



The dark side of the guidelines

2nd Interventional Radiologist under 40 Meeting

Interventional Oncology

8-10 Maggio 2017

Bologna

Società Medica Chirurgica - Palazzo dell'Archiginnasio



IV SESSIONE: FEGATO - HCC

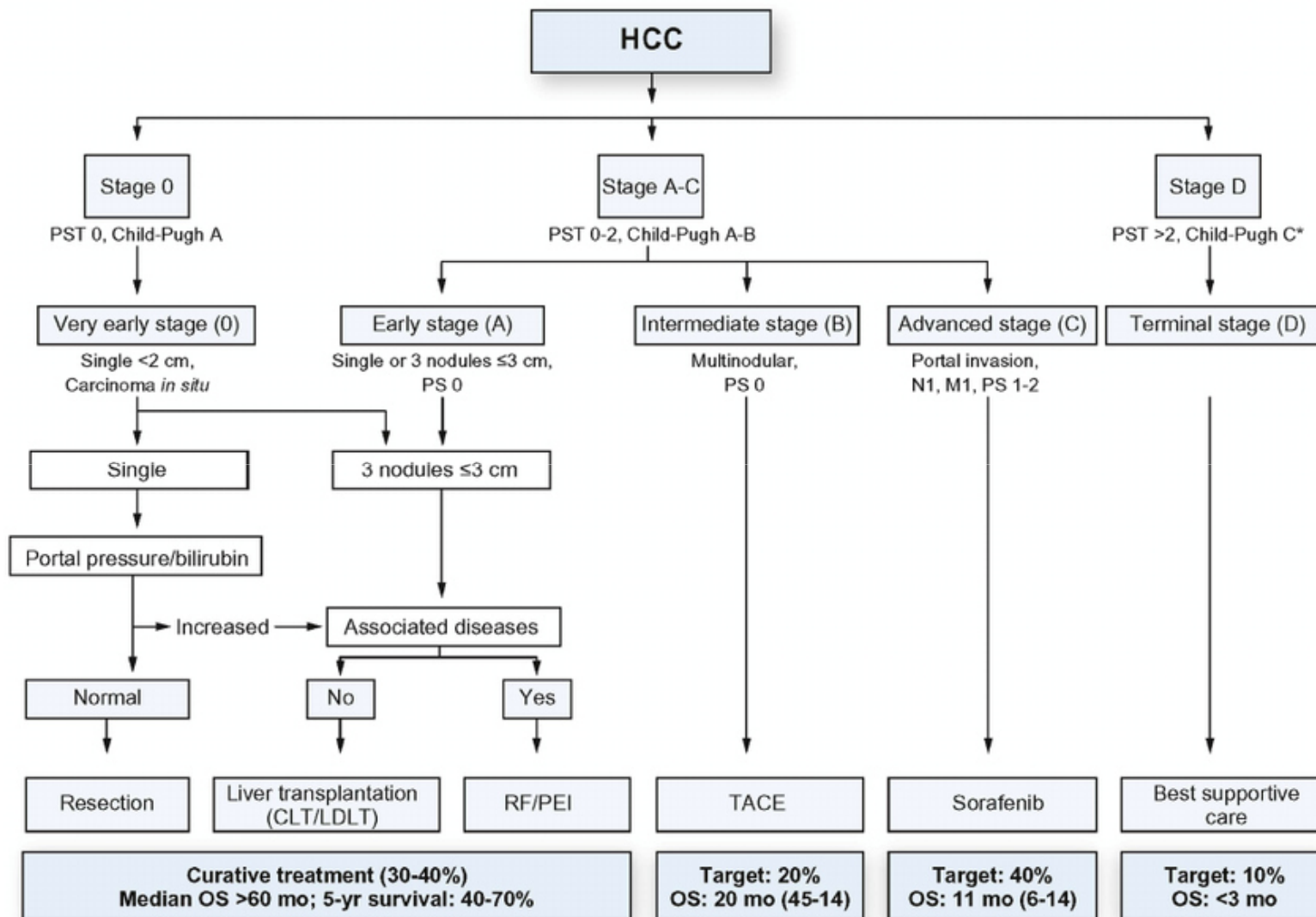
Trattamenti combinati: quando e come

Dott. Andrea Contegiacomo

Dipartimento di Scienze Radiologiche

Istituto di Radiologia, Fondazione Policlinico “A. Gemelli”

“Università Cattolica del Sacro Cuore” – Roma



APASL 2010

Various clinical studies, involving combination of transcatheter arterial chemoembolization followed by RFA [306] or hepatic arterial balloon occlusion during RFA [307], have been attempted to increase the ablated volume of RFA by reducing the cooling effect of the blood supply. Although the extension of necrotic area was achieved, it still remains unsettled whether these trials actually improve the prognosis or not.

EASL-EORTC 2012

considered as competitive alternatives to resection is uncertain
(evidence 1iA; recommendation 1C)

??

AASLD 2011

A recent trial comparing the combination of chemoembolization and radiofrequency suggested that this approach offered an improvement in survival as compared to chemoembolization or ablation alone.⁴⁷ However, this article was retracted by the publishing journal.

ESMO - ESDO 2012

risk in percutaneous than in laparoscopic series).

Neo-adjuvant or adjuvant therapies are not recommended to improve outcome of patients treated with resection or local ablation [II, B]. This recommendation is supported by a study of the Cochrane group that recently identified 12 RCTs with 343 patients, but concluded that there was no clear evidence for the efficacy of any of the adjuvant and neo-adjuvant protocols reviewed (including immunotherapy, retinoids, chemoembolization) [23]. The results of the STORM (Sorafenib as Adjuvant Treatment in the Prevention of

NCCN 2016

CLINICAL PRESENTATION

Unresectable
• Inadequate hepatic reserve^{aa}
• Tumor location

Evaluate whether patient is a candidate for transplant (See UNOS criteria under Surgical Assessment [HCC-3](#))^u

Transplant candidate

TREATMENT

• Refer to liver transplant center
• Consider bridge therapy as indicated^v

SURVEILLANCE

• Imaging^z every 3–6 mo for 2 y, then every 6–12 mo
• AFP, every 3–6 mo for 2 y, then every 6–12 mo
• See relevant pathway ([HCC-2](#) through [HCC-7](#)) if disease recurs

Not a transplant candidate

Options:^{bb}

• Locoregional therapy preferred^{cc, dd}
 ▶ Ablation
 ▶ Arterially directed therapies
 ▶ EBRT (conformal or stereotactic)^y (category 2B)
• Systemic therapy
 ▶ Sorafenib (Child-Pugh Class A [category 1] or B)^{aa, ee, ff}
 ▶ Chemotherapy^{gg}
 ◊ Systemic
 ◊ Intra-arterial
• Clinical trial
• Best supportive care

KLCSG - NCC 2014

CQ34 Does a combination of TACE and percutaneous ablation therapy improve prognosis?

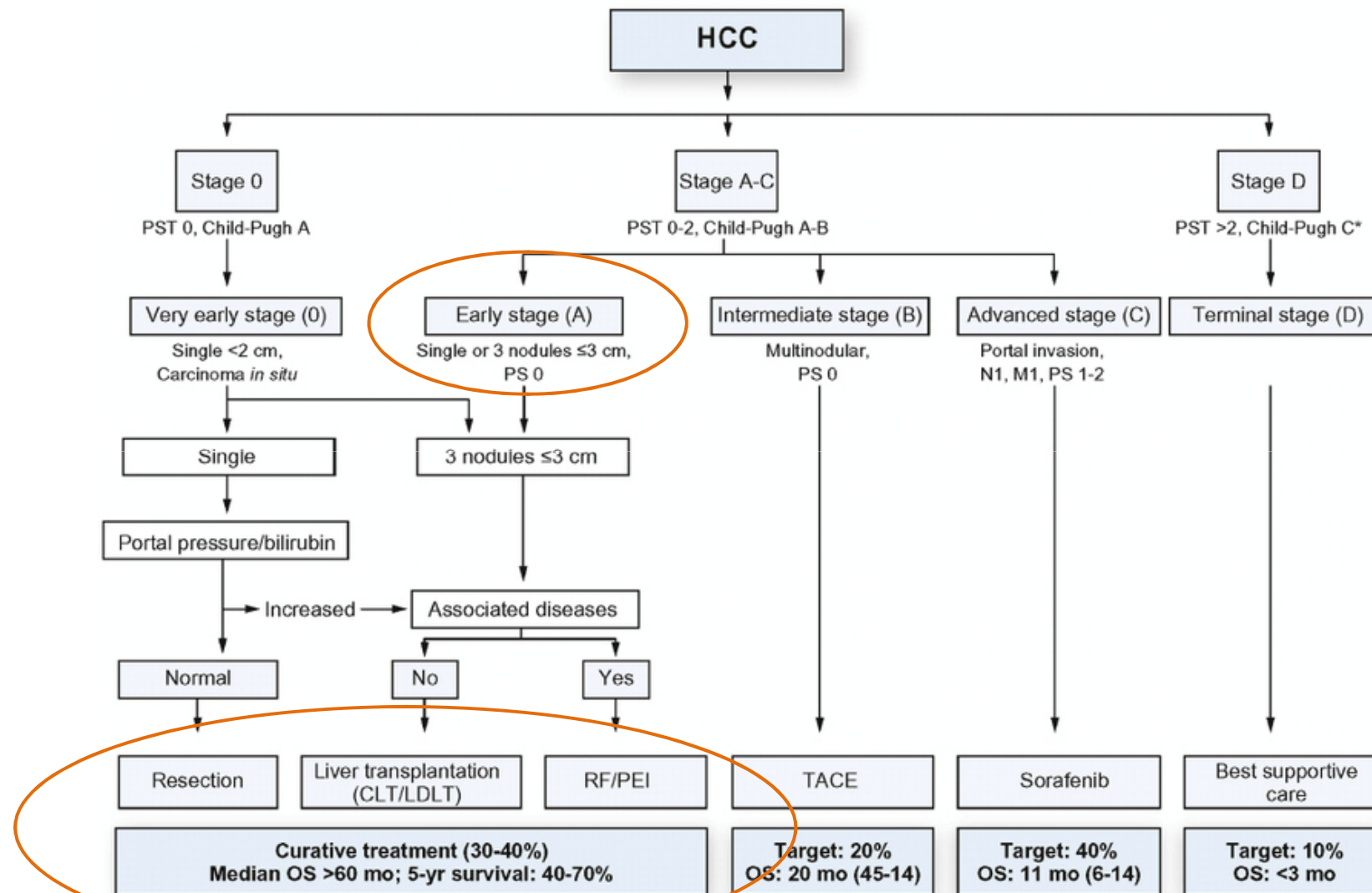
Recommendation

TACE before RFA extends the range of necrosis (**Grade A**).

A favorable prognosis can be expected if local control is achieved. However, there is inadequate evidence demonstrating that pretreatment with TACE will improve RFA outcomes (**Grade C1**).

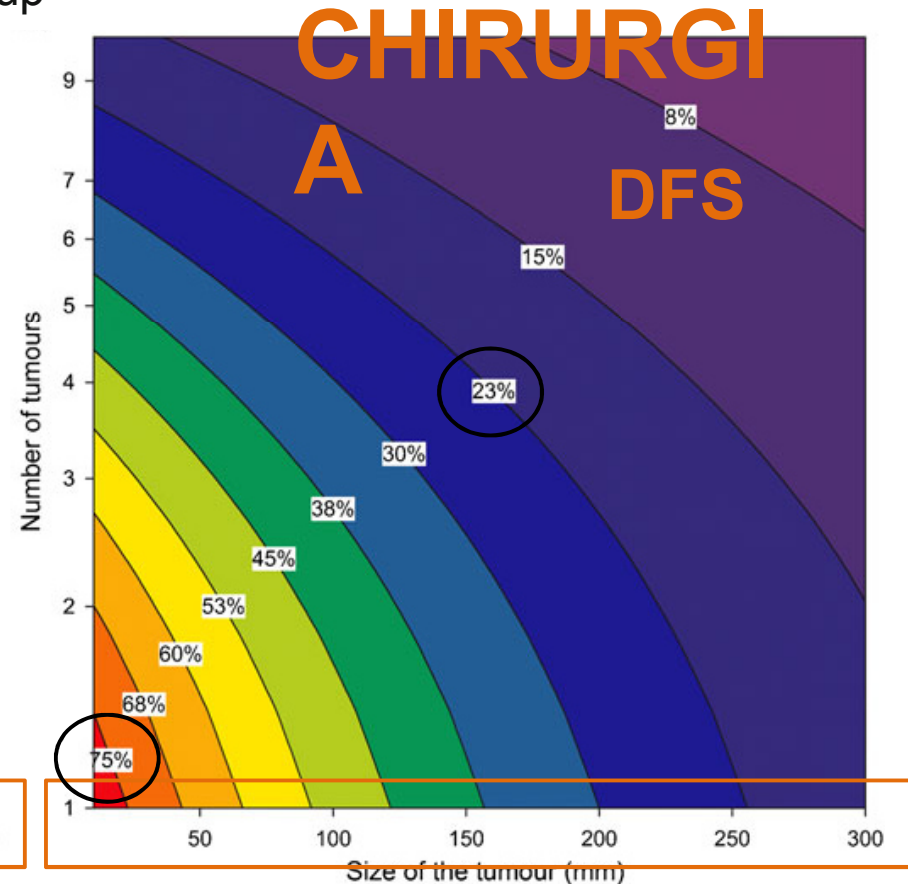
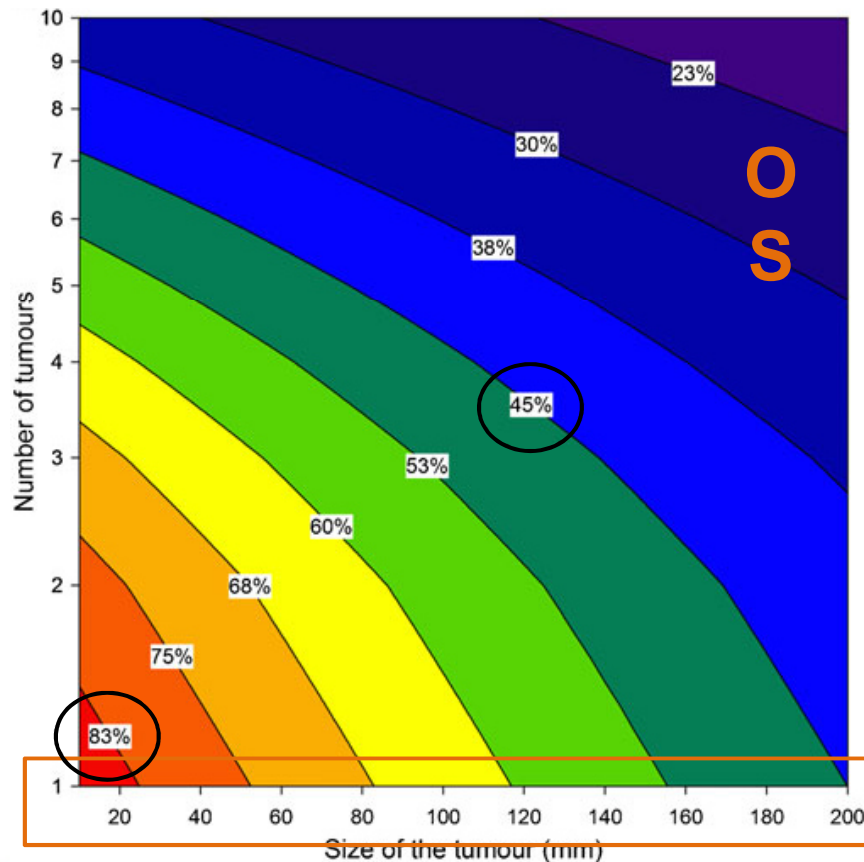


