



ΧΕΙΡΟΥΡΓΙΚΗ ΑΝΤΙΜΕΤΩΠΙΣΗ ΠΟΛΥ ΠΡΩΙΜΟΥ / ΠΡΩΙΜΟΥ ΣΤΑΔΙΟΥ ΗΚΚ (BCLC 0/A)

ΔΗΜΗΤΡΗΣ Π. ΚΟΡΚΟΛΗΣ

Χειρουργός

ΓΑΟΝΑ «Ο Άγιος Σάββας»

ΕΠΙΔΗΜΙΟΛΟΓΙΑ Early HCC

- Πρώιμος ΗΚΚ: Μονήρης βλάβη < 5 εκ
2-3 βλάβες ≤ 3 εκ
- Διάγνωση: 5-10% στη Δύση
30% στην Ιαπωνία (*surveillance!!!*)

5ετής επιβίωση: 50-70% μετά θεραπεία:

- α. Ηπατεκτομή RL
- β. Μεταμόσχευση LT
- γ. Ablation RFA

- MDTs

ΕΝΔΕΙΞΕΙΣ ΗΠΑΤΕΚΤΟΜΗΣ

Πρώιμο ΗΚΚ σε μη-κίρρωτικό ήπαρ

LR Θεραπεία Εκλογής

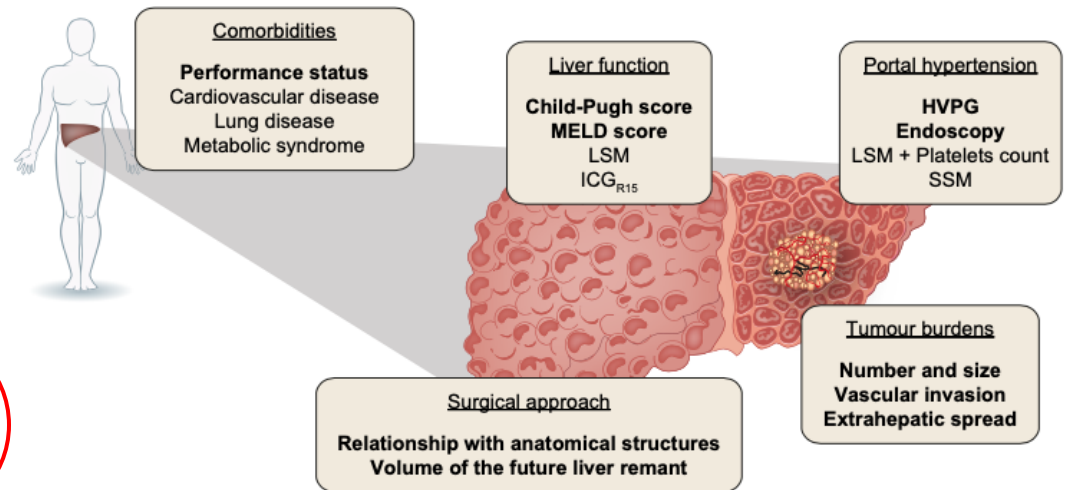
- 5year OS: 50%-70%
- M & M: 4% & 33%

- Επιβαρυντικοί παράγοντες

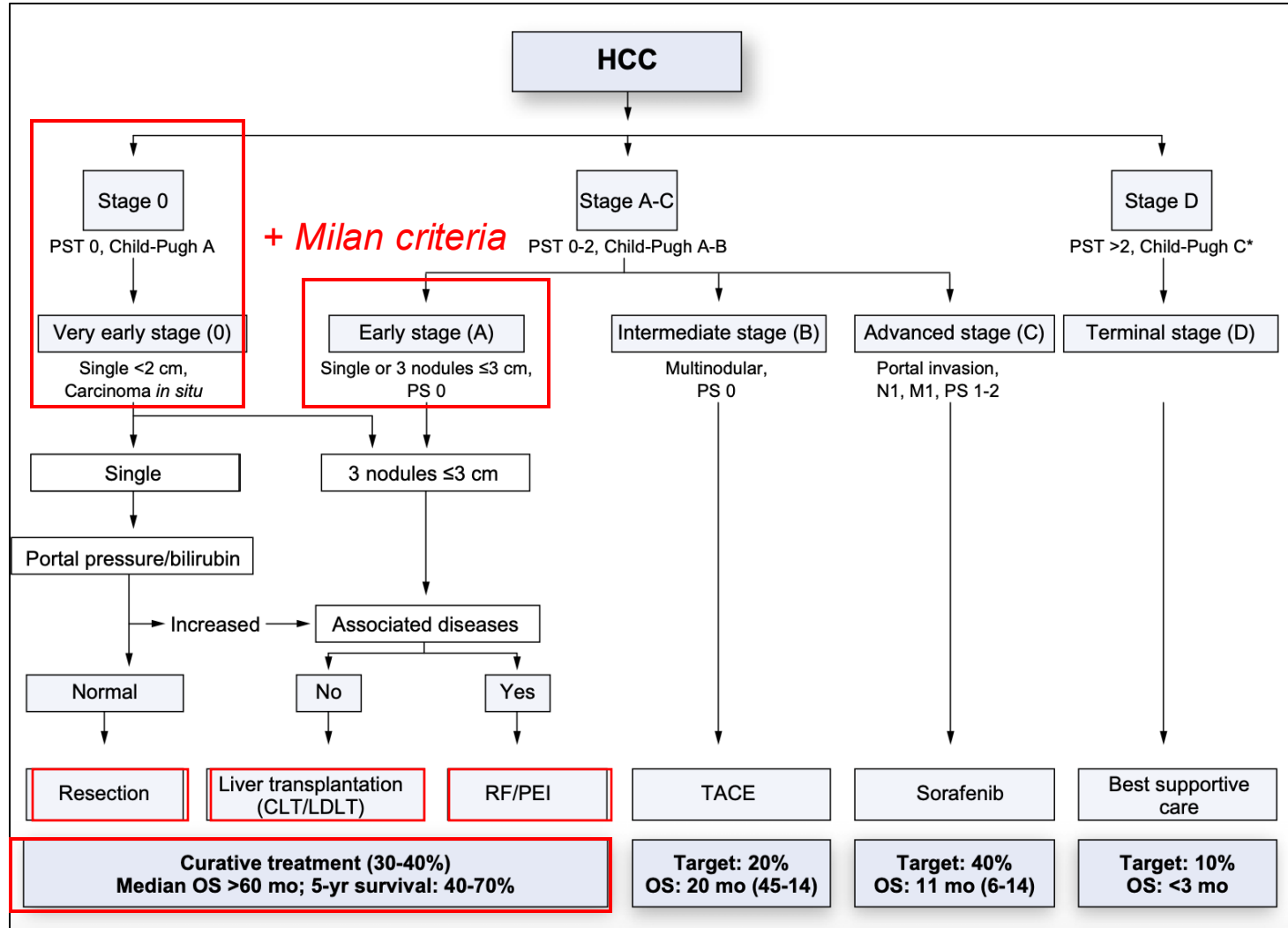
- α. Ίνωση
- β. Ενεργός Φλεγμονή
- γ. Στεάτωση

