NUHS
National University Health System

Predicting need for transplantation in resectable candidates in HCC

Pang Ning Qi

Conflicts of Interest

Nil

Defining the Patient Population

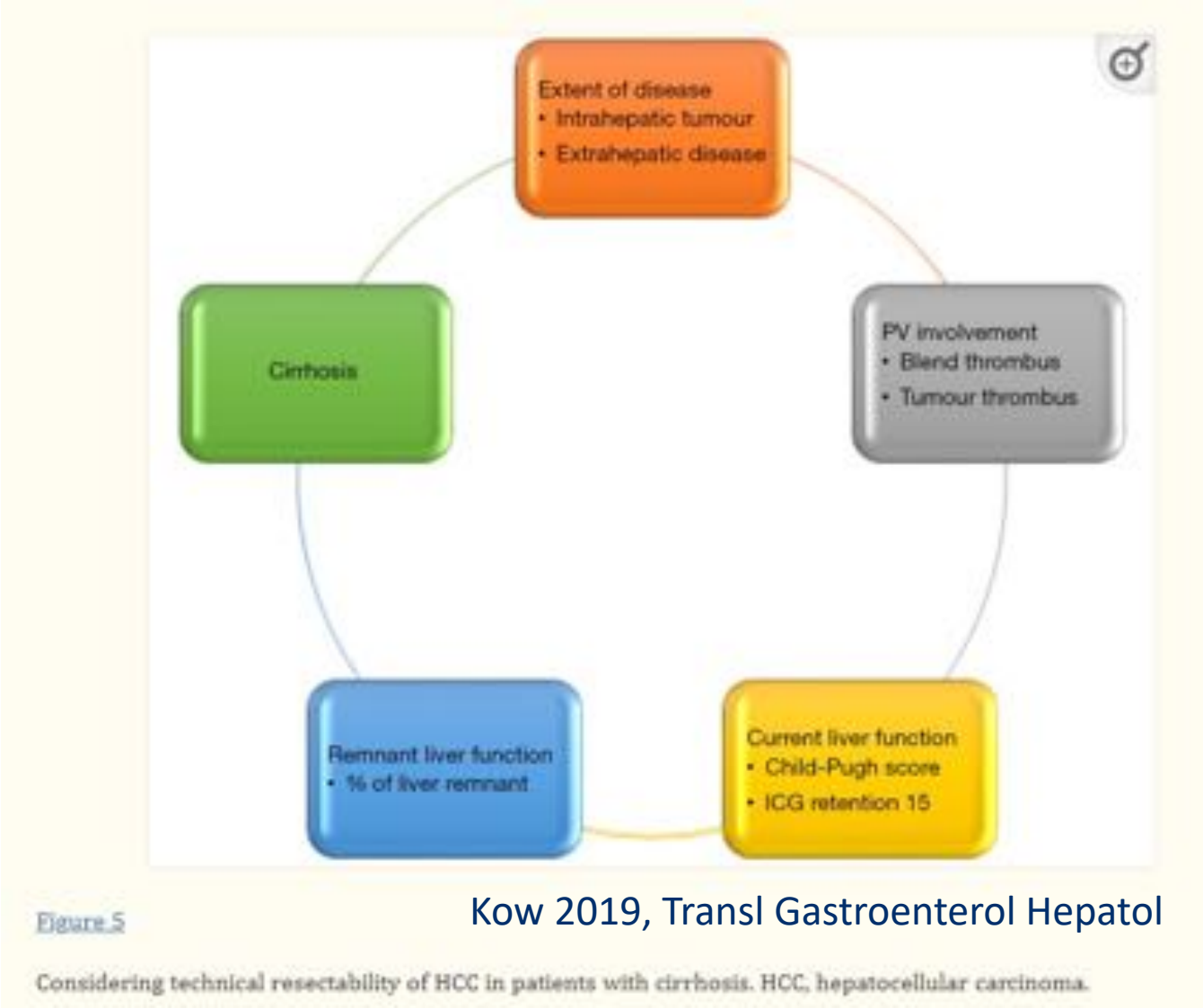
Resectable HCC

NOT

- Outcomes of LT vs LR in HCC patients

Rather, we want to understand in patients with resectable HCC

- Do they benefit from LT upfront (instead of resection)
- Do they benefit from LT after resection
  - Pre-emptive (de principe)
  - Salvage

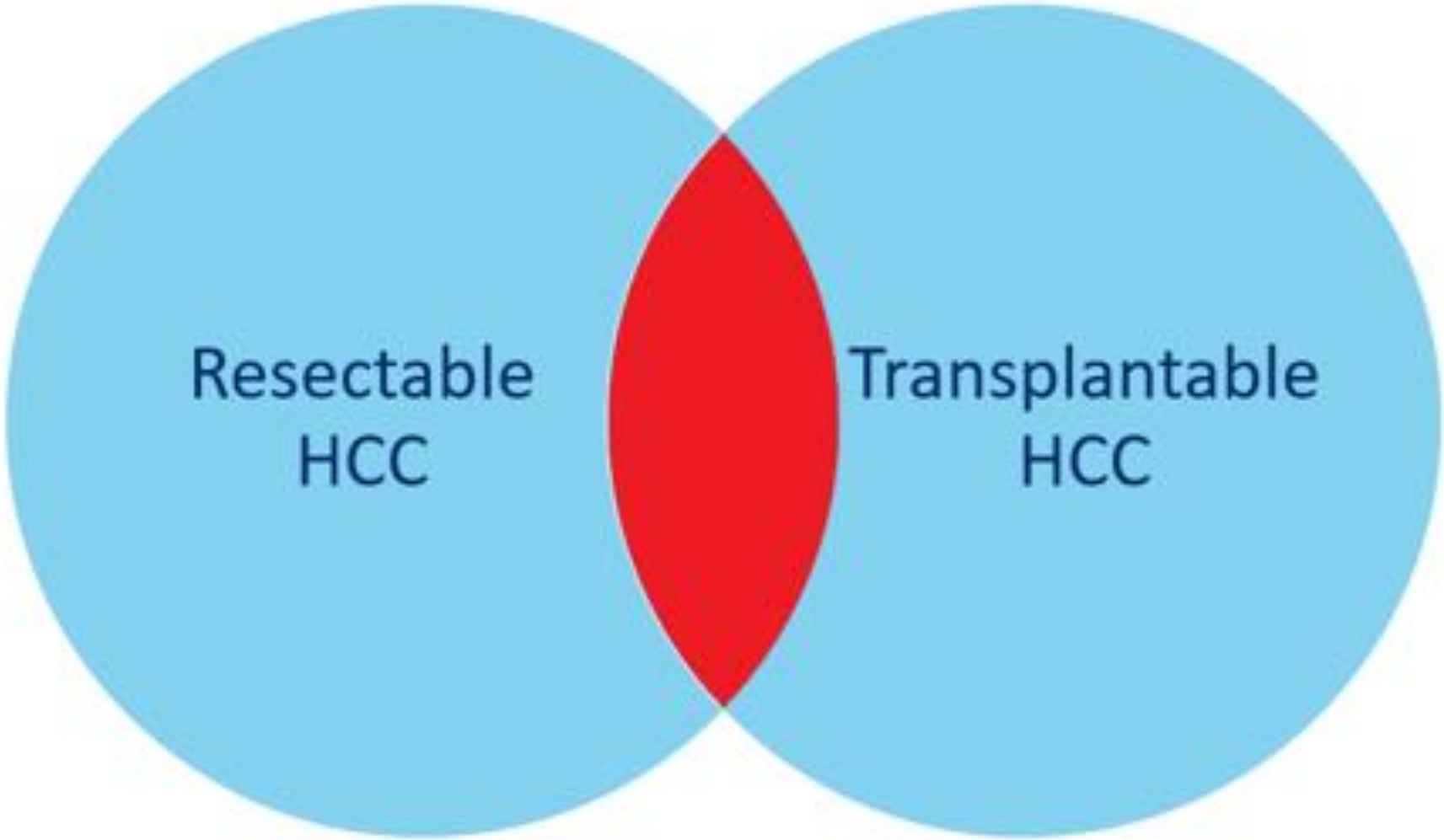


Kow 2019, Transl Gastroenterol Hepatol

Resectable and Transplantable

Predicting ~~need~~ benefit for transplantation in resectable candidates in HCC

Ultimate goal: improved OS



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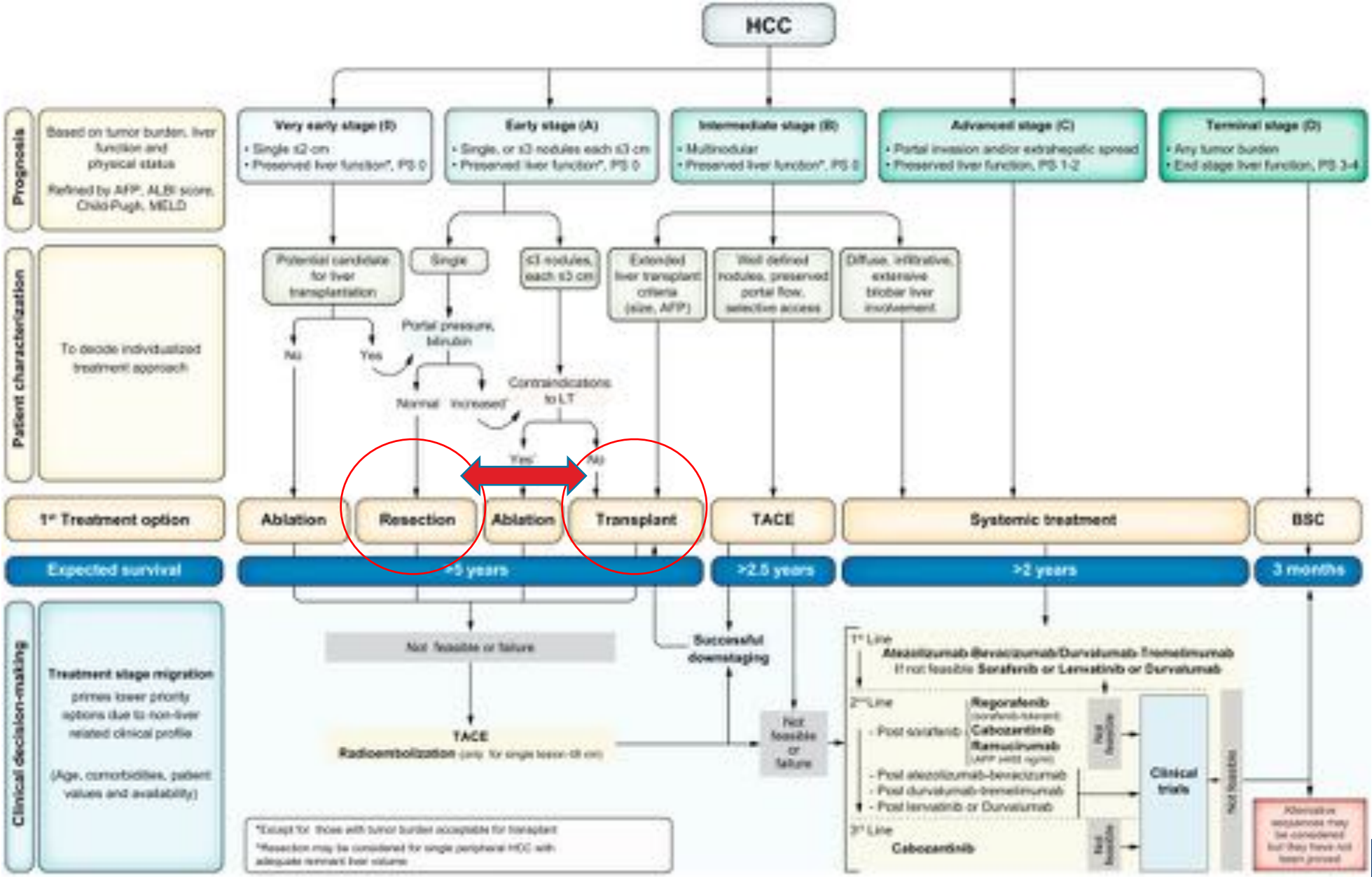
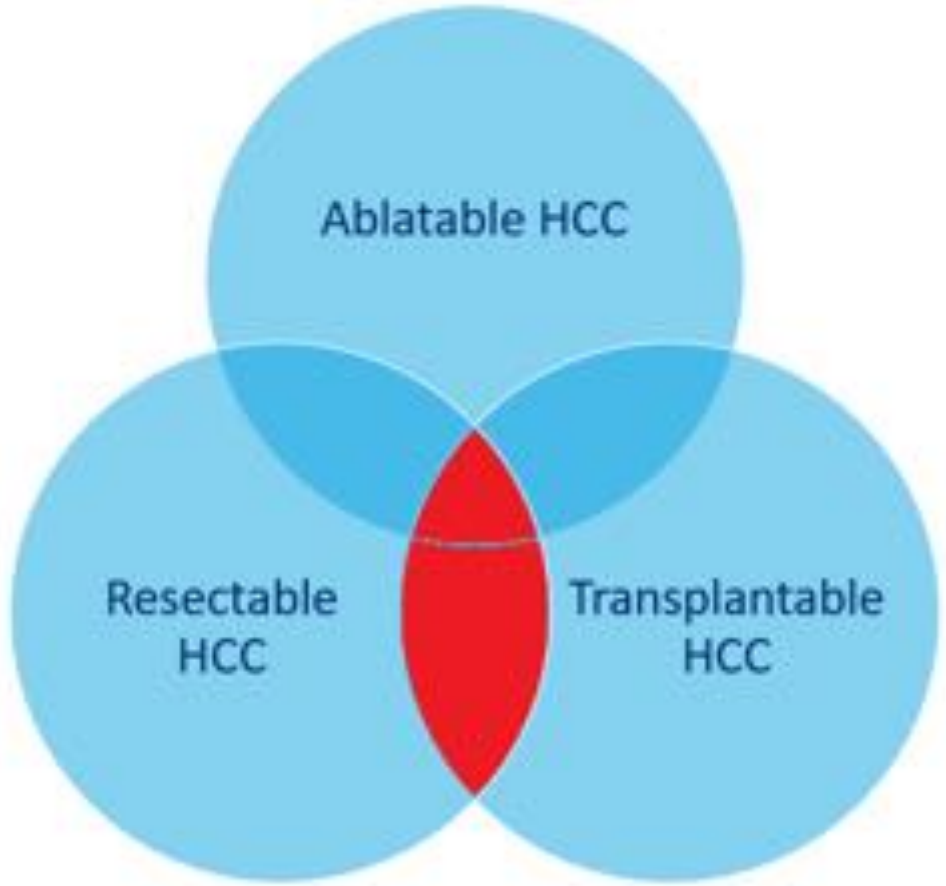


Other Variables - 1

Back of our mind – other treatment modalities

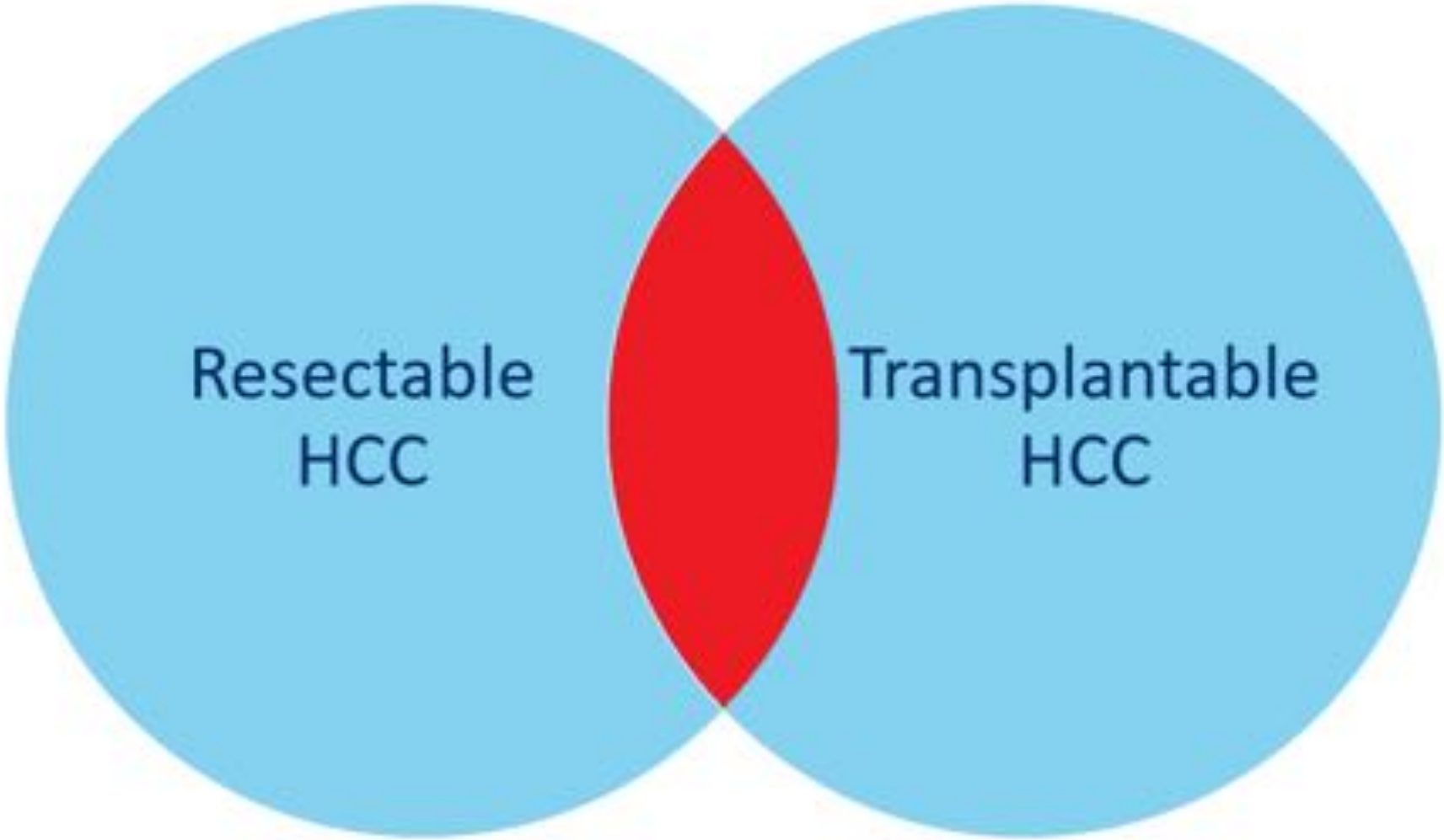
- Ablation
- Trans arterial therapy
- Systemic



