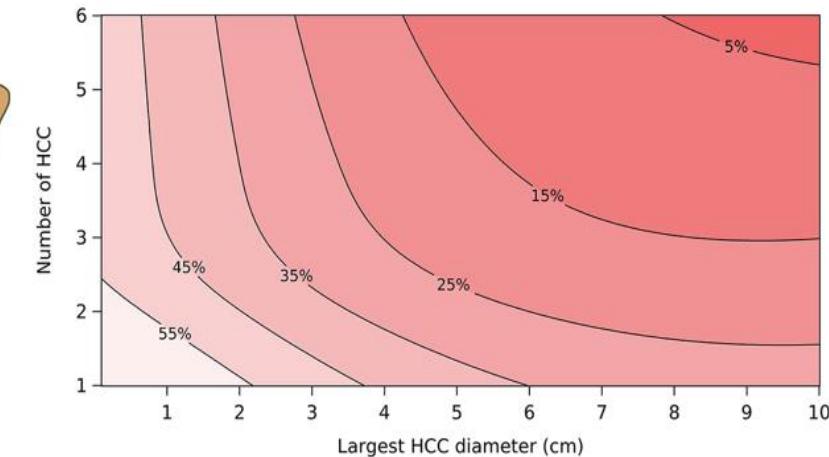
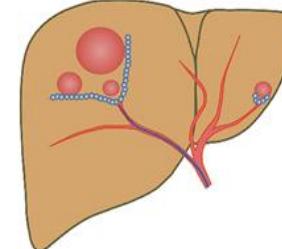
43.904 HCC

15.313 Resections

15.216 Ablations

13.375 TACE

◆TACE



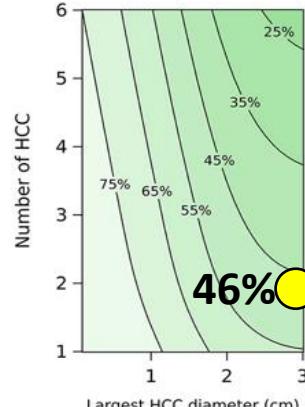
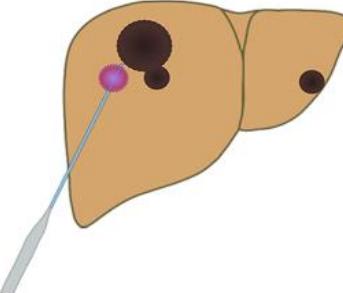
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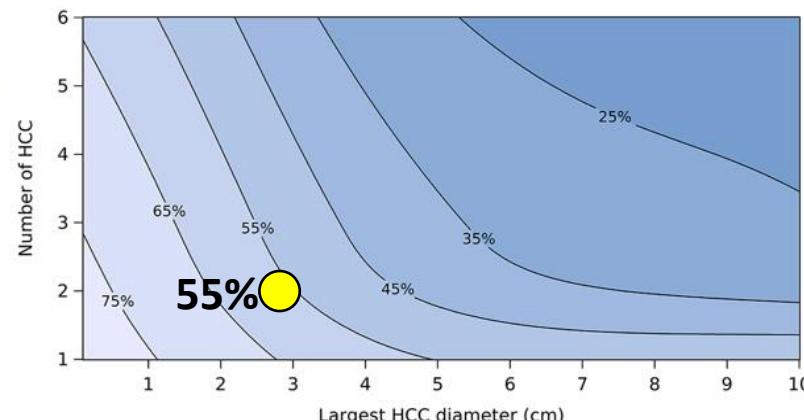
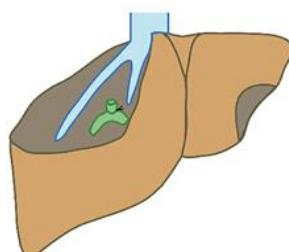
Am J Gastroenterol 2021

**43.904 HCC
15.313 Resections
15.216 Ablations
13.375 TACE**

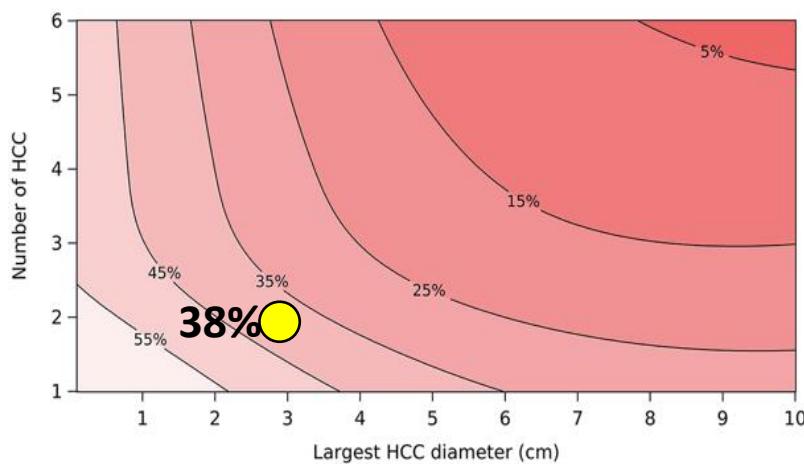
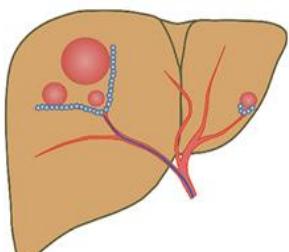
◆Ablation



◆Resection



◆TACE



Survival Calculator for Hepatocellular Carcinoma (HCC)

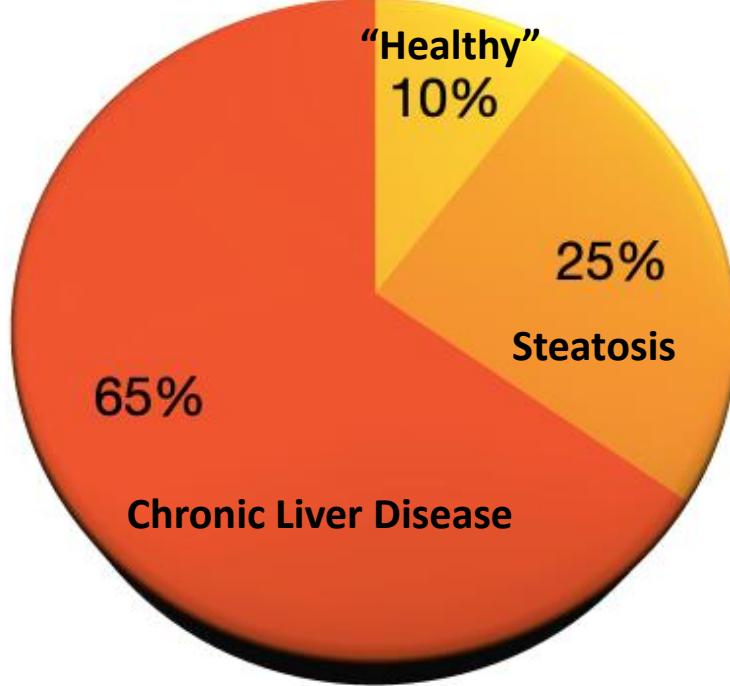
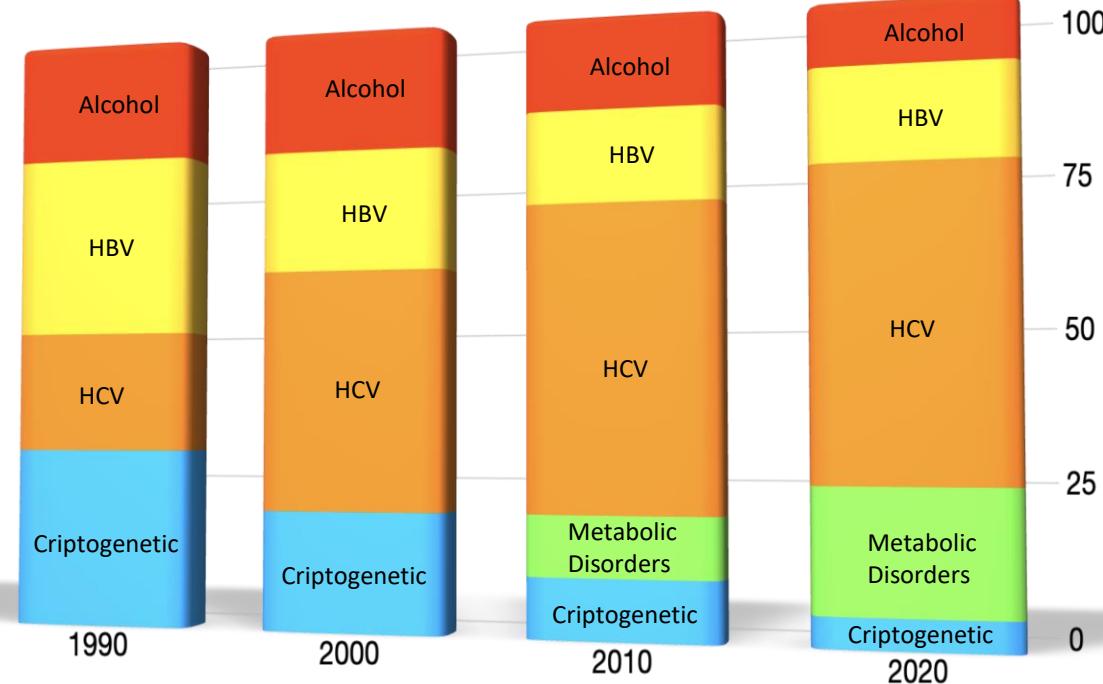
■ Resection, Trans-Arterial Chemoembolization (TACE), and Ablation

	Number	Largest diameter, cm
Select	2	3.0

	Overall survival†		
	1-year	3-year	5-year
Resection	91.1 %	71.5 %	55.4 %
TACE	89.6 %	60.3 %	38.2 %
Ablation‡	92.7 %	68.1 %	46.0 %



Epidemiology trends

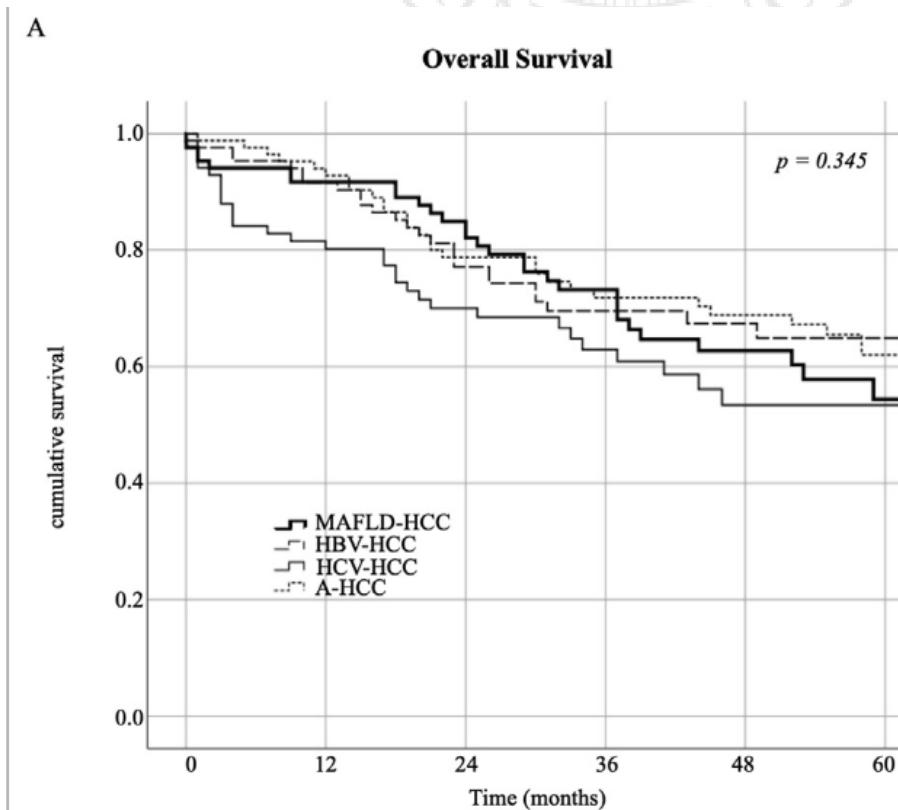


Extralesional liver

Hepatectomy for Metabolic Associated Fatty Liver Disease (MAFLD) related HCC: Propensity case-matched analysis with viral- and alcohol-related HCC

Conci S, Ruzzenente A et al.