- NAFLD!!!
- Metabolic syndrome!

30%



BCLC / EASL Clinical Practice Guidelines

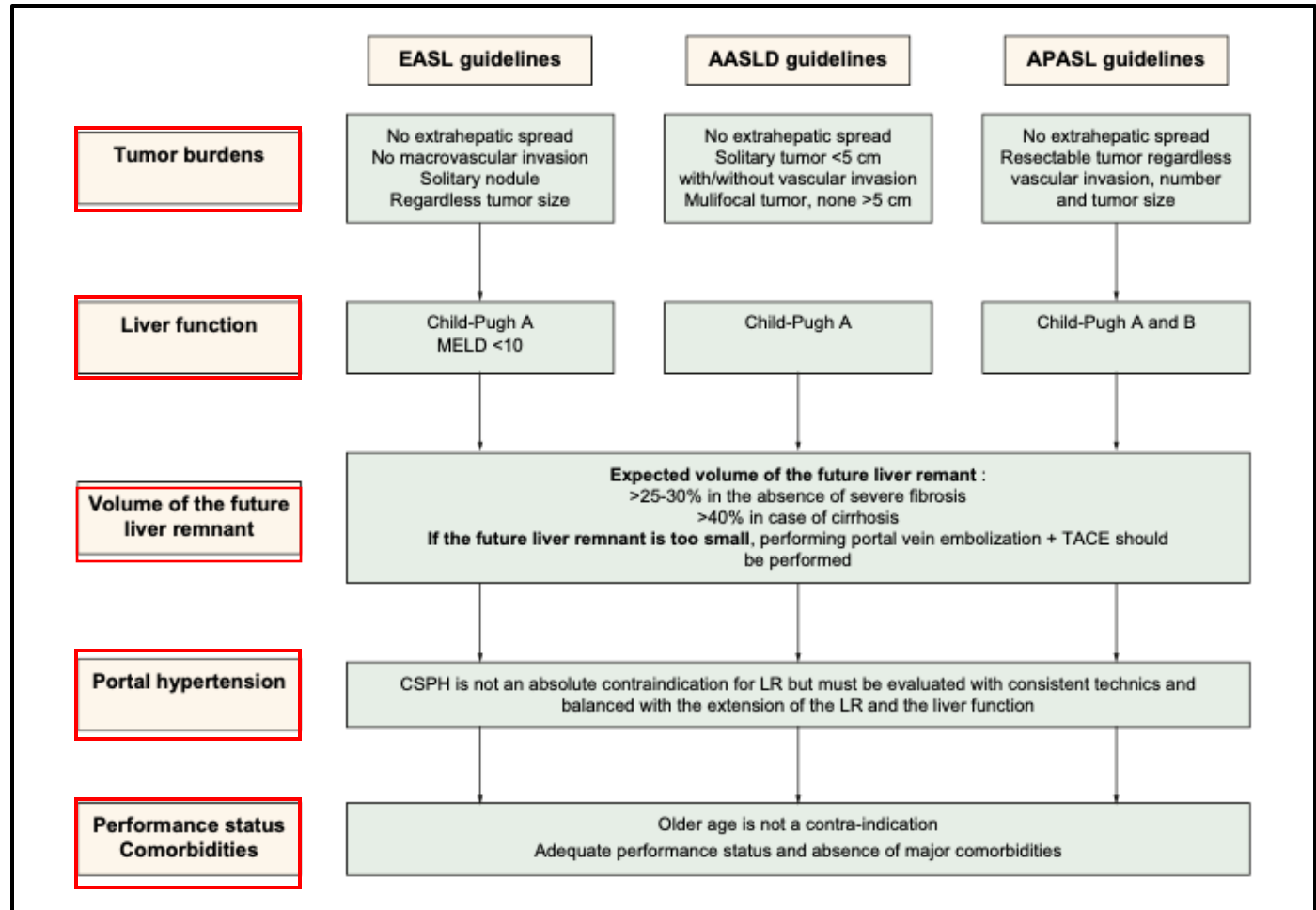


ΕΝΔΕΙΞΕΙΣ ΗΠΑΤΕΚΤΟΜΗΣ

Πρώιμο ΗΚΚ σε κίρρωτικό ήπαρ

Mortality 2-3%
Transfusion <10%

varices
HVPG>10
PLTs<100.000
splenomegaly



ΕΝΔΕΙΞΕΙΣ ΗΠΑΤΕΚΤΟΜΗΣ

ΗΚΚ σε κίρρωτικό ήπαρ

Child-Pugh A

Tumor n.	Tumor size (cm)	Therapy	AASLD (2010)	SEOM (2015)	EASL-EORTC (2012)	ESMO-ESDO (2012)	APASL (2010)	JSH (2013)	AIOM (2015)	S3 (2013)
Single	< 2	LR LT	● ●	● ●	● ●	● ●	● ○	● ○	● ●	● ●
Single	2.1 - 3	LR LT	● ●	● ●	● ●	● ●	● ○	● ○	● ●	● ●
Single	3.1 - 5	LR LT	● ●	● ●	● ●	● ●	● ○	● ○	● ●	● ●
Single	> 5	LR LT	● ○	● ○	● ○	● ○	● ○	● ○	● ○	● ○
2-3 tumors	≤ 3	LR LT	○ ●	○ ●	○ ●	● ●	● ○	● ○	● ●	● ●
2-3 tumors	> 3	LR LT	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○
> 4 tumors		LR LT	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○