Resectable and Transplantable

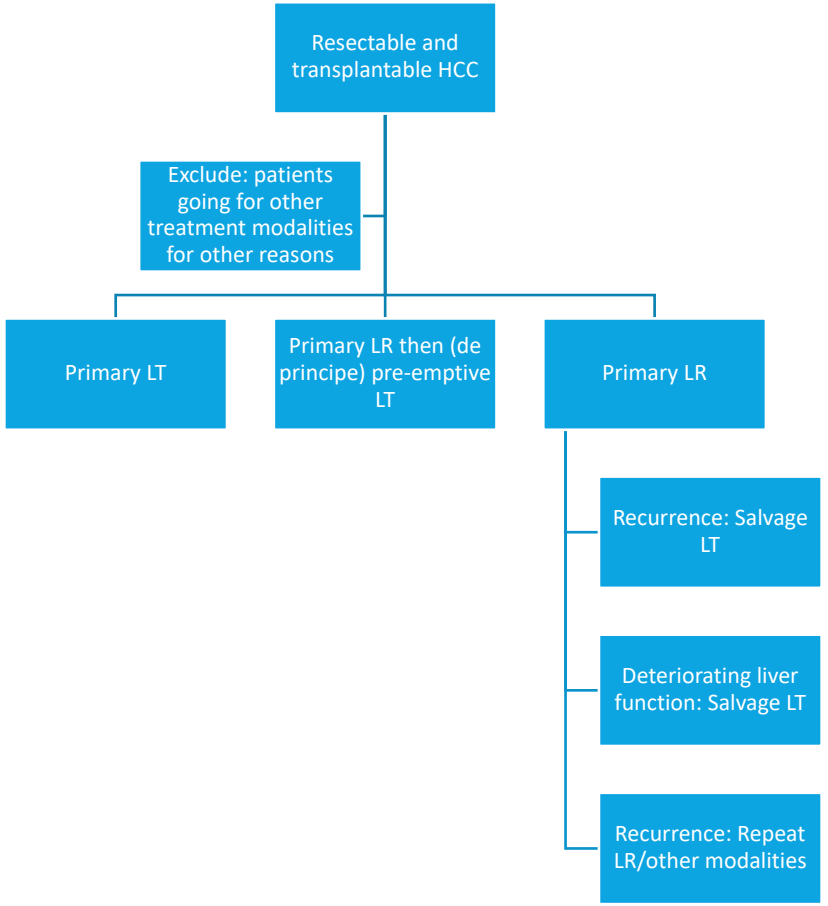
Predicting ~~need~~ benefit for transplantation in resectable candidates in HCC

Ultimate goal: improved OS



Resectable and Transplantable

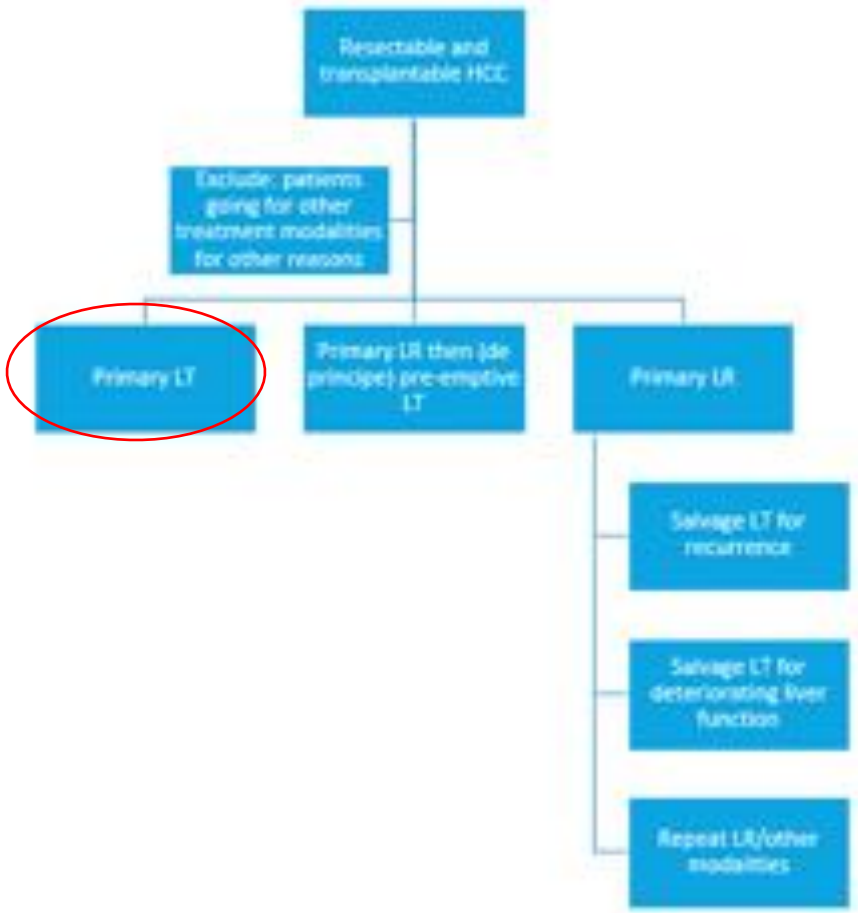
How to choose?



Liver Resection as a Bridge to Transplantation for Hepatocellular Carcinoma on Cirrhosis

A Reasonable Strategy?

René Adam, MD, PhD, Daniel Azoulay, MD, PhD, Denis Castaing, MD, Rony Eshkenazy, MD, Gérard Pascal, MD, Kentaro Hashizume, MD, Didier Samuel, MD, PhD, and Henri Bismuth, MD, FACS Hon.



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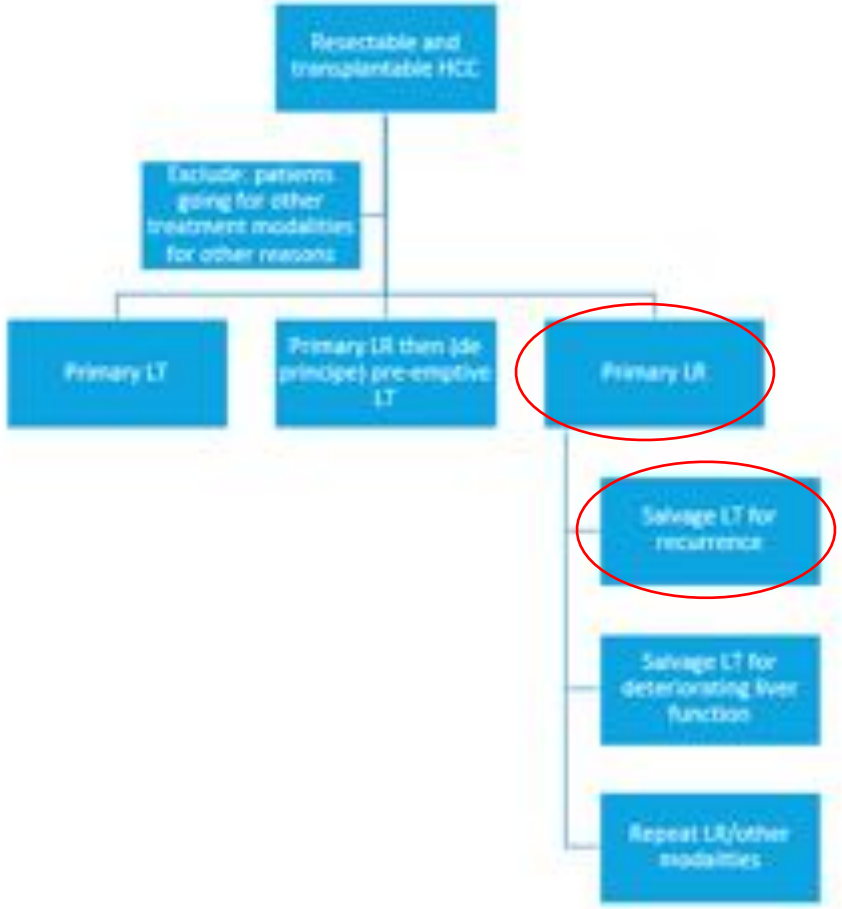

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- Salvage LT (n = 17) vs primary LT (n = 195)

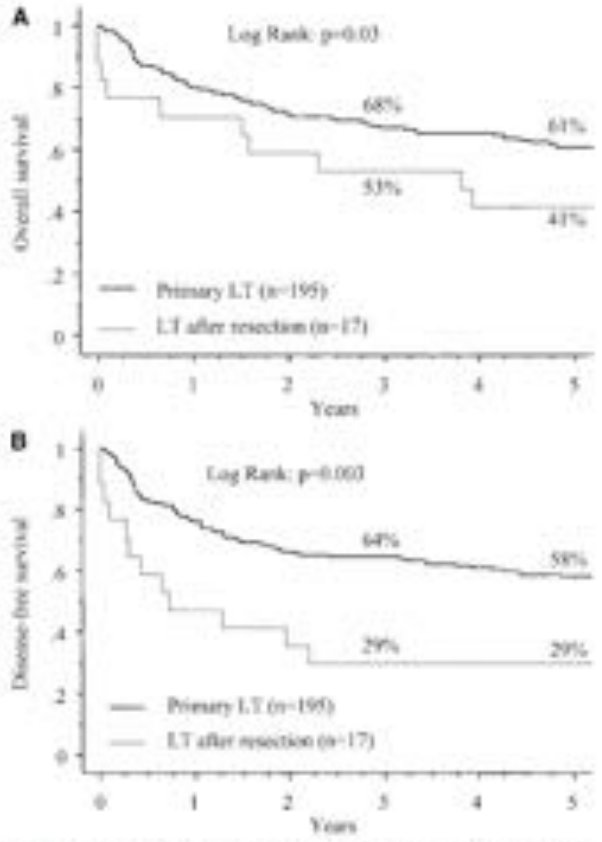

FIGURE 2. Comparison of survival between primary and secondary transplantation for HCC on cirrhosis. (A) overall survival; (B) disease-free survival.

Adam et al 2003, Ann Surg

Primary LR ± salvage (n = 98) LT vs primary LT (n = 195)

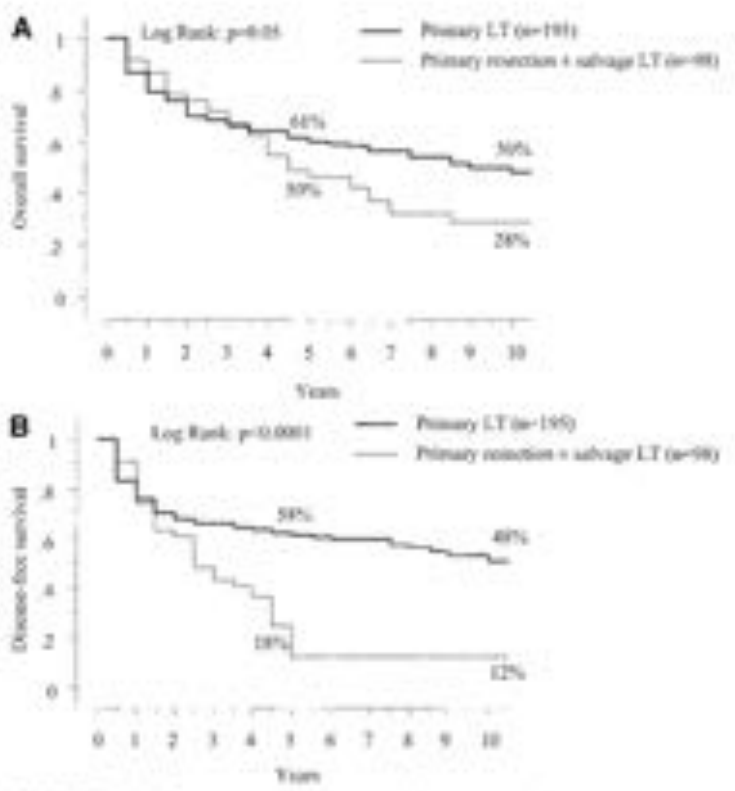

FIGURE 4. Comparison of survival between primary resection with possible transplantation and primary transplantation for HCC on cirrhosis (A) overall survival and (B) disease-free survival.

Liver Resection as a Bridge to Transplantation for Hepatocellular Carcinoma on Cirrhosis

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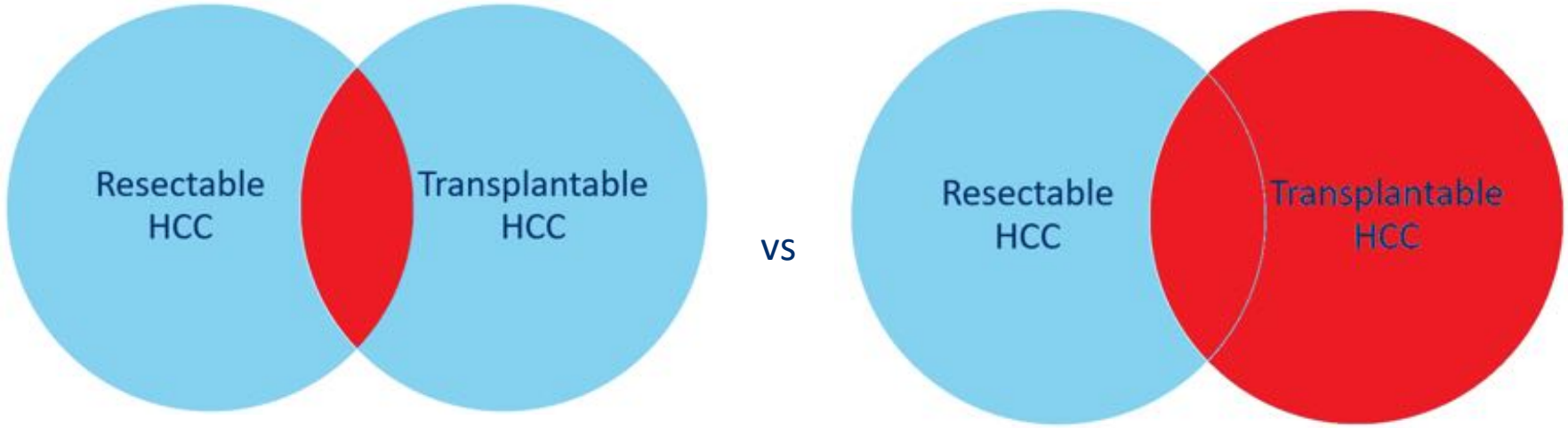
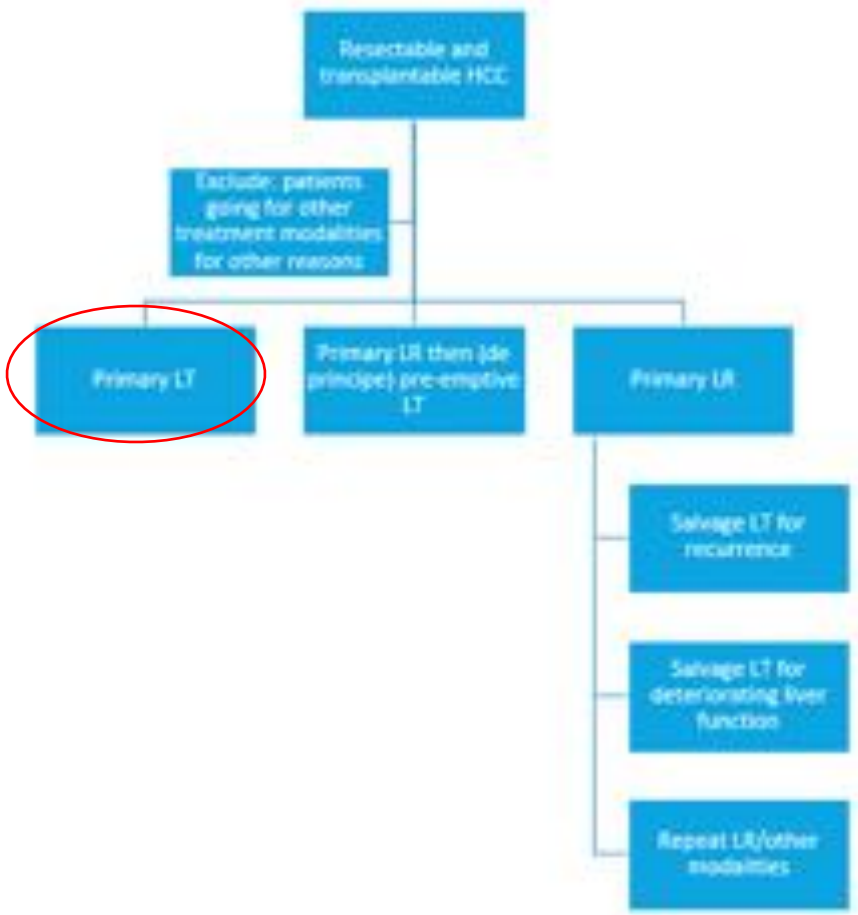
- LT after LR is associated with
  - Higher mortality
  - Increased risk of recurrence
  - LR impairs patient transplantability