	MAFLD-HCC	HBV-HCC	HCV-HCC	A-HCC	p-values
Cirrhosis	38%	59%	73%	66%	<0.001
Steatosis	90%	8%	8%	14%	<0.001
Portal Hypertension	7%	18%	22%	20%	< 0.001



	Number at risk	85	75	59	44	30	14
MAFLD-HCC	85	75	59	44	30	14	
HBV-HCC	85	72	56	36	27	16	
HCV-HCC	85	60	46	31	18	12	
A-HCC	85	76	60	52	42	33	



Trends in hospital volume and operative mortality in hepato-biliary surgery in Veneto region, Italy

Alfredo Guglielmi¹ · Marzia Triepi¹ · Laura Salmaso² · Ugo Fedeli² · Andrea Ruzzenente¹ · Mario Saia²

Received: 17 February 2023 / Accepted: 22 June 2023 / Published online: 3 July 2023

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2010-2021
7989 Hepatobiliary procedures

MORTALITY

2010-2013	2,2%
2014-2017	1,9%
2018-2021	1,4%



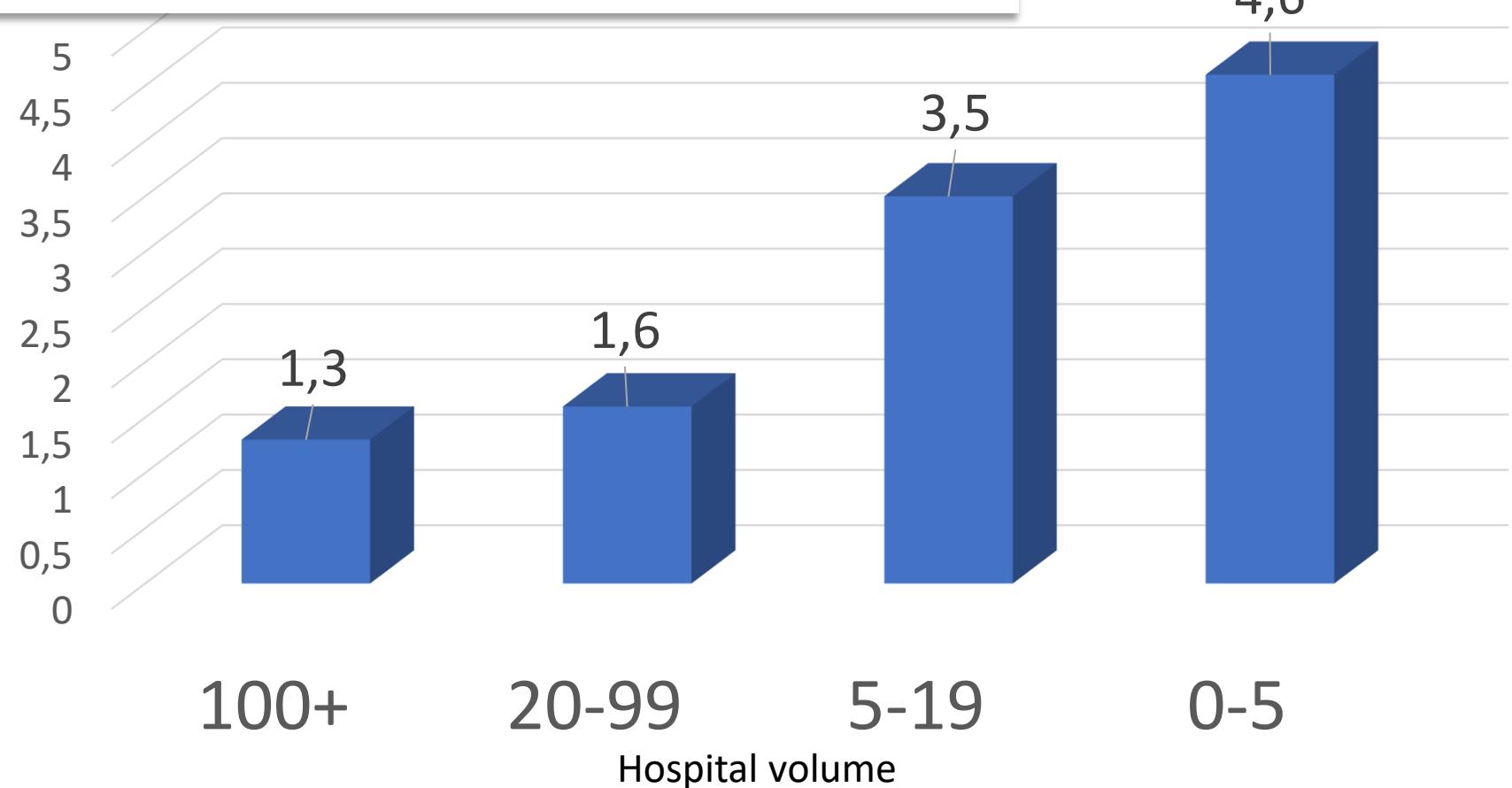
Trends in hospital volume and operative mortality in hepato-biliary surgery in Veneto region, Italy

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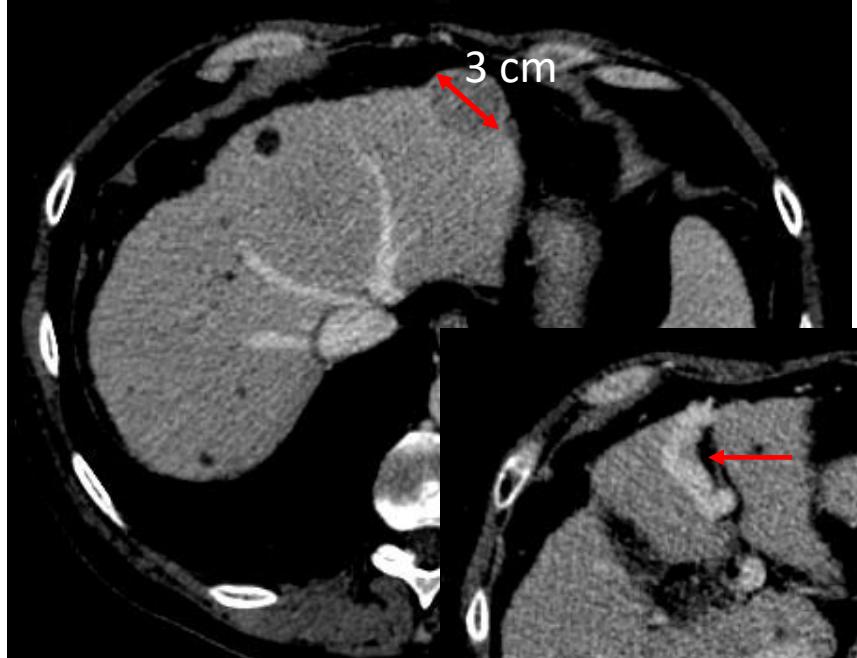
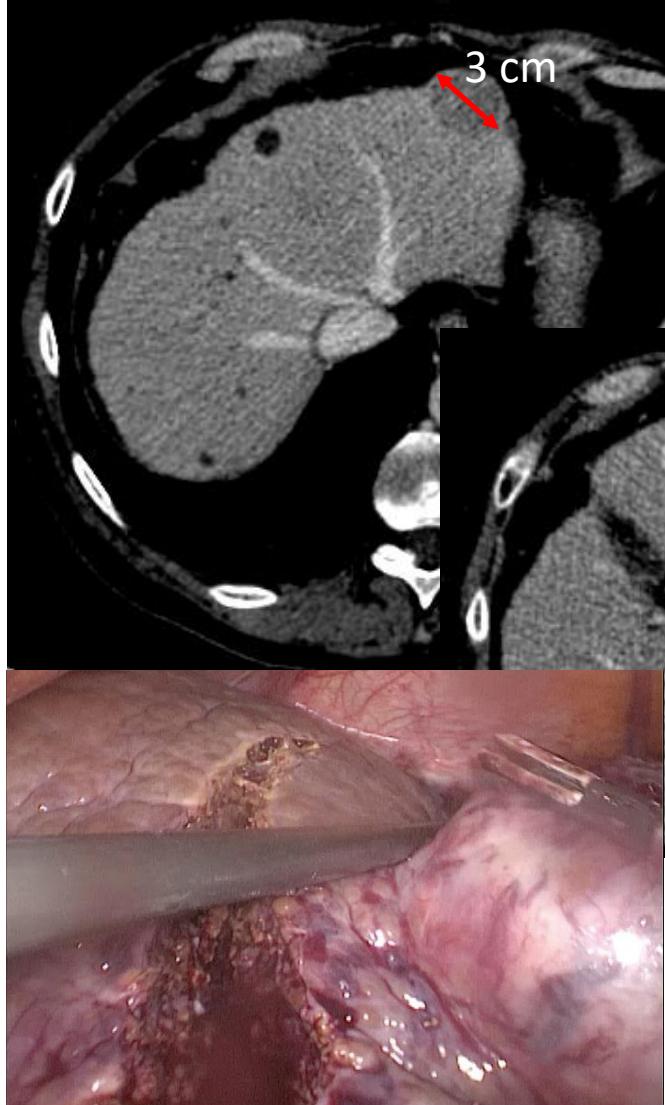
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MORTALITY & HOSPITAL VOLUME

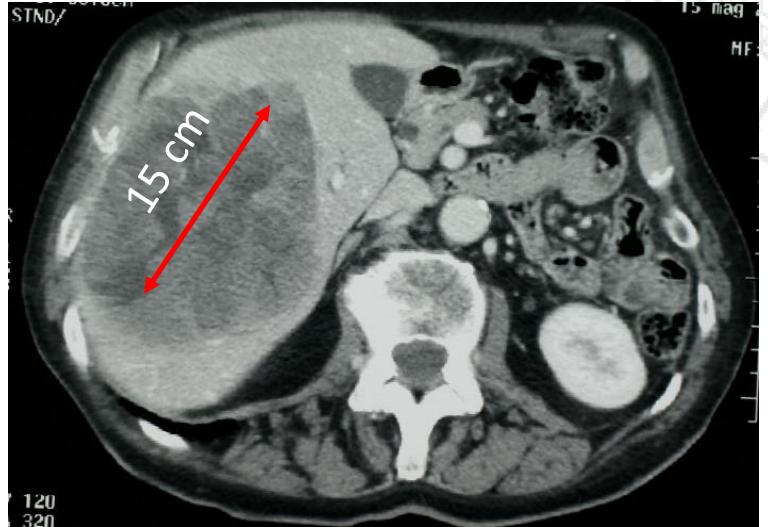


EARLY-VERY EARLY

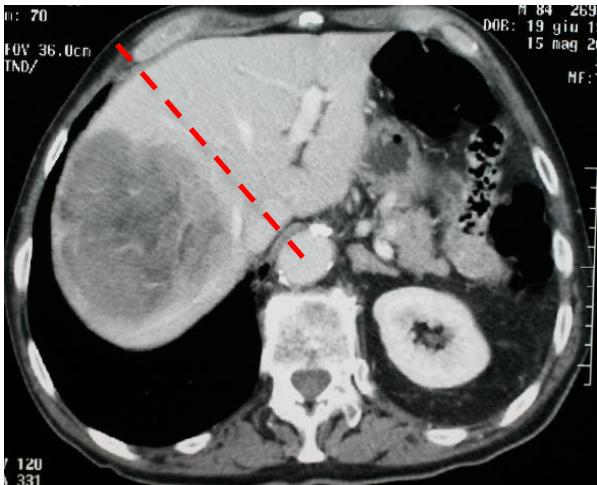


CHILD A6 – ICGR15 66,3%
- PLTS 65.000
Portal hypertension

INTERMEDIATE-ADVANCED



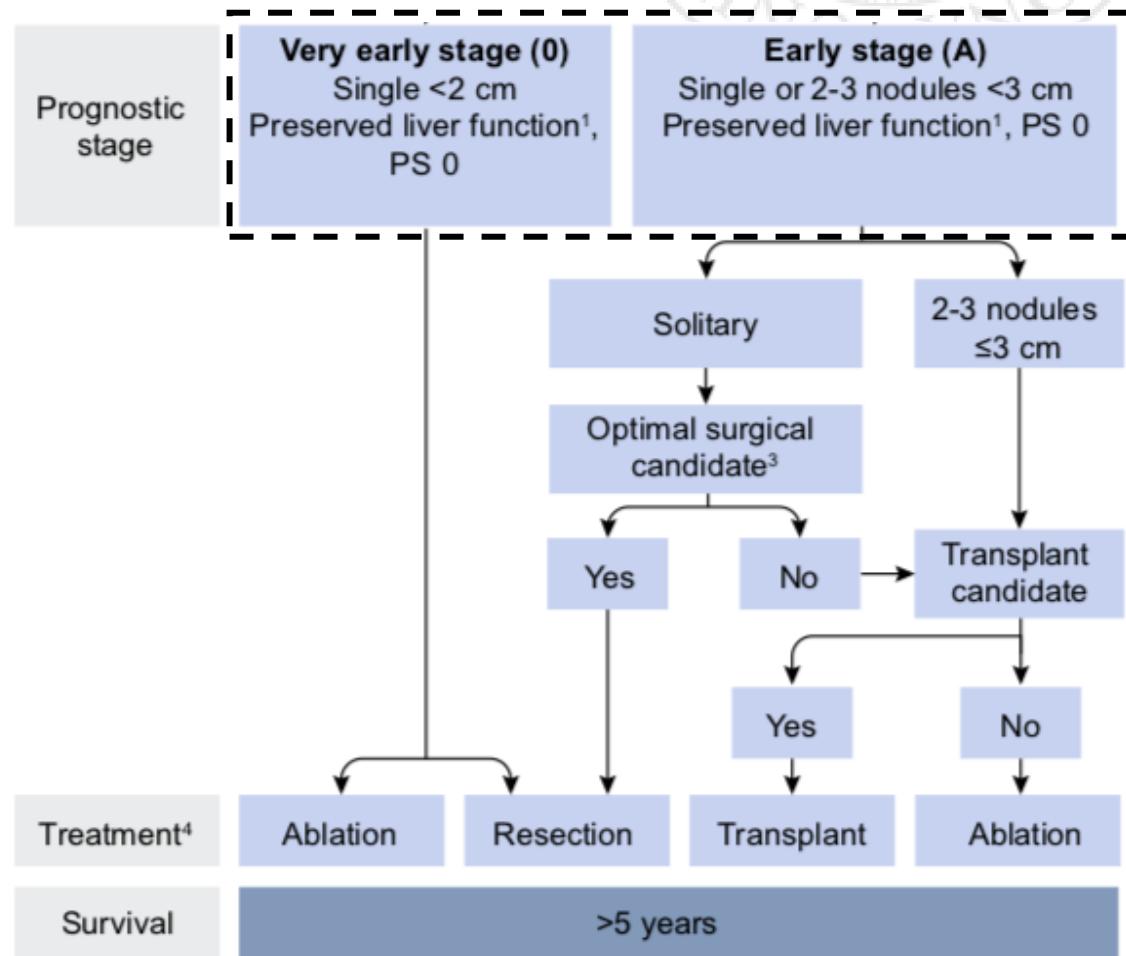
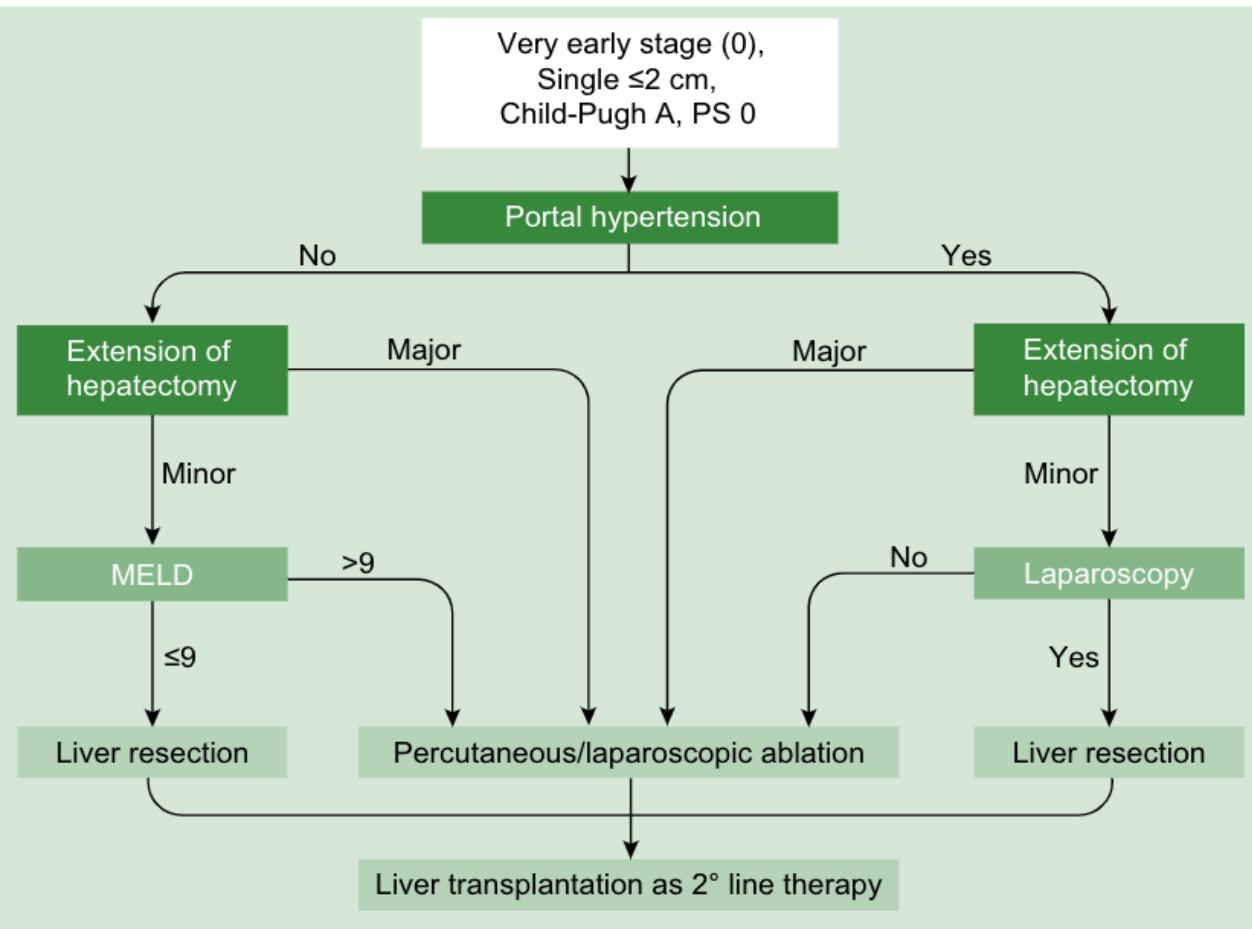
CHILD A5 – ICGR15 3,7%