Child-Pugh B

Therapy	AASLD (2010)	SEOM (2015)	EASL-EORTC (2012)	ESMO-ESDO (2012)	APASL (2010)	JSH (2013)	AIOM (2015)	S3 (2013)
LR LT	● ●	● ●	● ●	● ●	● ●	● ○	● ●	● ●
LR LT	● ●	● ●	● ●	● ●	● ●	● ○	● ●	● ●
LR LT	● ●	● ●	● ●	● ●	● ●	● ○	● ●	● ●
LR LT	● ○	● ○	● ○	● ○	○ ○	● ○	● ○	● ○
LR LT	○ ●	○ ●	○ ●	● ●	● ●	● ○	● ●	● ●
LR LT	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○
LR LT	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○

LR vs RFA for Early HCC

BCLC - 0

HCC $\leq$ 2cm

Same OS, DFS!!!

Less morbidity

Less overall cost

Close to:

- Hollow viscus
- Diaphragm
- Large vessels
- Portal triad

Then.....

- LR
- Lap RFA
- MWA, IRE

Study	Characteristics of the study	Characteristics of the patients	Endpoints	Morbidity/mortality
Lee et al. <i>Ann Surg</i> <i>Treat Res</i> 2018 ²⁸	Korea 2005–2008 RCT	29 LR vs. 34 RFA % cirrhosis n.d. % viral hepatitis n.d. 100% solitary tumour 24% HCC between 3–4 cm	OS at 3 years: 96.6% in LR vs. 97.1% in RFA ($p = \text{n.s.}$) DFS at 3 years: 66.7% in LR vs. 44.1% in RFA ($p = 0.071$)	37.9% in LR vs. 26.5% in RFA ($p = \text{n.s.}$) Deaths 3.4% in LR vs. 0% in RFA
Ng et al. <i>BJS</i> 2017 ²⁹	China 2002–2007 RCT	109 LR vs. 109 RFA % cirrhosis n.d. 90% viral hepatitis 91% solitary tumour 100% In Milan criteria	OS at 3 years: 80.6% in LR vs. 82.3% in RFA ($p = \text{n.s.}$) DFS at 3 years: 50.9% in LR vs. 46.6% in RFA ($p = \text{n.s.}$)	16.5% in LR vs. 9.2% in RFA ($p = \text{n.s.}$) Deaths 0.9% in LR vs. 0% in RFA
Fang et al. <i>JGHF</i> 2014 ³⁰	China 2000–2012	60 LR vs. 60 RFA 80% cirrhosis 90% viral hepatitis 80% solitary tumour 100% HCC $\leq$ 3 cm	OS at 3 years: 77.5% in LR vs. 82.5% in RFA ($p = \text{n.s.}$) DFS at 3 years: 41.3% in LR vs. 55.4% in RFA ($p = \text{n.s.}$)	27.5% in LR vs. 5% in RFA ($p < 0.05$) No deaths
Feng et al. <i>J Hepatol</i> 2012 ³¹	China 2005–2008 RCT	84 LR vs. 84 RFA 60% cirrhosis 84% viral hepatitis 60% solitary tumour 64% HCC between 2–4 cm	OS at 3 years: 74.8% in LR vs. 67.2% in RFA ($p = \text{n.s.}$) Recurrence at 3 years: 37.7% in LR vs. 49.6% in RFA ($p = \text{n.s.}$)	21.4% in LR vs. 9.5% in RFA ($p < 0.05$) No deaths
Huang et al. <i>Ann Surg</i> 2010 ³²	China 2003–2005 RCT	115 LR vs. 115 RFA 70% cirrhosis 93% viral hepatitis 55% solitary tumour 50% HCC between 3–5 cm More solitary tumour in LR Larger HCC in RFA group	OS at 3 years: 92% in LR vs. 76% in RFA ($p = 0.001$) Recurrence at 3 years: 34% in LR vs. 49% in RFA ($p = 0.024$)	28% in LR vs. 4% in RFA ($p < 0.05$) No deaths
Cheng et al. <i>Ann Surg</i> 2006 ³³	China 1999–2004 RCT	90 LR vs. 90 RFA % cirrhosis n.d. % viral hepatitis n.d. 100% solitary tumour 50% HCC between 3–5 cm	OS at 3 years: 73% in LR vs. 69% in RFA ($p = \text{n.s.}$) DFS at 3 years: 52% in LR vs. 60% in RFA ($p = \text{n.s.}$)	55% in LR vs. 4% in RFA ($p < 0.05$) Deaths 1.1% in LR vs. 0% in RFA
Lu et al. <i>Zhonghua Yi Xue Za Zhi</i> 2006 ³⁴	China RCT Written in Chinese	54 LR vs. 51 RFA % cirrhosis n.d. % viral hepatitis n.d. % solitary tumour n.d. 100% In Milan criteria	OS at 3 years: 86.4% in LR vs. 87.1% in RFA ($p = \text{n.s.}$) DFS at 3 years: 82.4% in LR vs. 51.3% in RFA ($p = \text{n.s.}$)	11.1% in LR vs. 7.8% in RFA ($p = \text{n.s.}$) % n.s. Deaths

LR vs RFA for Early HCC

Study Author (year)	Inclusion Criteria	OS	DFS/RFS	Postprocedure Outcomes	Comments
Chen et al (2006) ¹⁶	Solitary <5 cm; N = 180	4-year OS: RFA = 67.9%; LR = 64% (P = ns)	4-year DFS: RFA = 46.4%; LR = 51.6% (P = ns)	Mortality: RFA = 0%; LR = 1.1% (P = ns); major complications: RFA = 4%; LR = 55% (P < .05)	Authors emphasize equivalent long-term outcomes, as well as lower risk of complications (and shorter length of hospital stay) with RFA; notably, a number of patients withdrew from RFA arm and analysis was not on intention-to-treat basis
Huang et al (2010) ¹⁷	Milan criteria and amenable for both LR and RFA; N = 230	5-year OS: RFA = 54.7%; LR = 75.6% (P = .001)	5-year RFS: RFA = 28.6%; LR = 51.3% (P = .01)	Mortality: 0% for both groups; adverse events: RFA: 4%; LR: 28% (P < .05)	Authors recommend LR for management of HCC within Milan criteria despite increased complications and length of hospital stay
Feng et al (2012) ¹⁸	Maximum number of tumors = 2 and maximum tumor size <4 cm; N = 168	3-year OS: RFA = 67.2%; LR = 74.8% (P = .34)	3-year RFS: RFA = 49.6%; LR = 61.1% (P = .12)	Mortality: 0% for both groups; complications: RFA = 9.5%; LR = 21.4% (P = .01)	Authors emphasize overall similar long-term outcomes but caution the use of percutaneous ablation for lesions in difficult areas to get to, in which cases local recurrence is higher

BCLC – A

Single HCC 2-5 cm
Up to 3 lesions <3cm

LR first option!!!