- Caution should be exercised when ablating lesions near major vessels, major bile ducts, diaphragm, and other intra-abdominal organs.
- Ablation alone may be curative in treating tumors ≤3 cm. In well-selected patients with small properly located tumors, ablation should be considered as definitive treatment in the context of a multidisciplinary review. Lesions 3 to 5 cm may be treated to prolong survival using arterially directed therapies, or with combination of an arterially directed therapy and ablation as long as tumor location is accessible for ablation.^{1,2,3}
- Unresectable/inoperable lesions >5 cm should be considered for treatment using arterially directed or systemic therapy.⁴⁻⁶



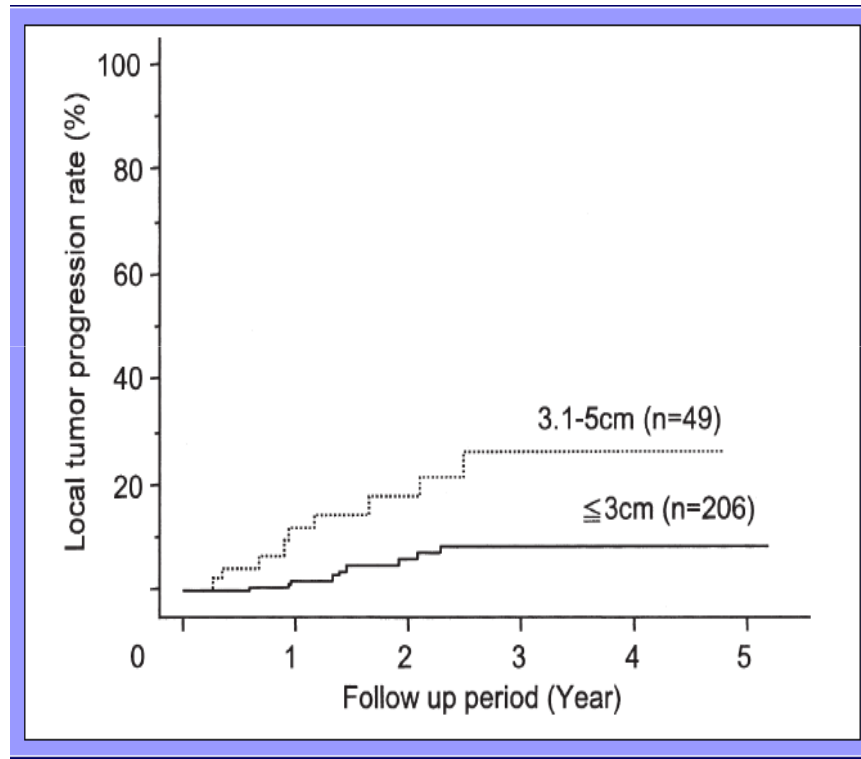
Singolo nodulo

Predicting Individual Survival After Hepatectomy for Hepatocellular Carcinoma: a Novel Nomogram from the BHCC East & West Study Group[^]



Singolo nodulo

RF



- **3 cm < A HCC < 5 cm**
Risposta completa 50-70%
- **HCC > 5 cm**
Risposta completa 30%
- **Elevati tassi di recidiva anche dopo risposta completa post-RFA**

Sede

- 10-25% delle lesioni difficilmente trattabili con RFA a causa della sede:
 - ✓ Lesioni sottocapsulari
 - ✓ Lesioni adiacenti al diaframma
 - ✓ Lesioni disposte lungo la superficie libera epatica
- Scarsa accessibilità/visualizzazione
- Rischio di complicanze (emorragiche)

Lencioni R, Radiology. 2005 Mar;234(3):961-7.

Ebara M, J Hepatol. 2005 Sep;43(3):458-64.

Llovet M, Hepatology. 2001 May;33(5):1124-9.

Kudo M, Oncology. 2010 Jul;78 Suppl 1:94-101.

Rhim H, AJR Am J Roentgenol. 2008 May;190(5):1324-30.

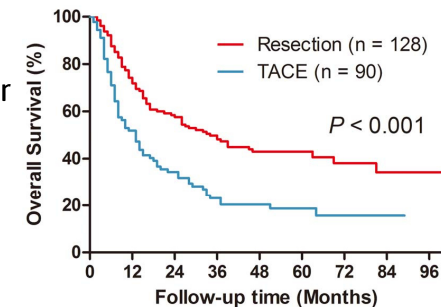
Quale trattamento?

- **No RFA** (Rischio complicanze/scarsa visualizzazione ed accessibilità alla lesione)

TACE
?



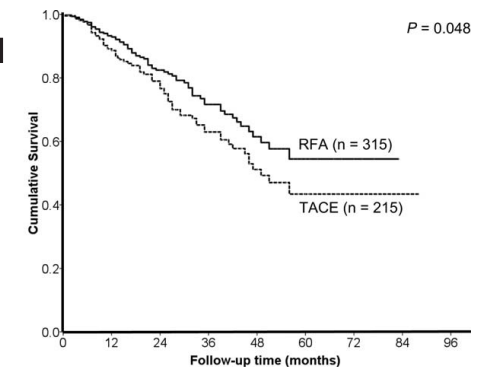
Comparison of Long-Term Survival of Patients with Solitary Large Hepatocellular Carcinoma of BCLC Stage A after Liver Resection or Transarterial Chemoembolization: A Propensity Score Analysis



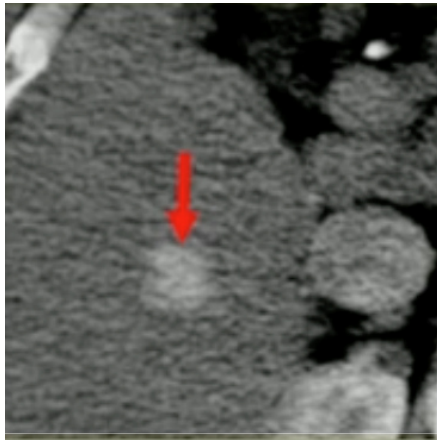
Comparison of Radiofrequency Ablation and Transarterial Chemoembolization for Hepatocellular Carcinoma Within the Milan Criteria: A Propensity Score Analysis

Chia-Yang Hsu,^{1,4,6} Yi-Hsiang Huang,^{2,4} Yi-You Chiou,^{1,5} Chien-Wei Su,^{1,4} Han-Chieh Lin,^{1,4} Rheun-Chuan Lee,^{1,5} Jen-Huey Chiang,^{1,5} Teh-Ia Huo,^{3,4} Fa-Yauh Lee,^{1,4} and Shou-Dong Lee^{1,4}

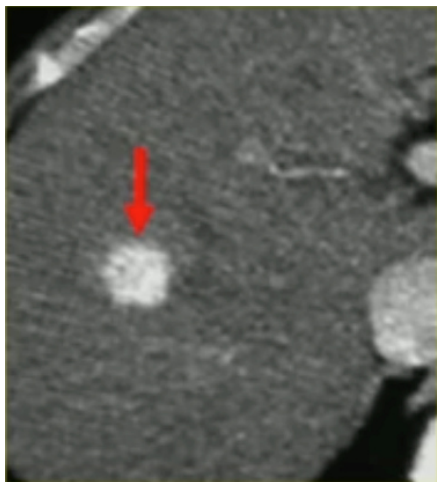
LIVER TRANSPLANTATION 17:556-566, 2011



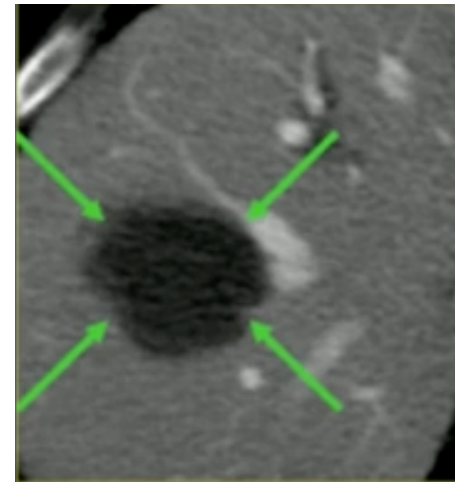
Quale trattamento?



TACE



RFA



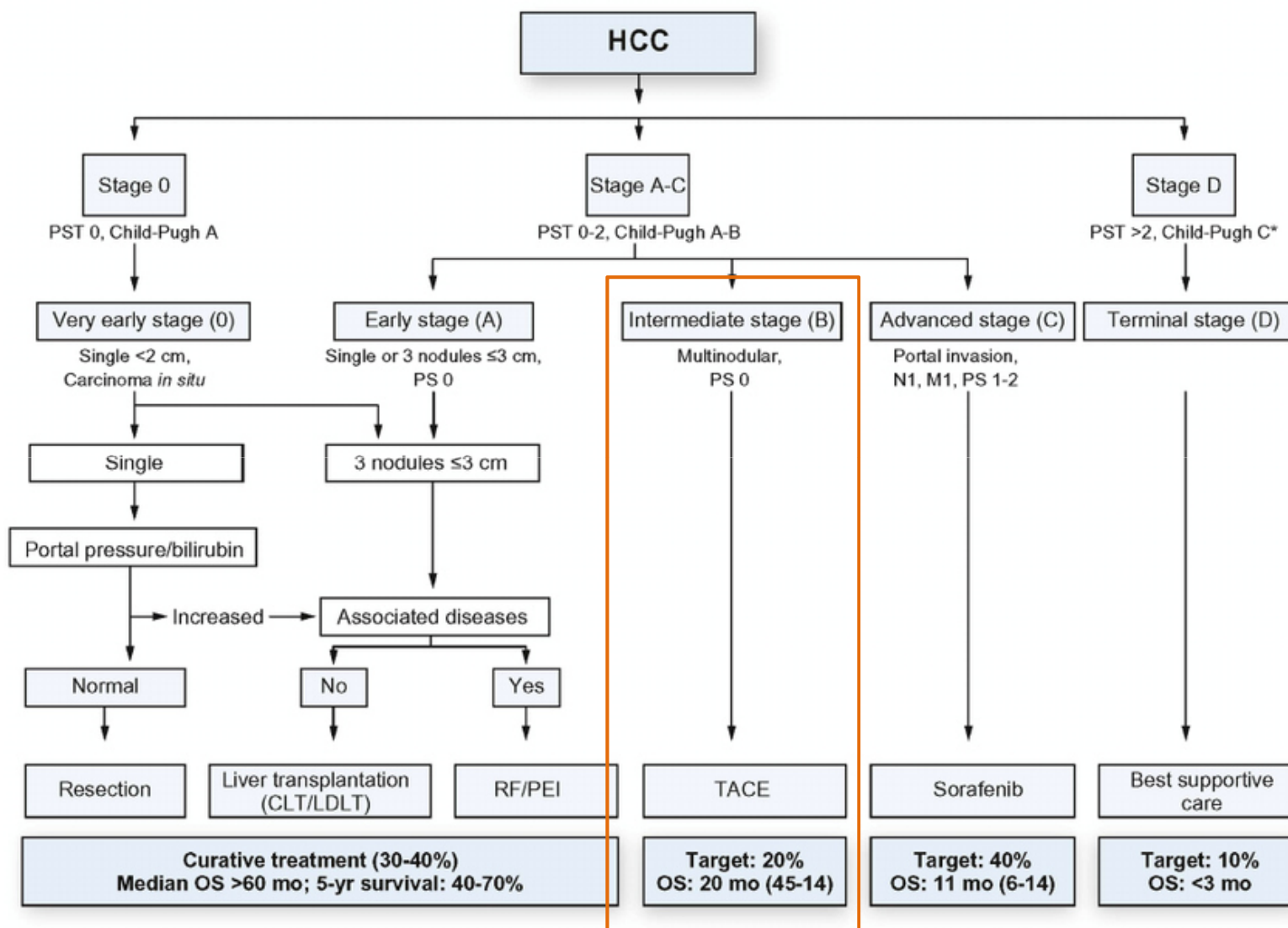
**Safety
Margin**

Quale trattamento?

- **TACE** è una tecnica in via di sviluppo (DEB-TACE/cTACE)
- Migliore **tollerabilità** del paziente
- Aumento della **sopravvivenza** nei pz avanzati
- **>70%** pz con **necrosi tumorale massiva** post-

TACE

**< 20% pz ottiene una
risposta completa**



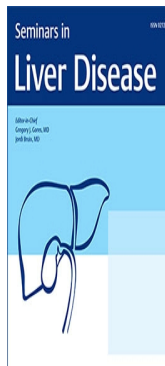
Intermediate HCC

➤ **Popolazione di pazienti estremamente eterogenea**

✓ **Tumor load**

✓ **Funzionalità epatica residua**

✓ **Età/ comorbidità**



Luigi Bolondi, MD¹ Andrew Burroughs, MBChBHons, FMedSci² Jean-François Dufour, MD³
 Peter R. Galle, MD, PhD⁴ Vincenzo Mazzaferro, MD⁵ Fabio Piscaglia, MD, PhD¹
 Jean Luc Raoul, MD, PhD⁶ Bruno Sangro, MD, PhD⁷

Heterogeneity of Patients with Intermediate (BCLC B) Hepatocellular Carcinoma: Proposal for a Subclassification to Facilitate Treatment Decisions

BCLC Sub-Stage	B1	B2	B3	B4
CPT score	5-6-7	5-6	7	8-9*
Beyond Milan and within Ut-7	IN	OUT	OUT	ANY
ECOG (Tumor Related) PS	0	0	0	0-1
PVT	NO	NO	NO	NO

➤ **Early stage**

Singolo HCC > 3cm

No RFA (sede, complicanze)

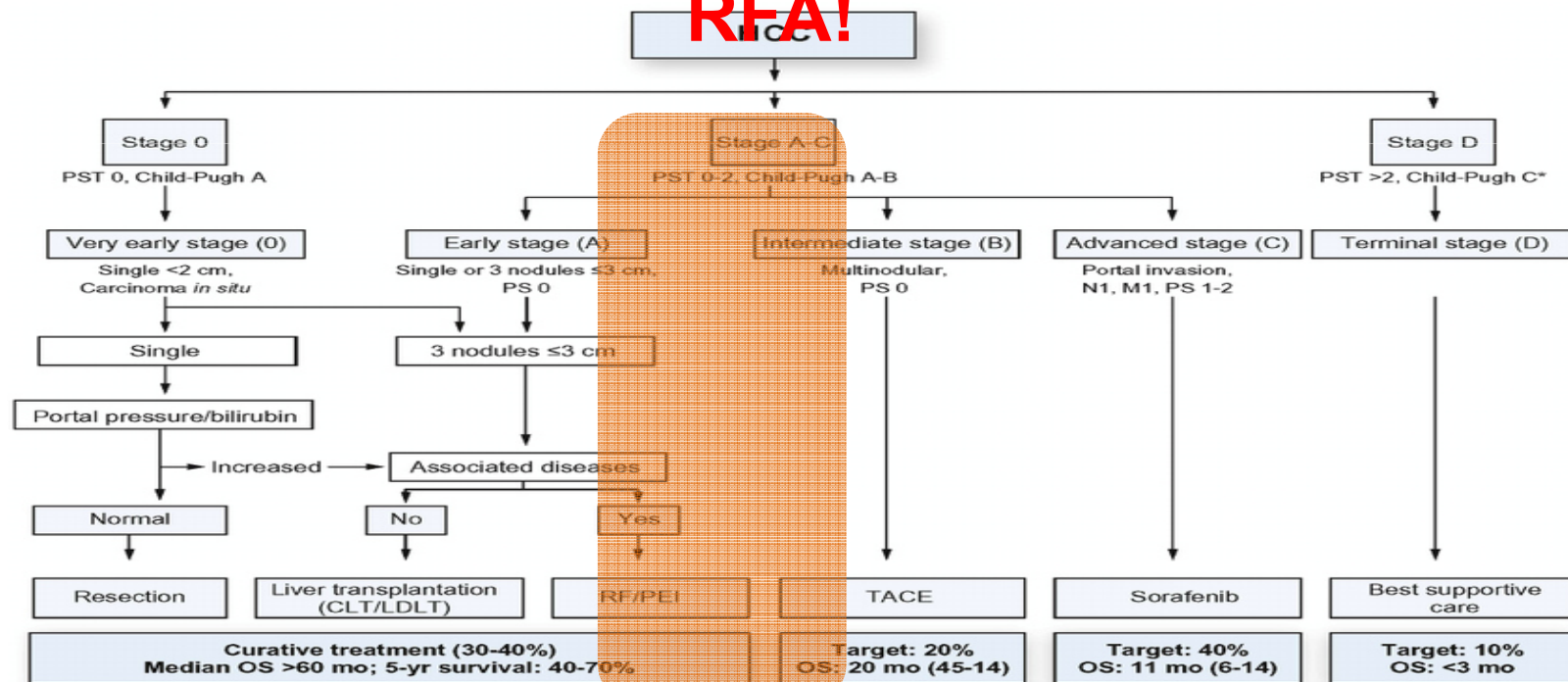
➤ **Intermediate stage**

Multinodulare (7)

Multinodulare (< 5 noduli)

Child-Pugh A

Espandere le indicazioni della RFA!