VERY EARLY – EARLY HCC

Personalized treatment of patients with very early hepatocellular carcinoma

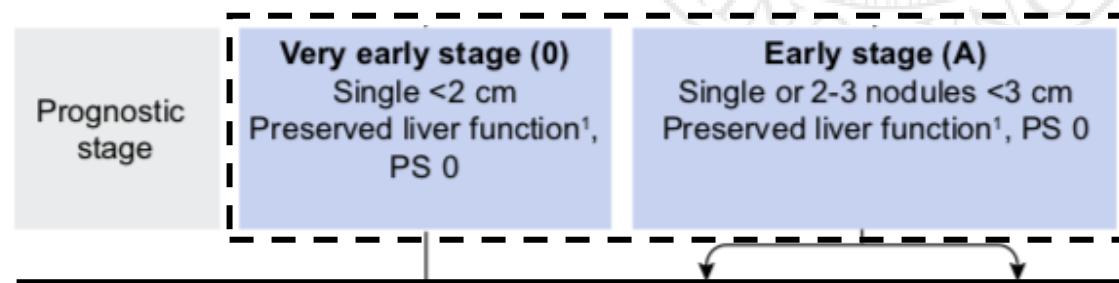
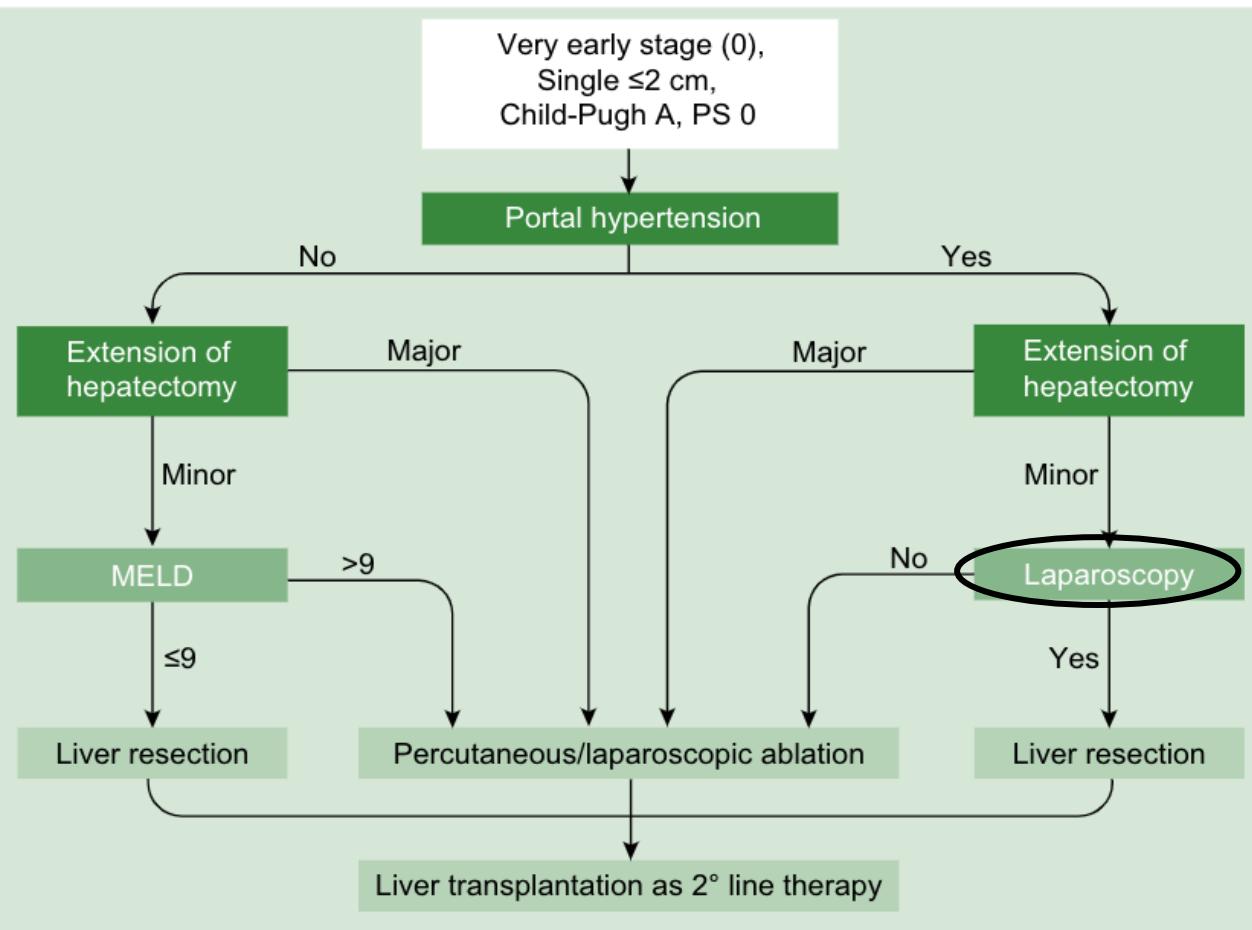
Vitale A et al.



EARLY HCC

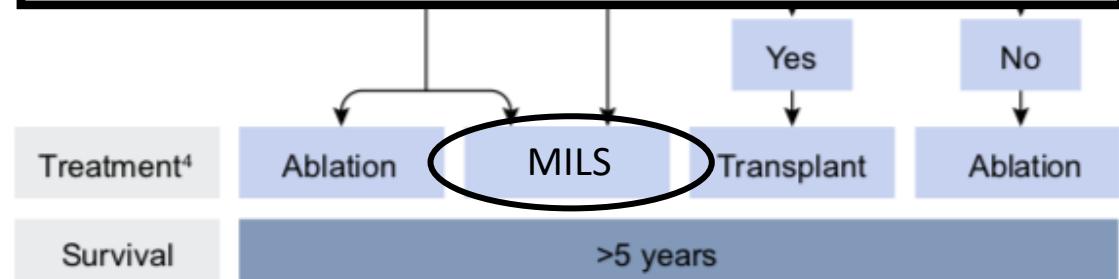
Personalized treatment of patients with very early hepatocellular carcinoma

Vitale A et al.



Il ruolo del chirurgo è decisivo negli stadi precoci della malattia (very early + early)

Chirurgia laparoscopica sempre più gold standard





Incidence of PHLF and ascites in HCC surgery

- ✓ Overall complication rate of **44%**
- ✓ Major complications in **9.5%**
- ✓ Postoperative ascites in **9.5%**
- ✓ Postoperative liver failure in **6 %**
- ✓ 90 days mortality **3.5%**



Original article
Benchmarking postoperative outcomes after open
liver surgery for cirrhotic patients with
hepatocellular carcinoma in a national cohort

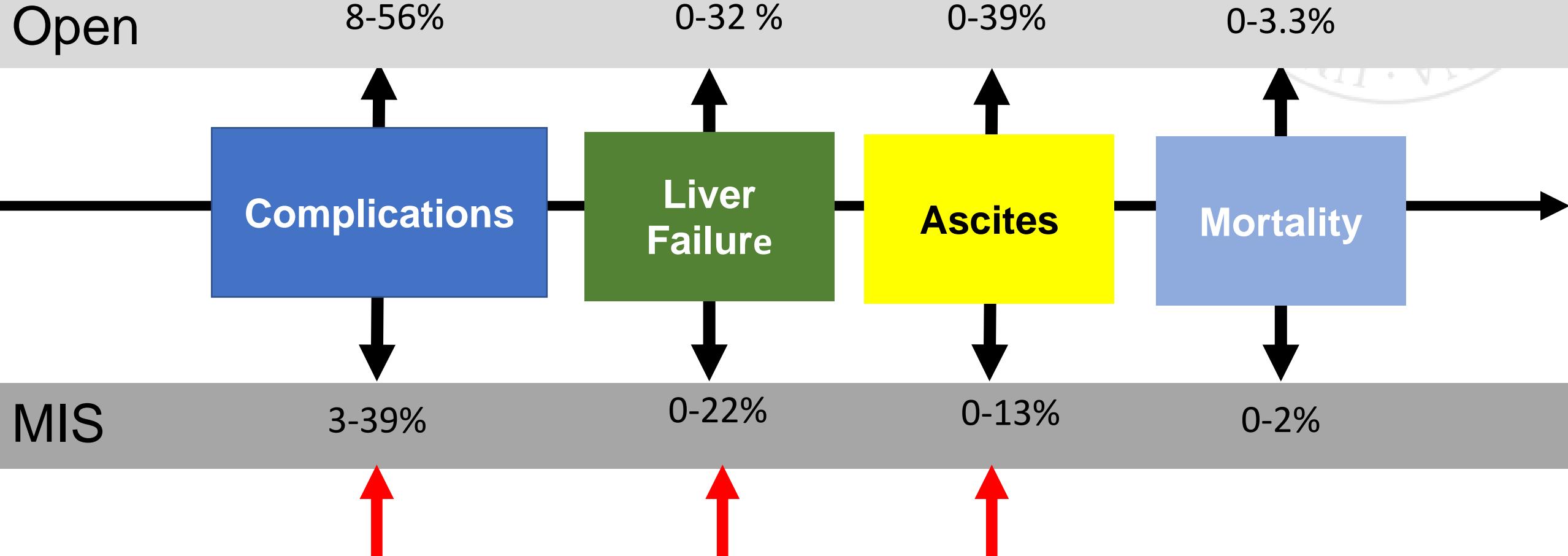
Simone Famularo^{1,2,3}, Nadia Russolillo⁴, Matteo Donadon^{1,2} & Federica Cipriani⁵, Francesco Ardito⁶,
Pasquale Perri⁷, Alessandro Gianni⁷, Francesca De Stefano⁸, Quirino Lisi⁹, Sarah Molinò¹⁰, Matteo Zanelli¹¹,
Maurizio Iaria¹², Giuliano La Barba¹³, Enrico Pinotti¹⁴, Paola Germani¹⁵, Simone Conci¹⁶, Cecilia Ferrari¹⁷, Luca
Fumagalli¹⁸ ... Davide Gaudesi¹⁹

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Surgery for HCC: MILS vs Open



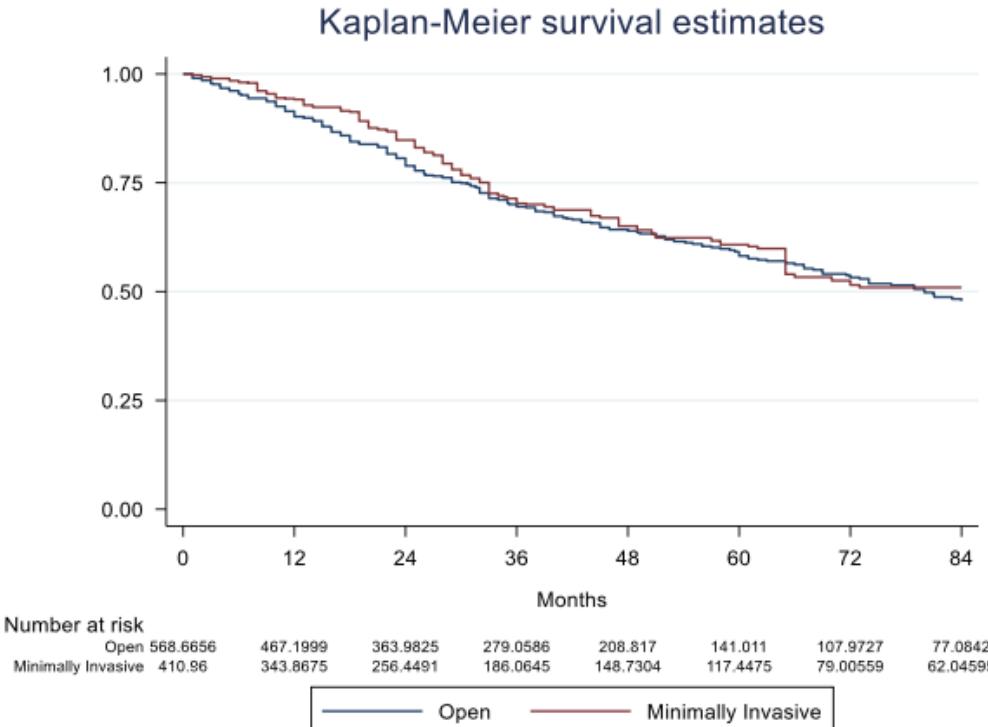
[Chen, Kim, Guro, Xu, Yoon, Di Sandro, Tsai , Untereiner,
Deng, Iwata, Ryu, Wu, Cheung, El Ghendi, Liu, Cipriani]