LR vs OLT in Early HCC

- LT η καλύτερη θεραπεία κίρρωτικού ασθενούς με κριτήρια Μιλάνου
 - α. Εκτομή όγκου
 - β. Θεραπεία υποκείμενης ηπατοπάθειας
- ΔΥΣΤΥΧΩΣ.....
 - α. Έλλειψη μοσχευμάτων
 - β. Μακρά λίστα αναμονής
 - γ. Κίνδυνος dropout λόγω εξέλιξης της νόσου
 - δ. Κοινωνικο-οικονομικοί παράγοντες
 - ε. Ειδικότητα θεράποντος ιατρού

Liver Resection and Transplantation in Hepatocellular Carcinoma

J. Belghiti D. Fuks

- LR for HCC

1-yr, 3-yr, 5-yr OS

85%, 64%, 45%

- Early HCC < 5 cm Child-Pugh A-B
5-yr OS 60-70%
- 5-yr Recurrence rate 18% - 72%!!!

Predictors for recurrence:

*tumor size, tumor number, microvascular invasion, grade,
satellite nodules, R1 resection, nonanatomic resection,
underlying cirrhosis*

Meta-analysis

Liver transplantation versus liver resection for hepatocellular carcinoma: a meta-analysis

Hepatobiliary Pancreat Dis Int 2014

REVIEW ARTICLE – HEPATOBILIARY TUMORS

Is Resection or Transplantation the ideal Treatment in Patients with Hepatocellular Carcinoma in Cirrhosis if Both Are Possible? A Systematic Review and Metaanalysis

Andrea Proneth, MD¹, Florian Zeman, MSc², Hans J. Schlitt, MD, FACS¹, and Andreas A. Schnitzbauer, MD^{1,3}

Ann Surg Oncol 2016

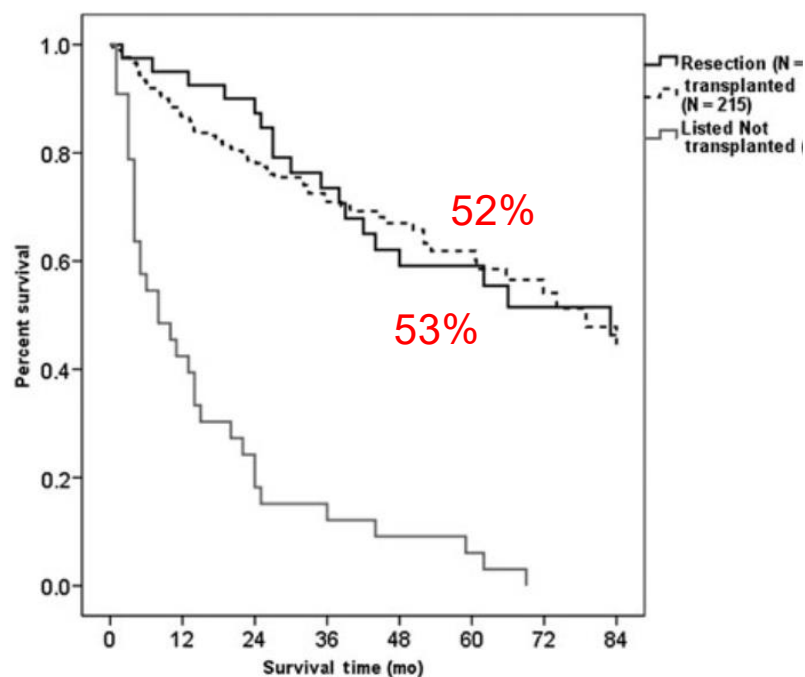
Postop Mortality – Morbidity ↑↑↑
1-year Survival ↓↓↓ OLT

5-year OS OLT 63% - LR 58%
 OLT 61% - LR 49%

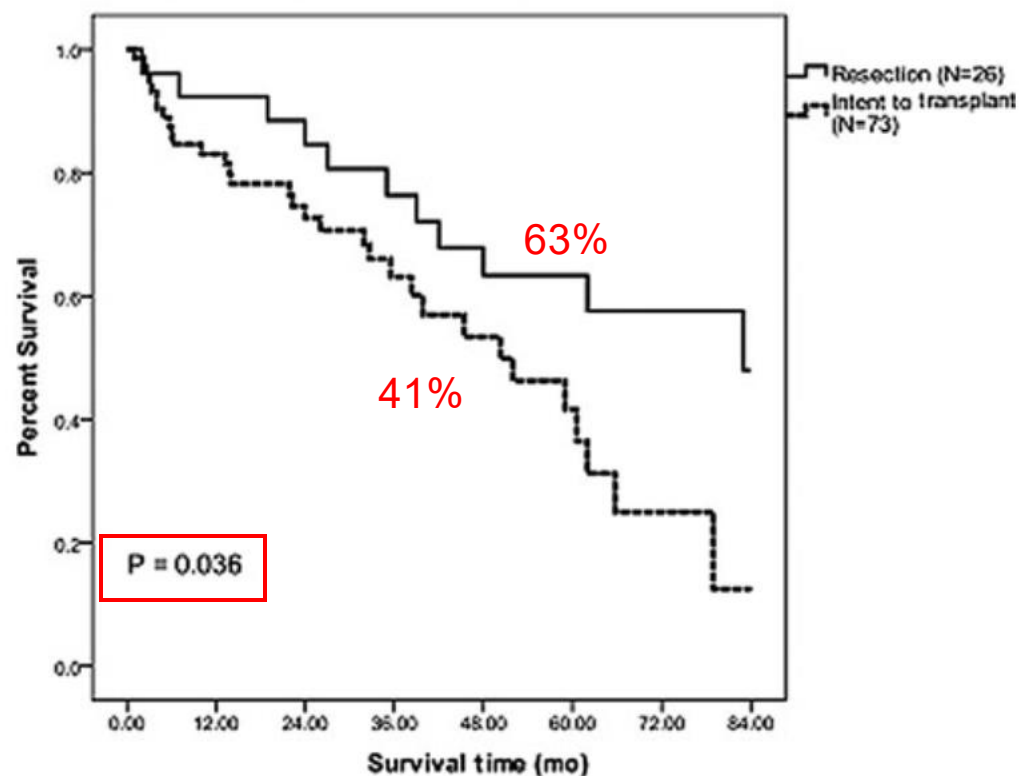
Equivalent OS – DFS for:
BCLC A
T < 5cm solitary lesions
No vascular invasion
MELD<10/ No CSPH