Quali limiti (e soluzioni?)

RF

- **Meccanismo di azione**
 - ✓ **Necrosi coagulativa**
 - “locale”**
- **Numero lesioni limitato**
- **Dimensioni delle lesioni**

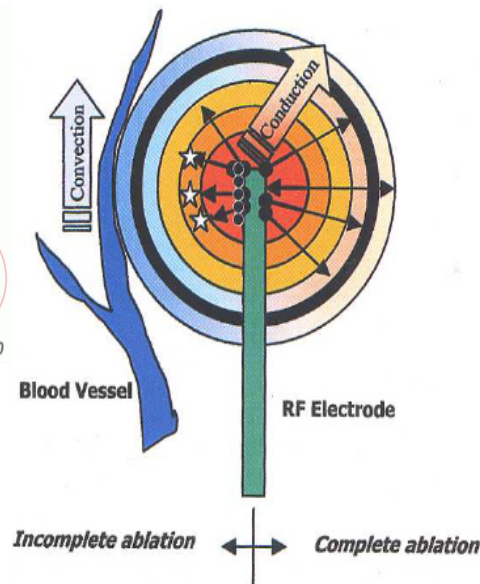
Bio-Heat Equation

$$\rho c \frac{\partial \theta}{\partial t} = \nabla^2 \theta - \left[\frac{Qc}{4\pi r^2} \right] \frac{\partial \theta}{\partial r} - \omega \rho c_b \theta + \frac{I_o^2 \sigma}{16\pi^2 r^4}$$

Coagulation = Energy x Tissue - Heat
Necrosis Deposited Interactions Loss

modified from Goldberg SN et al, AJR 2000

Heat-Sink Effect

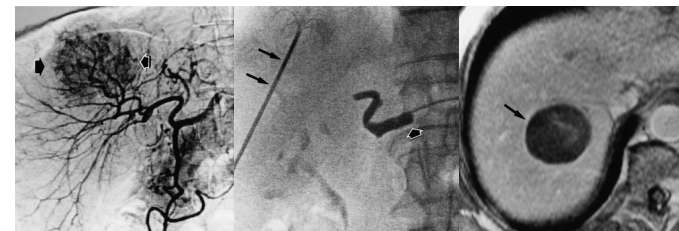


TAC

- **Numero di lesioni**
 - ✓ **Ischemia/tossicità**
 - “globale”**
- **Numero lesioni ∞**
- **Dimensioni delle lesioni**

Percutaneous Radio-frequency Thermal Ablation of Nonresectable Hepatocellular Carcinoma after Occlusion of Tumor Blood Supply¹
Rossi et al, 2000

Radiology



Quali limiti (e soluzioni?)

- **DANNO TERMICO**
- **ISCHEMIA**
-

CITOTOSSICITA'

RFA



TACE

Quale combinazione?

TAC



RF

E

A

- Occlusione del vaso afferente
- Riduzione dell'Heat-sink effect
- Estensione dell'area di trattamento della RFA
- Aumento del “safety margin” con coagulazione di noduli satelliti
- Trattamento di lesioni a distanza

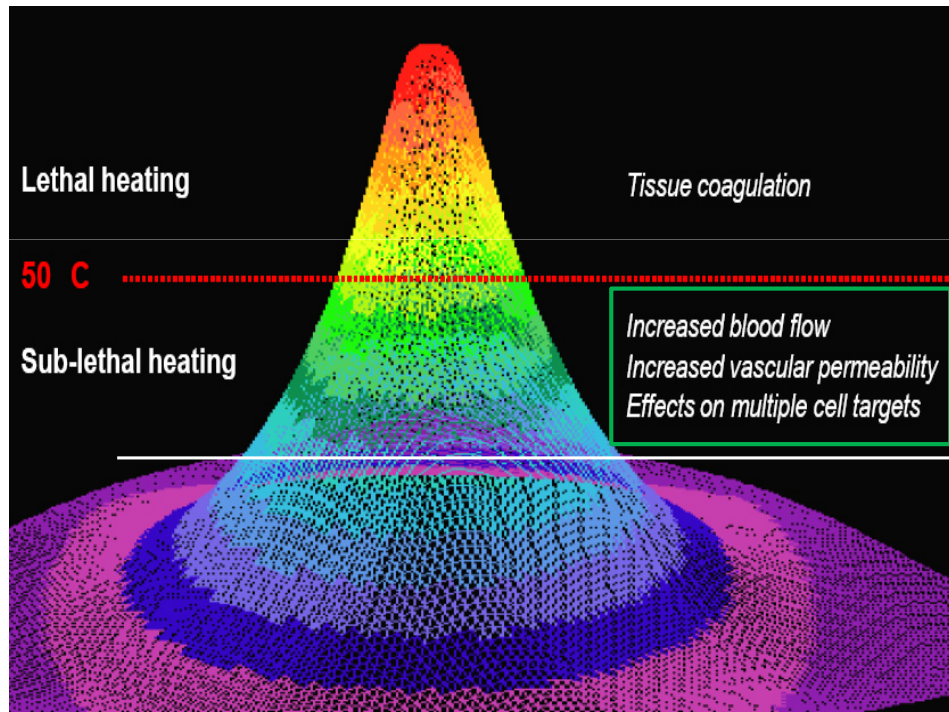
Quale combinazione?

RFA



TAC

E



- Concentrazione del farmaco nel **tessuto vitale residuo** (porzione centrale necrotica)
- **Minore resistenza cellulare** al danno cito-tossico del farmaco (esposizione a temperature sub-letali)
- Miglior **rilascio di farmaco** (iperemia)
- Trattamento **sanguinamenti**

Quale combinazione?



Radiology

Sequential or combined treatment? That is the question.

Iezzi R¹, Pompili M, Gasbarrini A, Bonomo L.

Dove stiamo andando?

Efficacy and safety of radiofrequency ablation and transcatheter arterial chemoembolization for treatment of hepatocellular carcinoma: A meta-analysis

Yulan Wang,¹ Tianxing Deng,² Li Zeng¹ and Weiqing Chen¹

Department of ¹Gastroenterology, Second Affiliated Hospital of Chongqing Medical University; and ²Urology, Second Affiliated Hospital, Third Military Medical University, Chongqing, China

Combination of radiofrequency ablation with transarterial chemoembolization for hepatocellular carcinoma: an up-to-date meta-analysis

Zhenyin Liu & Fei Gao & Guang Yang & Sristi Singh & Mingjian Lu & Tao Zhang & Zhihui Zhong & Fujun Zhang & Rijing Tang

META-ANALYSIS

Meta-analysis of radiofrequency ablation in combination with transarterial chemoembolization for hepatocellular carcinoma

Jia-Yan Ni, Shan-Shan Liu, Lin-Feng Xu, Hong-Liang Sun, Yao-Ting Chen

Radiofrequency ablation plus chemoembolization versus radiofrequency ablation alone for hepatocellular carcinoma: a meta-analysis of randomized-controlled trials

Zaiming Lu*, Feng Wen*, Qiyong Guo, Hongyuan Liang, Xiaonan Mao and Hongzan Sun

Efficacy and Safety of Radiofrequency Ablation Combined with Transcatheter Arterial Chemoembolization for Hepatocellular Carcinomas Compared with Radiofrequency Ablation Alone: A Time-to-Event Meta-Analysis

Xin Wang, PhD, Yanan Hu, PhD, Mudan Ren, MD, Xinlan Lu, PhD, Guifang Lu, PhD, Shuixiang He, PhD

All authors: Department of Gastroenterology, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province 710061, China

ORIGINAL ARTICLE

Radiofrequency ablation plus chemoembolization versus radiofrequency ablation alone for hepatocellular carcinoma: A systematic review and meta-analysis

Qi-Wen Chen^{a,b,1}, Hai-Feng Ying^{c,1}, Song Gao^{a,1}, Ye-Hua Shen^a, Zhi-Qiang Meng^a, Hao Chen^a, Zhen Chen^{a,*}, Wen-Jing Teng^d

Meta-analysis of transcatheter arterial chemoembolization plus radiofrequency ablation versus transcatheter arterial chemoembolization alone for hepatocellular carcinoma

De-jun Yang^{1,*}, Kun-lun Luo^{3,*}, Hong Liu^{3,*}, Bing Cai², Guo-qing Tao², Xiao-fang Su³, Xiao-juan Hou⁴, Fei Ye⁴, Xiang-yong Li³, Zhi-qiang Tian^{2,3,4}

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²Department of General Surgery, Wuxi People's Hospital Affiliated Nanjing Medical University, Wuxi 214023, China

³Department of General Surgery and Rehabilitation Medicine and Oncology, The 101st Hospital of Chinese PLA, Wuxi 214044, China

⁴Tumor Immunology and Gene Therapy Center, Eastern Hepatobiliary Surgery Hospital, The Second Military Medical University, Shanghai 200438, China

*These authors contributed equally to this work

Lu Z, *Eur J Gastroenterol Hepatol*. 2013 Feb;25(2):187-94.

Ni JY, *World J Gastroenterol*. 2013 Jun 28;19(24):3872-82.

Liu Z, *Tumour Biol*. 2014 Aug;35(8):7407-13.

Chen QW, *Clin Res Hepatol Gastroenterol*. 2016 Jun;40(3):309-14.

Wang Y, *Hepatol Res*. 2016 Jan;46(1):58-71.

Wang X, *Korean J Radiol*. 2016 Jan-Feb;17(1):93-102.

Yang DJ, *Oncotarget*. 2017 Jan 10;8(2):2960-2970.

The dark side of the guideline

AUTORE	ANNO	STUDI	RCT	TACE + RFA vs.	Overall Survival				Recurrence Free Survival			Tumor Size		
					1	2	3	5	1	3	5	< 3cm	3cm < X < 5cm	> 5cm
Lu Z.	2013	7	7	RFA								OS	1, 3, 5 OS	1, 3, 5 OS
Ni J.	2013	8	8	RFA								1 OS	1, 3, 5 OS	1, 3 OS
Liu Z.	2014	7	7	RFA										
Chen Q.	2015	8	8	RFA										
Wang Y.	2016	21	6	TACE										
				RFA								3, 5 RFS	1, 2, 3 OS - 1, 3 RFS	
Wang X.	2016	6	6	RFA										
Yang D.	2017	11	1	TACE					Non specificato					

AUTORE	TACE + RFA vs.	Child group	Tumor Progression	Tumor response	Complications
Lu Z.	RFA				
Ni J.	RFA				
Liu Z.	RFA				
Chen Q.	RFA				
Wang Y.	TACE				
	RFA	1, 3, 5 OS - 1, 3, 5 RFS Child-Pugh A			
Wang X.	RFA				
Yang D.	TACE			CR + PR	

- ++ Trattamento combinato
- Monoterapia = trattamento combinato
- Non valutato
- ++ Monoterapia

OS: Overall Survival

RFS: Recurrence Free Survival

TS: Tumor Size

CP: Complete response

PR: Partial Response

RCT: Randomized Control Trial

RFA: RadioFrequency Ablation

TACE: Trans-Arterial ChemoEmbolization

HCC non resecabile



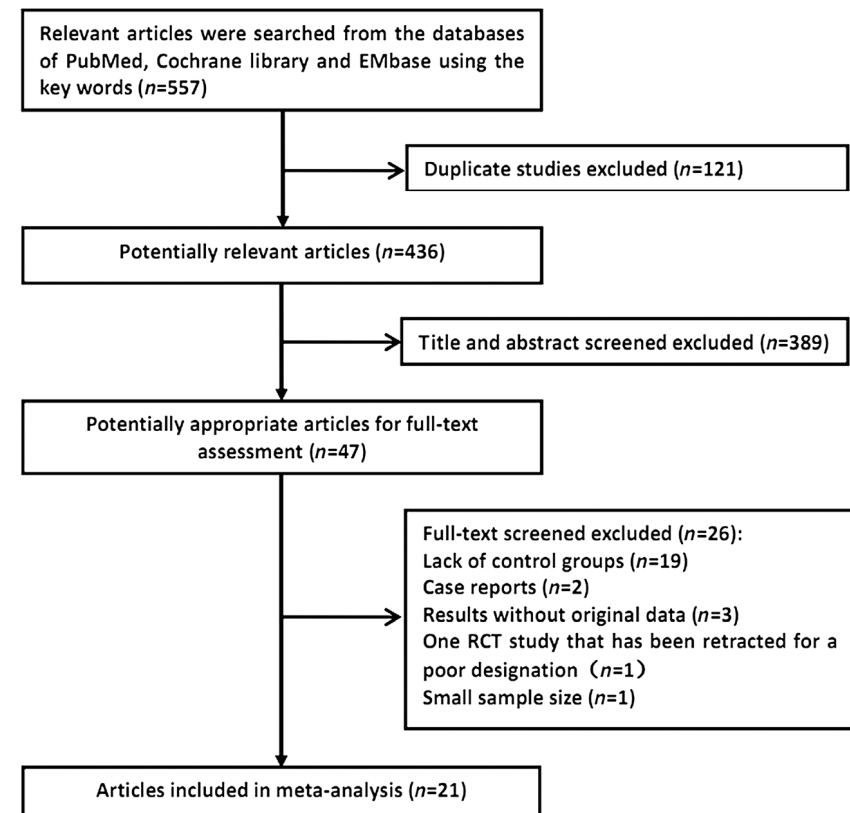
Hepatology Research 2016; 46: 58-71

Efficacy and safety of radiofrequency ablation and transcatheter arterial chemoembolization for treatment of hepatocellular carcinoma: A meta-analysis

Yulan Wang,¹ Tianxing Deng,² Li Zeng¹ and Weiqing Chen¹

Department of ¹Gastroenterology, Second Affiliated Hospital of Chongqing Medical University; and ²Urology, Second Affiliated Hospital, Third Military Medical University, Chongqing, China

- 21 studi, 6 RCT
- 3073 pz inclusi
- RFA + TACE vs monoterapia (RFA/TACE)