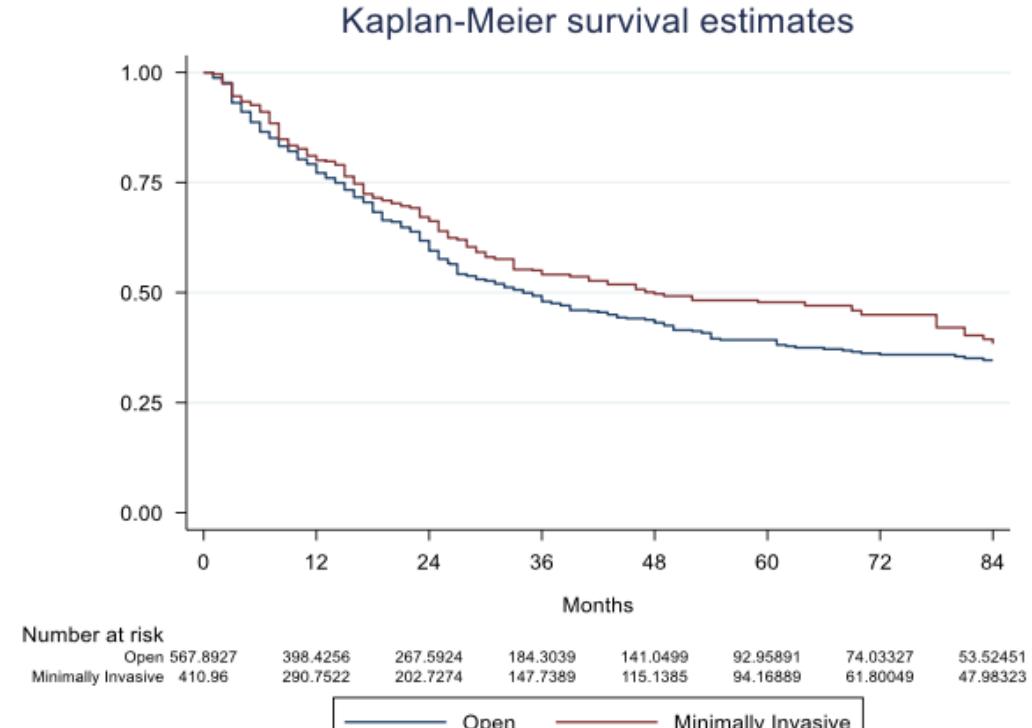
Long survival MILS vs OPEN

996 resections for HCC on metabolic syndrome → 580 open vs 416 MILS

OS



Disease free survival





Laparoscopic versus open resection of hepatocellular carcinoma in patients with cirrhosis: meta-analysis

Tousif Kabir ^{1,2}, Zoe Z. Tan², Nicholas L. Syn ³, Eric Wu ³, J. Daryl Lin ³, Joseph J. Zhao ³, Alvin Y.H. Tan¹, Yong Hui^{1,2}, Juinn H. Kam^{1,2} and Brian K. P. Goh ^{2,4,*}

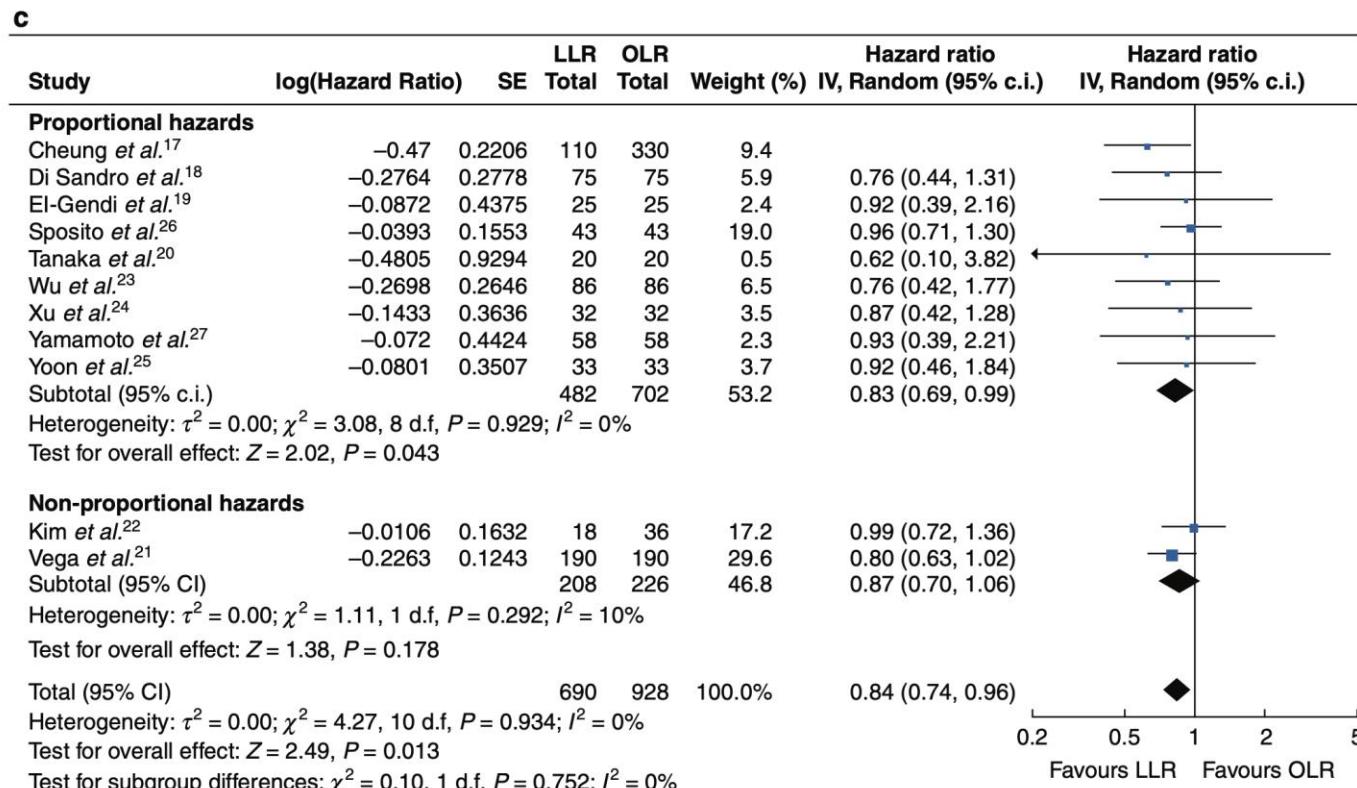
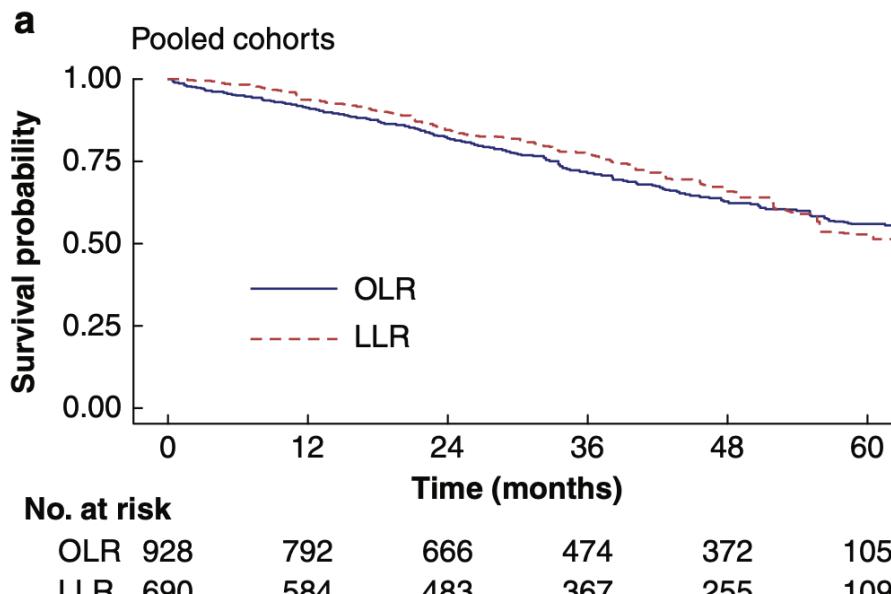
¹Department of General Surgery, Sengkang General Hospital, Singapore

²Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital, Singapore

³Yong Loo Lin School of Medicine, Singapore

⁴Duke NUS Medical School, Singapore

*Correspondence to: Brian K.P. Goh, Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital, 20 College Road, Singapore 169856
 (e-mail: bsgkp@hotmail.com)

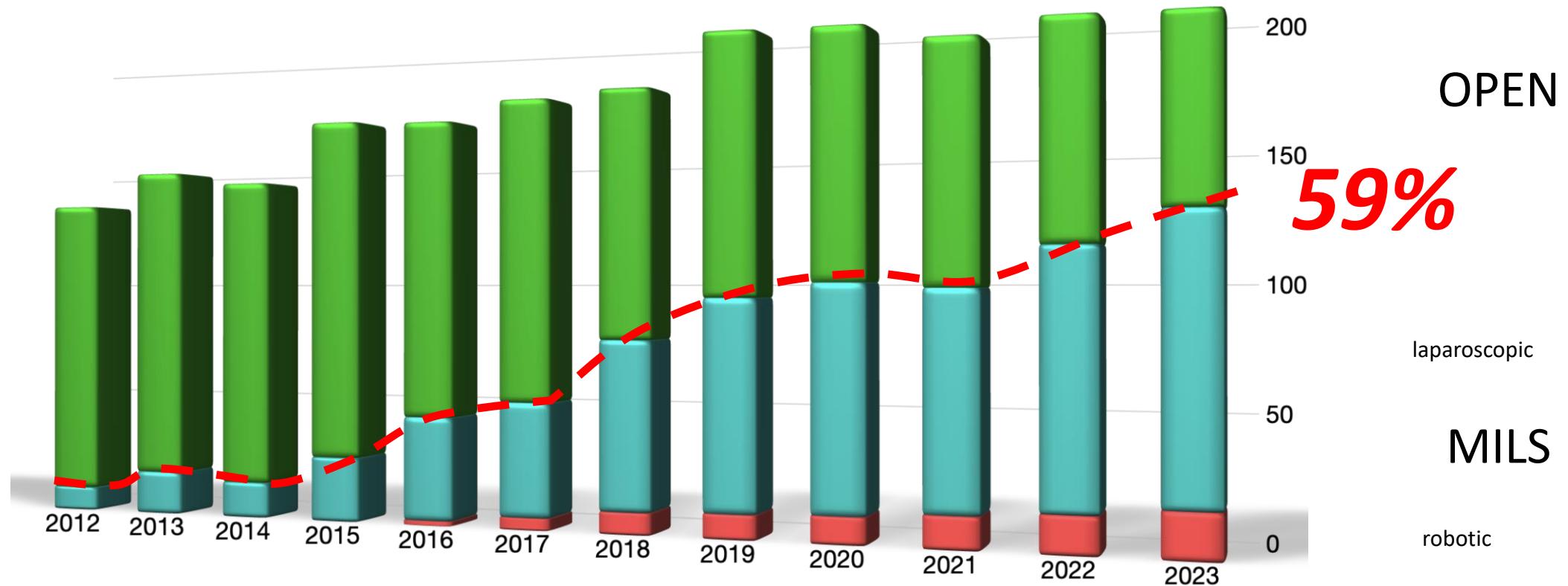


Evolution of Liver Surgery in Verona

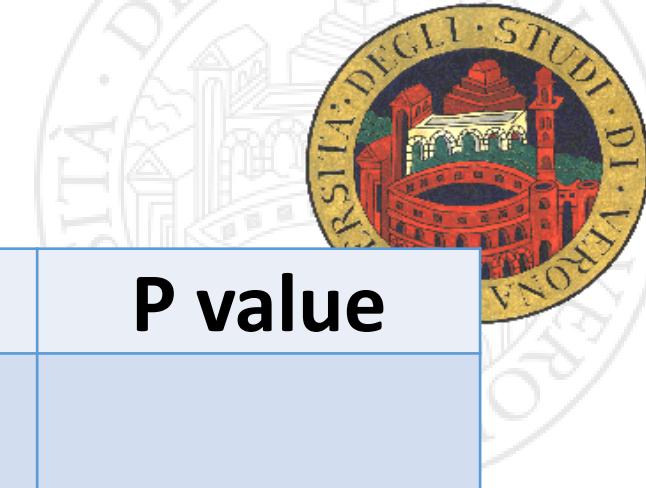


University of Verona
General and Hepatobiliary Surgery
GB Rossi Hospital

Hepatobiliary Resection
2012-2023
tot 2048 – MILS 753



Surgery for HCC



Variable	Open (n=356)	MILS (n=208)	P value
Overall Morbidity			
No	104 (57.3%)	140 (67.3%)	
Yes	152 (42.7%)	68 (32.7%)	0.019
Clavien-Dindo≥III			
No	249 (69.9%)	198 (95.2%)	
Yes	107 (30.1%)	10 (4.8%)	<0.001
PHLF			
No	297 (83.4%)	174 (91.6%)	
Yes	59 (16.6%)	16 (8.4%)	0.008
Length of Stay (days)	11 (± 8)	6 (± 3)	<0.001
90-Days mortality			
No	348 (98%)	207 (99.5%)	
Yes	8 (2%)	1 (0.5%)	0.042