Is Surgical Resection Superior to Transplantation in the Treatment of Hepatocellular Carcinoma?

Median waiting time to OLT: 48 days



B) Milan (<5cm) Criteria, MELD <10



LR vs OLT in Early HCC

- “Salvage” LT για υποτροπή μετά LR

Ανάλογα OS and DFS!!!

Μικροί όγκοι <5εκ

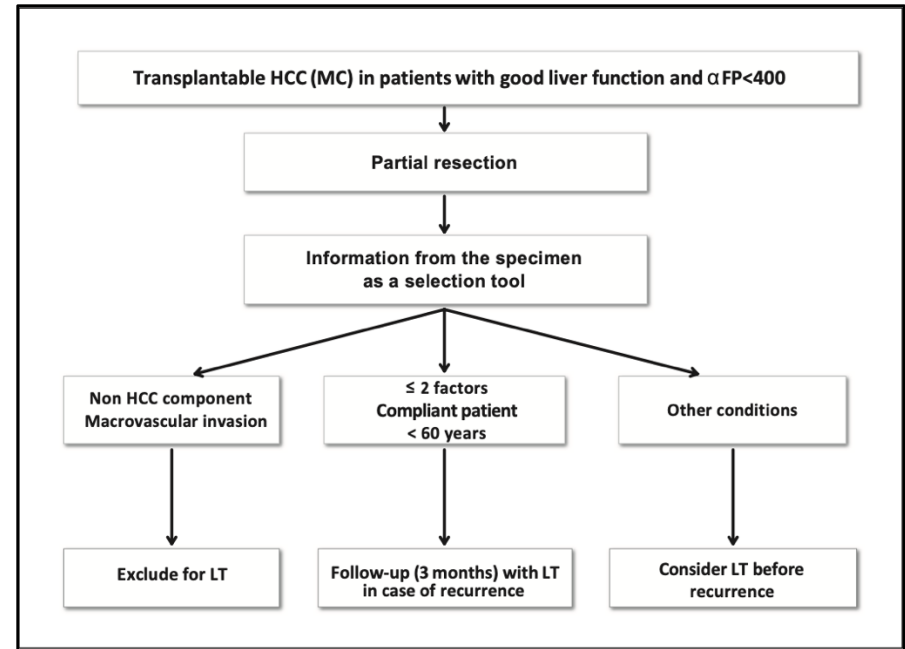
Μονήρεις βλάβες

Καλή διαφοροποίηση

Χωρίς δορυφορικά οζίδια

Χωρίς αγγειακή διήθηση

Κίρρωση (-)



- New Concept of “Up Front” LR

LT στην υποτροπή ΗΚΚ με «καλούς» προγνωστικούς δείκτες

ΕΞΑΤΟΜΙΚΕΥΜΕΝΗ προσέγγιση με βάση την ιστολογική της LR

Διαφύλαξη μοσχευμάτων

*Ann Surg Oncol 2018
J Gastrointest Surg 2016
Hepatology 2016*

Χειρουργική Προσέγγιση Πρώιμου ΗΚΚ

- Αξιολόγηση ηπατικής λειτουργίας

Child – Pugh A – B

MELD <10

- Ογκομέτρηση

CP score A/ No CSPH $\geq 40\%$ FLR

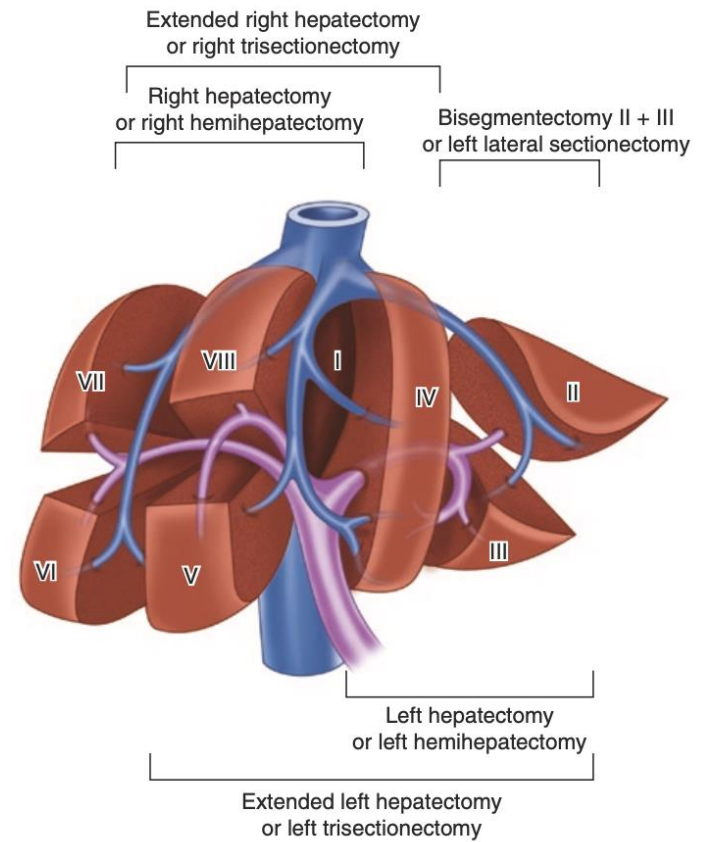
- Right Hemiliver 65-67%

- PVE

- PVE + TACE/+ HVE

- ALPPS

↓↓↓PHLF



Χειρουργική Προσέγγιση Πρώιμου ΗΚΚ

- R0 Εκτομή (> 1mm)
- Ανατομική εκτομή *Equal rate of PHLF*
↓↓↓ *Recurrence rate*
↑↑↑ *DFS*
- Parenchyma – sparing LR
- Laparoscopic LR