HCC non resectable

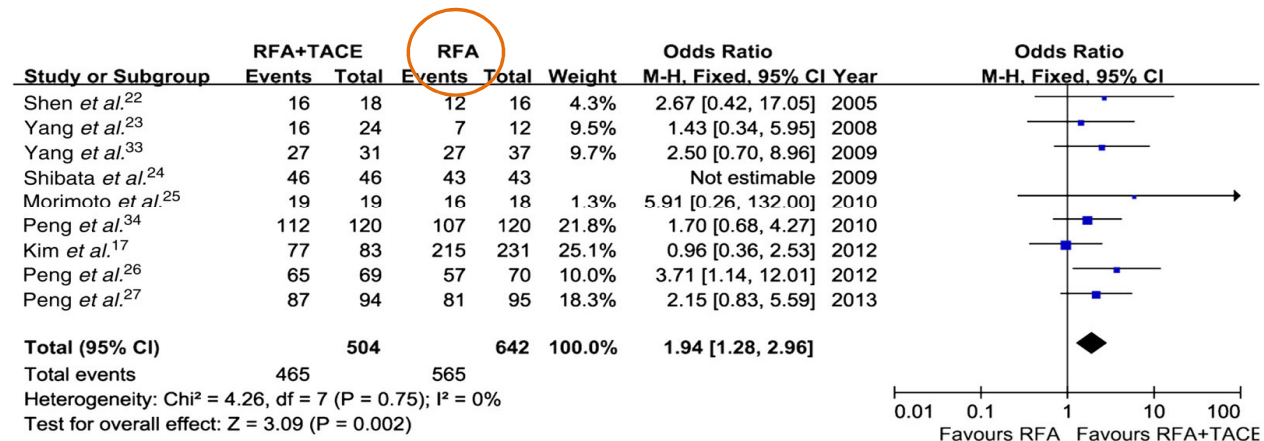


Hepatology Research 2016; 46: 58-71

Efficacy and safety of radiofrequency ablation and transcatheter arterial chemoembolization for treatment of hepatocellular carcinoma: A meta-analysis

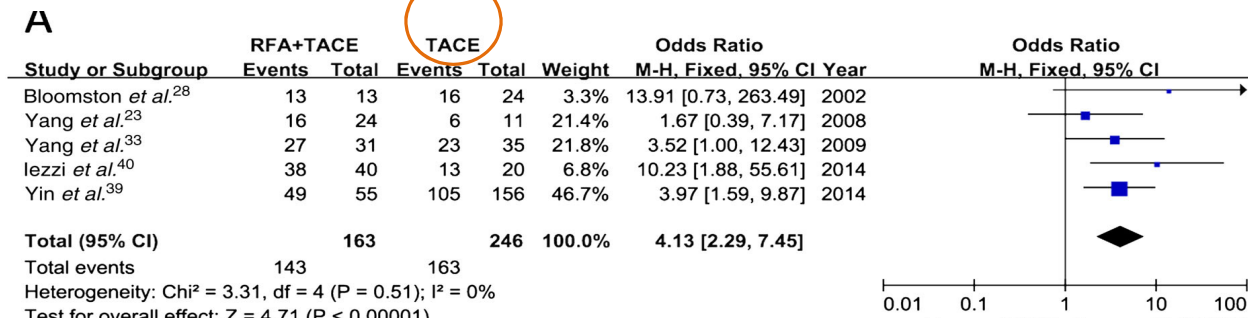
Yulan Wang,¹ Tianxing Deng,² Li Zeng¹ and Weiqing Chen¹

Department of ¹Gastroenterology, Second Affiliated Hospital of Chongqing Medical University; and ²Urology, Second Affiliated Hospital, Third Military Medical University, Chongqing, China



5yrs -

OS



HCC non resectable



Hepatology Research 2016; 46: 58-71

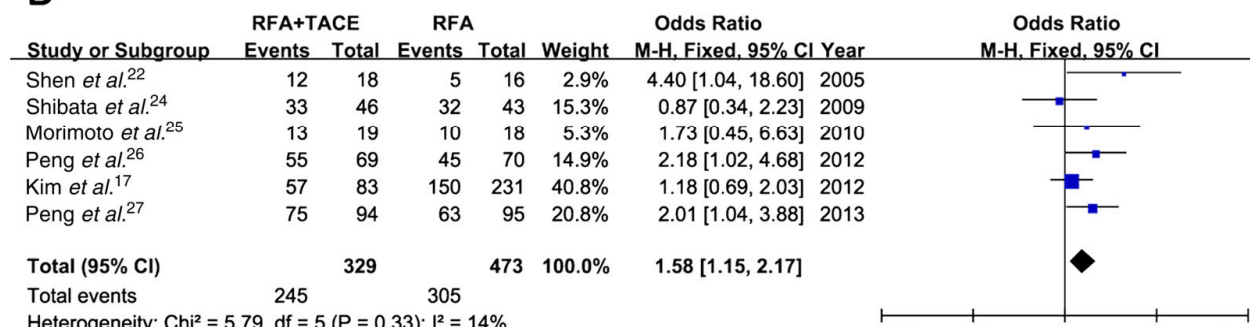
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Yulan Wang,¹ Tianxing Deng,² Li Zeng¹ and Weiqing Chen¹

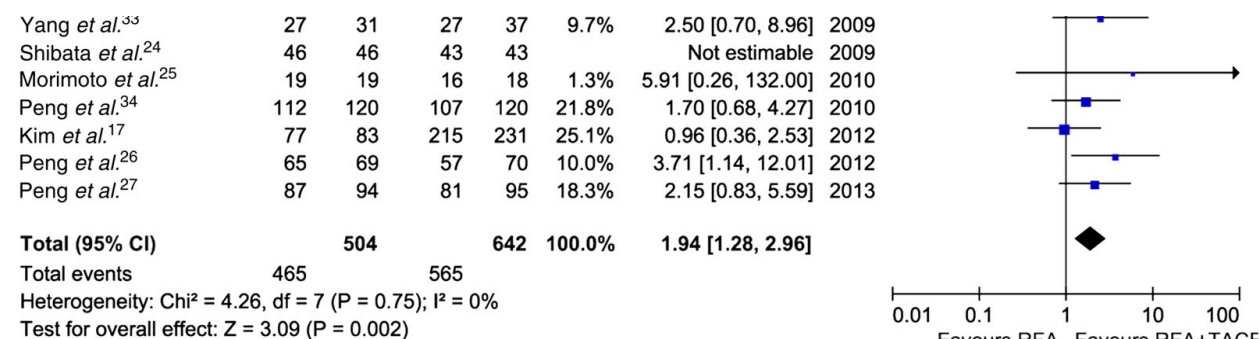
Department of ¹Gastroenterology, Second Affiliated Hospital of Chongqing Medical University; and ²Urology, Second Affiliated Hospital, Third Military Medical University, Chongqing, China

B

RFS



LTP



HCC non resectable



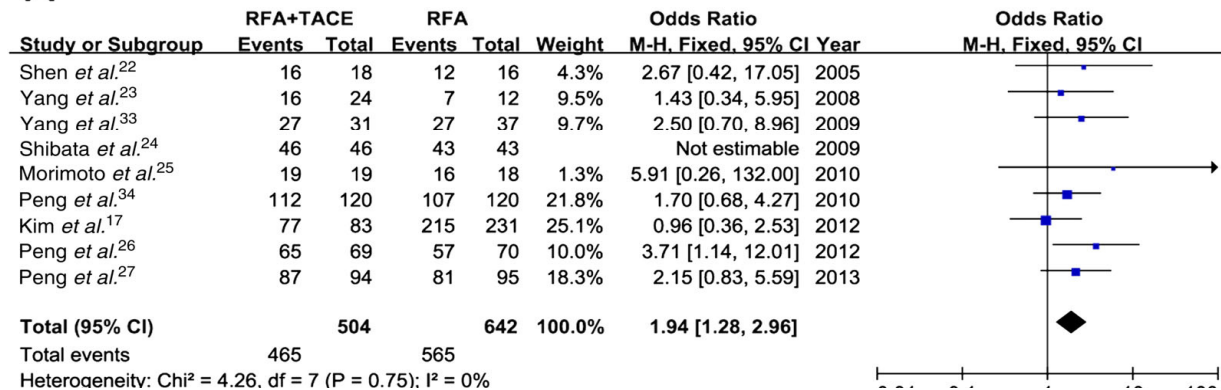
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Efficacy and safety of radiofrequency ablation and transcatheter arterial chemoembolization for treatment of hepatocellular carcinoma: A meta-analysis

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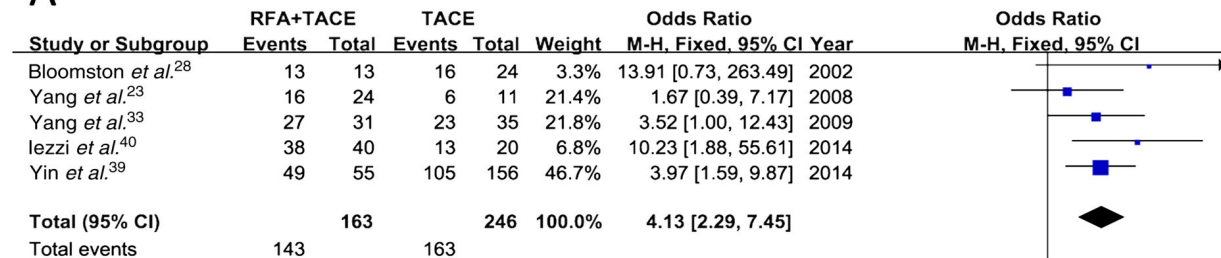
Department of ¹Gastroenterology, Second Affiliated Hospital of Chongqing Medical University; and ²Urology, Second Affiliated Hospital, Third Military Medical University, Chongqing, China

A



Complications

A



HCC non resecabile

Analisi univariata e multivariata fattori predittivi di insuccesso

Overall Survival

Variables	Univariate Analysis			Multivariate Analysis		
	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value
Age, per y	0.9864	0.9713–1.0017	0.0820			
Main tumor size, cm						Overall 0.0463
3.1–5.0						
5.1–7.0			0.1294			
7.1–10.0			0.0142			
Gender						
Female						
Male						
Child-Pugh class						
A						
B						
Number of tumors, n						0.0003
KPS						
70						
80						
90						
100						
Background liver disease						
Hepatitis B virus						
Hepatitis C virus						
Other						
AFP level, ng/mL						
<100						
100–400						
>400						
Treatment modality						Overall 0.0428
TACE + RFA	Reference			Reference		
TACE	1.9117	1.17–3.1892	0.0077	1.8342	1.0333–3.253	0.0204
RFA	2.0220	1.1864–3.4460	0.0096	1.8342	1.0333–3.1544	0.0283

Dimensioni > 7 cm

Numero di lesioni

Tipo di

trattamento

Recurrence free survival

Variables	Univariate Analysis			Multivariate Analysis		
	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value
Age, per y	0.9897	0.9746–1.0050	0.1842			
Main tumor size, cm						Overall 0.0120
3.1–5.0						
5.1–7.0			0.0102			
7.1–10.0			0.0093			
Gender						
Female						
Male						
Child-Pugh class						
A						
B						
Number of tumors, n						0.0001
KPS						
70						
80						
90						
100						
Background liver disease						
Hepatitis B virus						
Hepatitis C virus						
Other						
AFP level, ng/mL						
<100						
100–400						
>400						
Treatment modality						Overall 0.0389
TACE + RFA	Reference			Reference		
TACE	1.9251	1.141–3.2472	0.0134	1.8048	1.0558–3.0850	0.0163
RFA	1.9344	1.1369–3.2914	0.0150	1.8048	1.0558–3.0850	0.0309

Dimensioni > 5 cm

Numero di lesioni

Tipo di

trattamento

Che fare > 5 cm?

MWA vs RFA

Microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma: A systematic review and meta-analysis

Antonio Facciorusso, Marianna Di Maso & Nicola Muscatiello

CONCLUSIONS: Our results indicate a similar efficacy between the two percutaneous techniques with an apparent superiority of MWA in larger neoplasms.

Coagulation Areas Produced by Cool-Tip Radiofrequency Ablation and Microwave Ablation Using a Device to Decrease Back-Heating Effects: A Prospective Pilot Study

Francesca Di Vece · Paola Tombesi ·
Francesca Ermili · Cinzia Maraldi ·
Sergio Sartori

CONCLUSION: The MWA system can achieve significantly larger ablation areas than the internally cooled RFA system. Broader randomized trials are strongly warranted to investigate whether such superiority can translate into better long-term outcome of the ablation procedure.

JGH Journal of Gastroenterology and Hepatology

JGHF

doi:10.1111/jgh.13028

META ANALYSIS AND SYSTEMATIC REVIEW

Percutaneous thermal ablation for primary hepatocellular carcinoma: A systematic review and meta-analysis

Mohamed A Chinnaratha,^{*,†} Ming-yu Anthony Chuang,[†] Robert JL Fraser,^{*,†} Richard J Woodman^{*} and Alan J Wigg^{*,†}

Conclusion: Overall, both RFA and MWA are equally effective and safe, but MWA may be more effective compared to RFA in preventing LTP when treating larger tumors. Well-designed, larger, multicentre RCTs are required to confirm these findings.

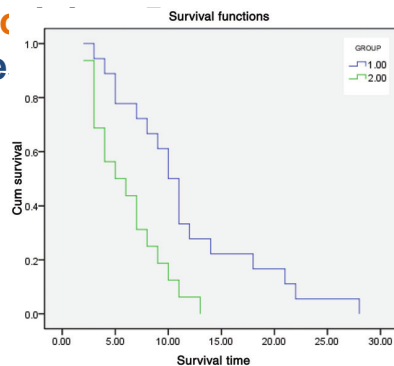
MWA + TACE

MWA Combined with TACE as a combined therapy for unresectable large-sized hepatocellular carcinoma

CUN LIU^{1,2,3}, PING LIANG, FANGYI LIU¹, YANG WANG¹, XIN LI¹, ZHIYU HAN¹, & CHANGCHUN LIU³

¹From the department of Interventional Ultrasound, Chinese PLA General Hospital, 28 Fuxing Road Beijing, 100853, P.R. China, ²From the department of ultrasound, Jinan Central Hospital, Shandong University, 105 Jiefang Xi Road Jinan, Shandong, 250013, P.R. China, and ³School of Control Science and Engineering, Shandong University, 73 Jingzhi Road Jinan, 250061 Shandong Province, P.R. China

- **Prospettico controllato**
- **TACE vs TACE + MWA**
- **34 pazienti consecutivi (18/16)**
- **Non resecabile**



- **> Overall Survival**
- **> Tumor response (Completa e Parziale)**
- **= Complications**

HEPATOLOGY

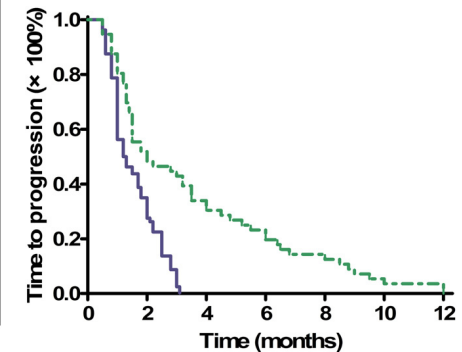
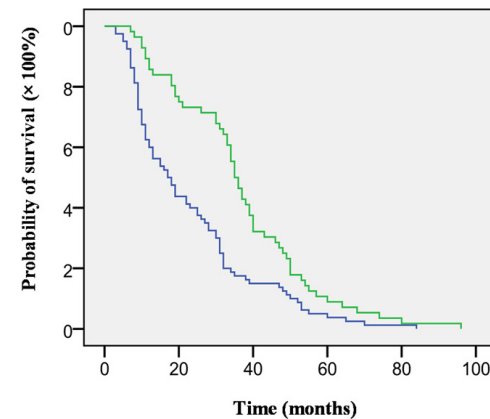
Large primary hepatocellular carcinoma: Transarterial chemoembolization monotherapy versus combined transarterial chemoembolization-percutaneous microwave coagulation therapy

Lin-Feng Xu, Hong-Liang Sun, Yao-Ting Chen, Jia-Yan Ni, Dong Chen, Jiang-Hong Luo, Jing-Xing Zhou, Ren-Mei Hu and Qi-Yun Tan