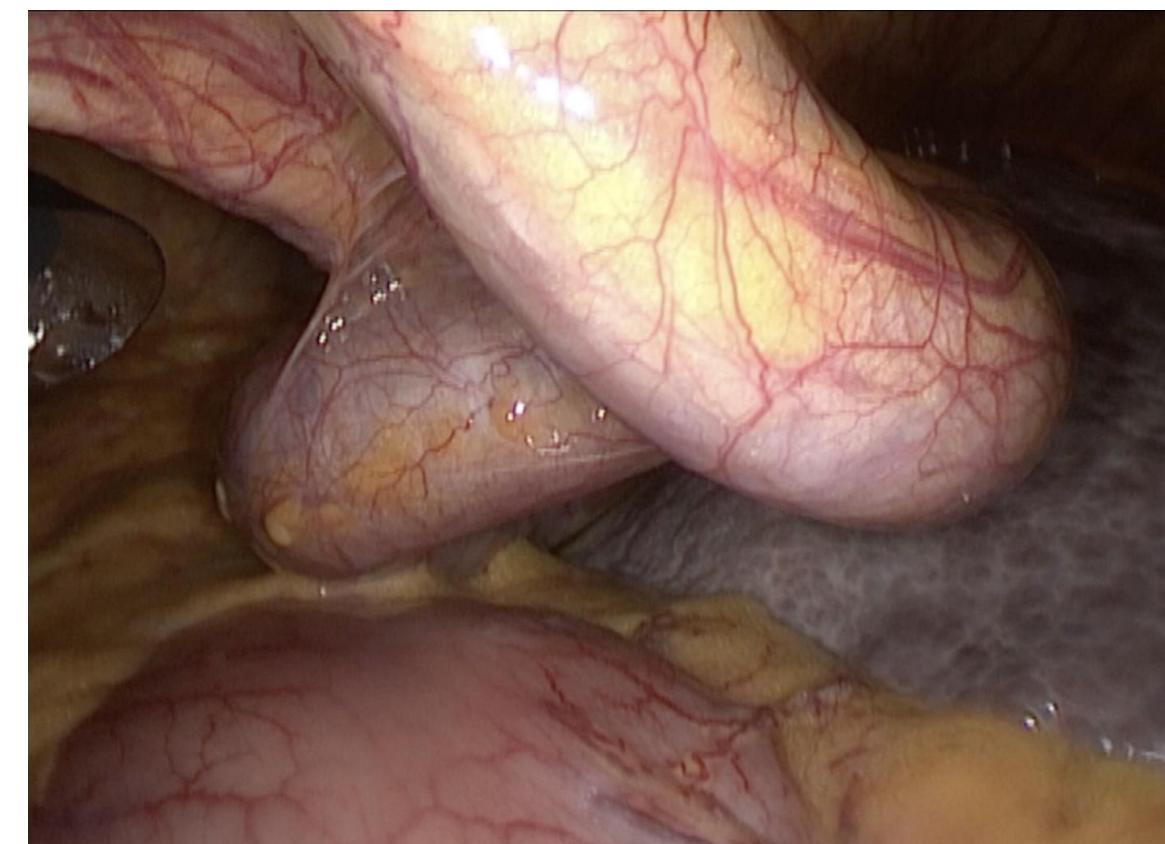
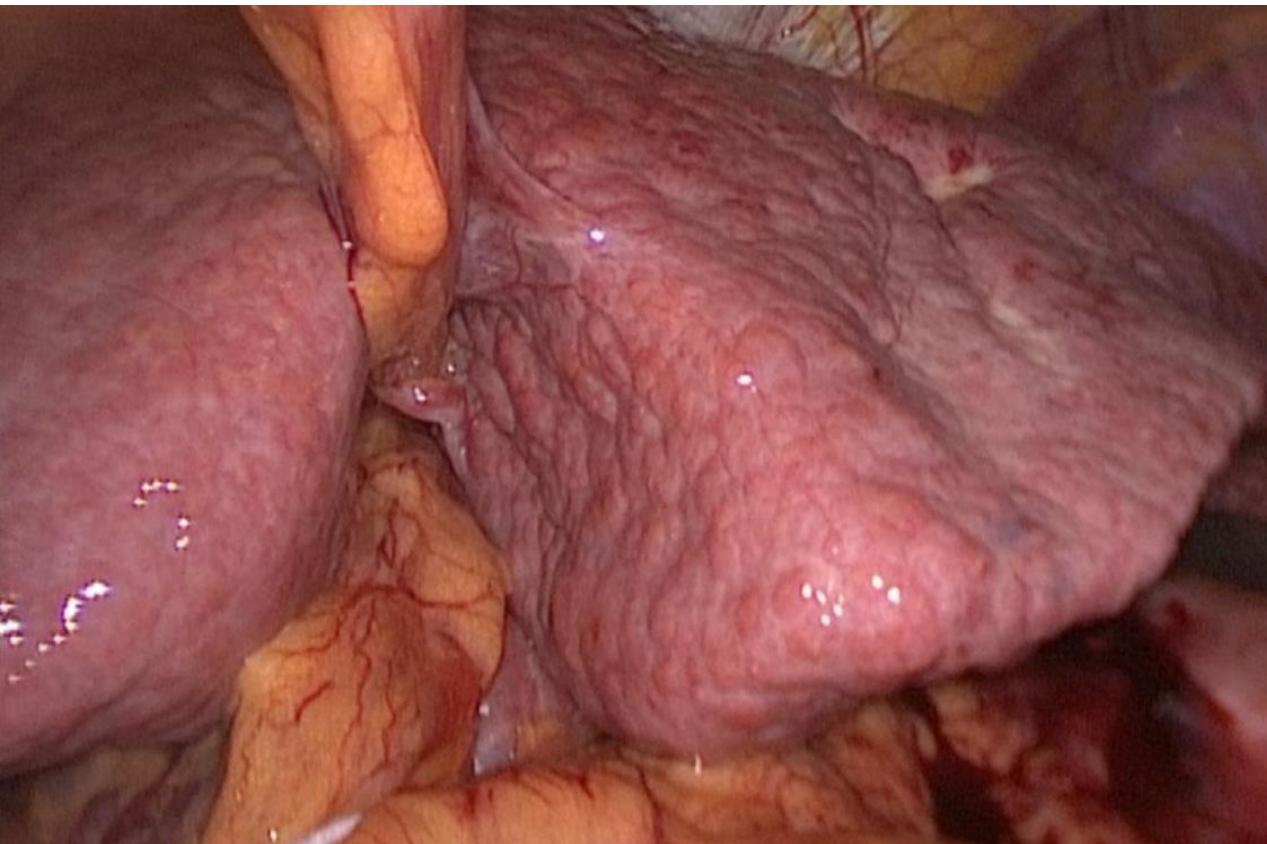
Surgery for HCC



Variable	OR (CI 95%)	P Value
ICG R15	1.068 (1.033-1.103)	<0.001
Portal Hypertension		
No	Ref	
Yes	2.524 (1.134-5.620)	0.023
Extent of resection		
Minor	Ref	
Major	2.223 (0.864-5.718)	0.098
MILS		
No	Ref	
Yes	0.380 (0.184-0.784)	0.009
Operative time	1.004 (1.001-1.008)	0.023

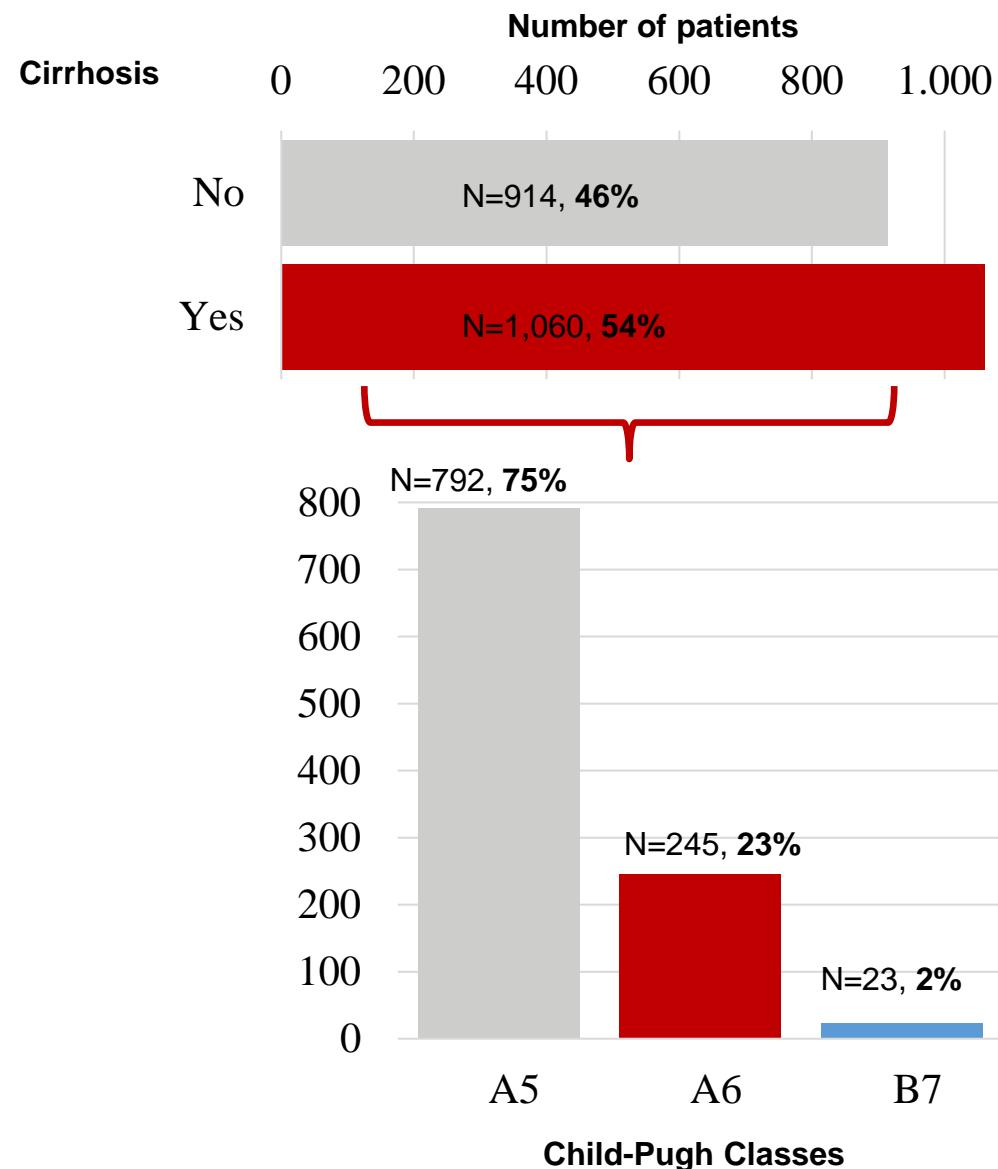


MILS in Impaired liver function





Total Number of Patients: 1,974

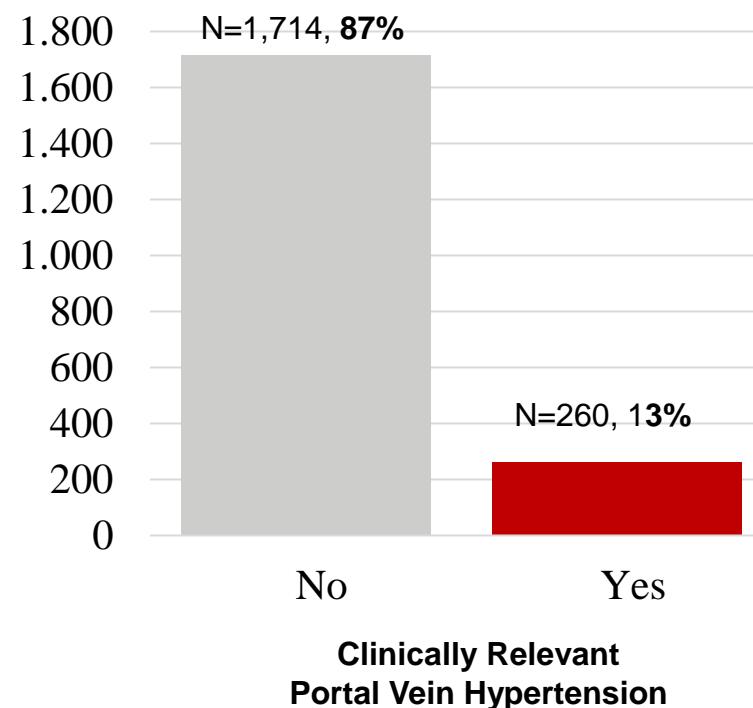


ORIGINAL ARTICLE – HEPATOBILIARY TUMORS

Minimally Invasive Versus Open Liver Resection for Hepatocellular Carcinoma in the Setting of Portal Vein Hypertension: Results of an International Multi-institutional Analysis

Andrea Ruzzenente, MD¹, Fabio Bagante, MD^{1,2}, Francesca Ratti, MD³, Laura Alaimo, MD¹, Hugo P. Marques, MD⁴, Silvia Silva, MD⁴, Olivier Soubrane, MD⁵, Itaru Endo, MD⁶, Kota Sahara, MD⁶, Eliza W. Beal, MD², Vincent Lam, MD⁷, George A. Poultsides, MD⁸, Eleftherios A. Makris, MD⁸, Irinel Popescu, MD⁹, Sorin Alexandrescu, MD⁹, Guillaume Martel, MD¹⁰, Aklike Workneh, MD¹⁰, Thomas J. Hugh, MD¹¹, Alfredo Guglielmi, MD¹, Luca Aldrighetti, MD³, and Timothy M. Pawlik, MD, MPH, PhD, FACS^{2,12}

CRPH → Plt count/ EOGvarices



ALL PATIENTS

Variables	Non-MIS patients	MIS patients	p-value
Number of Patients	458	458	-
Length of Stay, median (IQR)	7 days (5-10)	5 days (4-7)	<0.001
Complication			
No	62.2%	71.2%	0.015
Clavien-Dindo 1-2	21.0%	16.6%	
Clavien-Dindo ≥ 3	16.8%	12.2%	
90-Death			
No	96.7%	98.7%	0.046
Yes	3.3%	1.3%	

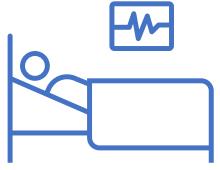
PORTAL HYPERTENSION

Non-MIS patients	MIS patients	p-value
89	89	-
8 days (5-10)	6 days (4-7)	<0.001
56.2%	70.8%	0.042
24.7%	11.2%	
19.1%	16.9%	
93.3%	96.6%	0.30
6.7%	3.4%	