Recurrence after Anatomic Resection Versus Nonanatomic Resection for Hepatocellular Carcinoma: A Meta-analysis

JZ Ye¹, ZG Miao¹, FX Wu¹, YN Zhao², HH Ye³, LQ Li^{4*}

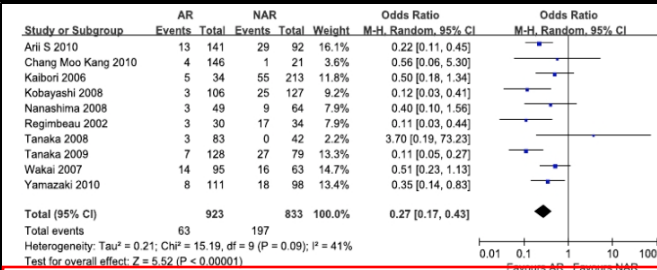


Figure 1. Results of the Meta-analysis on Local Intra-hepatic Recurrence

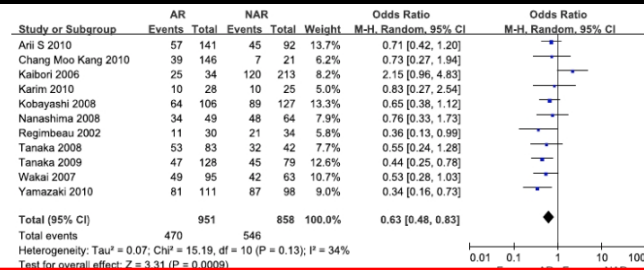


Figure 2. Results of the Meta-analysis on Overall Intra-hepatic Recurrence

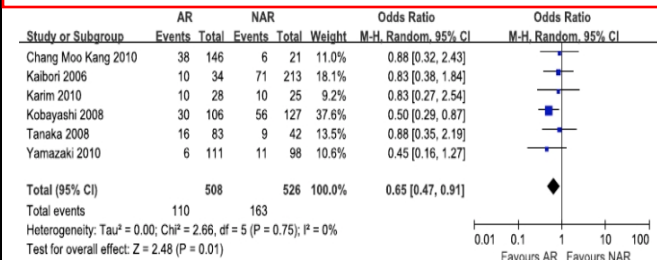


Figure 3. Results of the Meta-analysis on Early Intra-hepatic Recurrence

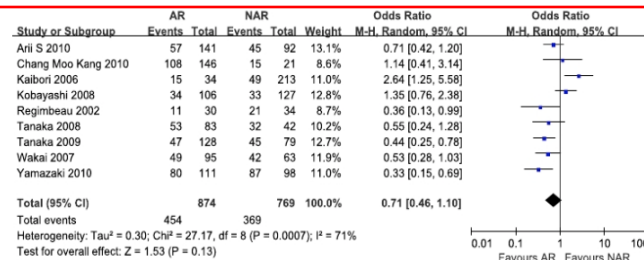


Figure 4. Results of the Meta-analysis on Late Intra-hepatic Recurrence

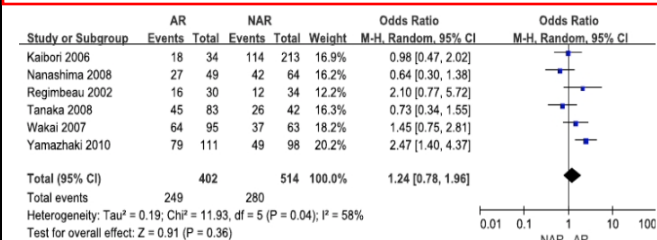


Figure 5. Results of the Meta-analysis on 5 Years Overall Survival

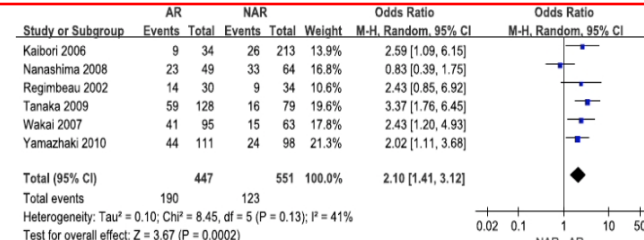
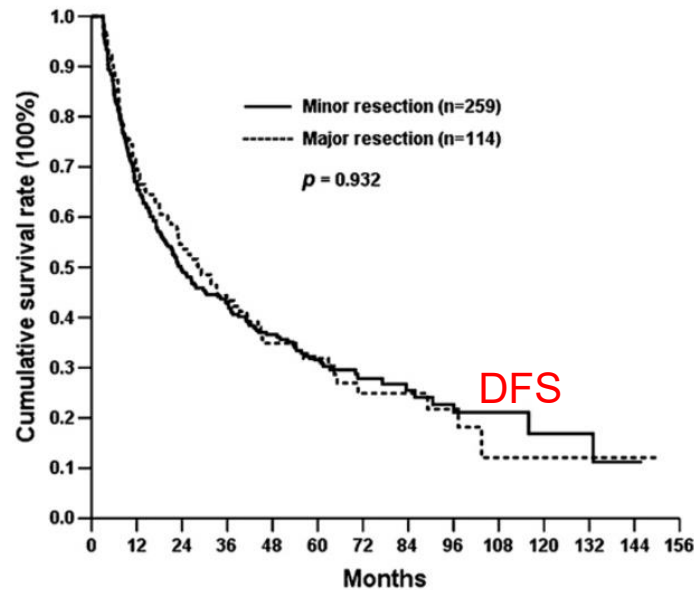
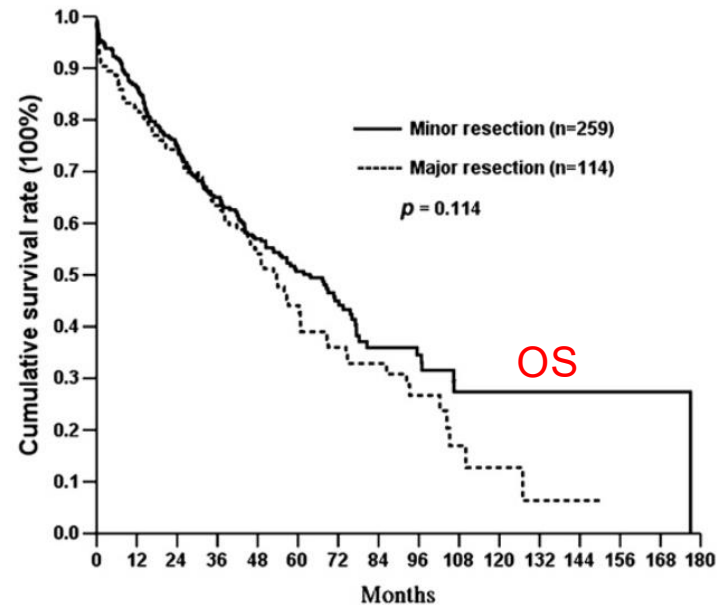