Department of Interventional Radiology, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, Guangdong Province, China

- **Retrospectivo**
- **TACE vs TACE + MWA**
- **136 pazienti consecutivi (88/56)**
- **Nodulo > 5 cm non resecabile**

Survival



- **> Overall Survival**
- **> Time to progression**
- **< Complications**

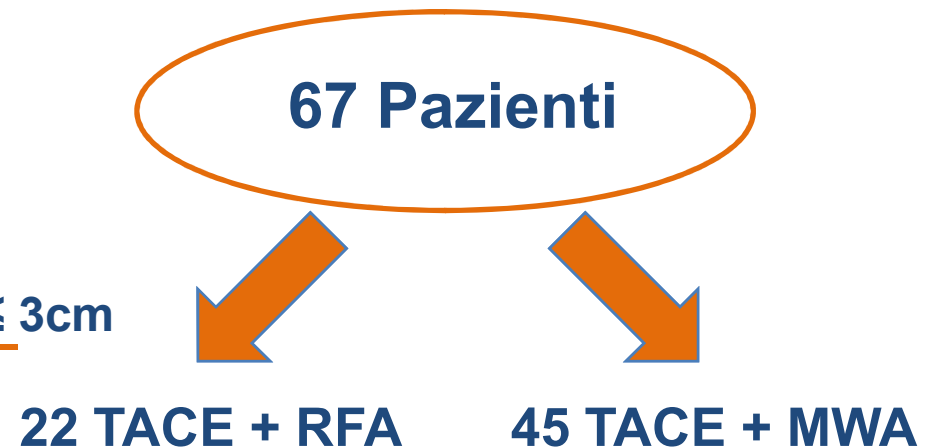
TACE + MWA vs TACE + RFA

Transarterial Chemoembolization Combined with Either Radiofrequency or Microwave Ablation in Management of Hepatocellular Carcinoma

Ashraf Omar Abdelaziz¹, Ahmed Hosni Abdelmaksoud², Mohamed Mahmoud Nabeel¹, Hend Ibrahim Shousha^{1*}, Ahmed Abdelmonem Cordie¹, Sherif Hamdy Mahmoud¹, Eman Medhat¹, Dalia Omran¹, Tamer Mahmoud Elbaz¹

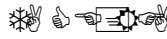
Caratteristiche dello studio

- Retrospektivo, monocentrico
- Child - Pugh A/B
- Singolo nodulo $\leq 5\text{cm}$ o ≤ 3 noduli $\leq 3\text{cm}$



		TACE+Microwave	
Complete response	18/22 (81.8%)		
	4/22 (18.2%)	2/45 (4.4%)	
Complete response			
Tumors 3-5cm			
Complete response		28/28 (100%)	0.01*
		0(0%)	

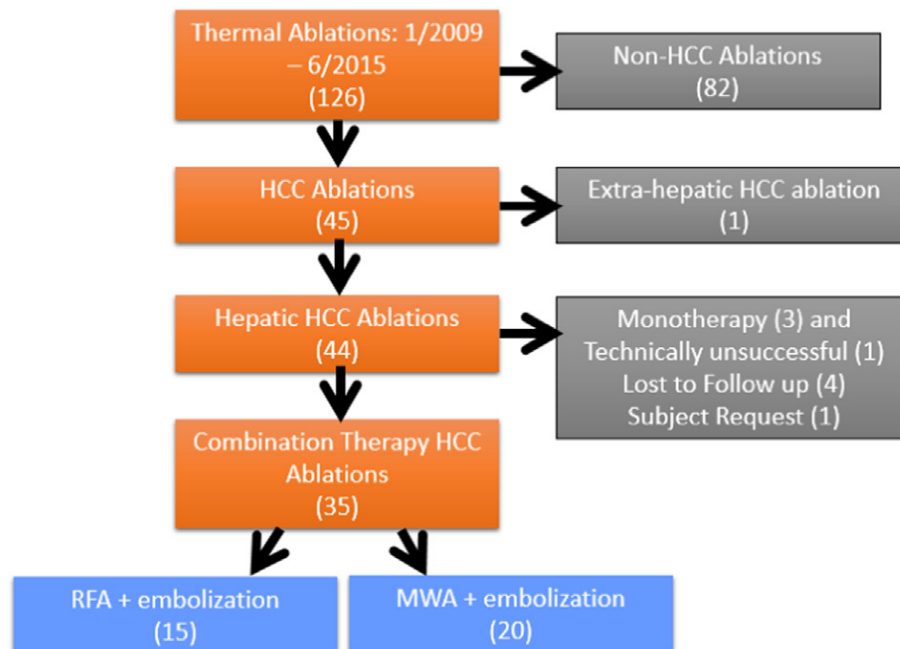
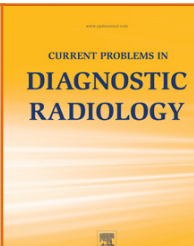
		TACE+Microwave (n.45)	
	4 (18.2%)		0.9
	0 (0.0%)	1 (2.2%)	0.5
Abdominal LNs	0 (0.0%)	0 (0.0%)	-
	1 (4.5%)	0 (1.5%)	
Ascites			0.9
		4 (8.9%)	0.2

	Total patients		TACE+Microwave	
Overall survival 				0.08
1 year	80.10%		83.30%	
2 years	55%			
3 years				
Overall survival in relation to tumor size 				0.3
focal lesion > 3cm		21 months	22 months	
				0.1
1 year			81.20%	
2 years		42%		
3 years		14%		

Finally, we conclude that TACE-MWA led to better response rates than TACE-RFA with tumors 3-5 cm. No difference between both lines of treatment for small tumors (less than 3 cm). Better response rates did not efficiently correlated with better survival rates.

Radiofrequency vs Microwave Ablation After Neoadjuvant Transarterial Bland and Drug-Eluting Microsphere Chembolization for the Treatment of Hepatocellular Carcinoma^{☆,☆☆}

Lindsay M. Thornton, MD^{a,*}, Roniel Cabrera, MD, MS^b, Melissa Kapp, ARNP^c, Michael Lazarowicz, MD^a, Jeffrey D. Vogel, MD^a, Beau B. Toskich, MD^a

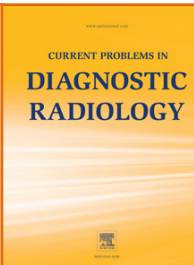


MELD			
Avg	8.7	9.3	0.125
Range	6-16	6-15	
Child Pugh score			0.16
% of A	12 (80%)	11 (55%)	
% of B	3 (20%)	9 (45%)	
BCLC stage			0.14
% very early (0)	4 (27%)	1 (5%)	
% early (A)	11 (73%)	19 (95%)	
Previous treatment			0.73
	9 (60%)	10 (50%)	

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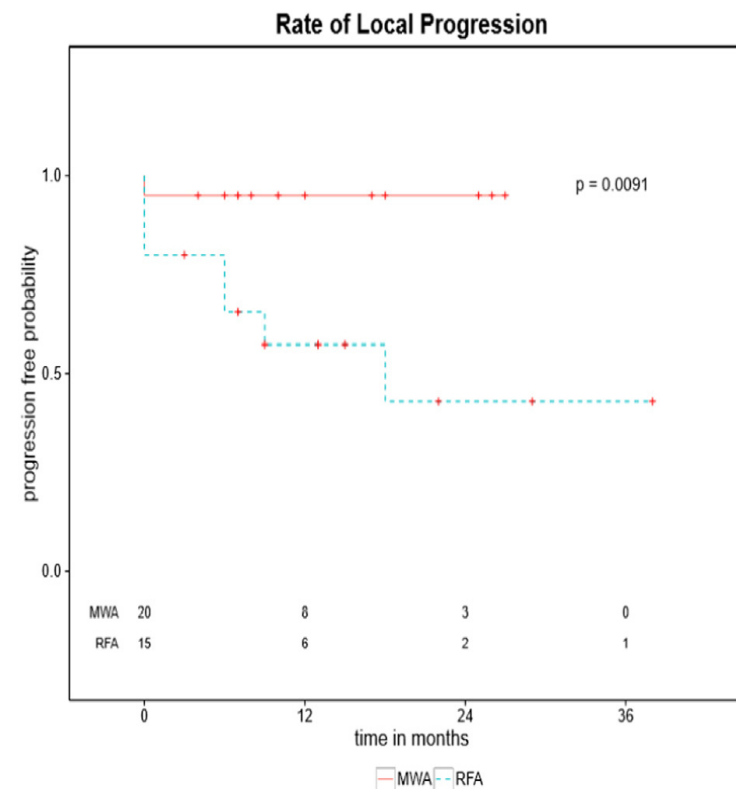
Neoadjuvant here Chembolization for ☆☆

lissa Kapp, ARNP^c,
oskich, MD^a



	1/15 (7%)	8/20 (40%)	0.048
Complications	3/15 (20%)	2/20 (10%)	0.377
Type of embolization			
TACE	3/15 (20%)	9/20 (45%)	0.50
TAE	12/15 (80%)	11/20 (55%)	

	RFA	MWA	P value
<i>Outcomes</i>			
Complete response	12/15 (80%)	19/20 (95%)	0.29
Median postop MELD	7	9.25	0.25
Median follow-up	18	14	0.071
Transplanted	2	5	0.681



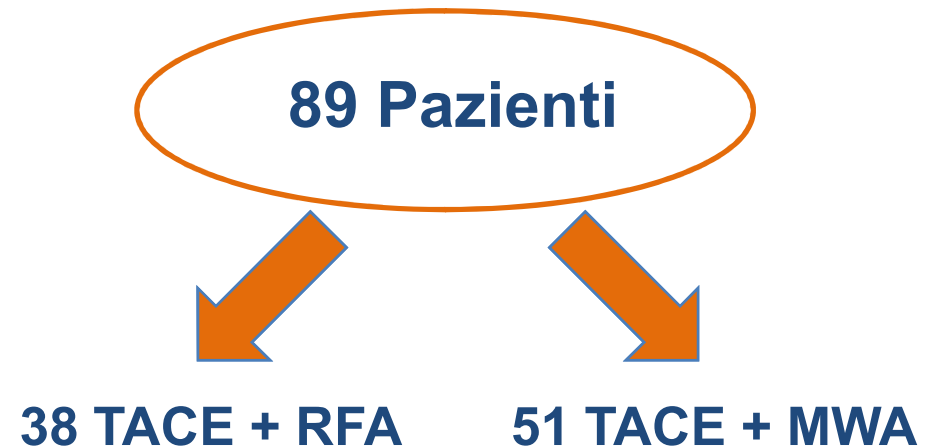
Comparison of Combination Therapies in the Management of Hepatocellular Carcinoma: Transarterial Chemoembolization with Radiofrequency Ablation versus Microwave Ablation

Michael Ginsburg, MD, Sean P. Zivin, MD, Kristen Wroblewski, MS, Taral Doshi, MD, Raj J. Vasnani, MD, and Thuong G. Van Ha, MD



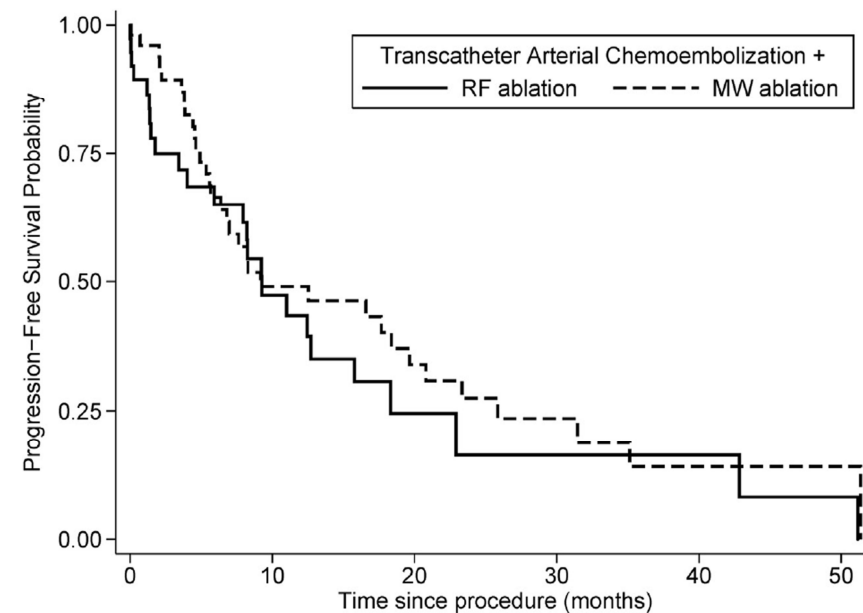
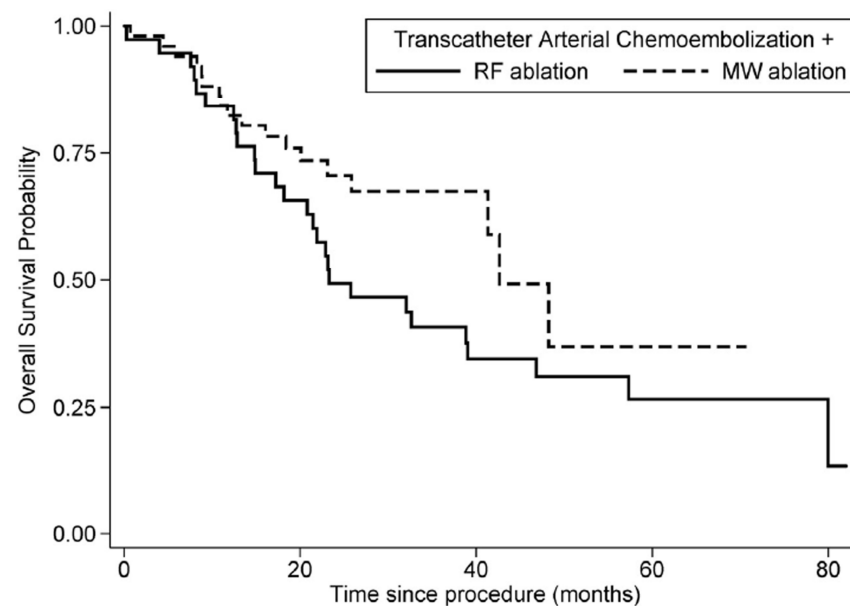
Caratteristiche dello studio

- Retrospektivo, monocentrico
- Child - Pugh A/B
- BCLC A/B/C
- Dimensioni 1,6 cm – 12,5 cm



Comparison of Combination Therapies in the Management of Hepatocellular Carcinoma: Transarterial Chemoembolization with Radiofrequency Ablation versus Microwave Ablation

Michael Ginsburg, MD, Sean P. Zivin, MD, Kristen Wroblewski, MS, Taral Doshi, MD, Raj J. Vasnani, MD, and Thuong G. Van Ha, MD



Used in isolation, there are hypothesized benefits to MW ablation, having demonstrated higher average intratumoral temperatures, larger ablation zones, and less susceptibility to the heat sink effect (17) compared with RF ablation. However, in this study, such theoretical technical advantages were not demonstrated in practice. It is possible that combination therapy lessens the advantage that MW ablation has over RF ablation on the heat sink effect because transcatheter arterial chemoembolization would mitigate such an advantage at least theoretically. Additionally, combination therapy with the two different ablative modalities had no significant differences in safety, with low complication rates for both groups.