- Note: patient population for LT upfront may not have been upfront resectable



Resection Prior to Liver Transplantation for Hepatocellular Carcinoma

Jacques Belghiti, MD, Alexandre Cortes, MD,* Eddie K. Abdalla, MD,* Jean-Marc Régimbeau, MD,* Kurumboor Prakash, MD,* François Durand, MD,† Daniele Sommacale, MD,* Federica Dondero, MD,* Mickael Lesurtel, MD,* Alain Sauvanet, MD,* Olivier Farges, MD, PhD,* and Reza Kianmanesh, MD**



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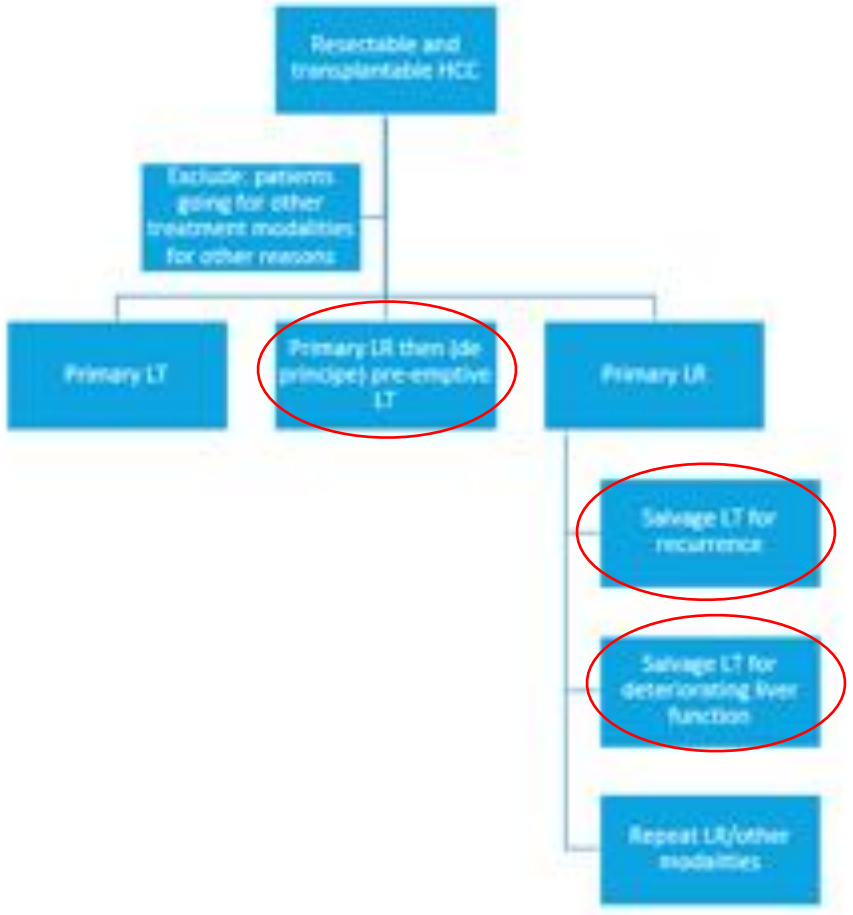

- Primary LT (n = 70) vs secondary LT (n = 18)
    - Secondary LT for recurrence, deterioration of liver function, pre-emptive

- LT after LR does NOT impair long term survival

- Note: patient population for LT upfront may not have been upfront resectable

Resection Prior to Liver Transplantation for Hepatocellular Carcinoma

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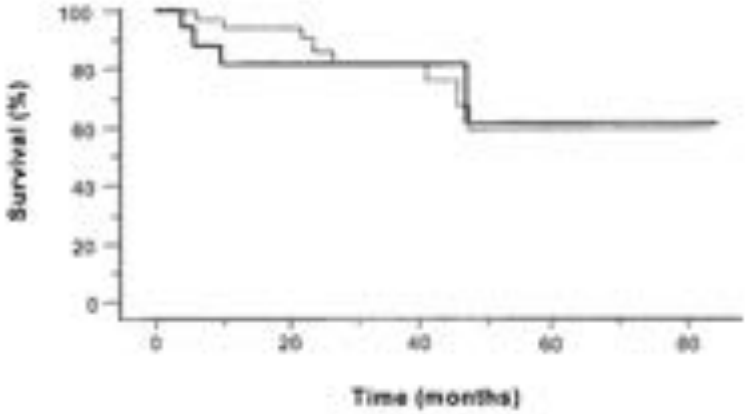
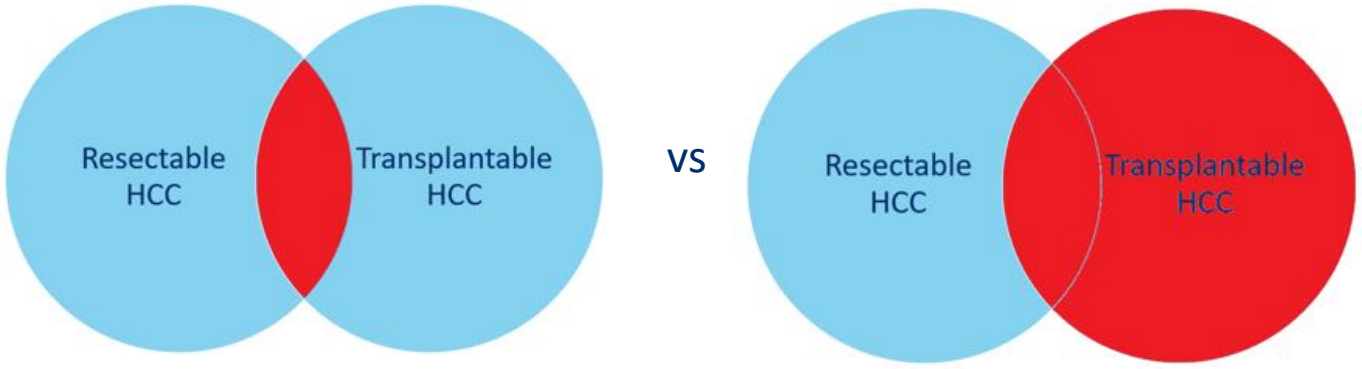


FIGURE 2. Kaplan-Meier survival plots for PLT versus SLT groups. The survival rates measured from the time of liver transplantation in the group of patients who underwent primary (—) versus secondary (···) liver transplantation for HCC. There was a single death (5.6%) in the first 30 days postoperatively in the SLT group and 4 postoperative deaths (5.7%) in the PLT group. Patients who died in the postoperative period were excluded.

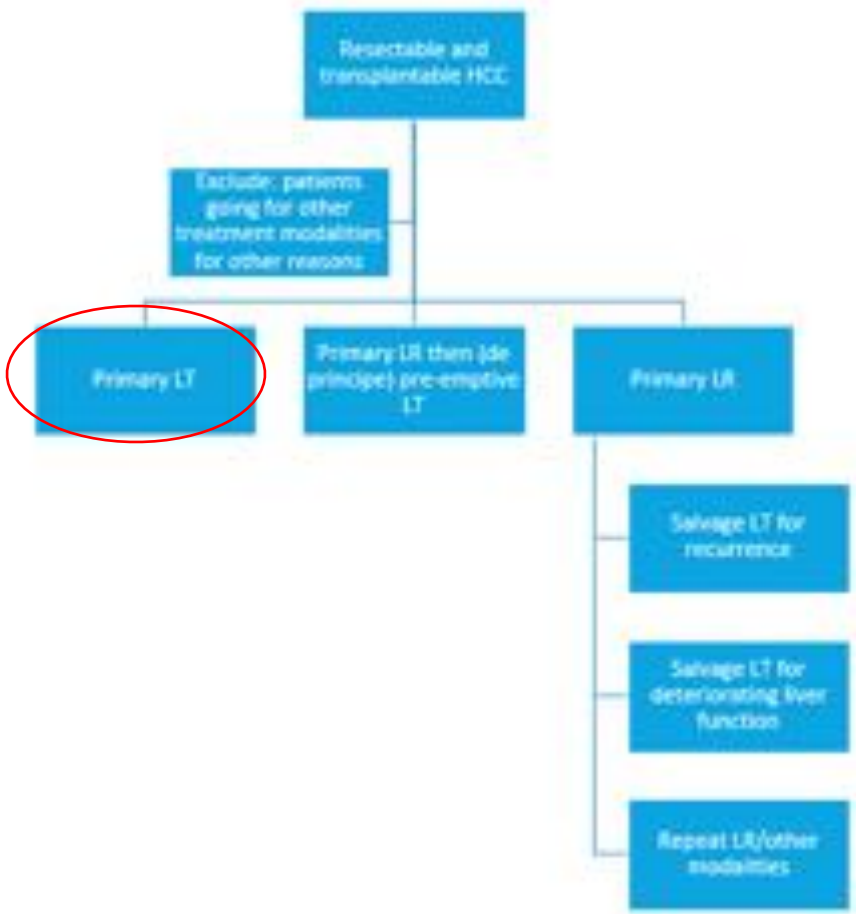


Belghiti et al 2003, Ann Surg

Salvage Liver Transplantation Is a Reasonable Option for Selected Patients Who Have Recurrent Hepatocellular Carcinoma after Liver Resection

Zhenhua Hu[1,2,3], Jie Zhou[1,2,3], Xiaofeng Xu[1,2,3], Zhiwei Li[1,2,3], Lin Zhou[1,2,3], Jian Wu[1,2,3], Min Zhang[1,2,3], Shusen Zheng[1,2,3]*

1 Department of Hepatobiliary and Pancreatic Surgery, First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China, 2 Key Laboratory of Combined Multi-Organ Transplantation, Ministry of Public Health, First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China, 3 Key Laboratory of Organ Transplantation, First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China



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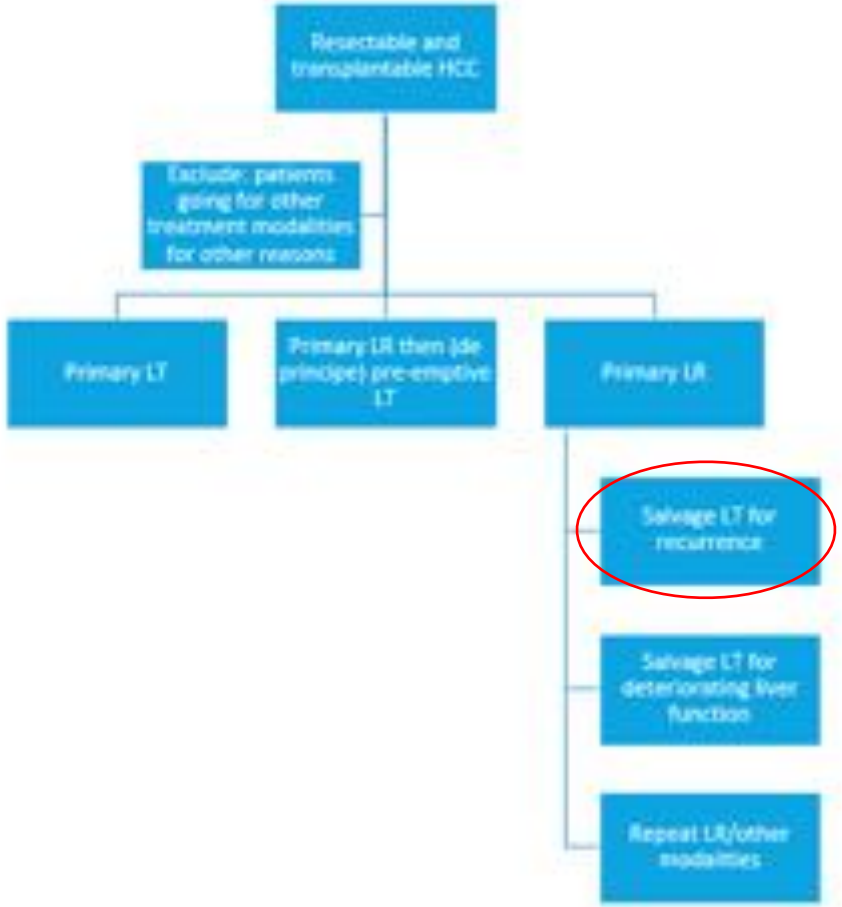

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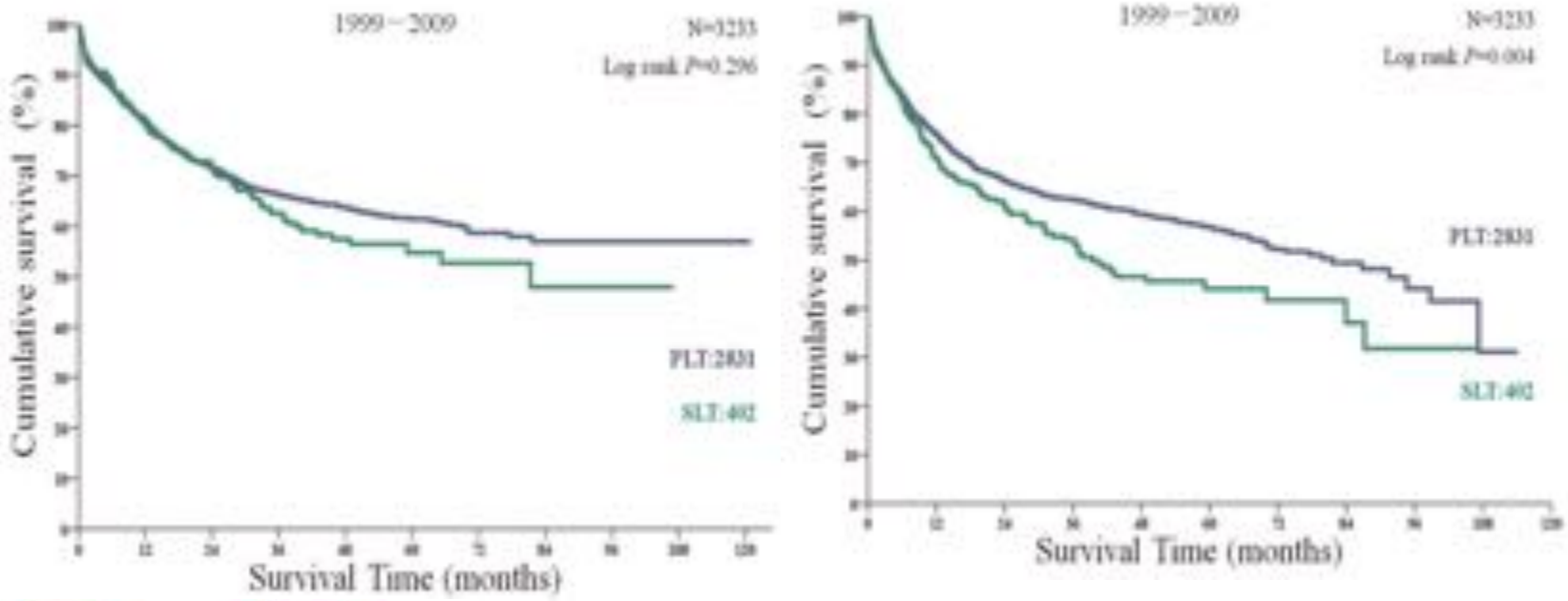
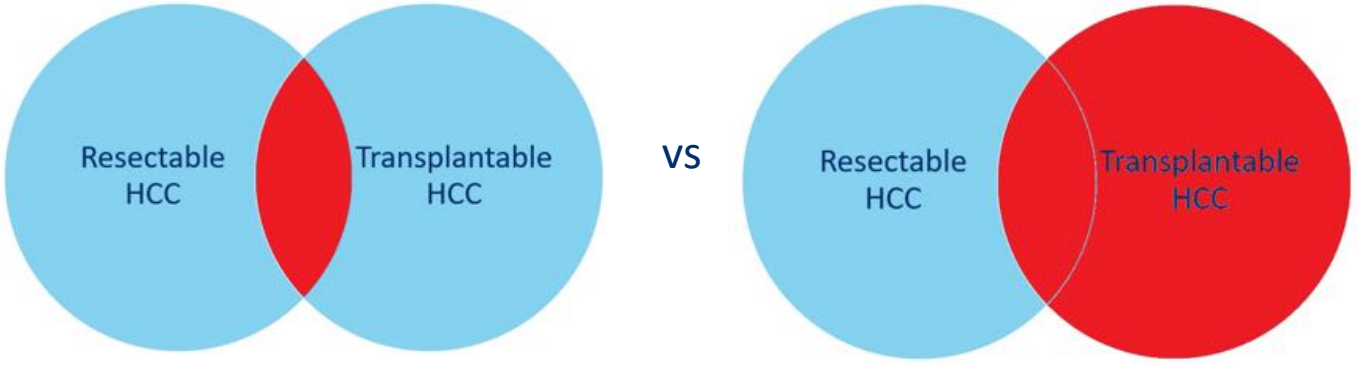
- Primary LT (n = 6087) vs secondary LT (n = 888) for recurrence