Figure 6. Results of the Meta-analysis on 5 Years Disease-free Survival

Minor versus major hepatic resection for small hepatocellular carcinoma (HCC) in cirrhotic patients: A 20-year experience



No. at risk					
Minor resection	155	97	49	20	4
Major resection	70	41	21	8	1

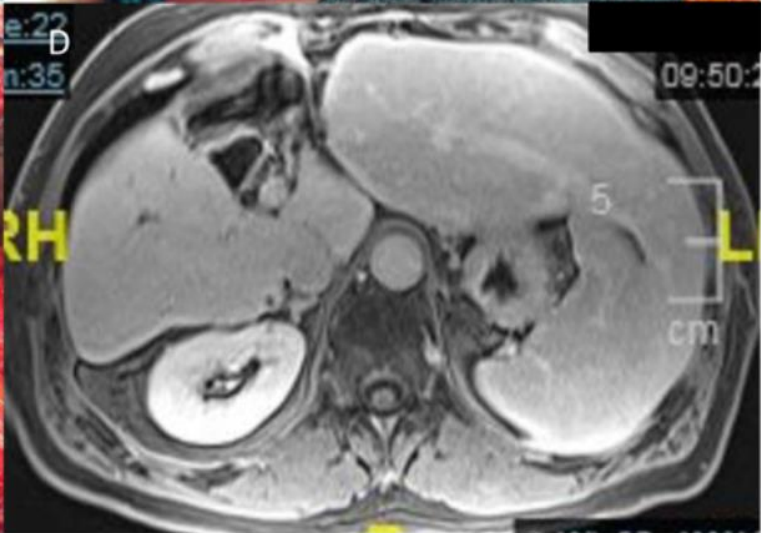
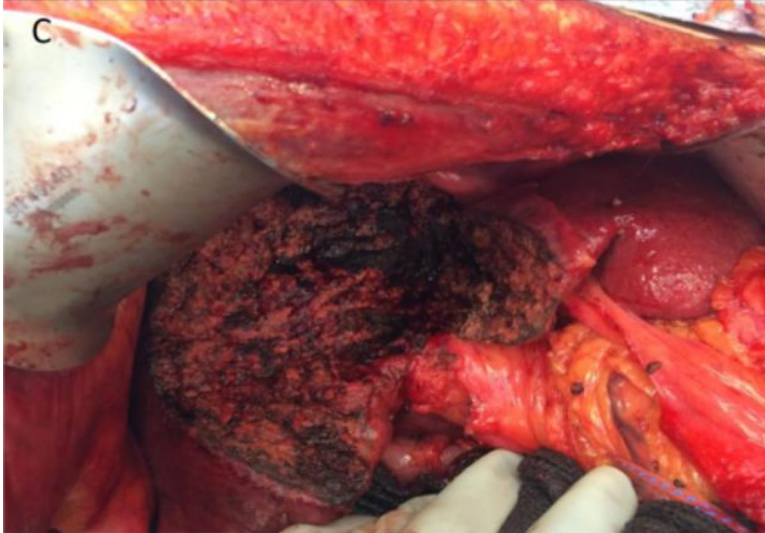