TACE + RFA vs HR

Transcatheter Arterial Chemoembolization Plus Radiofrequency Ablation Therapy for Early Stage Hepatocellular Carcinoma

Comparison With Surgical Resection

Tatehiro Kagawa, MD¹; Jun Koizumi, MD²; Sei-ichiro Kojima, MD¹; Naruhiko Nagata, MD¹; Makoto Numata, MD¹; Norihito Watanabe, MD¹; Tetsu Watanabe, MD³; Tetsuya Mine, MD¹; and the Tokai RFA Study Group

Radiofrequency Ablation Combined with Transcatheter Arterial Chemoembolization for the Treatment of Single Hepatocellular Carcinoma of 2 to 5 cm in Diameter: Comparison with Surgical Resection

Jin Woong Kim, MD¹, Sang Soo Shin, MD^{2,3}, Jae Kyu Kim, MD², Sung Kyu Choi, MD⁴, Suk Hee Heo, MD², Hyo Soon Lim, MD², Young Hoe Hur, MD⁵, Chol Kyoong Cho, MD², Yong Yeon Jeong, MD², Heoung Keun Kang, MD²

Departments of ¹Radiology and ²Surgery, Chonnam National University Hwasun Hospital, Hwasun 519-763, Korea; Departments of ³Radiology, ⁴Internal Medicine and ⁵Center for Aging and Geriatrics, Chonnam National University Medical School, Gwangju 501-757, Korea

Early-Stage Hepatocellular Carcinoma: Radiofrequency Ablation Combined with Chemoembolization versus Hepatectomy¹

Koichiro Yamakado, MD
Atsuhiko Nakatsuka, MD
Haruyuki Takaki, MD
Hajime Yokoi, MD
Masanobu Usui, MD
Hiroyuki Sakurai, MD
Shuji Tsaji, MD
Katsuya Shiraki, MD
Hiroyuki Fuke, MD
Shinji Uemoto, MD
Kan Takeda, MD

Purpose: To retrospectively evaluate the long-term results of radiofrequency (RF) ablation combined with chemoembolization (combination therapy) as compared with hepatectomy for the treatment of early-stage hepatocellular carcinoma (HCC).

Materials and Methods: The study was approved by the institutional review board, and informed consent was waived. Patients with early-stage HCC were included if they underwent either combination therapy or hepatectomy and met the following inclusion criteria: no previous treatment for HCC, three or fewer tumors with a maximum diameter of 3 cm or less

Radiology

Yoshitaka Takuma, MD
Hiroyuki Takabatake, MD

Comparison of Combined Transcatheter Arterial Chemoembolization and Radiofrequency Ablation with Surgical Resection by Using Propensity Score Matching in Patients with Hepatocellular Carcinoma within Milan Criteria¹

Purpose: To retrospectively compare the outcome of combined transcatheter arterial chemoembolization (TACE) and radiofrequency ablation (RFA) with surgical resection by using propensity score matching in patients with hepatocellular carcinoma within Milan criteria.

Transcatheter Arterial Chemoembolization Plus Radiofrequency Ablation Therapy for Early Stage Hepatocellular Carcinoma

Comparison With Surgical Resection

Tatehiro Kagawa, MD¹; Jun Koizumi, MD²; Sei-ichiro Kojima, MD¹; Naruhiko Nagata, MD¹; Makoto Numata, MD¹; Norihito Watanabe, MD¹; Tetsu Watanabe, MD³; Tetsuya Mine, MD¹; and the Tokai RFA Study Group

Randomized clinical trial

Randomized clinical trial of chemoembolization plus radiofrequency ablation *versus* partial hepatectomy for hepatocellular carcinoma within the Milan criteria

H. Liu¹, Z.-G. Wang¹, S.-Y. Fu¹, A.-J. Li¹, Z.-Y. Pan¹, W.-P. Zhou¹, W.-Y. Lau² and M.-C. Wu¹

¹Third Department of Hepatic Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, and ²Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong, China

Correspondence to: Professor W.-P. Zhou, Third Department of Hepatic Surgery, Eastern Hepatobiliary Surgery Hospital, 225 Changhai Road, Shanghai 200438, China (e-mail: chphwp@126.com)

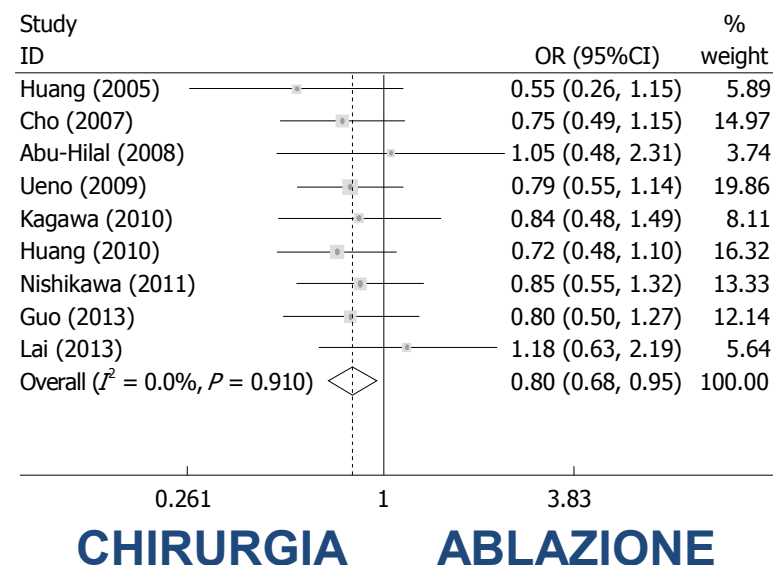
COMBINATO vs HR

Clinical outcome of small hepatocellular carcinoma after different treatments: A meta-analysis

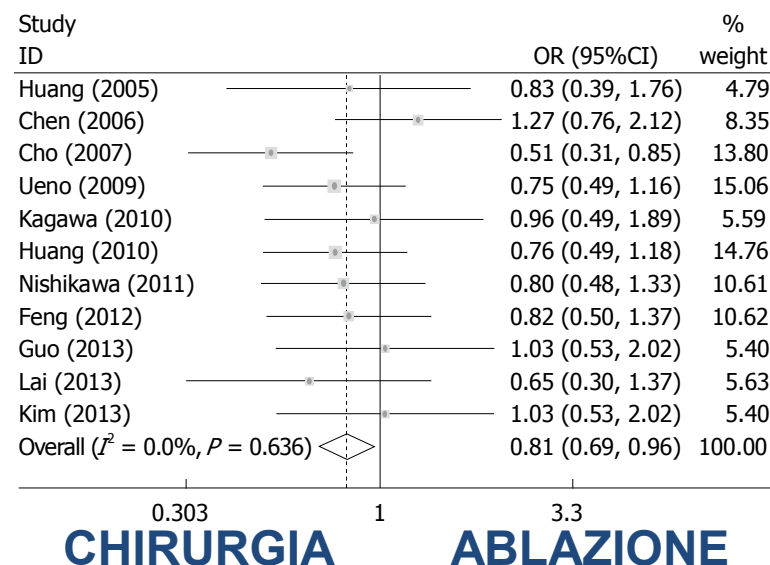


World Journal of
Gastroenterology

Wei Dong, Ting Zhang, Zhen-Guang Wang, Hui Liu



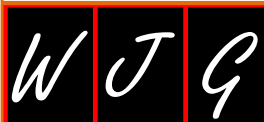
5 yrs OS



3 yrs RFS

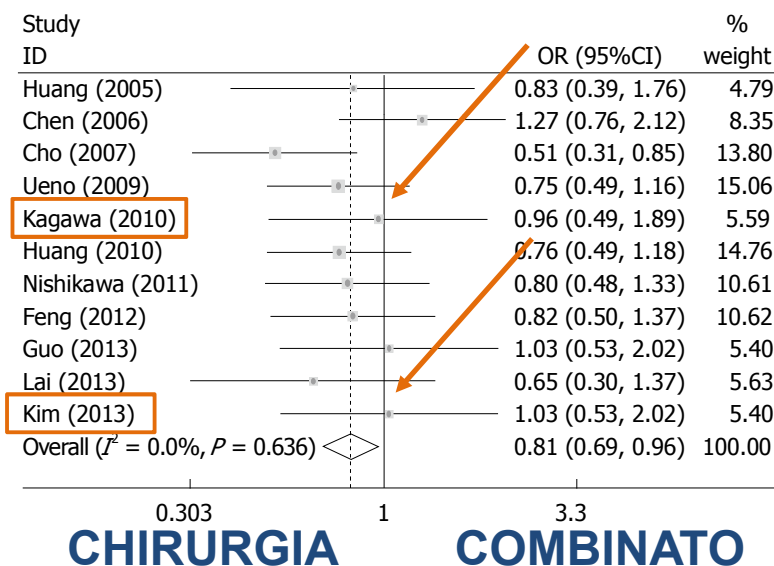
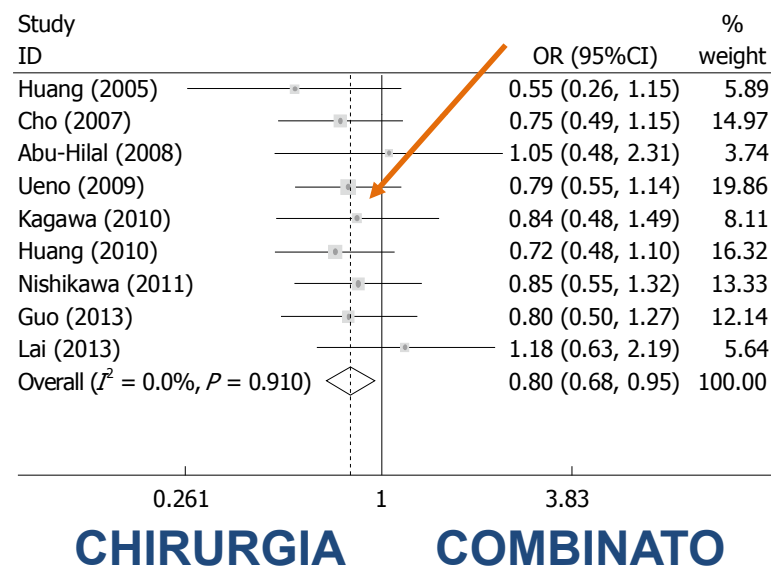
COMBINATO vs HR

Clinical outcome of small hepatocellular carcinoma after different treatments: A meta-analysis



World Journal of
Gastroenterology

Wei Dong, Ting Zhang, Zhen-Guang Wang, Hui Liu



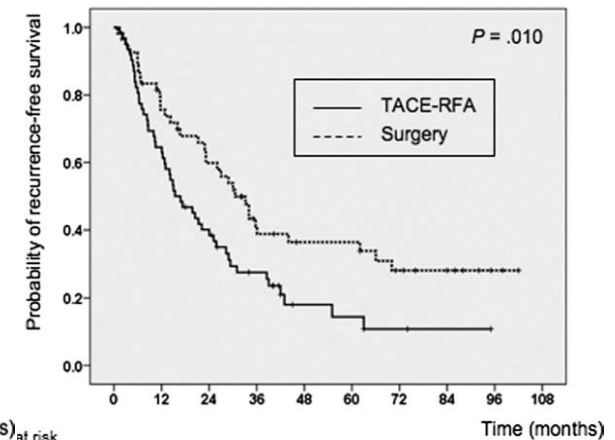
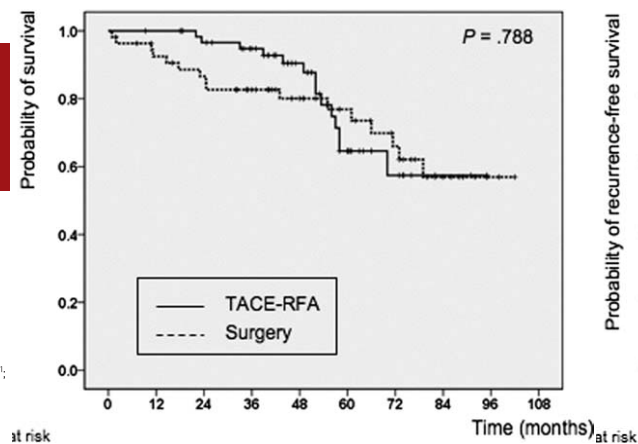
COMBINATO vs HR



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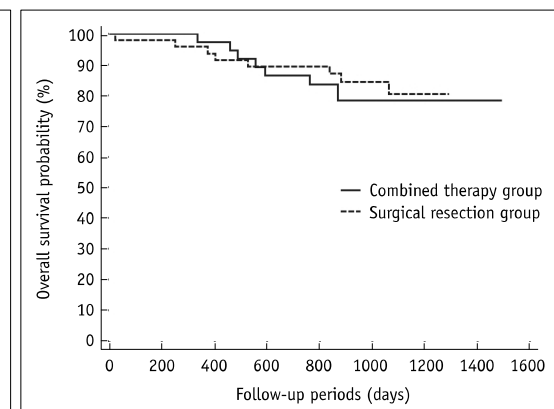
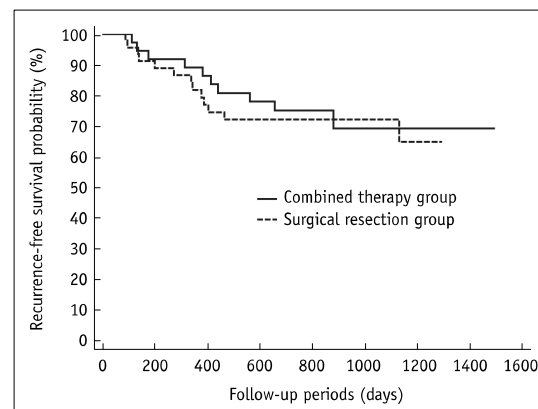


Radiofrequency Ablation Combined with Transcatheter Arterial Chemoembolization for the Treatment of Single Hepatocellular Carcinoma of 2 to 5 cm in Diameter: Comparison with Surgical Resection

Korean Journal of Radiology



Jin Woong Kim, MD¹; Sang Soo Shin, MD^{2,3}; Jae Kyu Kim, MD²; Sung Kyu Choi, MD⁴; Suk Hee Heo, MD²; Hyo Soon Lim, MD²; Young Hoe Hur, MD⁵; Chol Kyocho Cho, MD⁵; Yong Yeon Jeong, MD²; Heoung Keun Kang, MD²

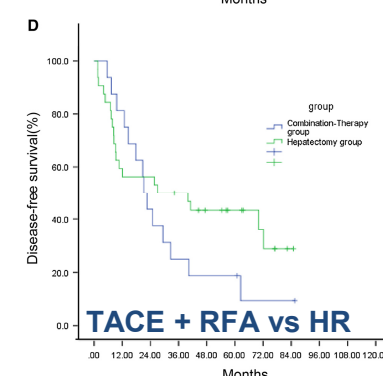
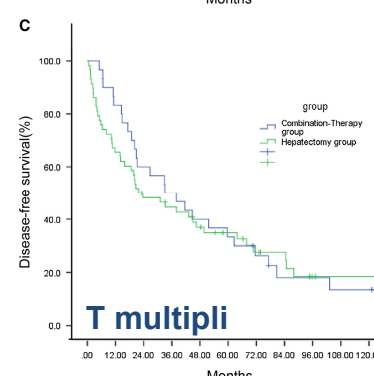
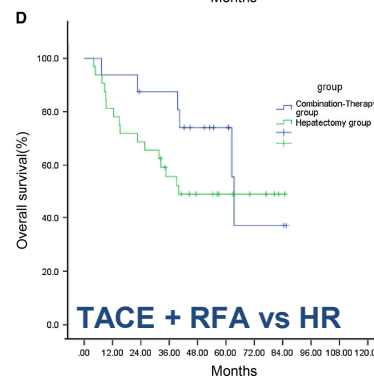
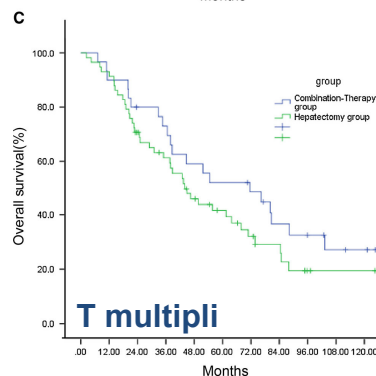
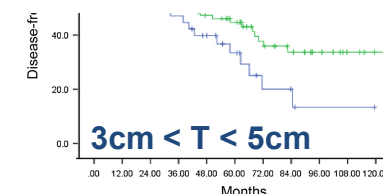
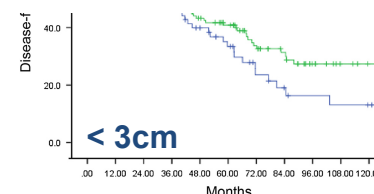
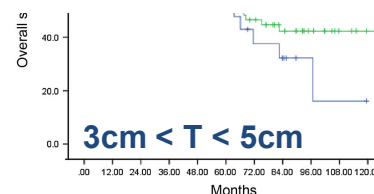
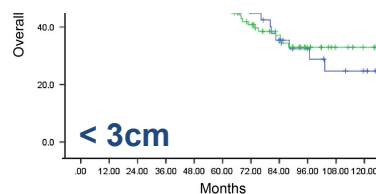


COMBINATO vs HR

Radiofrequency ablation combined with transarterial chemoembolization versus hepatectomy for patients with hepatocellular carcinoma within Milan criteria: a retrospective case-control study

A. K. Bholee^{1,2} · K. Peng^{2,3} · Z. Zhou^{1,2} · J. Chen^{1,2} · L. Xu^{1,2} · Y. Zhang^{1,2} · M. Chen^{1,2}

no significant difference was identified in either OS or DFS for patients with single tumor smaller than 3.0 cm, 3.0–5.0 cm, and multiple tumors. Multivariate analysis *Conclusion* TACE + RFA is safe and as effective as hepatectomy for patients with HCC within Milan criteria.