- Hangzhou criteria
- OS similar
- DFS improved in primary LT





DFS

Hu et al 2012, PLoS ONE

Liver transplant offers a survival benefit over margin negative resection in patients with small unifocal hepatocellular carcinoma and preserved liver function

Andrew J. Benjamin [a], Talia B. Baker [a], Mark S. Talamonti [b], Adam S. Bodzin [a], Andrew B. Schneider [a], David J. Winschester [b], Kevin K. Roggin [a], David J. Bentrem [c], Nicholas R. Suss [b], and Marshall S. Baker [b,*]

- US registry data
- MELD<12 and tumour <3cm included
- Liver resection (n-219) vs transplant (n=241)

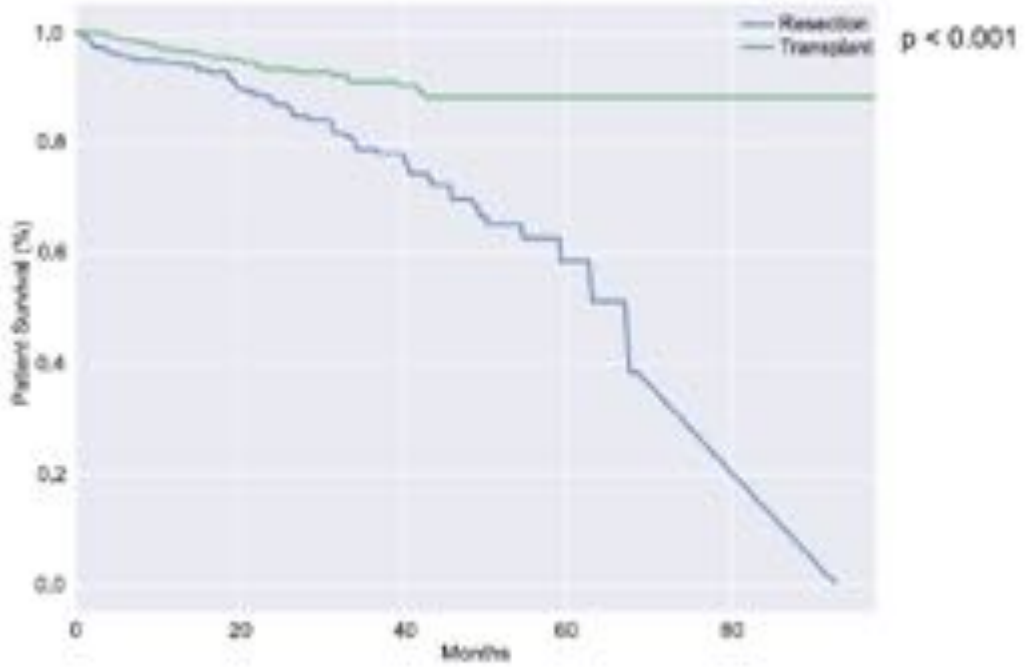


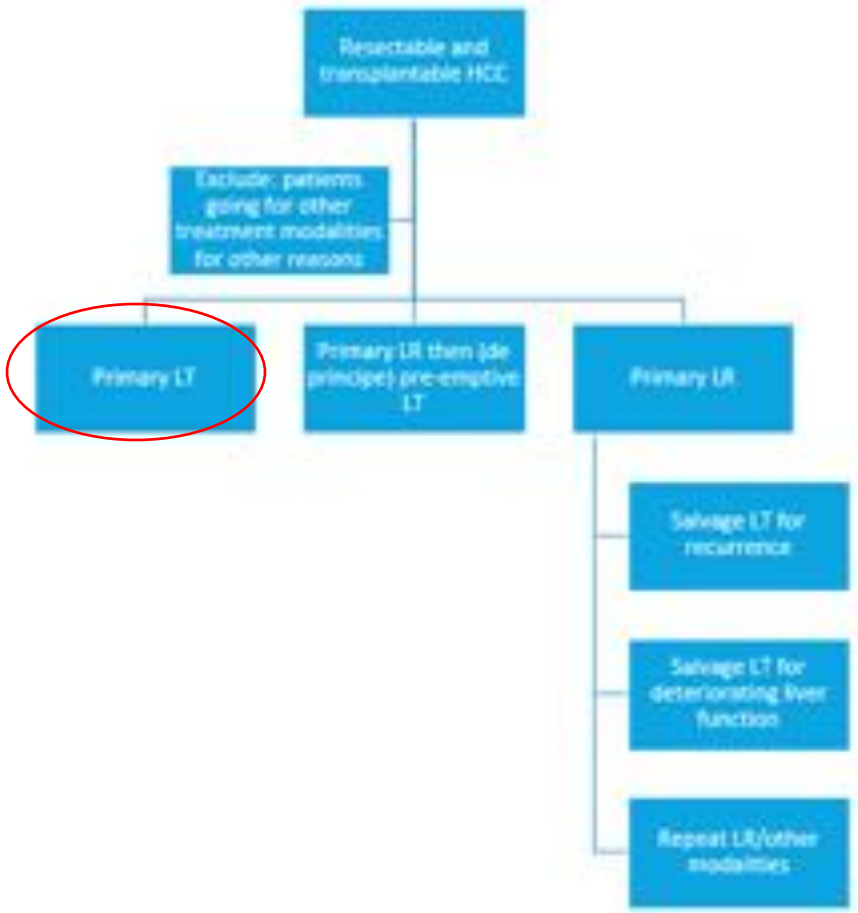
Fig. 3. Kaplan-Meier survival estimates comparing liver resection and orthotopic liver transplant.

Benjamin et al 2017, Surgery

Review

Salvage versus Primary Liver Transplantation for Hepatocellular Carcinoma: A Twenty-Year Experience Meta-Analysis

Gian Piero Guerrini *, Giuseppe Esposito, Tiziana Olivieri, Paolo Magistri, Roberto Ballarin, Stefano Di Sandro and Fabrizio Di Benedetto



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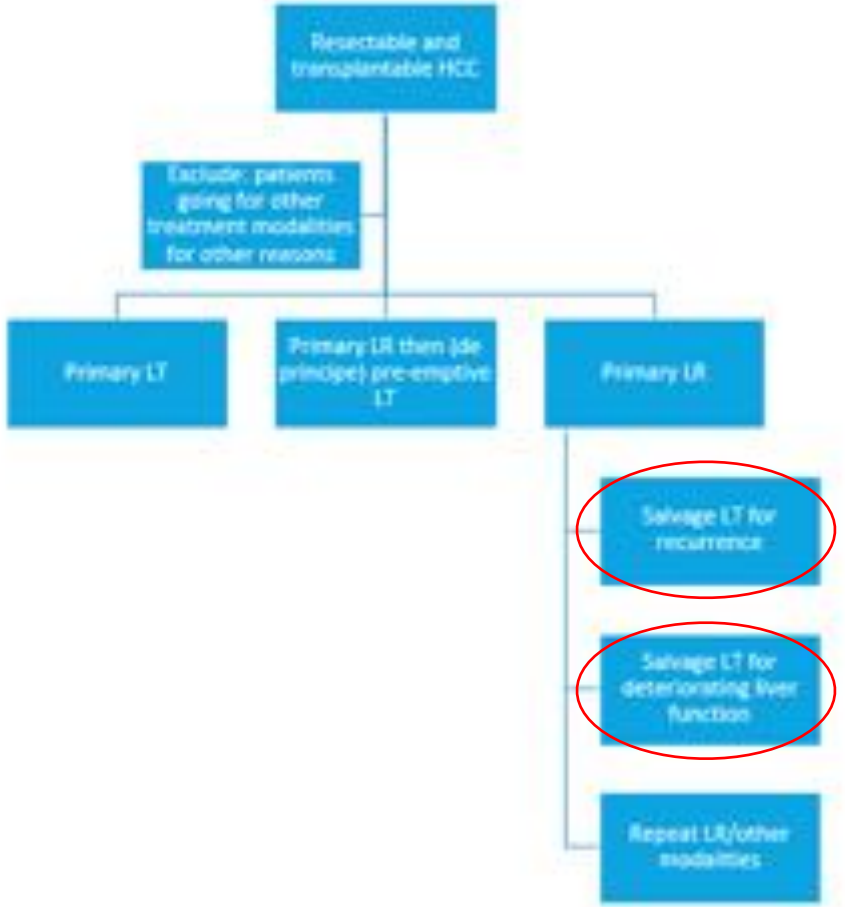

Meta-analysis 1

- 25 studies with 11275 patients

Review

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Table 1. Summary of studies included in the Meta-analysis.

n.	Author	Region	Year	Study Period	Study Design	Sample Size		Follow-Up (mo)		LDLT/DDLT	MINORS (Quality)
						SLT	PLT	SLT	PLT		
1	Adam [29]	France	2003	1984–2000	OCS (R)	57	195	49	51	DDLT	25
2	Belghiti [30]	France	2003	1993–2001	OCS (R)	18	70	56.2	56.2	DDLT	25
3	Margarit [31]	Spain	2005	1988–2002	OCS (P)	6	36	NA	NA	NA	20
4	Hwang [32]	Korea	2007	1997–2006	OCS (R)	37	200	30.7	40.1	LDLT	22
5	Vennarecci [33]	Italy	2007	2003–2006	OCS (P)	9	37	26.3	26.3	NA	23
6	Del Gaudio [34]	Italy	2008	1996–2005	OCS (R)	16	147	26.2	36	DDLT	23
7	Kim [35]	Korea	2008	2005–2007	OCS (NA)	15	31	18.3	18.7	DDLT + LDLT	20
8	Shao [36]	China	2008	2003–2005	OCS (P)	15	62	18	22.4	DDLT	22
9	Chenqai [37]	France	2009	1990–2007	OCS (R)	18	136	57.6	576	DDLT	21
10	Sapisochin [38]	Spain	2010	1990–2007	OCS (P)	17	34	70	70	NA	22
11	Hu [39]	China	2012	1999–2009	OCS (R)	888	6087	15.2	15	DDLT + LDLT	22
12	Kaido [40]	Japan	2012	1999–2009	OCS (R)	19	48	77	77	LDLT	22
13	Liu [41]	China	2012	2003–2011	OCS (R)	39	180	30	33	DDLT + LDLT	22
14	Moon [42]	Korea	2012	1996–2008	OCS (R)	17	169	27.3	39	LDLT	21
15	De Carlis [43]	Italy	2013	2000–2009	OCS (R)	26	153	NA	NA	NA	22
16	Guerrini [44]	Italy	2014	2000–2011	OCS (P)	28	198	44.2	44.2	DDLT + LDLT	22
17	Abe [45]	Japan	2015	2003–2011	OCS (R)	15	45	66.3	73.2	LDLT	22
18	Bhangui [46]	France	2015	1990–2012	OCS (P)	31	340	62	62	DDLT	23
19	Vasavada [47]	China	2015	2002–2012	OCS (R)	18	91	NA	NA	LDLT	22
20	Wang [48]	China	2016	2003–2011	OCS (P)	76	295	32.4	32.4	DDLT	23
21	Shan [49]	China	2017	2006–2015	OCS (R)	28	211	35	35	DDLT + LDLT	21
22	Yong [50]	Taiwan	2018	2000–2015	OCS (R)	100	100	NA	NA	LDLT	22
23	Chan [51]	Taiwan	2019	2003–2018	OCS (R)	58	245	NA	NA	LDLT	22
24	Gao [52]	Singapore	2019	2006–2017	OCS (P)	14	35	43.9	43.9	DDLT + LDLT	22
25	Hwan [53]	Korea	2020	2007–2018	OCS (R)	125	500	NA	NA	LDLT	23

Guerrini et al 2022, Cancers

Review

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- 5y OS better in primary LT
  - SLT 53.9% and PLT 56.5% (OR 0.68, 95% CI 0.56 to 0.82 p < 0.0001)

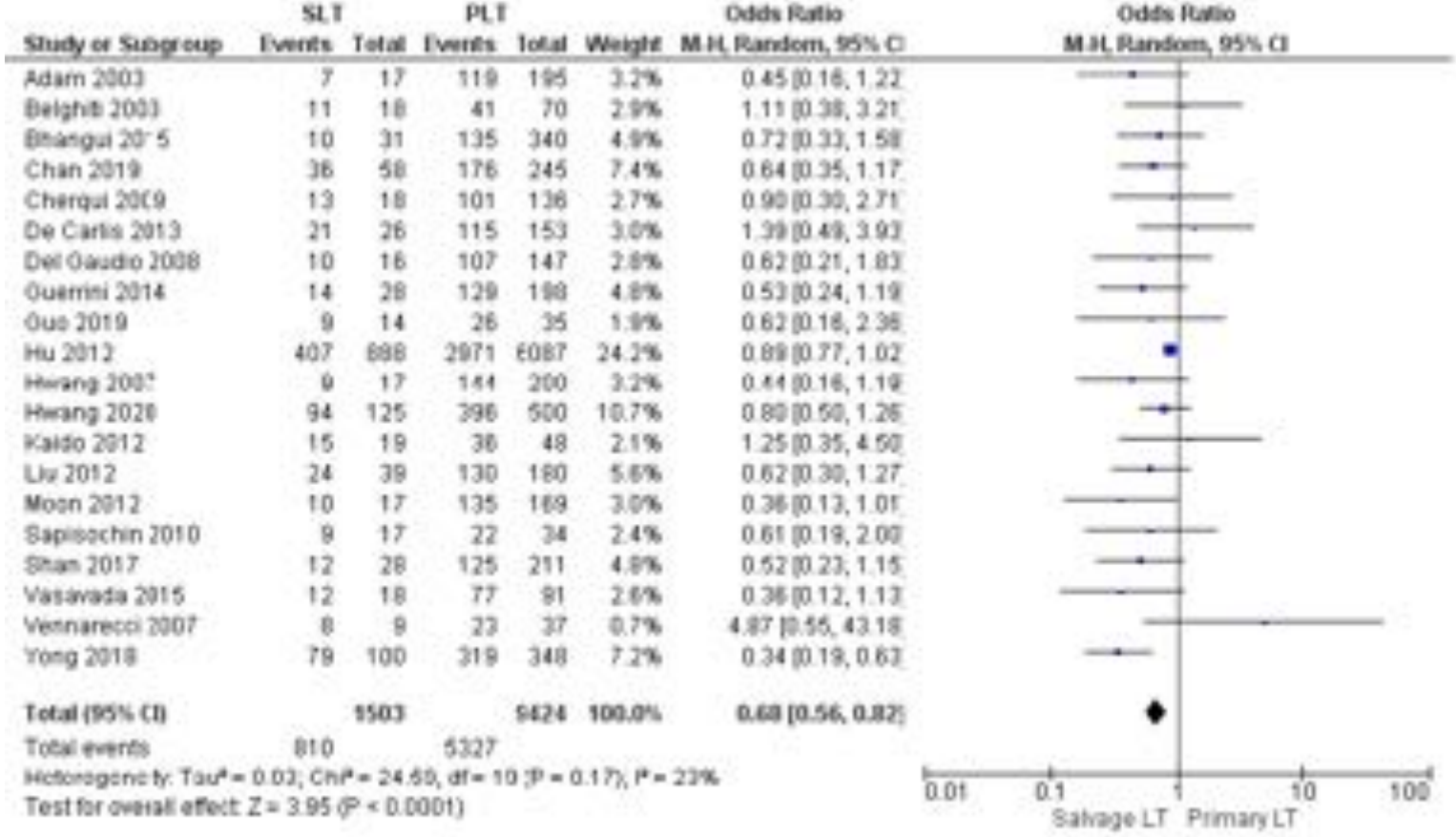
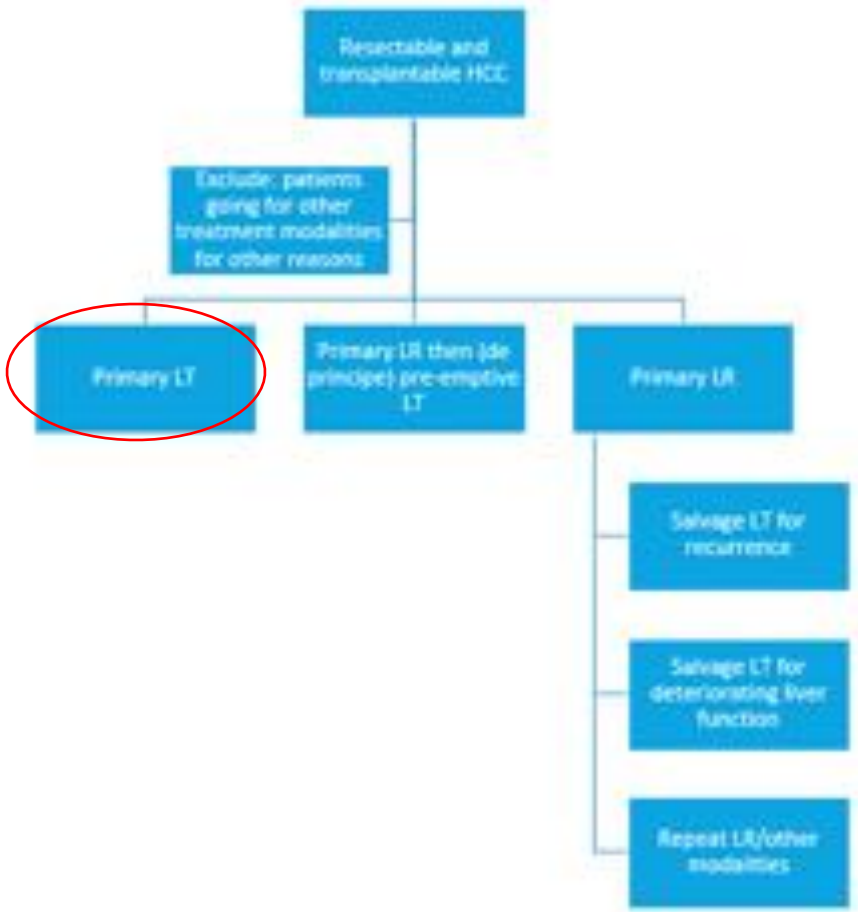


Figure 18. 5-year overall survival rates.