No. at risk					
Minor resection	219	162	93	30	17
Major resection	92	69	35	16	2

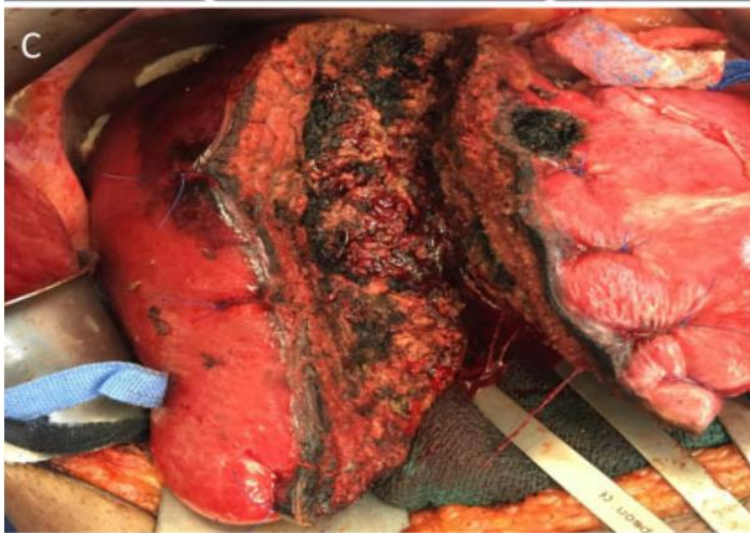
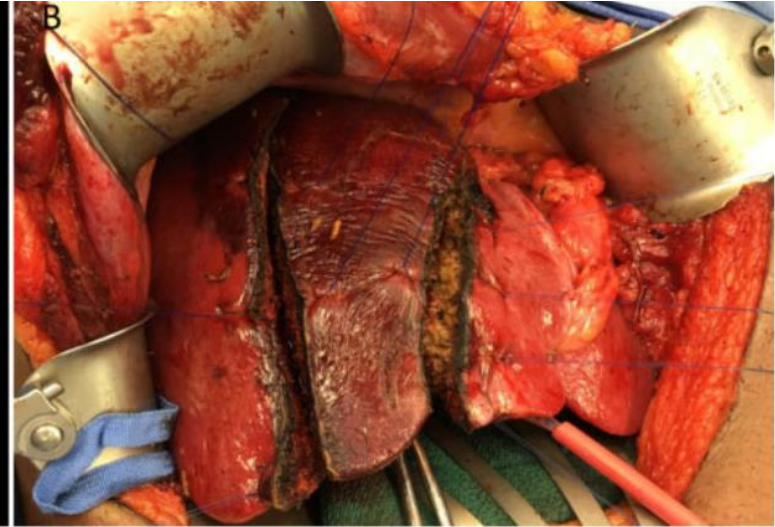
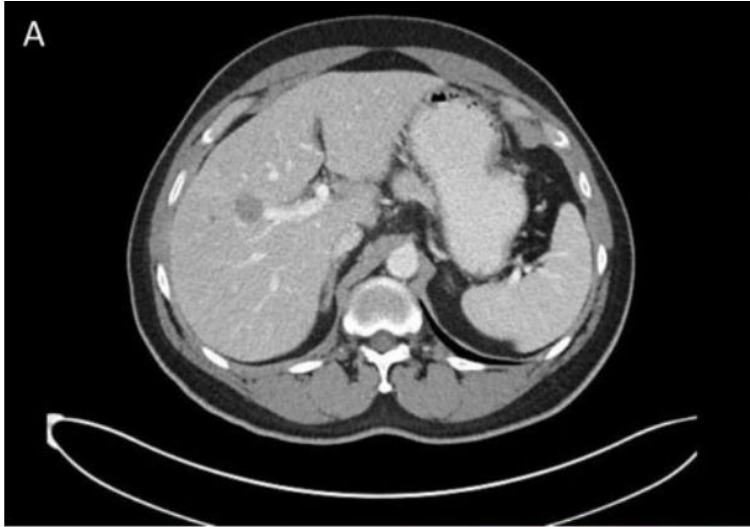
Parenchyma-sparing LR

Author, year	No. of patients	Findings	5-year OS	DSS
<i>Right-sided tumors</i>				
Fisher, 2013 [37]	RPS = 100 RH = 480	↑ PHLF in RH (1% RPS vs 9% RH, $p < 0.001$)	n/a	n/a
Yip, 2015 [38]	RPS = 49 RH = 32	No difference PHLF (2% RPS vs 9% RH, $p = 0.34$)	(84% RPS vs 76% RH, $p = 0.77$)	(52% RPS vs 53% RH, $p = 0.86$)
<i>Central tumors</i>				
Lee, 2015	<i>Matched</i> CH = 63 EH = 63	↑ Pringle time in CH (50 vs 36 min, $p = 0.04$) ↓ Blood loss in CH (800 vs 500 mL, $p = 0.01$) A post-op bilirubin > 4 mg/dL was observed in 2% CH vs 39% EH ($p < 0.01$)	n/a	n/a
Chen, 2014 [40]	CH = 118 RE = 47 LE = 33	↑ PHLF in RE (11% CH vs 2% RE, $p = 0.03$) but no difference between CH and LE ↓ Rate of R0 resection in CH (67% vs 83% RE and 85% RE, $p < 0.05$)	(29% CH vs 30% EH, $p = 0.58$)	(17% CH vs 27% EH, $p = 0.11$)
Lee, 2014 [100] systemic review of CH cases	CH = 895	Operative time = 115–627 min Pringle was used in majority of cases Intraop blood loss = 380–2450 mL	32–67%	17–32%

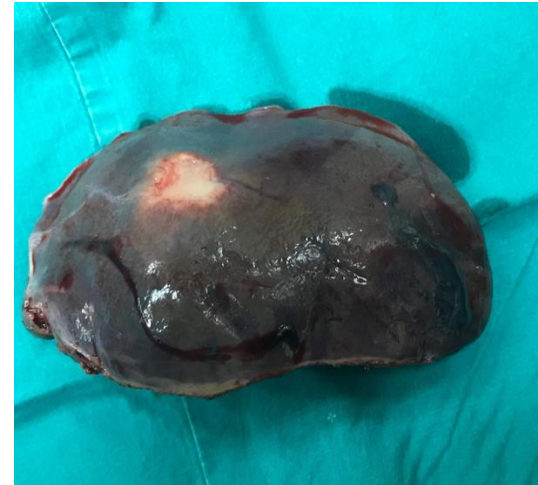
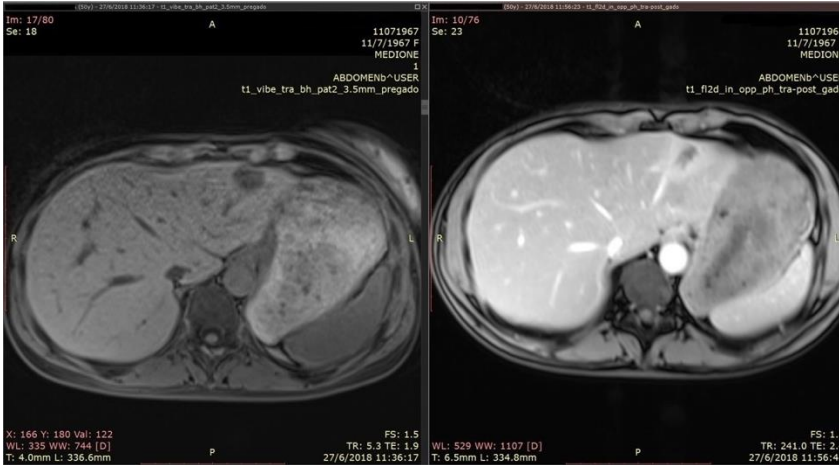
Parenchyma-sparing LR



Parenchyma-sparing LR



Λαπαροσκοπική Ηπατεκτομή



Male 53yrs of age
HBV +
Child-Pugh A
Normal Bilirubin / No CSPH
HCC 3.5cm left lobe
AFP 256

Laparoscopic Left Lateral Sectionectomy