OS

DFS

Randomized clinical trial

Randomized clinical trial of chemoembolization plus radiofrequency ablation versus partial hepatectomy for hepatocellular carcinoma within the Milan criteria

H. Liu¹, Z.-G. Wang¹, S.-Y. Fu¹, A.-J. Li¹, Z.-Y. Pan¹, W.-P. Zhou¹, W.-Y. Lau² and M.-C. Wu¹

¹Third Department of Hepatic Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, and ²Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong, China

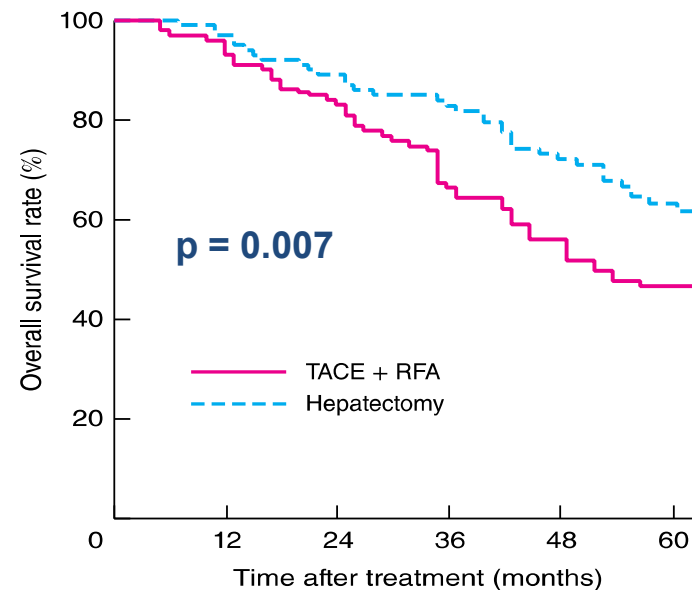
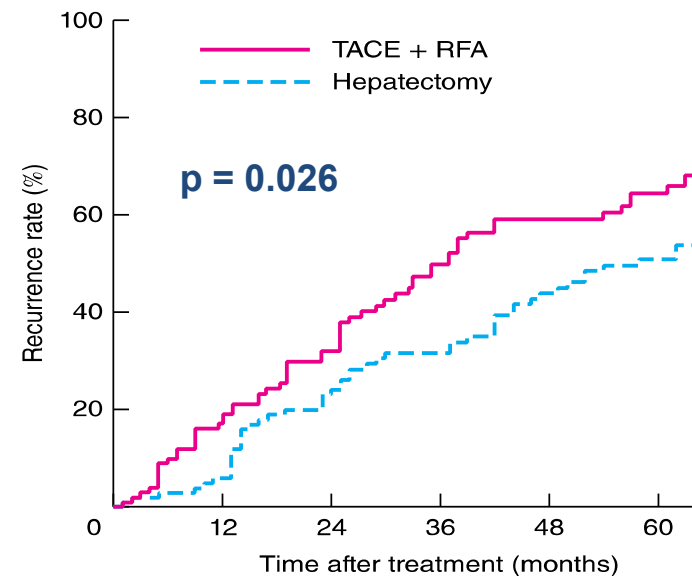
Correspondence to: Professor W.-P. Zhou, Third Department of Hepatic Surgery, Eastern Hepatobiliary Surgery Hospital, 225 Changhai Road, Shanghai 200438, China (e-mail: ehphwp@126.com)

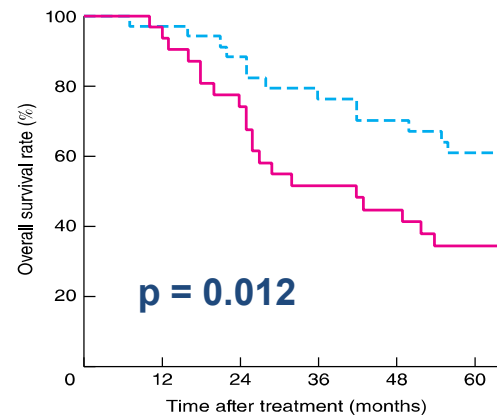
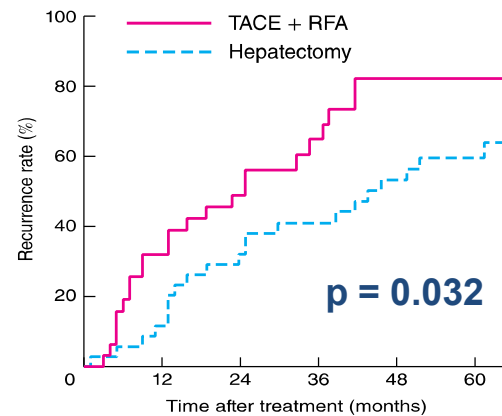
Criteri di inclusione

- 18 ≤ età ≤ 80, 200 pz
- No trattamenti pregressi per HCC
- Criteri di Milano
- Child - Pugh A/B
- Candidabile CH/RFA+TACE

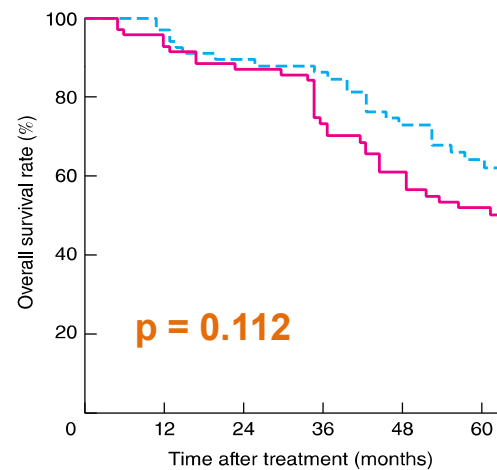
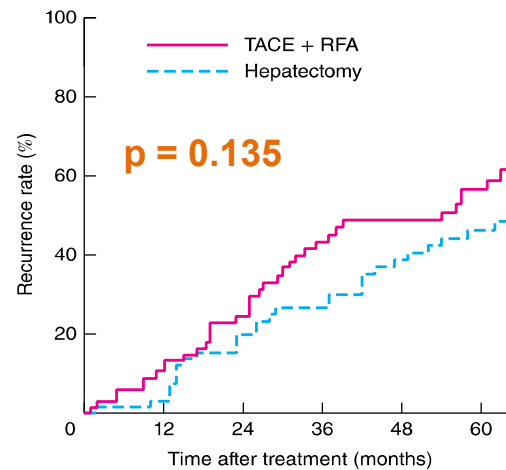
Criteri di esclusione

- Metastasi
- Infiltrazione portale
- Controindicazioni a CH, RFA, TACE





> 3cm



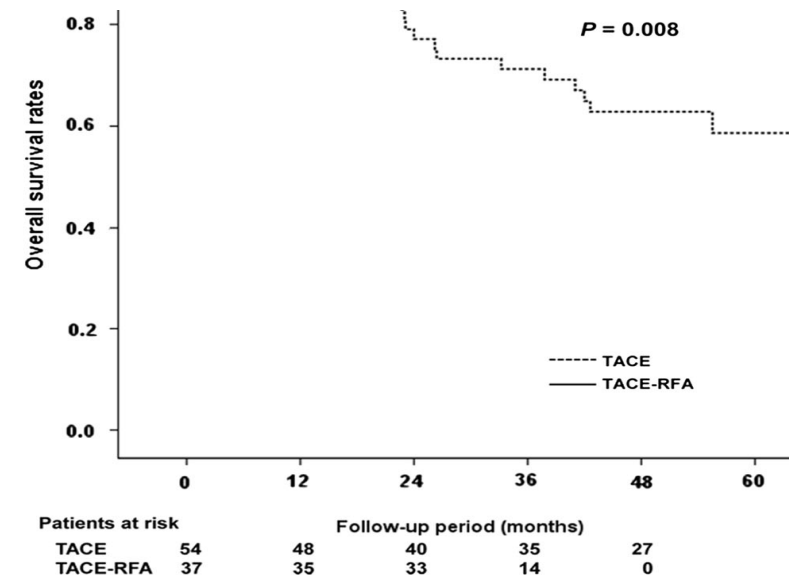
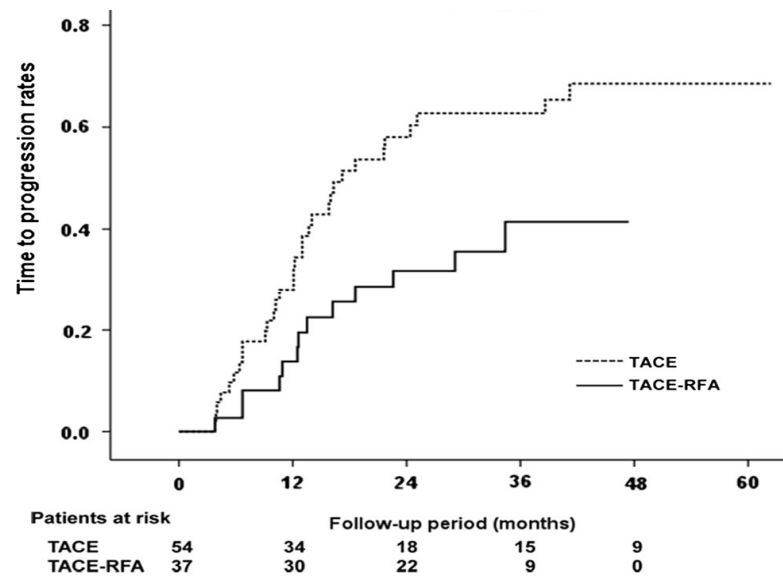
≤ 3cm

There was no 30- or 90-day mortality after treatment in either group. The incidence of complications in the partial hepatectomy group was 23.0 per cent versus 11.0 per cent in the TACE + RFA group ($P = 0.024$). Complications

EARLY STAGE (NO RFA)

Early Stage Hepatocellular Carcinomas Not Feasible for Ultrasound-Guided Radiofrequency Ablation: Comparison of Transarterial Chemoembolization Alone and Combined Therapy with Transarterial Chemoembolization and Radiofrequency Ablation

Dongho Hyun¹ · Sung Ki Cho¹ · Sung Wook Shin¹ · Kwang Bo Park¹ · Hong Suk Park¹ · Sung Wook Choo¹ · Young Soo Do¹ · In-wook Choo¹ · Min Woo Lee¹ · Hyunchul Rhim¹ · Hyo Keun Lim¹



EARLY STAGE (NO RFA)

Lesioni complesse

Lesione sottodiaframmatica di 4,5 cm

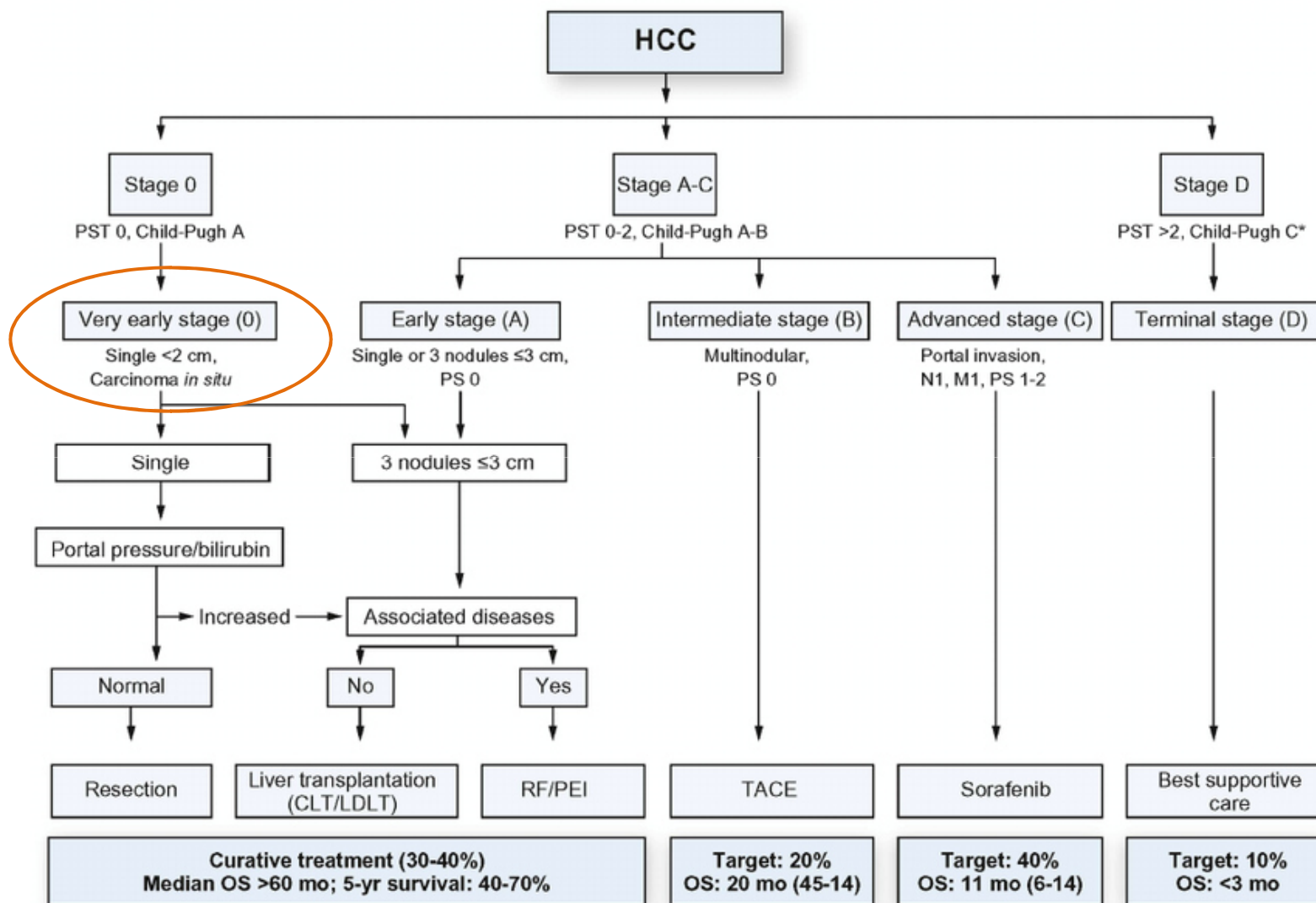


EARLY STAGE (NO RFA)

Lesioni complesse

Lesione sottodiaframmatica di 4,5 cm





Radiofrequency ablation versus hepatic resection for the treatment of hepatocellular carcinomas 2 cm or smaller: a retrospective comparative study.