Original Article

Liver resection versus liver transplantation for hepatocellular carcinoma within Milan criteria: a meta-analysis of 18,421 patients

Jin Hean Koh[1#], Darren Jun Hao Tan[1#], Yuki Ong[1], Wen Hui Lim[1], Cheng Han Ng[1], Phoebe Wen Lin Tay[1], Jie Ning Yong[1], Mark D. Muthiah[1,2,3], Eunice X. Tan[1,2,3], Ning Qi Pang[3,4], Beom Kyung Kim[1,6], Nicholas Syn[1,7], Alfred Kow[3,4], Brian K. P. Goh[8,9], Daniel Q. Huang[1,2,3]^



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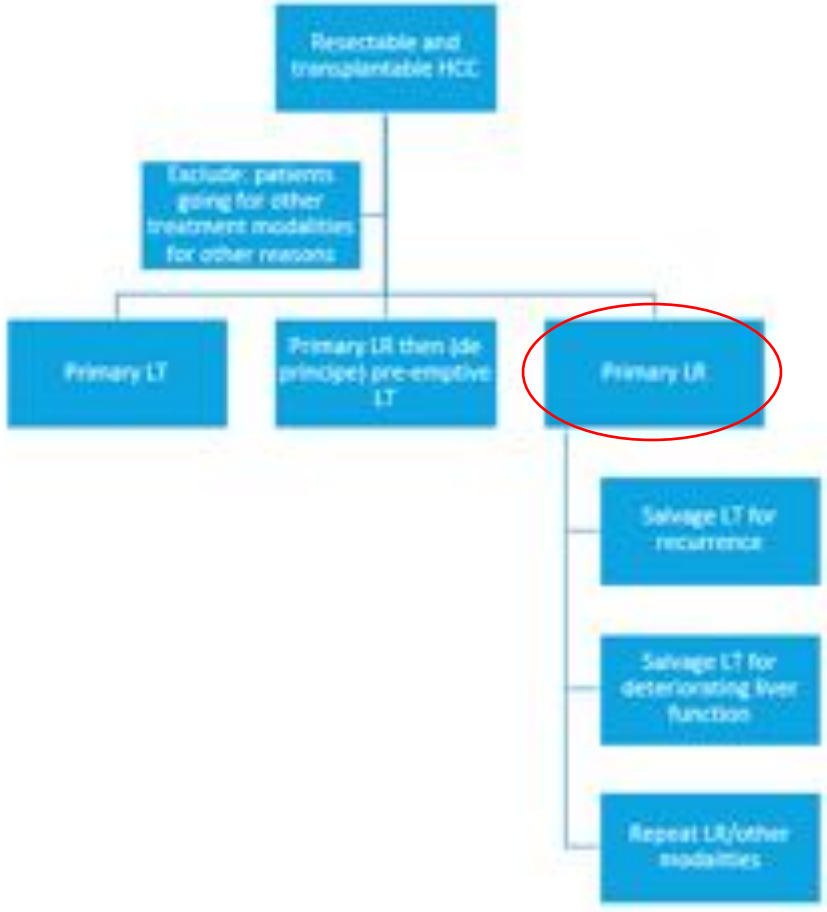
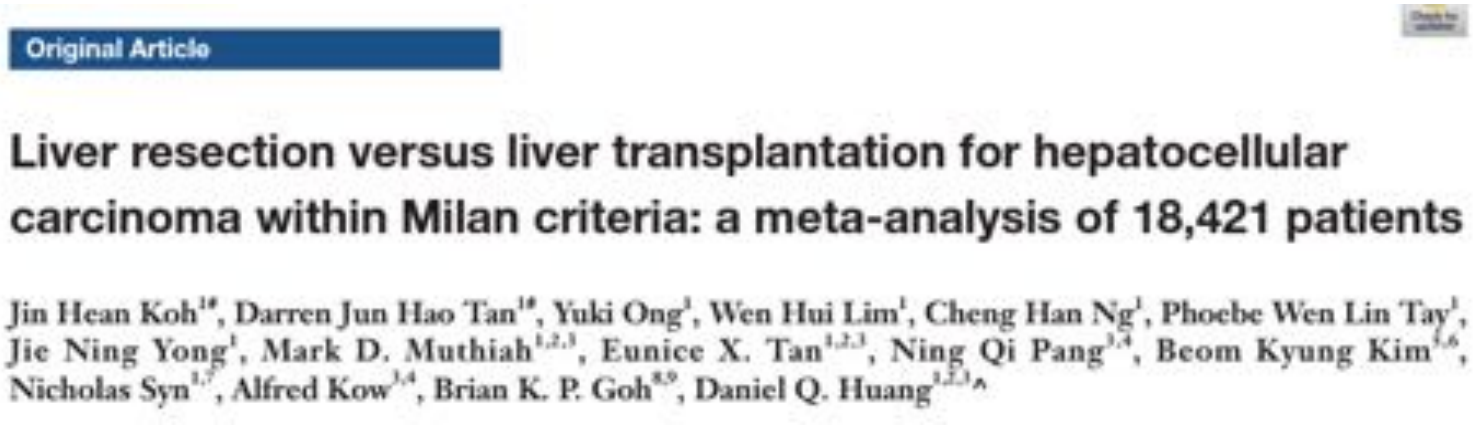


Meta-analysis 2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- Within Milan criteria
- Population includes resectable and non resectable HCC patients
  - Proportion of cirrhosis patient differed between groups
- Results generally favoured LT

Koh et al 2022, HepatoBiliary Surg Nutr

[Input data classification]

- LR showed poorer OS HR = 1.44; 95% CI: 1.14–1.81; P<0.01] and DFS (HR =2.71; 95% CI: 2.23–3.28; P<0.01) compared to LT

- Similar to previous the meta-analysis shown, but different groups compared!

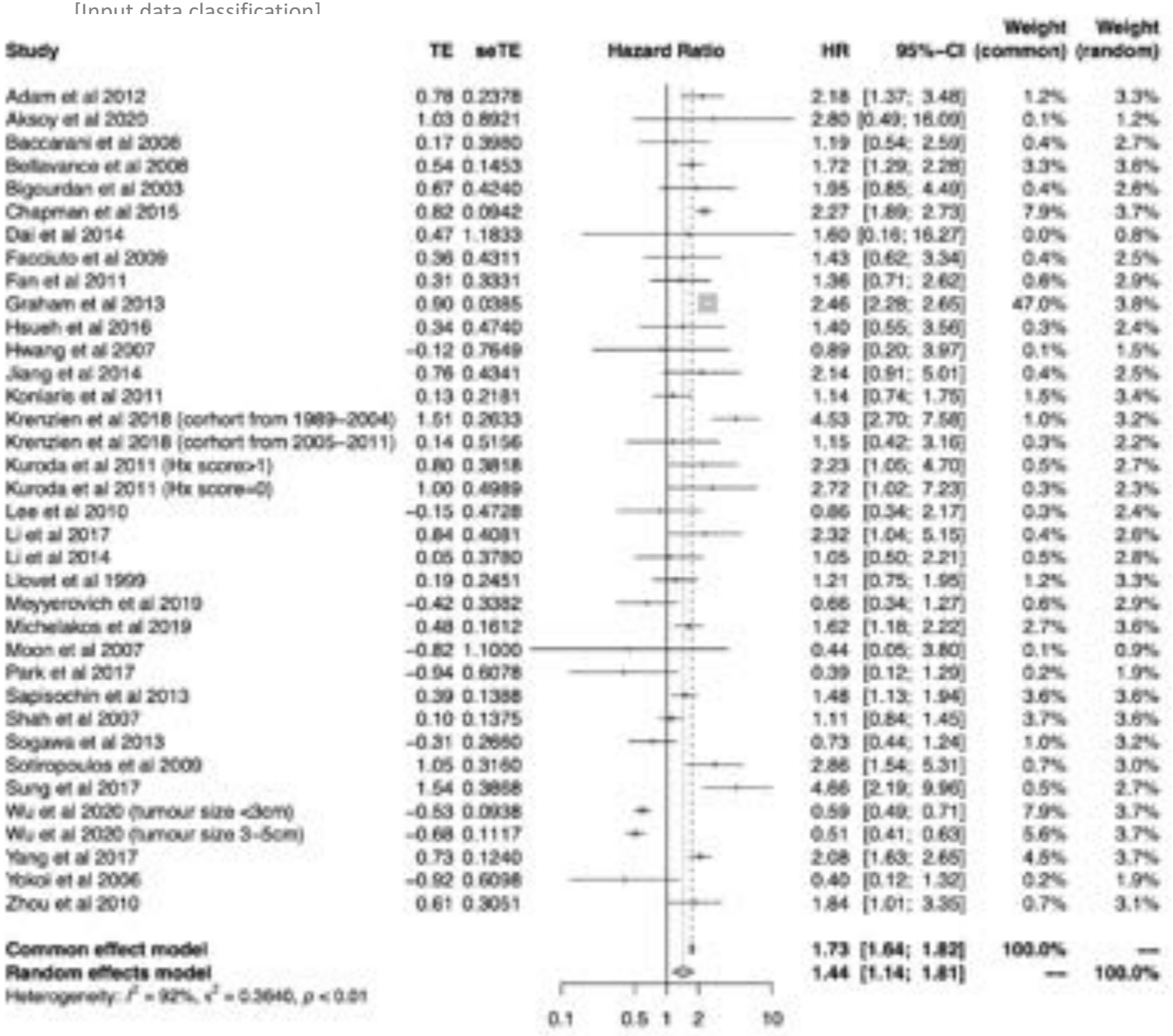


Figure 2 Forest plot for OS among patients who underwent LR versus LT for HCC. HR, hazard ratio; CI, confidence interval; OS, overall survival; LR, liver resection; LT, liver transplantation; HCC, hepatocellular carcinoma.

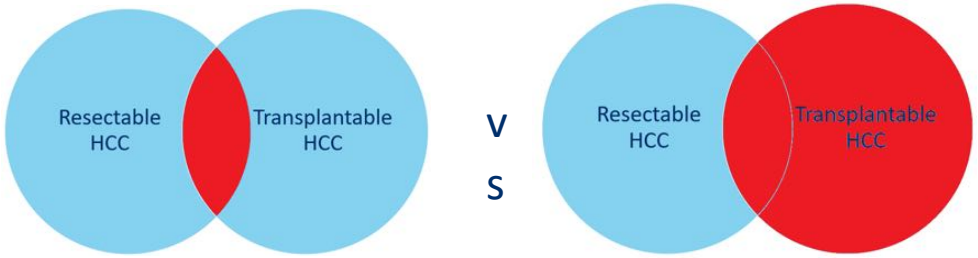
Table 1 Patient demographics and tumour characteristics, by treatment

Characteristics	Number of studies (total sample size)	LT (95% CI)	Number of studies (total sample size)	LR (95% CI)	P
Male (%)	23 (2,344)	81.13 (76.83–84.79)	23 (3,656)	75.30 (69.43–80.36)	0.086
Age (years)	23 (2,386)	53.74 (51.59–55.90)	24 (3,676)	57.05 (54.47–59.63)	0.054
Cirrhosis (%)	21 (2,047)	95.51 (94.52–96.32)	22 (3,145)	87.19 (85.97–88.31)	<0.001
HBV (%)	20 (2,125)	39.45 (16.42–68.37)	21 (3,296)	47.67 (27.57–68.56)	0.658
HCV (%)	17 (1,991)	33.56 (18.37–53.15)	18 (2,993)	19.79 (11.10–32.76)	0.184
ALD (%)	12 (1,279)	13.52 (6.21–26.95)	12 (435)	14.83 (7.83–26.28)	0.851
NASH (%)	7 (808)	5.60 (3.13–9.80)	7 (1,024)	9.22 (5.59–14.85)	0.193
Microvascular invasion (%)	19 (1,864)	15.23 (9.04–24.53)	20 (2,960)	19.83 (12.63–29.75)	0.434
Poorly differentiated (%)	12 (1,005)	11.77 (8.39–16.26)	12 (2,107)	14.84 (8.90–23.71)	0.447
Tumour size (cm)	17 (1,256)	2.74 (2.40–3.08)	17 (1,658)	3.24 (2.79–3.68)	0.084
Uninodular HCC (%)	17 (2,029)	89.67 (88.25–90.94)	17 (3,073)	91.15 (90.09–92.11)	0.08
LDLT (%)	16 (1,336)	78.07 (75.88–80.11)	–	–	–
Asian centres	12 (923)	96.97 (92.38–99.97)	–	–	–
Non-Asian centres	4 (413)	46.06 (41.91–50.26)	–	–	–
DDLT (%)	11 (746)	19.89 (17.93–22.01)	–	–	–
Asian centres	5 (201)	3.03 (2.10–4.36)	–	–	–
Non-Asian centres	6 (545)	48.44 (44.27–52.64)	–	–	–

LT, liver transplantation; LR, liver resection; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; ALD, alcoholic liver disease; NASH, non-alcoholic steatohepatitis; HCC, hepatocellular carcinoma; LDLT, living donor liver transplantation; DDLT, deceased donor liver transplantation.

Issues with the evidence comparing LR to LT

Across various studies:



- Patient selection different
  - Different LT criteria (Milan, UCSF etc)
  - Cirrhotic vs non-cirrhotic
- Most studies compare primary LT vs secondary LT BUT definition of secondary LT different
  - LT after recurrence (salvage LT)
  - Pre-emptive LT after initial resection
  - Pre-emptive LT after initial resection when liver function deteriorates
  - Were secondary LT patients upfront transplantable?

Despite the difficulties

Evidence so far…

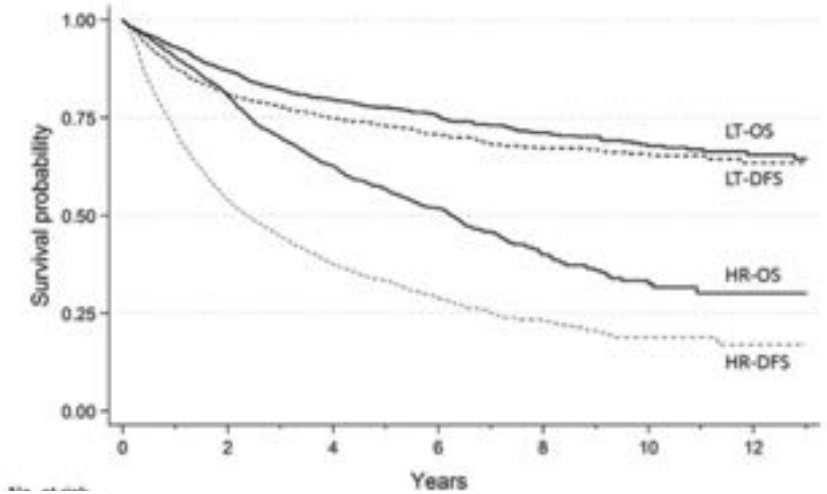
Generally, most authors seem to conclude that

- Primary LT seems to improve survival (OS vs DFS) compared to strategies involving LR
- But given practical considerations specific to LT, secondary LT after LR is an accepted treatment strategy

Liver Transplantation and Hepatic Resection can Achieve Cure for Hepatocellular Carcinoma

Antonio Daniele Pinna, MD, Tian Yang, MD,† Vincenzo Mazzaferro, MD, PhD,‡ Luciano De Carlis, MD, FEBS,§ Jian Zhou, MD, PhD,¶ Sasan Roayaie, MD,|| Feng Shen, MD, PhD,† Carlo Sposito, MD, PhD,† Matteo Cescon, MD, PhD,* Stefano Di Sandro, MD, PhD,§ He Yi-feng, MD,¶ Philip Johnson, MD, FRCP,** and Alessandro Cucchetti, MD**

- LT (n = 1218) vs LR (n = 2068)
- Estimated statistical cure
- Cure fraction of LT outperformed LR across all transplant criteria, esp for multiple tumours, even after accounting for drop out up to 20%



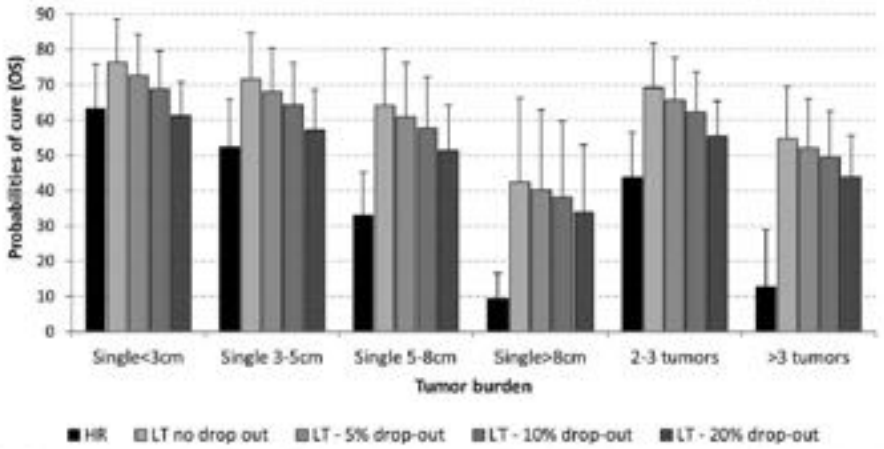


FIGURE 2. Graphical representation of cure fraction estimated on overall survival (OS), when cure was defined solely as the chance of being alive, regardless of tumor recurrence, equal to that of the general population. In fact, it can be argued that in presence of increased efficacy of therapeutic strategies for HCC recurrence, principally after hepatic resection, patients can still experience long-term survivals. Therefore, cure was estimated considering HCC as a chronic illness requiring continuing therapeutic options.