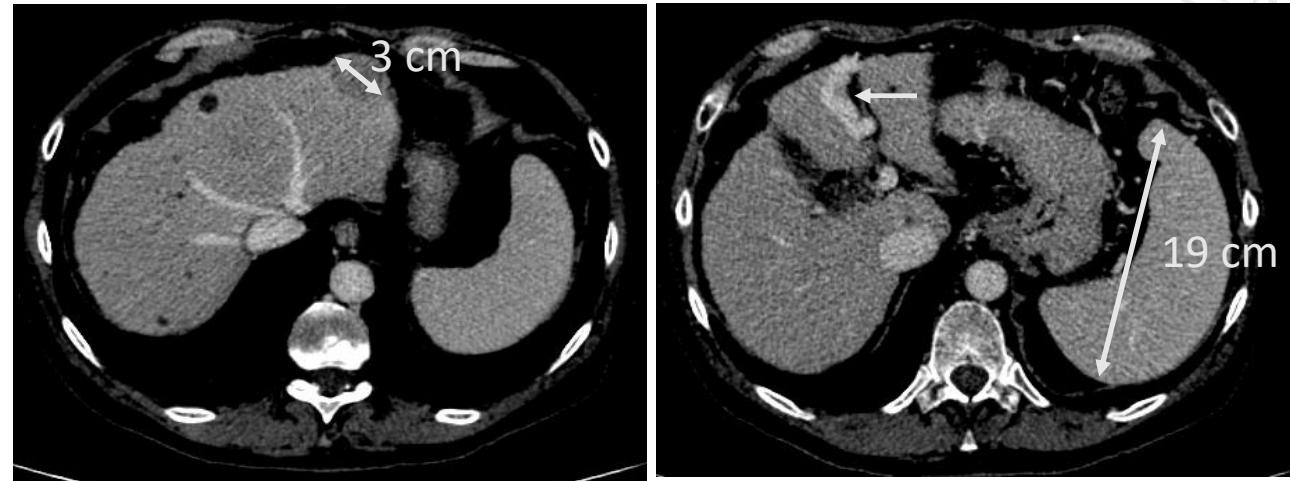
EARLY HCC



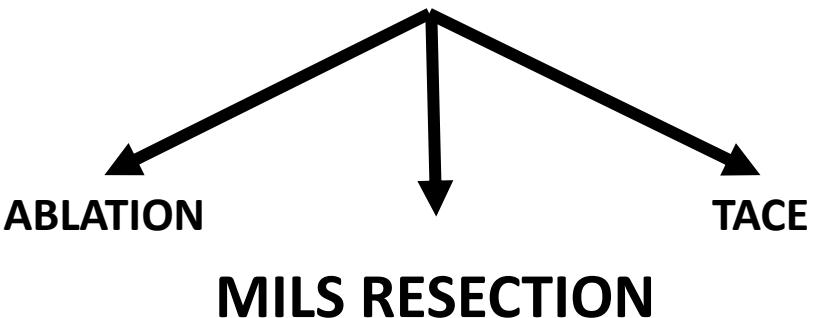
UNIVERSITÀ
di VERONA



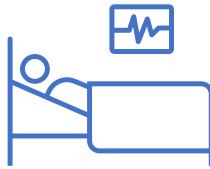
75 anni, M
HCC 3 cm
Child A6
ICGR15 66.3%
PLT 65.000



Therapeutic options



EARLY HCC



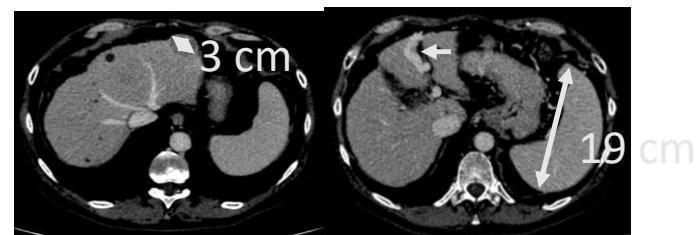
75 anni, M

HCC 3 cm

Child A6

ICGR15 66.3%

PLT 65.000

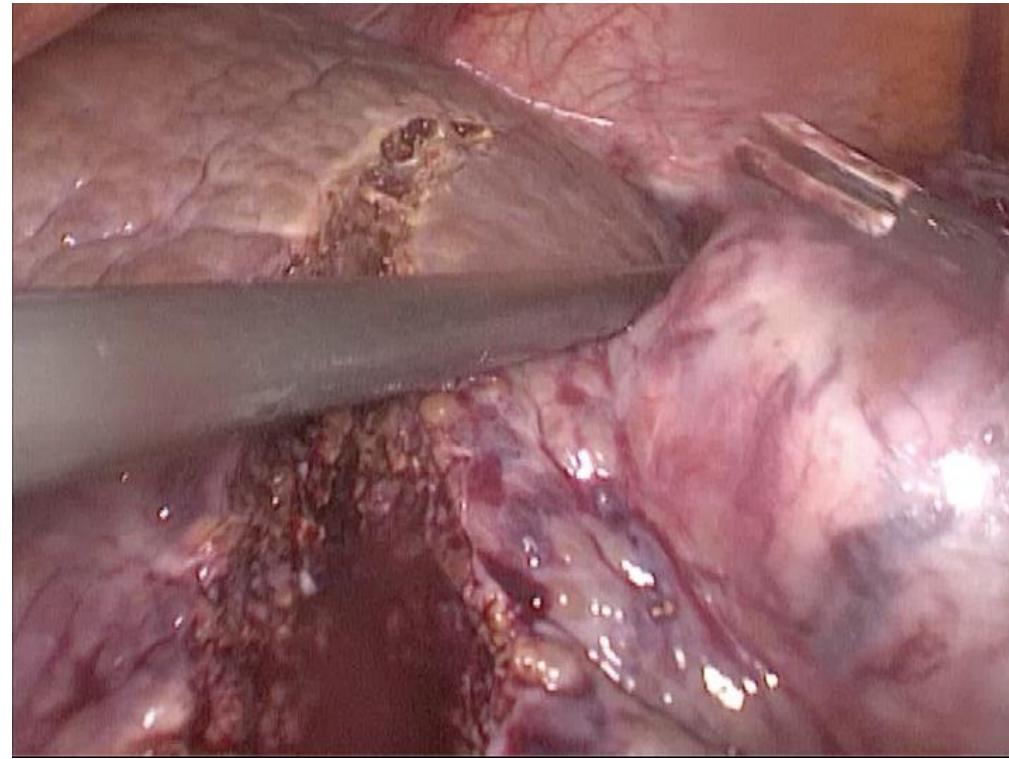


Therapeutic options

ABLATION

TACE

MILS RESECTION



Laparoscopic liver resection facilitates salvage liver transplantation for hepatocellular carcinoma

Alexis Laurent · Claude Tayar · Marion Andréoletti ·
Jean-Yves Lauzet · Jean-Claude Merle ·
Daniel Cherqui



24 trasplants (LT) after resection

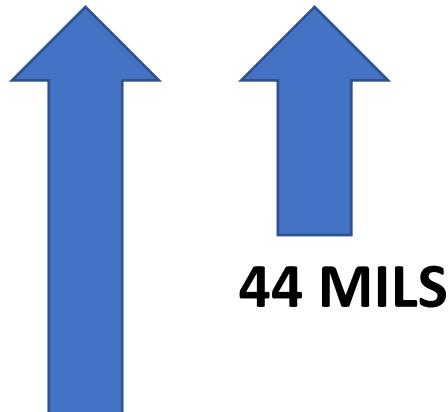
	Laparoscopy N 12	Open N 12	P value
Time LT (h)	6.2 (4.1-9)	8.5 (4.5-9.4)	< 0.05
Blood losses (mL)	1200 (400-2700)	2300 (1000-3200)	< 0.05

The Role of Salvage Transplantation in Patients Initially Treated With Open Versus Minimally Invasive Liver Surgery: An Intention-to-Treat Analysis



Giovanni B. Levi Sandri ^{1*}, Quirino Lai ^{2*}, Matteo Ravaioli,³ Stefano Di Sandro,⁴ Emanuele Balzano,⁵ Duilio Pagano,⁶ Paolo Magistri,⁷ Fabrizio Di Benedetto,⁷ Massimo Rossi,² Salvatore Gruttaduria,⁶ Paolo De Simone ⁵, Giuseppe M. Ettorre,¹ Luciano De Carlis,⁴ Matteo Cescon,³ Marco Colasanti,¹ Gianluca Mennini,² Matteo Serenari,³ Fabio Ferla,⁴ Giovanni Tincani,⁵ Fabrizio Di Francesco,⁶ and Cristiano Guidetti⁶

**211 SALVAGE LT
FOR HCC RECURRENTCE**

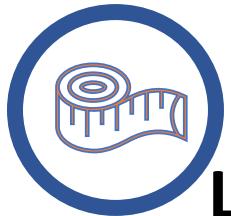
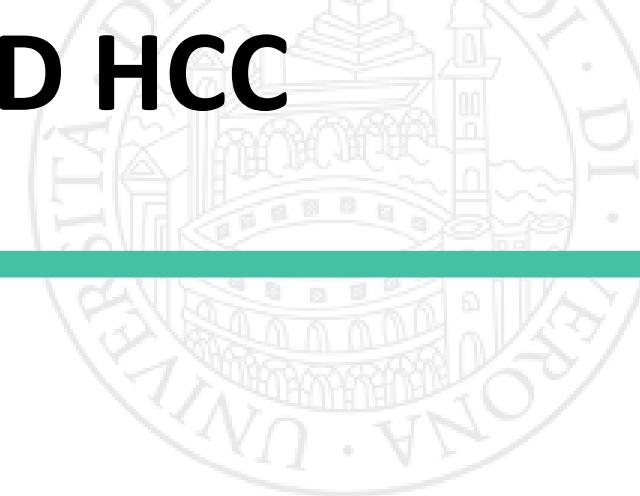


167 “OPEN” LIVER RESECTION

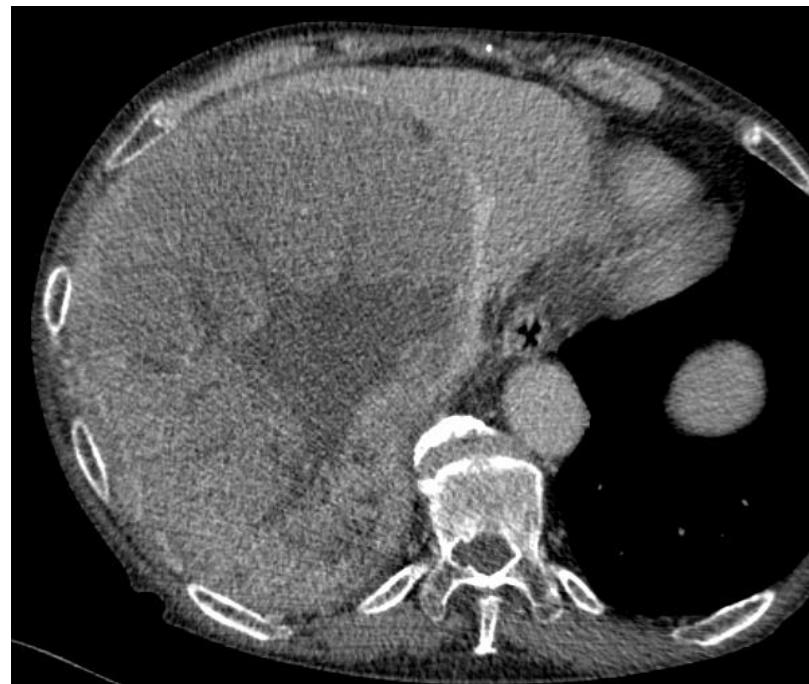
Risk factors for deaths after LT

	Protective factor	Variables	Univariate Analysis				Multivariate Analysis			
			Wald	OR	95% CI	P Value	Wald	OR	95% CI	P Value
		logAFP at LR	7.04	1.97	1.19-3.25	0.008	5.59	2.18	1.14-4.15	0.02
		MELD	3.10	1.08	0.99-1.18	0.08	3.47	1.10	1.00-1.22	0.06
		MILS	5.44	0.30	0.11-0.83	0.02	5.91	0.22	0.07-0.75	0.02
		Male sex	2.74	5.86	0.72-47.53	0.10	—	—	—	—
		Major lesion diameter	2.28	1.03	0.99-1.06	0.13	—	—	—	—
		Wait-list duration	0.85	1.02	0.98-1.07	0.36	—	—	—	—
		HCV	0.51	0.68	0.24-1.97	0.48	—	—	—	—
		Age at LR	0.32	0.99	0.93-1.04	0.57	—	—	—	—
		Post-LR LOS ≥ 10 days	0.28	0.69	0.17-2.72	0.59	—	—	—	—
		Microvascular invasion	0.24	1.27	0.49-3.32	0.62	—	—	—	—

SURGERY IN INTERMEDIATE-ADVANCED HCC



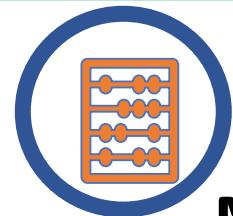
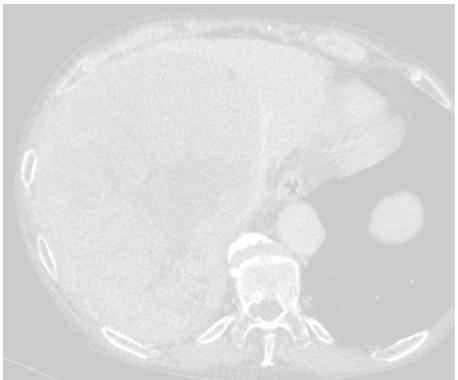
Large HCC



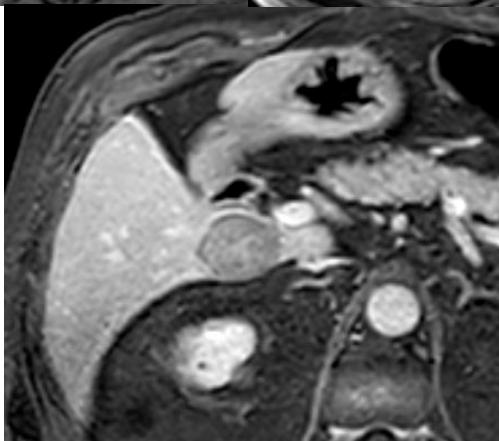
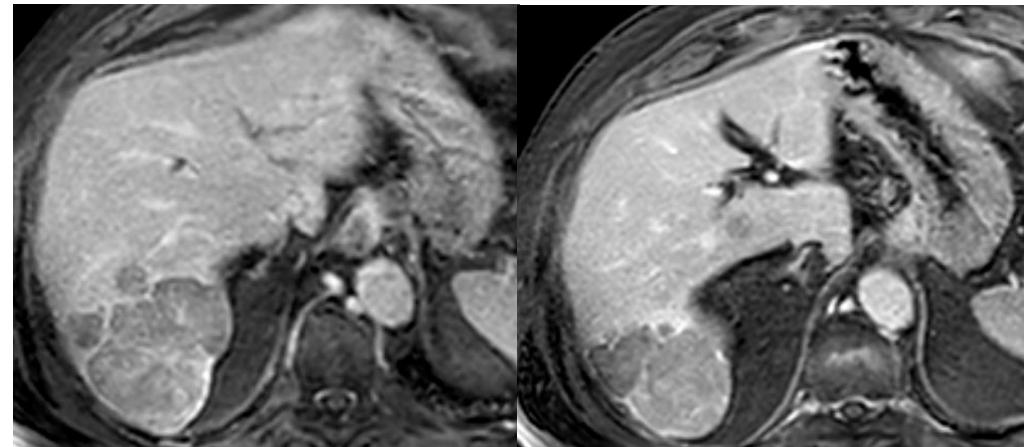
SURGERY IN INTERMEDIATE-ADVANCED HCC