Peng ZW¹, Lin XJ, Zhang YJ, Liang HH, Guo RP, Shi M, Chen MS.

CONCLUSION: The efficacy and safety of percutaneous RF ablation were better than those of surgical **resection** in patients with HCC measuring 2 cm or smaller, especially those with central HCC.

Comparison of Combined Transcatheter Arterial Chemoembolization and Radiofrequency Ablation with Surgical Resection by Using Propensity Score Matching in Patients with Hepatocellular Carcinoma within Milan Criteria¹

Yoshitaka Takuma, MD
Hiroyuki Takabatake, MD
Youichi Morimoto, MD
Nobuyuki Toshikuni, MD
Takahisa Kayahara, MD
Yasuhiro Makino, MD
Hiroshi Yamamoto, MD

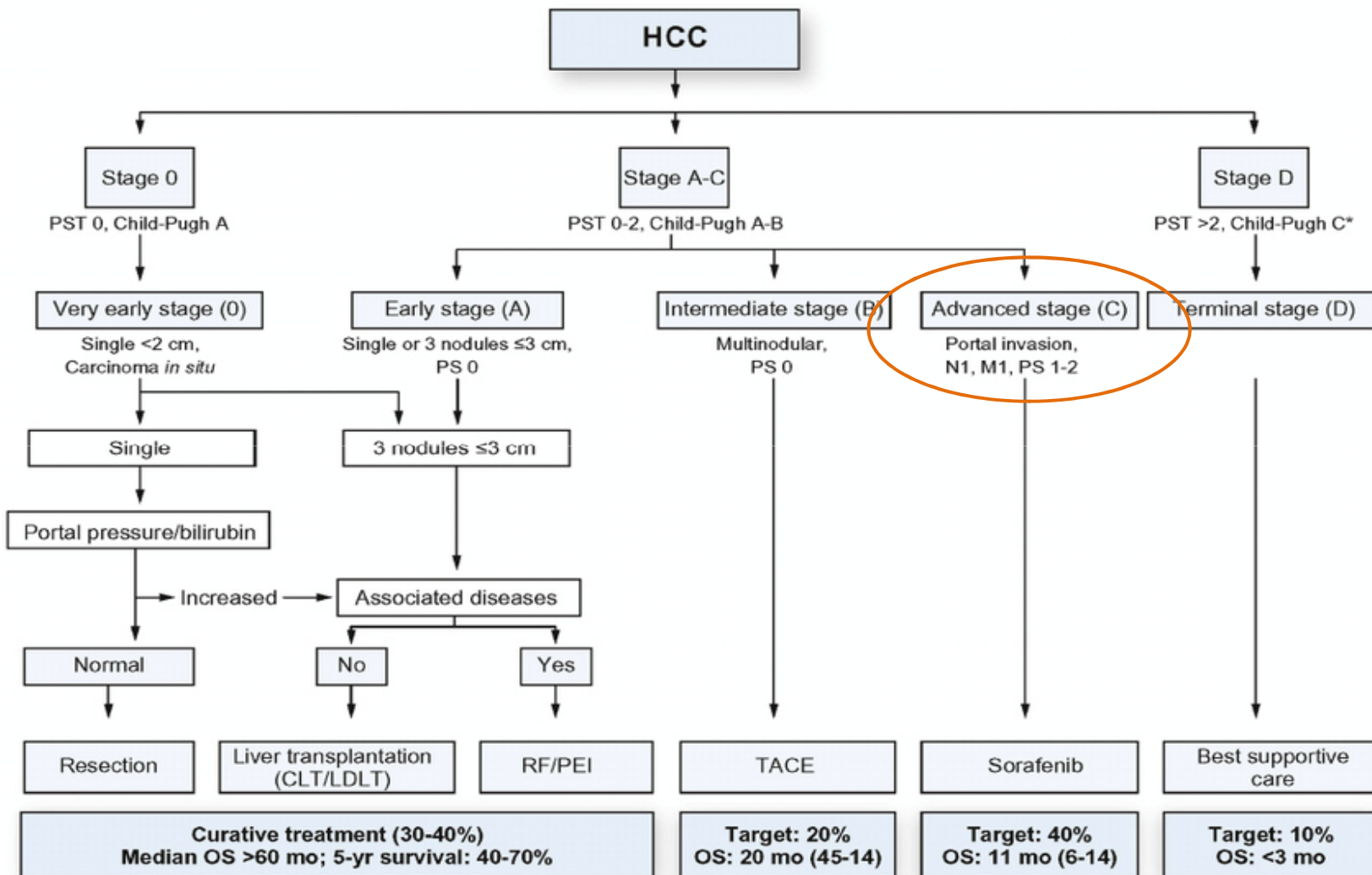
Overall Survival

	(OS)	3	5
TACE - RFA	100	90	78
CHIRURGIA	96	96	83

Disease free survival

	1 (DFS)	3	5
TACE - RFA	91	47	40
CHIRURGIA	89	68	28

No significatività!



Transcatheter arterial chemoembolization combined with radiofrequency ablation can improve survival of patients with hepatocellular carcinoma with portal vein tumour thrombosis: Extending the indication for ablation?

J.-s. Zheng^{*,a}, J. Long^a, B. Sun, N.-n. Lu, D. Fang, L.-y. Zhao, N. Du

Caratteristiche studio

- Retrospettivo
- 134 pz (TACE + RFA)
- BCLC grado C, PVTT (tipo I,II e III)
- Child - Pugh A/B

Risultati

	TACE + MWA
1yr OS	63%
3yr OS	40%
5yr OS	23%
Median survival (mesi)	29,5

ORIGINAL ARTICLE

Microwave ablation of hepatocellular carcinoma with portal vein tumor thrombosis after transarterial chemoembolization: a prospective study

Jiang Long¹ · Jia-sheng Zheng¹ · Bin Sun¹ · Ningning Lu¹

Caratteristiche studio

- Prospettico controllato
- 60 pz (TACE + MWA) vs 54 pz (TACE)
- BCLC grado C, PVTT (tipo I,II e III)
- Child - Pugh A/B

Risultati

	TACE + MWA	TACE
1yr OS	48%	33
3yr OS	23%	20
Median survival (mesi)	13,5	9,5

CONCLUSIONE

NI

- I **trattamenti combinati** sono un'arma importante nel trattamento dell'HCC, ma sono esclusi (o quasi) dalle **linee guida** delle più importanti società scientifiche e dal **BCLC** il quale non è attualmente sufficiente a garantire un corretto **"incasellamento terapeutico"**
- Numerose Metanalisi recenti hanno confermato che i **trattamenti combinati** migliorano **OS** e **RFS** del **Paziente** con HCC di dimensioni **tra 3 cm e 5 cm**, rispetto alle monoterapie RFA e TACE, a parità di rischi procedurali
- Nel paziente con **tumore < 3cm** il trattamento combinato TACE + RFA ha evidenziato risultati equiparabili a quelli della **chirurgia** in termini di **OS** e **RFS** mostrando inoltre maggiore **sicurezza procedurale**

CONCLUSIO

NI

- Nell'HCC > 5 cm entrambe TACE + RFA e TACE + MWA migliorano l'Overall Survival rispetto ai trattamenti singoli, significative differenze tra le due metodiche
- Ruolo importante nel paziente complesso
- Non ci sono indicazioni al trattamento combinato nel paziente very early
- L'applicazione dei trattamenti combinati nel paziente advanced è oggi solo una prospettiva

CONCLUSIONI

Come possiamo migliorare?

- Integrare alcuni dati importanti (es: **Child-Pugh**, **Performance Status**), nel tentativo di delineare **nuove categorie del BCLC**
- Aumentare il numero di **lavori di confronto** tra **trattamenti combinati**, con la **chirurgia** e con **altri trattamenti**

Necessità di **studi randomizzati** e/o **multicentrici** per dare maggiore “peso scientifico” alle evidenze già presenti ed identificare **nuove “vie percorribili”**

The dark side of the guidelines



GRAZIE!

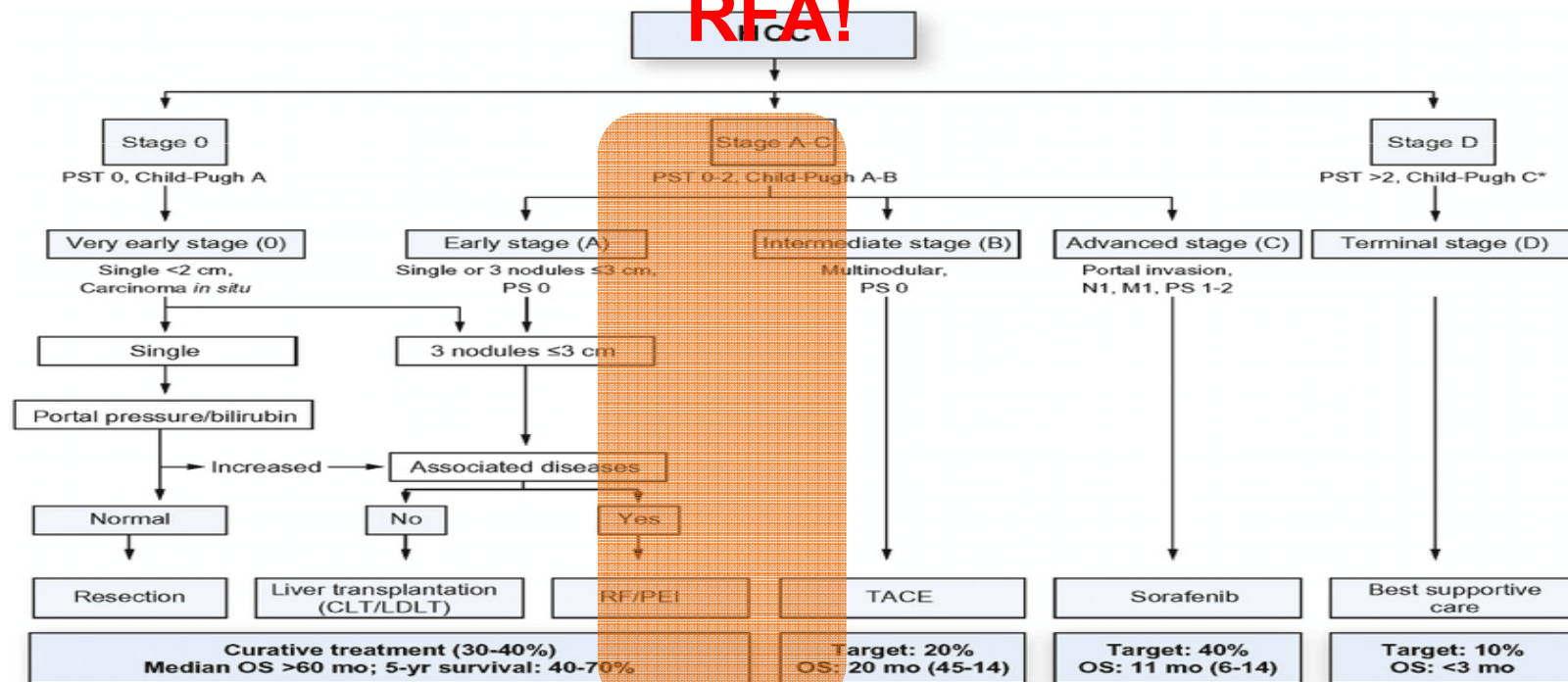
1st Interventional Radiologist under 40 Meeting

Emergencies in Interventional Radiology

➤ **Aumentare** il tasso
di pazienti
candidabili a
trattamenti curativi

➤ **Ridurre** le indicazioni
per i trattamenti
palliativi

**Espandere le indicazioni della
RFA!**



Radiofrequency ablation combined with percutaneous ethanol injection for hepatocellular carcinoma: a systematic review and meta-analysis

Zheng Li, Kai Zhang, Shu-Mei Lin, Deng-Hai Mi, Nong Cao, Zhi-Zhen Wen & Zhong-Xin Li

- 13 lavori
- 9 RCT
- 5 RFA + PEI vs PEI/RFA (1 RCT, 3 CCT, 1 CCS)
- RFA + PEI > RFA (> PEI)
- 1, 1.5, 2, 3 OR ↑
- Local recurrence

Febbre

Study and year	Region	Design	P/T	Treatment arms (n)	Aetiology: HBV/HCV (n)	No. of tumours (1/≥2) (%)	Main HCC mean size (cm)	Mean treatment sessions per tumour	Mean follow-up (months)
Livraghi et al. (1999) [20]	Italy	RCT	86 (112)	RFA (42) PEI (44)	5/33 6/34	79/21 77/23	2.3 2.5	1.2 4.8	10 10
Lencioni et al. (2003) [21]	Italy	RCT	102 (142)	RFA (52) PEI (50)	6/22 9/20	77/23 62/38	2.8 2.8	1.1 5.4	22.9 22.4
Lin et al. (2004) [22]	Taiwan, China	RCT	157 (186)	RFA (52) PEI (105)	35/16 74/30	73/27 77/23	2.9 2.8	1.6 4.6	24.5 24
Lin et al. (2005) [23]	Taiwan, China	RCT	124 (154)	RFA (62) PEI (62)	41/20 42/19	79/21 79/21	2.5 2.3	1.3 4.9	28 26
Shiina et al. (2005) [24]	Japan	RCT	232 (379)	RFA (118) PEI (114)	18/90 11/98	61/39 53/47	NR NR	2.1 6.4	37 35
Brunello et al. (2008) [25]	Italy	RCT	139 (177)	RFA (70) PEI (69)	6/44 0/47	77/23 79/21	2.4 2.3	NR NR	26.1 25.3
Giorgio et al. (2011) [26]	Italy	RCT	271 (271)	RFA (128) PEI (143)	61/81 [§] 56/87	100/0 100/0	2.3 2.3	5 8	22 22
Azab et al. (2011) [27]	Egypt	RCT	90 (98)	RFA (30) PEI (30)	NR NR	NR NR	NR NR	1.5 7.7	18 18
Shankar et al. (2004) [28]	America	CCT	50 (58)	RFA-PEI (30) RFA (20)	NR NR	NR NR	8.8 8.4	NR NR	NR NR
Kurokohchi et al. (2005) [29]	Japan	CCT	75 (NR)	RFA-PEI (30) RFA (15)	NR NR	NR NR	2.5 3.0	NR NR	NR NR
Zhang et al. (2007) [30]	China	RCT	133 (210)	RFA-PEI (66) RFA (158 [§])	65/2 61/5	61/39 64/36	NR NR	NR NR	32.2 33.5
Wong et al. (2008) [31]	Taiwan, China	CCT	142 (208)	RFA-PEI (50 [§]) PEI (12)	NR NR	NR NR	2.8 NR	NR NR	9.8 NR
Cha et al. (2013) [32]	Korea	CCS	20 (20)	RFA-PEI (8)	NR	NR	NR	NR	NR

RCT: randomised controlled trial; CCT: controlled clinical trial; CCS: case control study; RFA: radiofrequency ablation; PEI: percutaneous ethanol injection; HCC: hepatocellular carcinoma; P: patient; T: tumour; HBV: hepatitis B virus; HCV: hepatitis C virus; NR: not reported in the text.

[§]Aetiologies of 14 patients ineligible for RFA and shifted to PEI were not provided. Accordingly, we extracted the data from randomisation.

#Here is the number of tumours instead of the number of patients because this trial divided groups by the tumour characteristics.