Pinna et al 2018, Ann Surg

Risk factors for early mortality after hepatectomy for hepatocellular carcinoma

Chao-Wei Lee, MD[a,b,c], Hsin-I Tsai, MD[c,d], Chang-Mu Sung, MD[a,e], Chun-Wei Chen, MD[e], Shu-Wei Huang, MD[e], Wen-Juei Jeng, MD, PhD[e], Tsung-Han Wu, MD[a], Kun-Ming Chan, MD[a,b], Ming-Chin Yu, MD[a,b,c,*], Wei-Chen Lee, MD[a,b], Miin-Fu Chen, MD[a,b]

- A review of 3383 patients

Table 6

Risk Assessment for early Mortality (RAM) score for hepatectomy for hepatocellular carcinoma.

Variables	Score allocation*	Total score	No. (% of total)	6-mo mortality (%)	Total score	No. (% of total)	6-mo mortality (%)
Diabetes mellitus	1	0	36 (1.8)	1 (2.8)	6	203 (10.5)	27 (13.3)
Albumin ≤3.5 g/dL	2	1	36 (1.8)	2 (5.6)	7	112 (5.7)	21 (18.75)
α-fetoprotein >200 ng/mL	2	2	532 (27.5)	11 (2.1)	8	76 (3.9)	12 (15.8)
Major resection†	1	3	308 (15.9)	10 (3.2)	9	39 (2.0)	9 (25.6)
Blood loss >800 mL	1	4	288 (14.9)	20 (6.9)	10	6 (0.3)	2 (33.3)
Major surgical complications‡	3	5	299 (15.5)	30 (10)	Total	1935 (100)	145 (7.5)

RAM score§	Score	6-mo mortality (%)	
Class I	0–6	101 (5.9)	$P<0.001$
Class II	7–9	42 (18.5)	
Class III	10	2 (33.3)	

* The regression coefficients (*B*) were multiplied by 2 and rounded to integer in order to calculate the RAM score.
† Includes trisegmentectomy, right/left lobectomy, and extended right/left lobectomy.
‡ Major surgical complications include grade III–IV surgical complications.
§ AUC = 0.725, $P<0.001$. When cutoff score is 4.5, the sensitivity and specificity for 6-month mortality was 0.705 and 0.648, respectively.

Lee et al 2016, Medicine (Baltimore)

Poor Prognostic Factors for Resection

- Portal HTN
- Multifocal HCC
- Impaired liver function

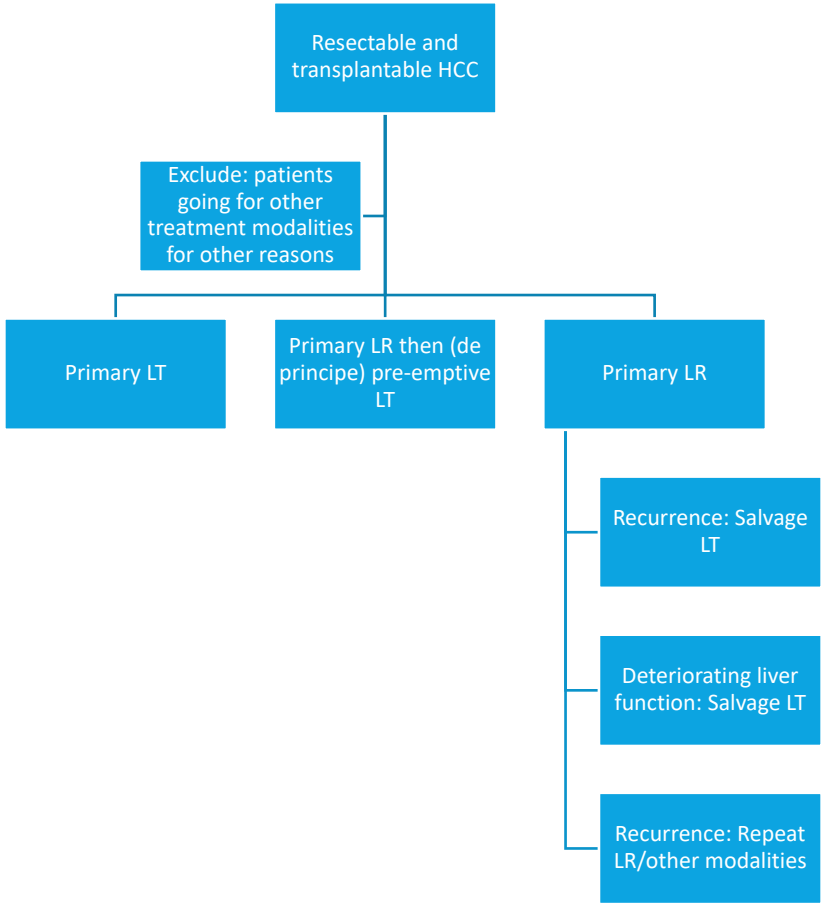
Why consider LR then?

- Practical considerations for LT
  - Availability of organ
    - Different considerations between DDLT vs LDLT?
  - Costs of LT
  - Long term immunosuppressants
  - Specialized multidisciplinary team

- LR can serve as
  - Bridging therapy to LT to prevent waitlist drop out (pre-emptive)
  - Definitive curative treatment (until recurrence: then salvage LT)

Resectable and Transplantable

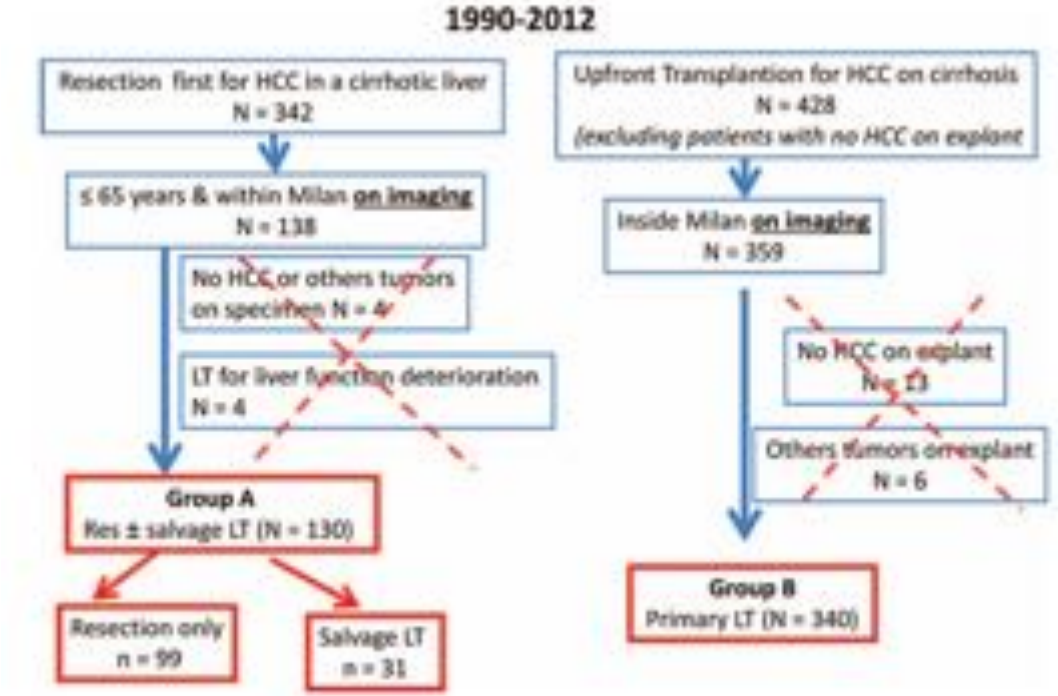
How to choose?



Salvage Versus Primary Liver Transplantation for Early Hepatocellular Carcinoma: Do Both Strategies Yield Similar Outcomes?

Prashant Bhangui, MD,†‡ Marc Antoine Allard, MD,*†§ Eric Vibert, MD, PhD,*†¶ Daniel Cherqui, MD,*†¶*
Gilles Pelletier, MD,†¶ Antonio Sa Cunha, MD,*†§ Catherine Guettier, MD,*†¶*
Jean-Charles Duclos Vallee, MD,†¶ Faouzi Saliba, MD,*†¶ Henri Bismuth, MD,**
Didier Samuel, MD, PhD,†¶ Denis Castaing, MD,*†¶ and René Adam, MD, PhD*†§*

- Note: patient population for LT upfront may not have been upfront resectable
- Only looked at cirrhotic patients



Bhangui et al 2016, Ann Surg

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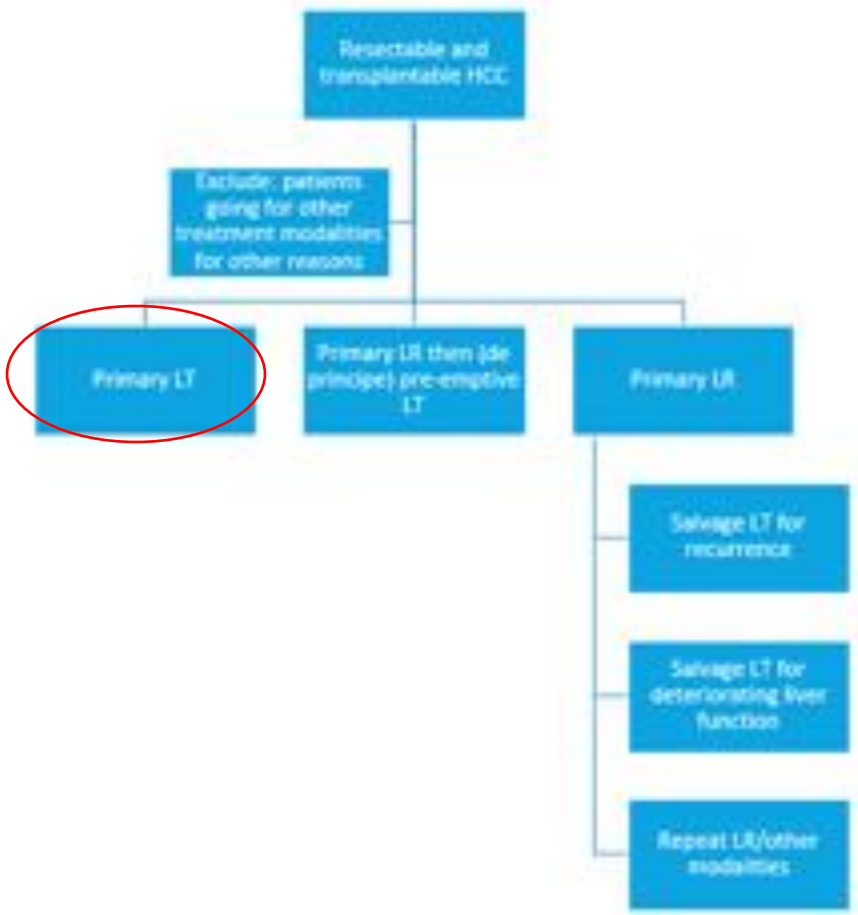

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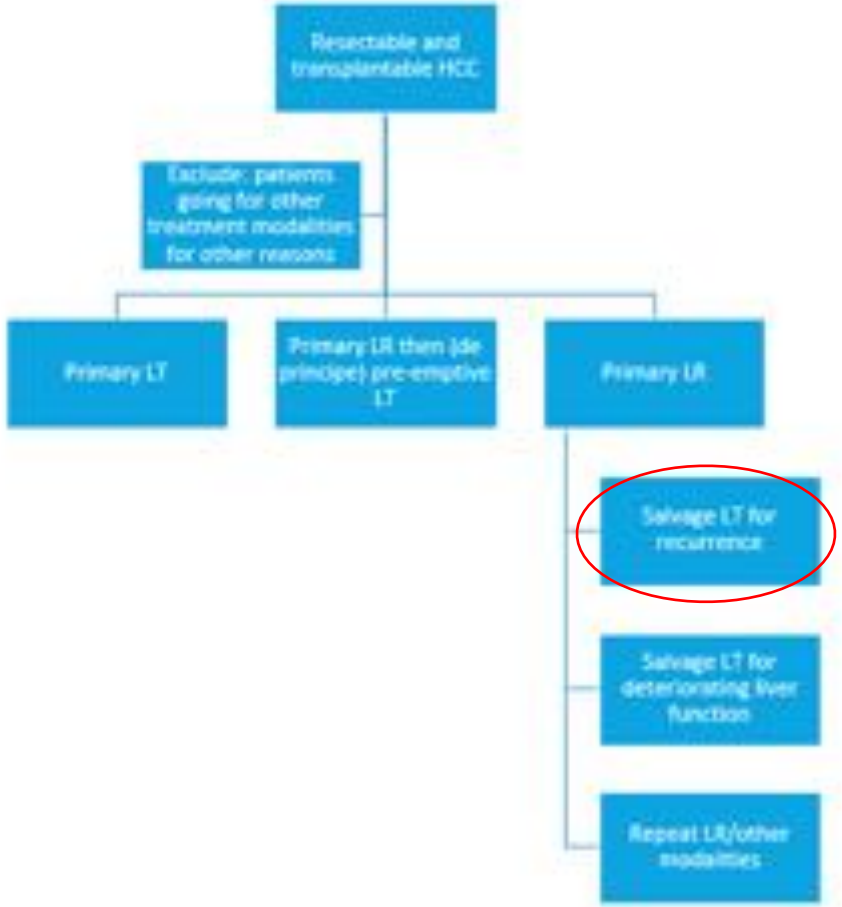

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TABLE 2. Multivariate Analysis for Overall and Disease-free Survival (n = 470)

	HR	95% Confidence Interval Lower	Upper	P
Overall survival				
Resection ± SLT strategy	1.882	1.175	3.015	0.002
Microvascular tumor invasion	1.682	1.218	2.324	0.0003
Disease-free survival				
Resection ± SLT strategy	37.95	6.51	16.68	<0.0001
Microvascular tumor invasion	7.02	3.74	8.63	0.001
Satellite tumor nodules	9.34	3.48	7.94	0.04

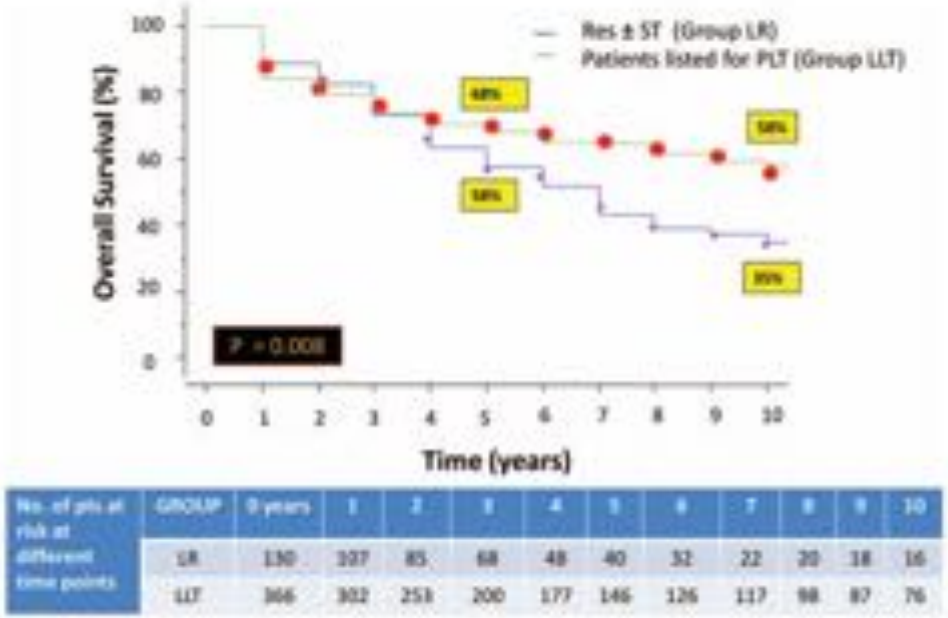
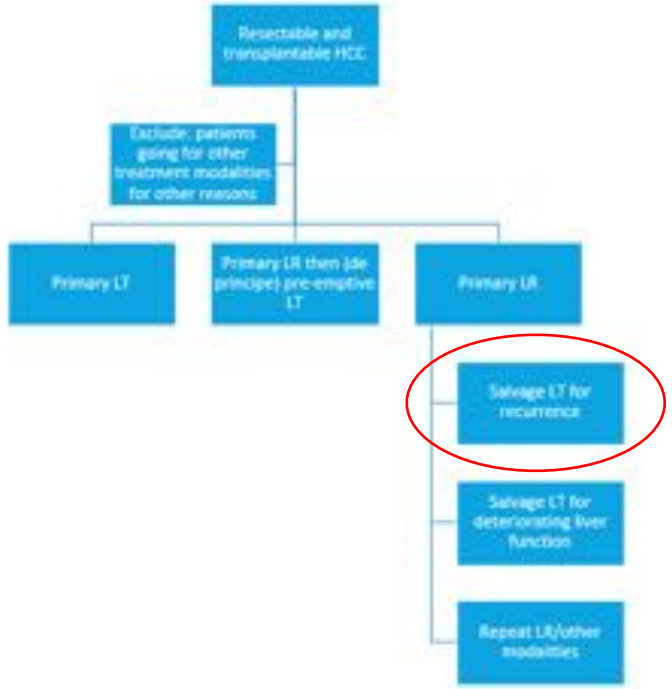


FIGURE 2. Overall survival resection ± salvage LT [group LR] (n = 130) versus patients listed for PLT (including drop-outs) [group LLT] (n = 366). Res, resection.