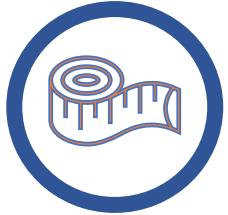
Large HCC



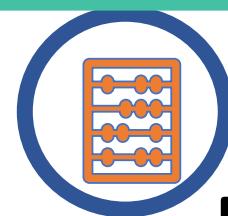
Multifocality



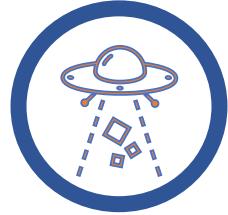
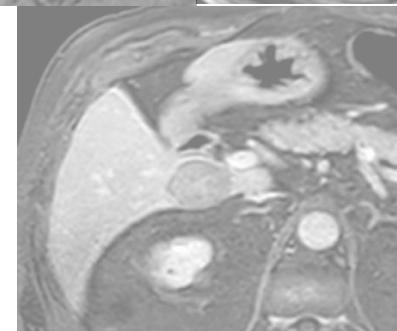
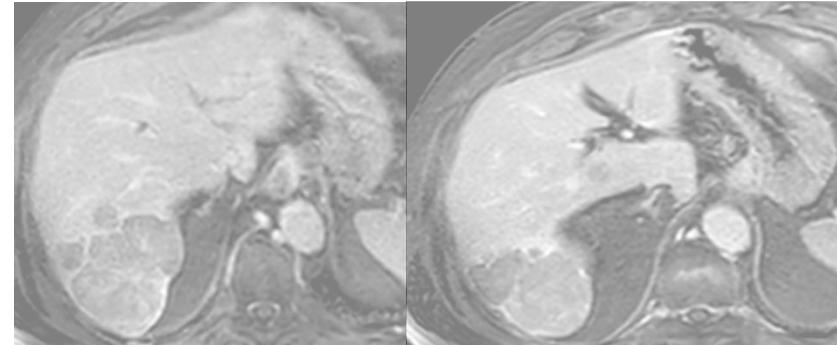
SURGERY IN INTERMEDIATE-ADVANCED HCC



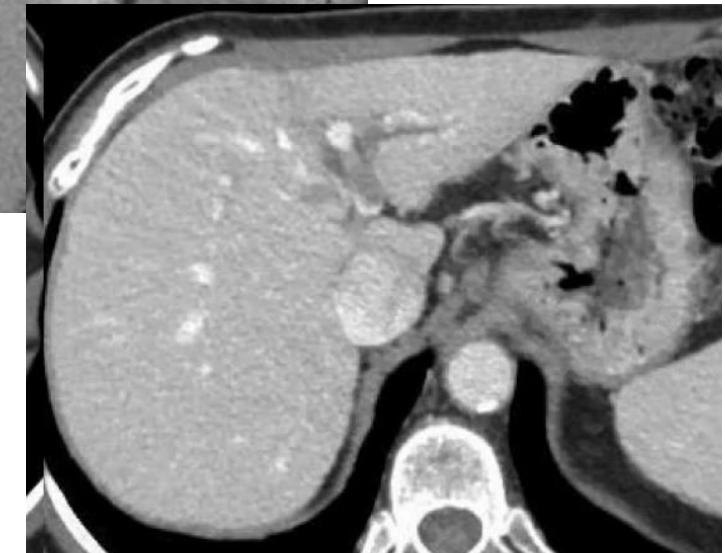
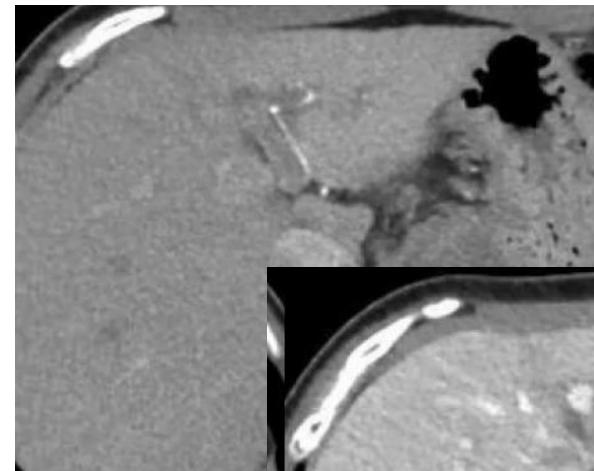
Large HCC



Multifocality

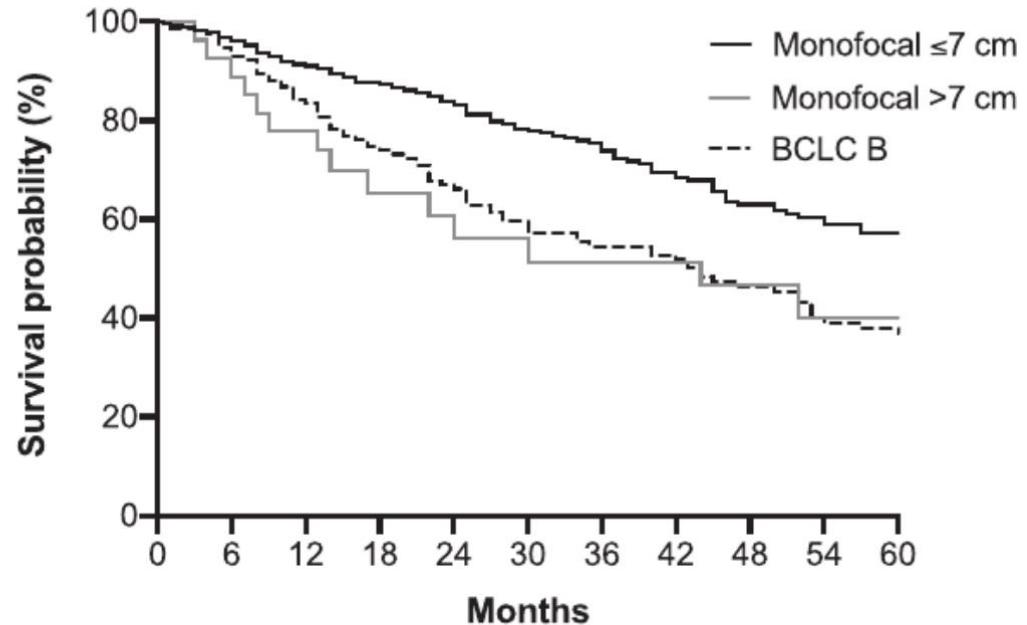


Vascular Invasion



LARGE HCC

Monofocal hepatocellular carcinoma: How much does size matter?
Pelizzaro et ITA.LI.CA group



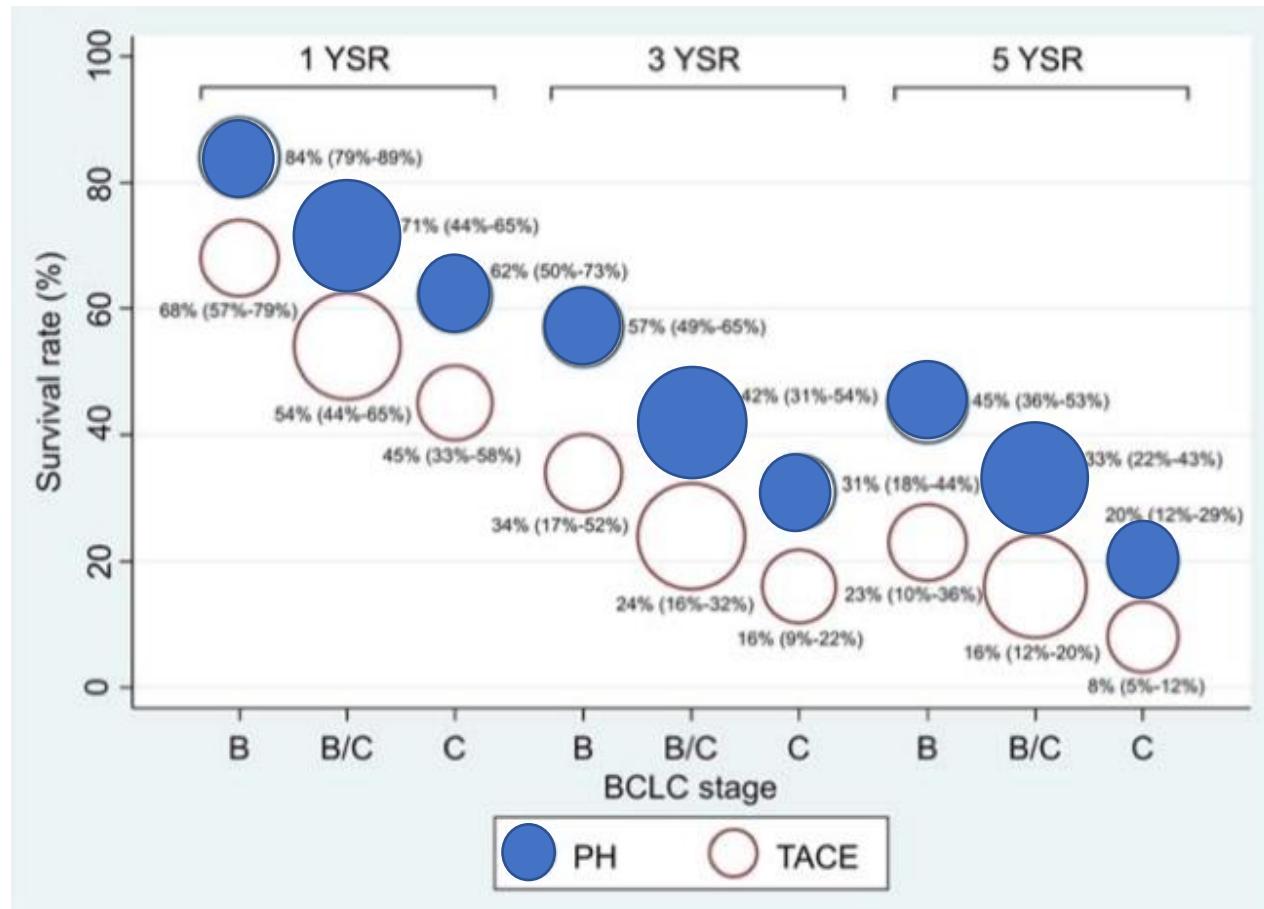
Patients at risk:

Monofocal ≤ 7 cm	279	262	234	211	186	164	144	126	97	83	73
Monofocal > 7 cm	27	25	37	26	20	17	16	15	11	9	9
BCLC-B	160	144	120	99	84	72	64	59	47	38	35

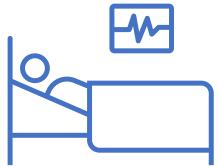
	5-Y SURV (%)	MEDIAN OS	HR
RESECTION	38	44	0.18
ABLATION	31	37	0.25
TACE	23	28	0.32
SYSTEMIC	0	8	0.52
BSC	0	8	Ref.

MULTINODULAR

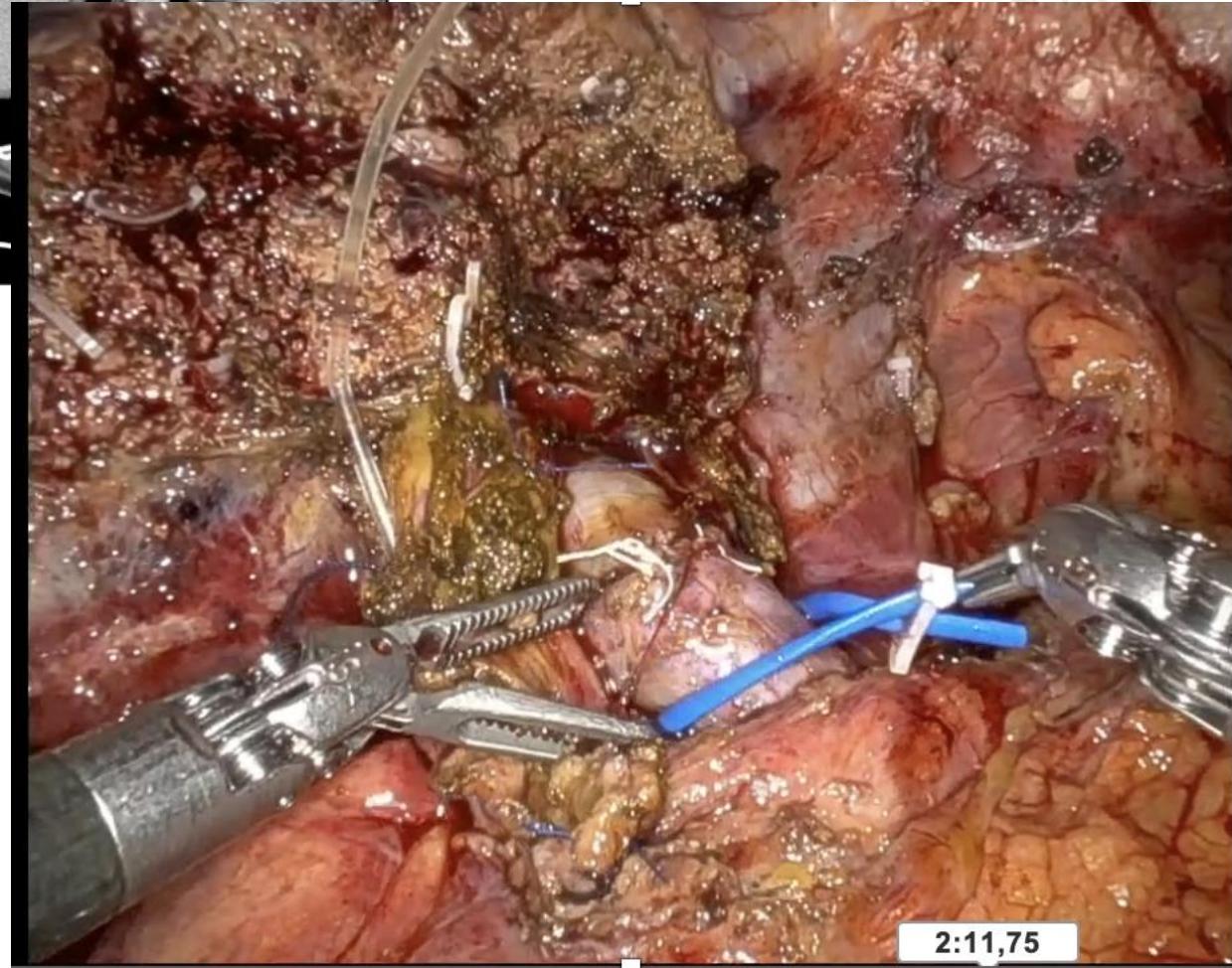
Hepatic resection compared to chemoembolization in intermediate- to advanced-stage hepatocellular carcinoma: A meta-analysis of high-quality studies
Hyun et Al.