- Upfront resection and microvascular tumor invasion were poor prognostic factors for both OS and DFS, presence of satellite tumor nodules additionally predicted worse DFS.

- ITT analysis: LT better 5-yr/10-yr OS compared with LR (68%/58% vs. 58%/35%; p = 0.008)

- For patients who managed to undergo salvage LT, post-op and long term outcomes seem similar to primary LT
- However, the feasibility of salvage LT was 34% (31/90)
  - Tumours progressing beyond Milan, cannot be listed
  - Patient age above cut-off for LT
  - Progression while on waiting list



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- De principe (n = 63) vs salvage LT (n = 48)
- 5y OS higher in de principe group 84.6 versus 74.8 %, p=0.017

When Should We Propose Liver Transplant After Resection of Hepatocellular Carcinoma? A Comparison of Salvage and *De Principe* Strategies

Ecoline Tribillon[1] · Louise Barbier[1] · Claire Goumard[2] · Sabine Irtan[1] · Fabiano Perdigao-Cotta[2] · François Durand[3] · Valérie Paradis[4] · Jacques Belghiti[1] · Olivier Scatton[2] · Olivier Soubrane[1]

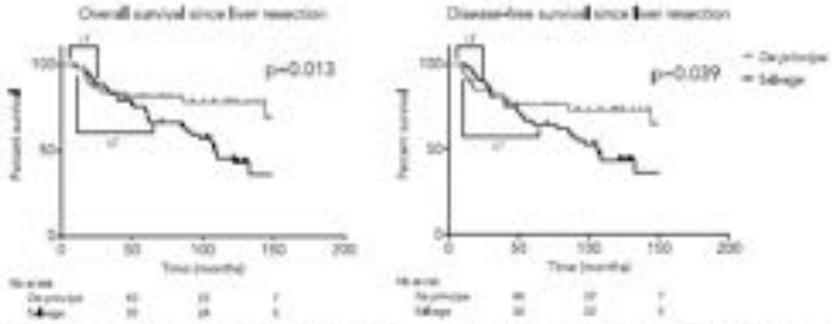

Fig. 2 Overall and disease-free survivals since liver resection in 63 patients enlisted before recurrence (*de principe*), and 48 patients enlisted at recurrence (*salvage*), following liver resection for hepatocellular carcinoma (intention-to-treat analysis). The mean time ± standard deviation between liver resection and liver transplantation is figured for each group

Tribillon et al 2016, J Gastrointest Surg

When Should We Propose Liver Transplant After Resection of Hepatocellular Carcinoma? A Comparison of Salvage and *De Principe* Strategies

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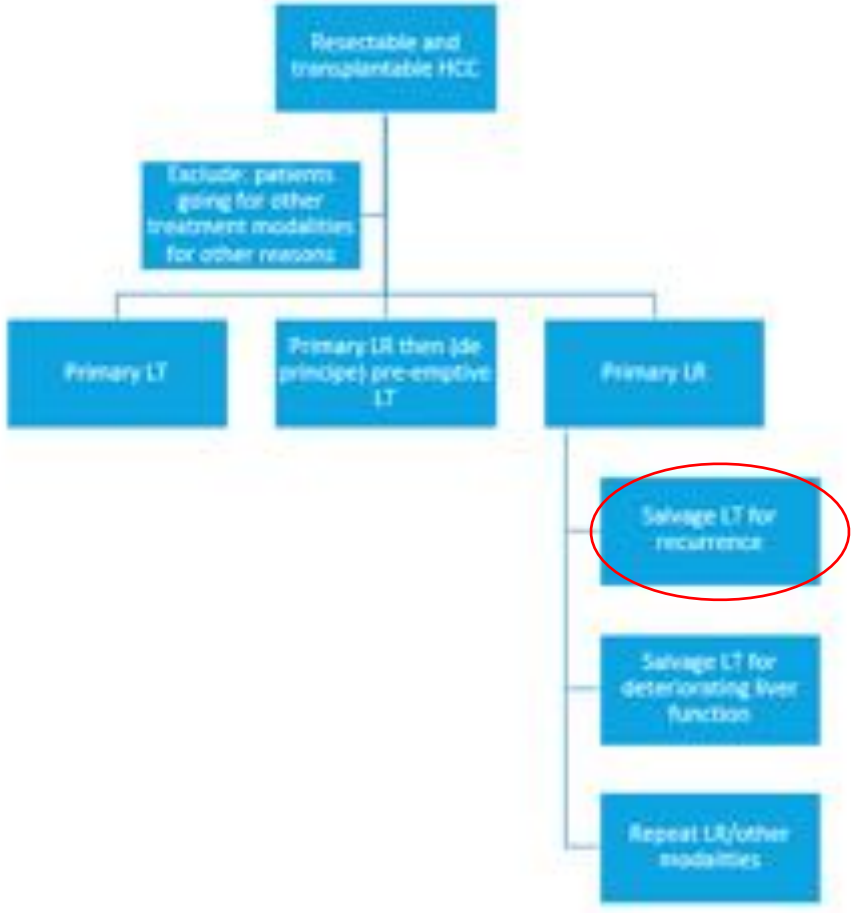
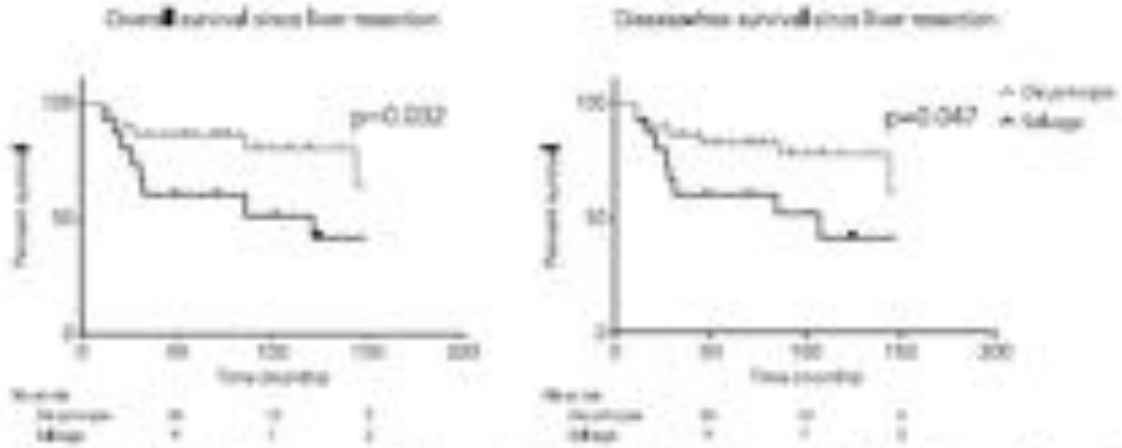


Subgroup analysis for high-risk patients



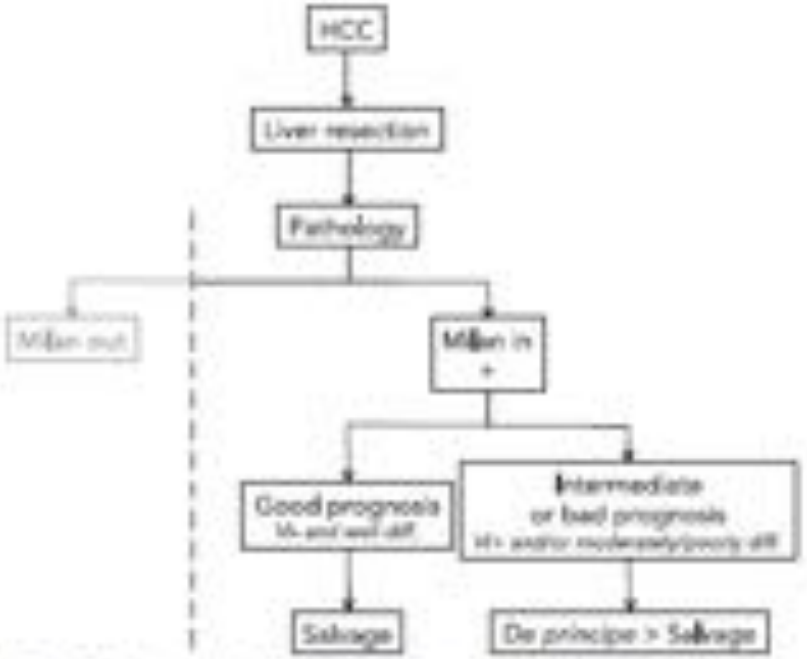


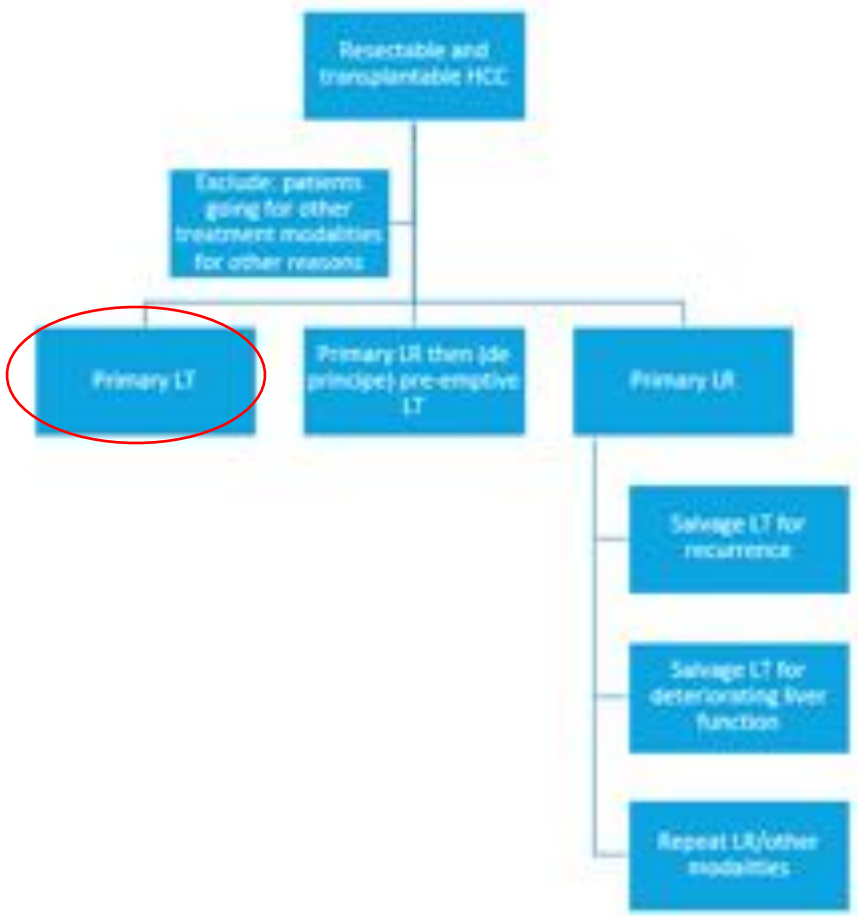
Fig. 7 Proposition for a therapeutic strategy after liver resection for hepatocellular carcinoma. *VI−* no vascular invasion, *VI+* vascular invasion, *diff.* differentiation

Fig. 6 Overall and disease-free survival since liver resection in a sub-group of 36 patients enlisted before recurrence (*de principe*), and 15 patients enlisted at recurrence (*salvage*), all of them with intermediate or bad pathological prognostic factors on the resected specimen (intention-to-treat analysis). Intermediate or bad pathological prognostic factors were defined as follows: Milan in + at least one factor among vascular invasion/moderately or poorly differentiated

In the good pathological prognostic factors sub-group (n=22), the 5-year overall and disease-free survivals were not different between de principe and salvage groups (p=0.305 and p=0.292, respectively).

Proposal of Prognostic Survival Models before and after Liver Resection for Hepatocellular Carcinoma in Potentially Transplantable Patients

Stefano Di Sandro, MD, PhD, Carlo Sposito, MD, Andrea Lauterio, MD, FEBS, Marc Najjar, MD, Michele Droz dit Busset, MD, Vincenzo Buscemi, MD, Maria Flores Reyes, MD, Riccardo De Carlis, MD, Vincenzo Mazzaferro, MD, Luciano De Carlis, MD, FEBS



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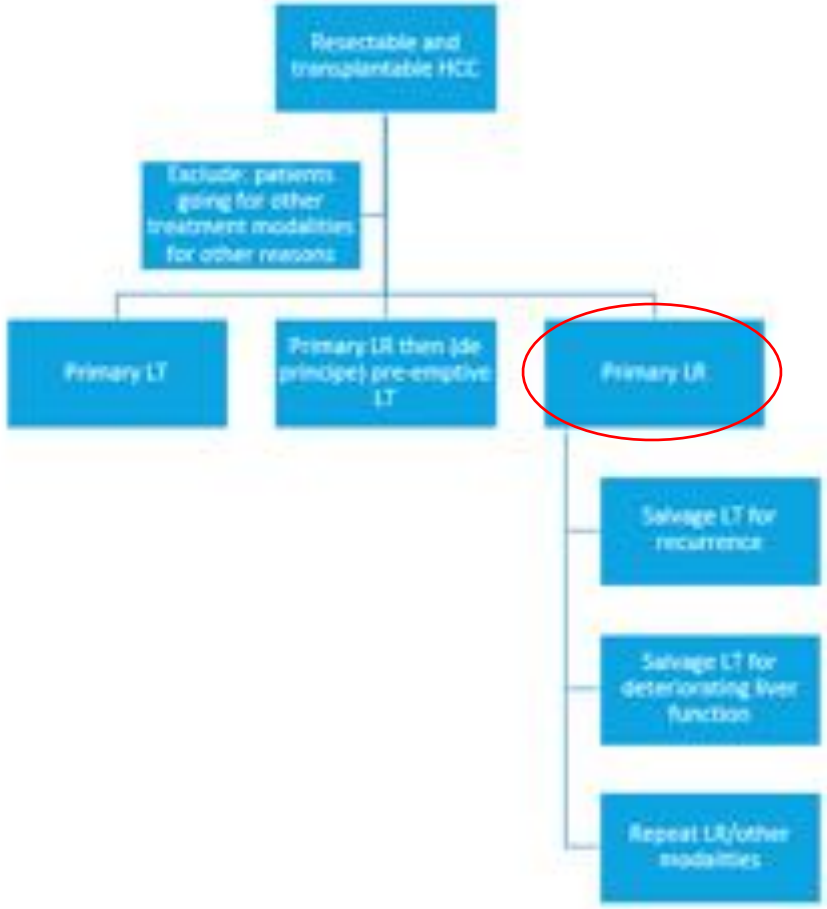

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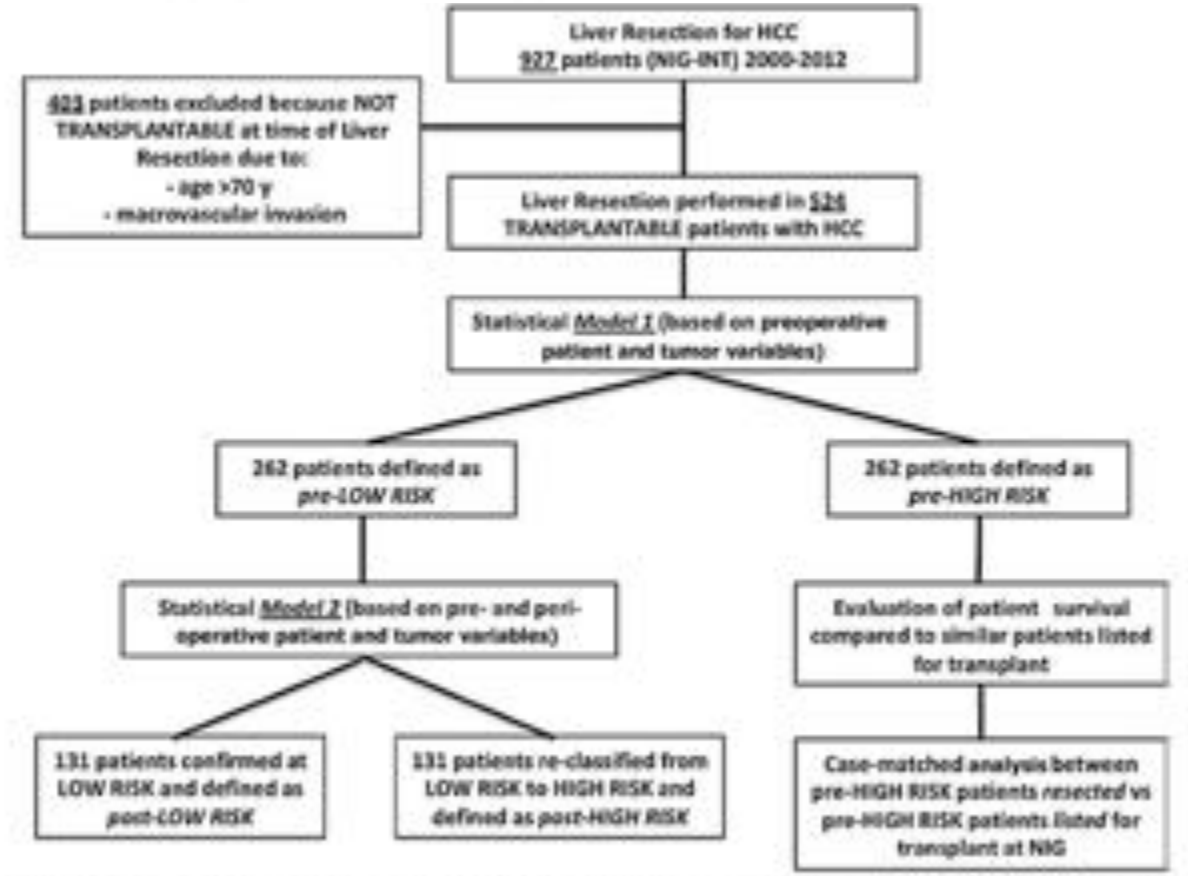

Figure 1. Study design and study cohort. HCC, hepatocellular carcinoma; INT, Istituto Nazionale Tumori; NIG, Niguarda Ca' Granda Hospital.