MACROSCOPIC VASCULAR INVASION



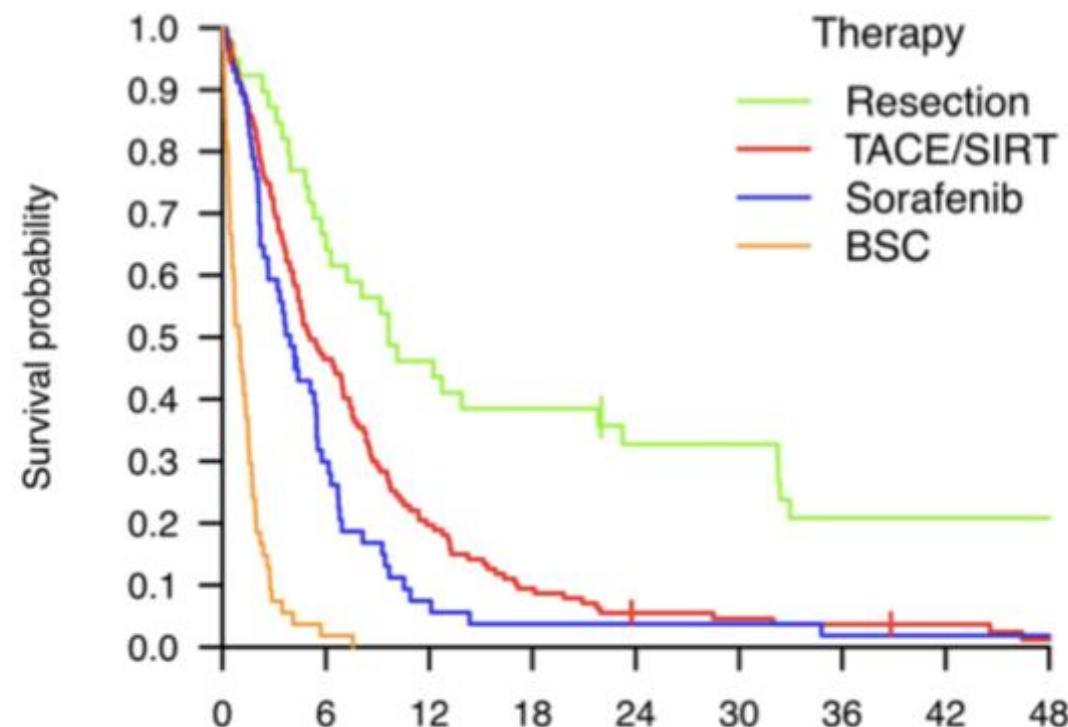
69 Years, F
HCC 2 cm with left
portal invasion
CHILD A5;
ICG R15 6.5%
Plts 247.000



The impact of portal vein tumor thrombosis on survival in patients with hepatocellular carcinoma treated with different therapies: A cohort study

Mähringer-Kunz A et Al.

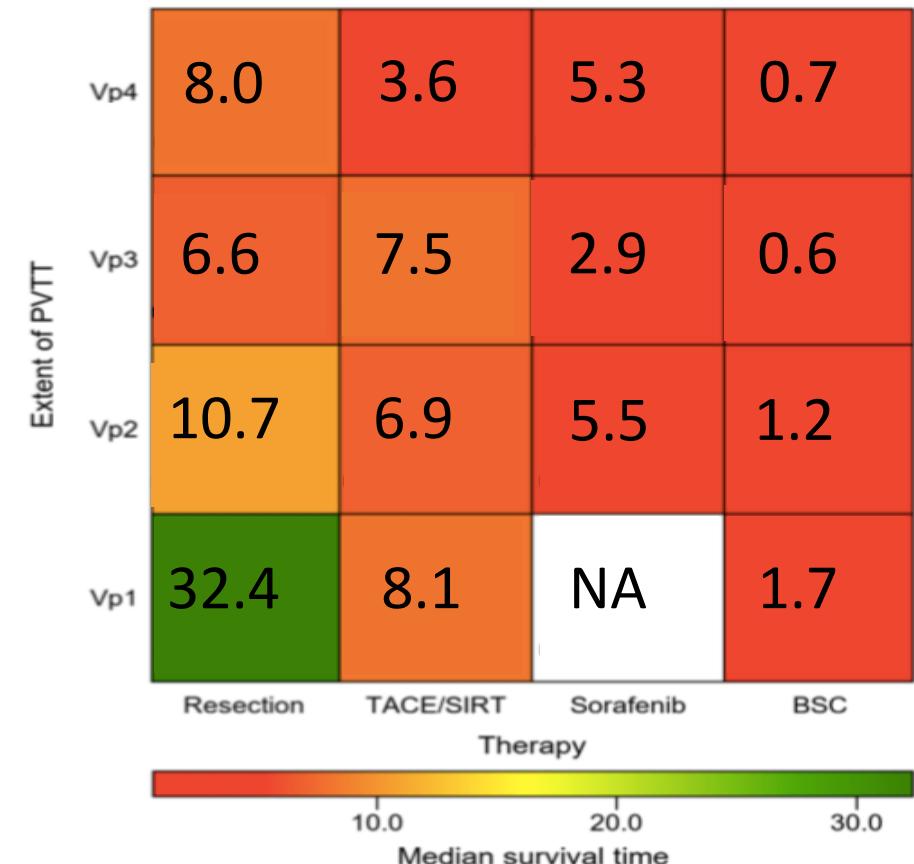
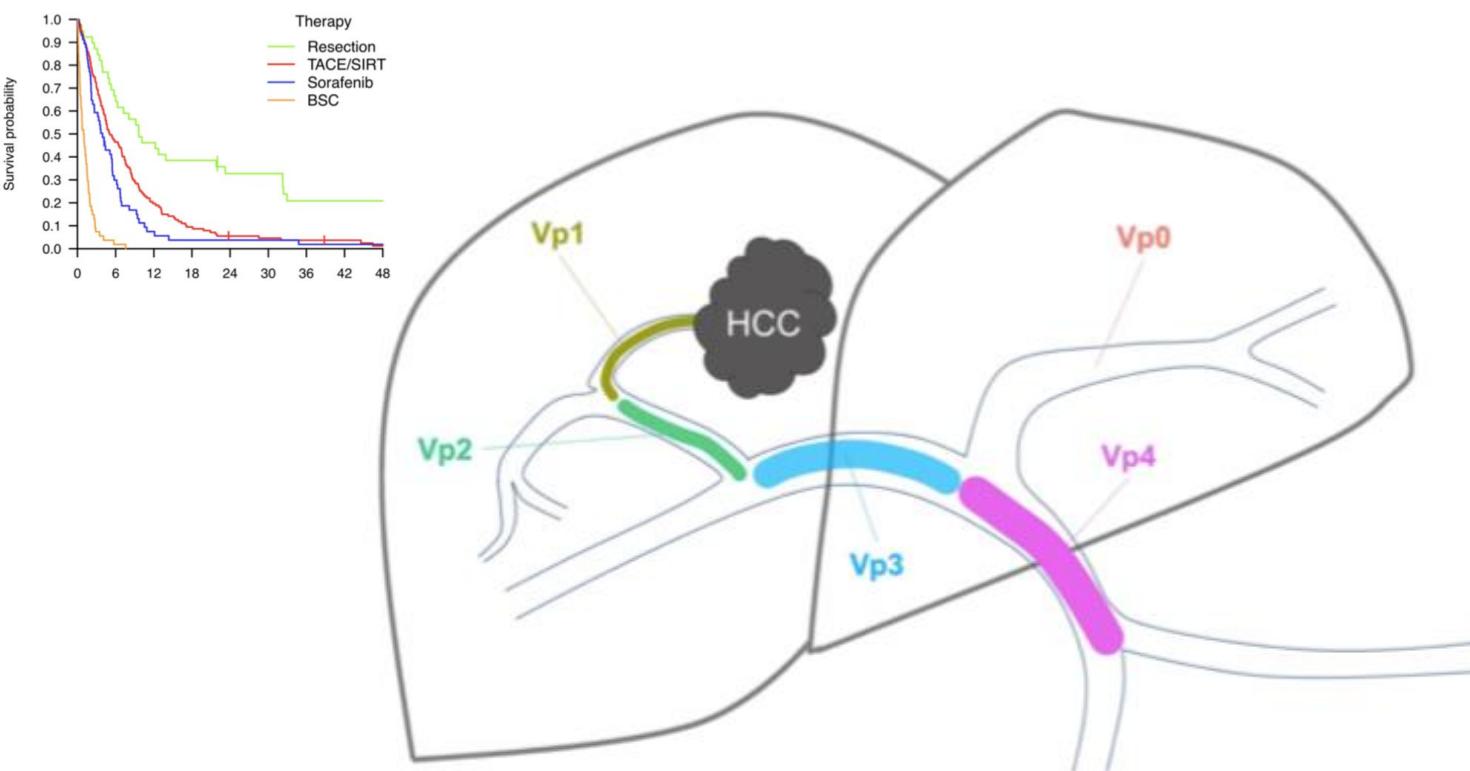
278 HCC CON MACROSCOPIC VASCULAR INVASION



MACROSCOPIC VASCULAR INVASION

The impact of portal vein tumor thrombosis on survival in patients with hepatocellular carcinoma treated with different therapies: A cohort study
Mähringer-Kunz A et Al.

278 HCC CON MACROSCOPIC VASCULAR INVASION



HCC INTERMEDIATE ADVANCED



RISK OF LIVER
FAILURE

BORDERLINE RESECTABLE
UNRESECTABLE

ONCOLOGICAL
FACTORS

TECHNICAL
DIFFICULTY

BORDERLINE RESECTABLE UNRESECTABLE



CONVERSION THERAPY

Original Paper

Liver Cancer 2021;10:320–329
DOI: 10.1159/000514313

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Accepted: January 7, 2021
Published online: March 30, 2021

Downstaging and Resection of Initially Unresectable Hepatocellular Carcinoma with Tyrosine Kinase Inhibitor and Anti-PD-1 Antibody Combinations

Xiao-Dong Zhu^a Cheng Huang^a Ying-Hao Shen^a Yuan Ji^b Ning-Ling Ge^c Xu-Dong Qu^d
Lingli Chen^b Wen-Kai Shi^e Mei-Ling Li^a Jin-Jin Zhu^a Chang-Jun Tan^a Zhao-You Tang^a
Jian Zhou^a Jia Fan^a Hui-Chuan Sun^a

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^eDepartment of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China

Surgical resection in 10 out of 63

ADJUVANT THERAPY

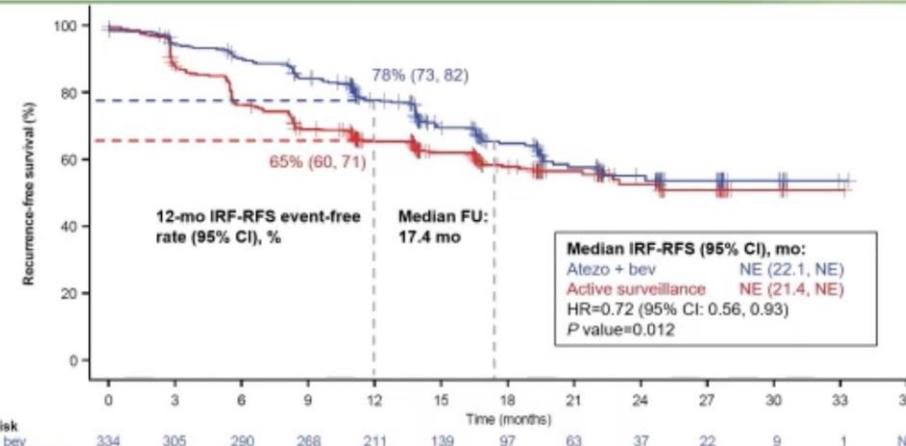
ORAL PRESENTATIONS - PROFFERED ABSTRACTS | MAY 29 2023

Abstract CT003: IMbrave050: Phase 3 study of adjuvant atezolizumab + bevacizumab versus active surveillance in patients with hepatocellular carcinoma (HCC) at high risk of disease recurrence following resection or ablation **FREE**

Pierce Chow; Minshan Chen; Ann-Lii Cheng; Ahmed O. Kaseb; Masatoshi Kudo; Han Chu Lee; Adam Yopp; Jian Zhou; Lu Wang; Xiaoyu Wen; Jeong Heo; Won Young Tak; Shinichiro Nakamura; Kazushi Numata; Thomas Uggen; David Hsiehchen; Edward Cha; Stephen P. Hack; Qinshu Lian; Jessica Spahn; Chun Wu; Shukui Qin

AACR ANNUAL MEETING 2023
APRIL 14-19 • #AACR23

Primary endpoint: IRF-assessed RFS was significantly improved with ateo + bev vs active surveillance



CONCLUSIONI

- 1 Panorama del paziente con HCC è cambiato**
- 2 La terapia chirurgica dell'hcc è in costante evoluzione**
- 3 Sempre piu' necessaria una stadiazione ad hoc del paziente con HCC – Molecolare → Casadei-Gardini**
- 4 Fondamentale l'approccio multidisciplinare al paziente con epatocarcinoma**