Based on mortality risk

Di Sandro et al 2018, JACS

Table 4. Models 1 and 2 Parameter Estimates for the Multivariable Regression Model for Overall Survival According to Preoperative Factors

Parameter	Concordance index	95% CI	Estimate	SE	p Value
Model 1	0.67	0.63–0.71			
Cirrhosis	—	—	0.55	0.25	0.03
Aspartate aminotransferase, IU/L	—	—	0.005	0.001	0.001
α-Fetoprotein					
≤20 ng/mL	—	—	0 (*reference*)	*reference*	*reference*
20–400 ng/mL	—	—	0.32	0.18	0.08
>400 ng/mL	—	—	0.60	0.21	0.006
Model for End-Stage Liver Disease score	—	—	0.08	0.03	0.003
No. of lesions at imaging					
1	—	—	0 (*reference*)	*reference*	*reference*
2	—	—	0.51	0.18	0.008
≥3	—	—	0.79	0.28	0.004
Diameter of the largest lesion at imaging, cm	—	—	0.06	0.02	0.001
Model 2	0.65	0.60–0.71			
Satellitosis	—	—	0.70	0.17	<0.0001
Microvascular invasion	—	—	0.49	0.17	0.003

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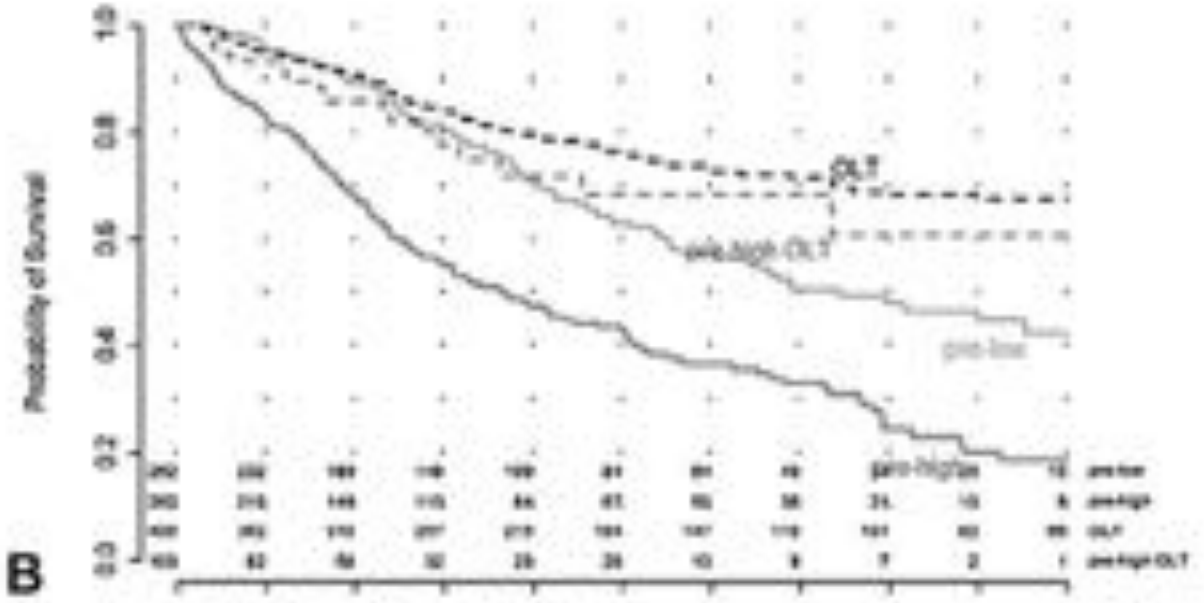
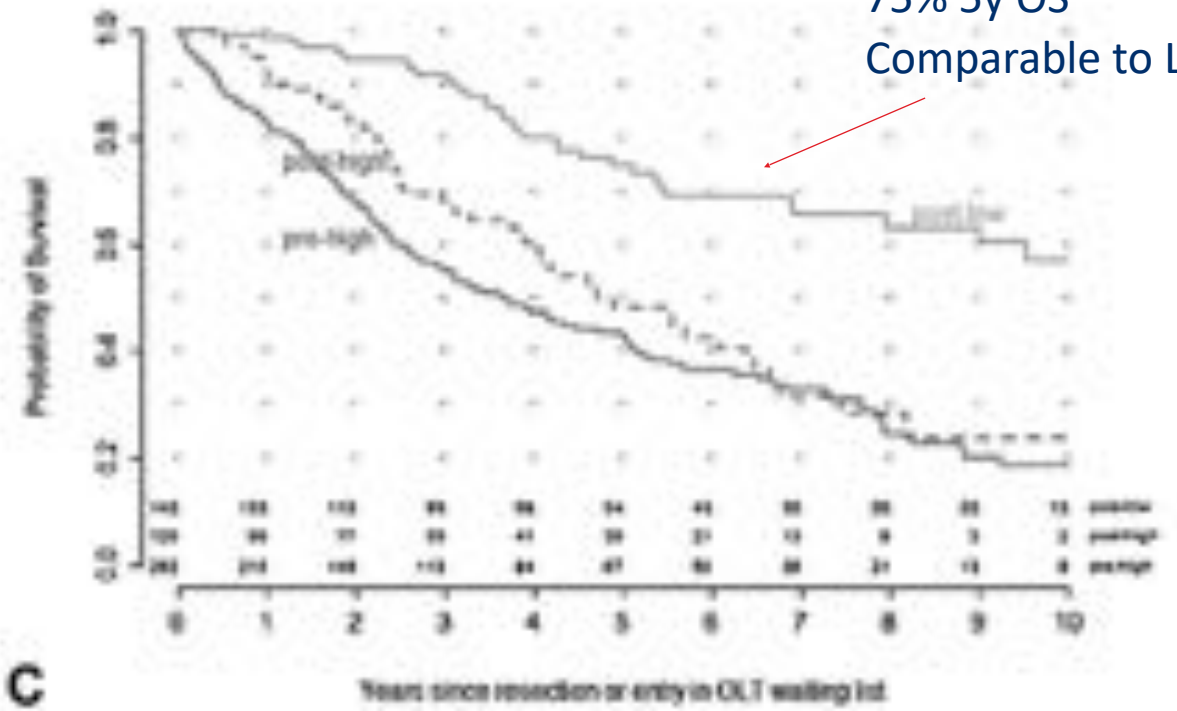
- 5y OS pre-high risk LR vs LT: 43% vs 68%; p<0.001
- 5y OS (pre-low but) post-high risk LR vs pre-low LT: 48% vs 76%
- 5y OS (pre-low with) post-low risk LR vs pre-low LT: 75% vs 76%

- Conclusion: Survival with LR is only comparable with LT for post-low risk patients
  - Otherwise, LT confers greater survival benefit





75% 5y OS
Comparable to LT

- To determine pre-low/high risk , look at A
- To look at post resection low/high risk, look at B

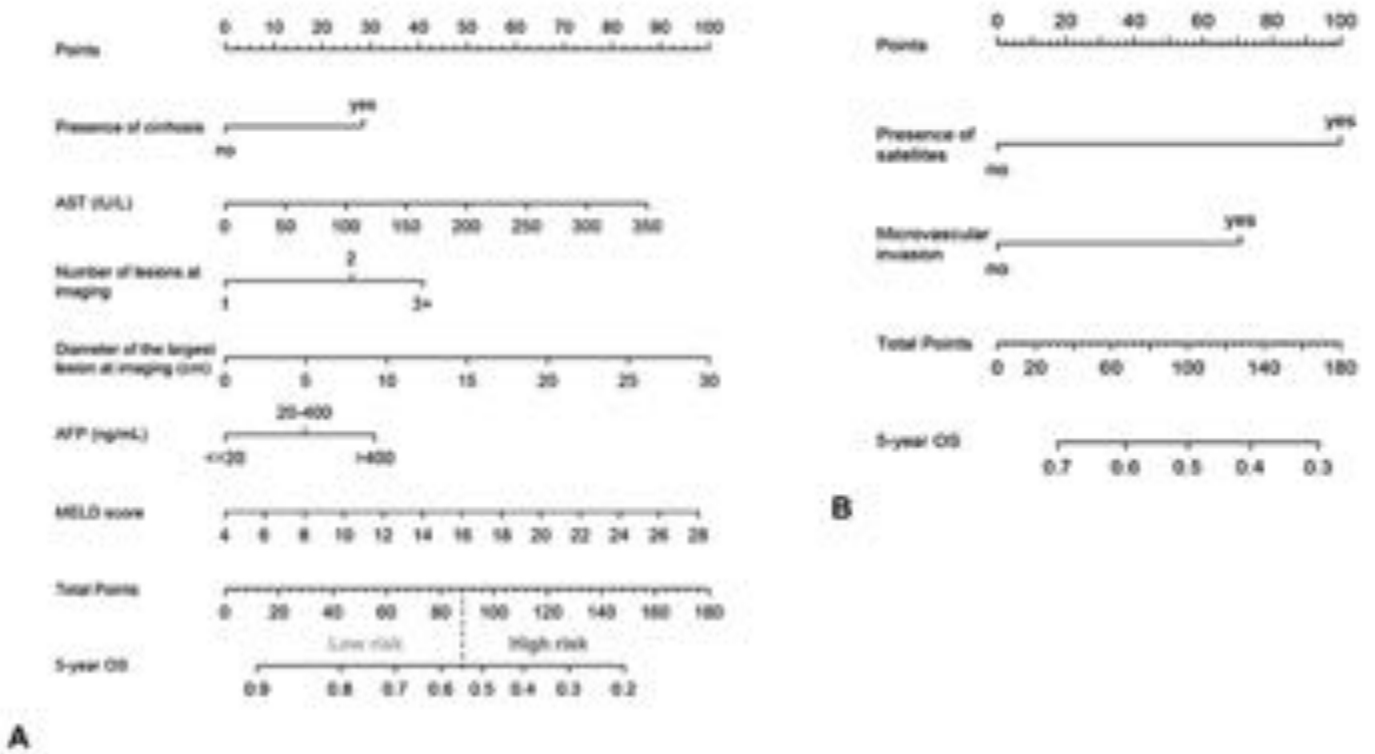


Figure 3. (A) Overall survival nomogram to predict the risk class of resected hepatocellular carcinoma (HCC) patients according to preoperative risk factors. (B) Overall survival nomogram to reclassify according to postoperative risk factors the risk of HCC patients initially classified at low risk according to preoperative risk factors (pre-low group). To use the nomogram, locate the value of each prognostic risk factor and draw a vertical line up to the points axis to obtain the relative score. Add together the score for all the prognostic factors and locate the total score on the total points axis and its associated risk class. AFP, α-fetoprotein; AST, aspartate aminotransferase; MELD, Model for End-Stage Liver Disease; OS, overall survival.

Additional Dimensions – not just LR vs LT

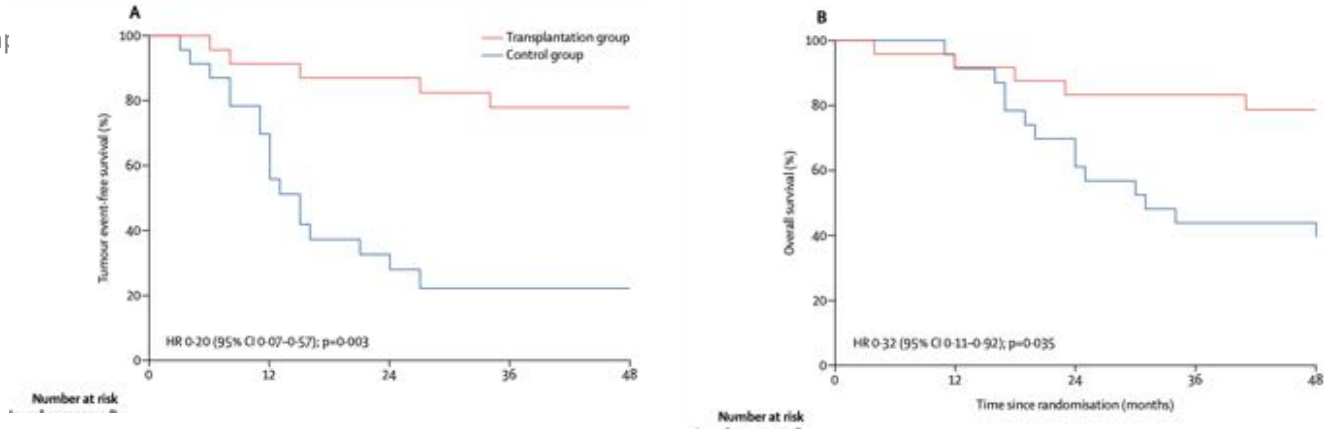
- Practical considerations for LT
  - Availability of organ
    - Different considerations between DDLT vs LDLT?
  - Costs of LT
  - Long term immunosuppressants
  - Specialized multidisciplinary team

- Disease factors
  - Presence of cirrhosis
  - Number of nodules, diameter of largest nodule
  - AFP
  - MELD
  - Satellite nodules, microvascular invasion
  - Patients beyond transplant criteria, role of locoregional downstaging + LT vs LR
  - LR as a downstaging strategy?

- Other treatment modalities

Liver transplantation in hepatocellular carcinoma after tumour downstaging (XXL): a randomised, controlled, phase 2b/3 trial

Vincenzo Mazzaferro, Davide Citterio, Sherrie Bhoori, Marco Bongini, Rosalba Miceli, Luciano De Carlis, Michele Colledan, Mauro Salizzoni, Renato Romagnoli, Barbara Antonelli, Marco Vivarelli, Giuseppe Tisone, Massimo Rossi, Salvatore Gruttadauria, Stefano Di Sandro, Riccardo De Carlis, Maria Grazia Lucà, Massimo De Giorgio, Stefano Mirabella, Luca Belli, Stefano Fagiuoli, Silvia Martini, Massimo Iavarone, Gianluca Svegliati Baroni, Mario Angelico, Stefano Ginanni Corradini, Riccardo Volpes, Luigi Mariani, Enrico Regalia, Maria Flores, Michele Droz dit Busset, Carlo Sposito



- Child's A-B7
- Tumour downstage with locoregional, surgical or systemic therapies
- 3 month sorafenib observation period
- Patients with partial or complete responses according to mRECIST randomly assigned
- Control group: sequences of locoregional and systemic treatment at time of demonstrated tumour progression
- Intervention: LT

- LR only accounts for 9% (LT) and 5%(control) – but shows LR as a potential downstaging strategy

Mazzaferro et al 2020, Lancet Oncol

- Future considerations
  - Precision medicine
  - Immunotherapy

IMbrave 050: a Phase III trial of atezolizumab plus bevacizumab in high-risk hepatocellular carcinoma after curative resection or ablation

Stephen P Hack, Jessica Spahn, Minshan Chen, Ann-Lii Cheng, Ahmed Kaseb, Masatoshi Kudo, Han Chu Lee, Adam Yopp, Pierce Chow & Shukui Qin

Review Article | Published: 30 July 2018

Molecular therapies and precision medicine for hepatocellular carcinoma

Josep M. Llovet, Robert Montal, Daniela Sia & Richard S. Finn

Nature Reviews Clinical Oncology **15**, 599–616 (2018) | Cite this article

Conclusions

- Most patients with resectable HCC will have a survival benefit from upfront LT
- Unfortunately LT candidates outnumber potential donors
- Careful analysis of each case should be done
  - Patients at low risk of HCC recurrence should be considered for LR
    - LT = LR
  - Patients at higher risk of HCC recurrence should be considered for upfront LT, or pre-emptive salvage LT, or salvage LT after recurrence
    - Upfront LT > pre-emptive salvage LT > salvage LT after recurrence
- Arrival of effective adjuvant treatment may completely change this paradigm

Thank you.


NUHS
National University Health System
National University Hospital
Ng Teng Fong General Hospital
Alexandra Hospital
Jurong Community Hospital
National University Polyclinics
Jurong Medical Centre
National University Cancer Institute Singapore
National University Heart Centre Singapore
National University Centre for Oral Health Singapore
NUS
NUS
NUS