PROGRAMA

29º CONGRESO
SETH
A Coruña
15 - 17 noviembre 2023
Palexco

TOP PAPERS 2023

SELECCIÓN DE CANDIDATOS

The novel SALT-M score predicts 1-year post-transplant mortality in patients with severe acute-on-chronic liver failure

Ruben Hernaez[1,2,3,*,#], **Constantine J. Karvellas**[4,#], Yan Liu[2,3], Sophie-Caroline Sacleux[5,6], Saro Khemichian[7], Lance L. Stein[8], Kirti Shetty[9], Christina C. Lindenmeyer[10], Justin R. Boike[11], Douglas A. Simonetto[12], Robert S. Rahimi[13], Prasun K. Jalal[3], Manhal Izzy[14], Michael S. Kriss[15], Gene Y. Im[16], Ming V. Lin[17], Janice H. Jou[18], Brett E. Fortune[19], George Cholankeril[3], Alexander Kuo[20], Nadim Mahmud[21], Fasiha Kanwal[1,2,3], Faouzi Saliba[5], Vinay Sundaram[20,‡,†], Thierry Artzner[22,‡], Rajiv Jalan [23,24,25,‡], for the Multi-Organ Dysfunction and Evaluation for Liver Transplantation (MODEL) Consortium[§]

- n=521

- MELD Na medio: 40 (36-40)

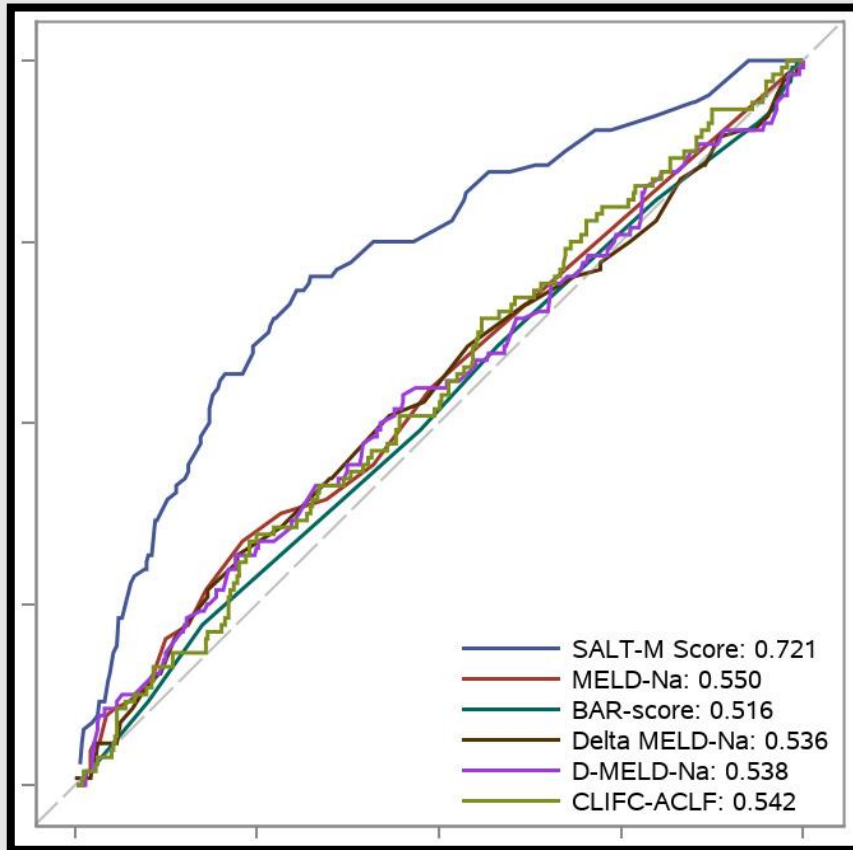- >50% con aminas/diálisis

- Mortalidad al año del 19%

MORTALIDAD

- Edad ≥ 50 años
- IMC
- Uso de aminas
- Fallo respiratorio
- Diabetes mellitus

ESTANCIA HOSPITALARIA

- Recuento leucocitario
- Infección fúngica
- Infección bacterias multirresistentes
- Diálisis

P(death within 1 year after LT)= 1/[1 + exp(-(-3.412 + 0.366*(Age>50) + 0.032*BMI + 0.414*one pressor + 1.192*two or more pressors + 0.599*respiratory failure + 0.417*diabetes mellitus))]*100%

Hernáez R et al. The novel SALT-M score predicts 1-year post-transplant mortality in patients with severe acute-on-chronic liver failure. J Hepatol 2023;717-27

Score	AUROC (95% CI)	p-value (vs. Sundaram score)
Sundaram ACLF-LT-M	0.72* (0.69-0.76)	--
MELD-Na [21]	0.55 (0.48-0.61)	<.0001
BAR score [25]	0.52 (0.45-0.58)	<.0001
Delta-MELD [22]	0.54 (0.48-0.60)	<.0001
D_MELD [23]	0.54 (0.47-0.60)	<.0001
CLIF-C-ACLF [24]	0.54 (0.48-0.60)	<.0001

Hernáez R et al. The novel SALT-M score predicts 1-year post-transplant mortality in patients with severe acute-on-chronic liver failure. J Hepatol 2023;717-27

UNOS Down-Staging Criteria for Liver Transplantation of Hepatocellular Carcinoma: Systematic Review and Meta-Analysis of 25 Studies

Darren Jun Hao Tan,[*,a] Wen. Hui Lim,[*,a] Jie Ning Yong,[*,a] Cheng Han Ng,[*] Mark D. Muthiah,[*,‡,§] Eunice X. Tan,[*,‡,§] Jieling Xiao,[*] Snow Yunni Lim,[*] Ansel Shao Pin Tang,[*] Xin Hui Pan,[*] Tousif Kabir,[‖,¶] Glenn K. Bonney,[#] Raghav Sundar,[*,**] Nicholas Syn,[*,‡‡] Beom Kyung Kim,[§§,‖‖] Yock Young Dan,[*,§,‡‡] Mazen Noureddin,[¶¶] Rohit Loomba,[##] and Daniel Q. Huang[*,‡,§,##]

UNOS-DS Criteria	Bologna Criteria
Inclusion: HCC exceeding Milan criteria but meeting one of the following: 1. Single lesion 5.1 - 8 cm 2. 2 - 3 lesions each < 5 cm with the sum of the maximal tumor diameters < 8 cm 3. 4 - 5 lesions each < 3 cm with the sum of the maximal tumor diameters < 8 cm Absence of vascular invasion or extra-hepatic disease based on cross-sectional imaging	**Inclusion:** HCC exceeding Milan criteria but meeting one of the following: 1. Single lesion ≤ 8 cm 2. Bifocal lesions each ≤ 5 cm 3. Multiple lesions < 6, each ≤ 4 cm, with the sum of the maximal tumor diameters ≤ 12 cm Absence of vascular invasion or extra-hepatic disease based on cross-sectional imaging
Criteria for successful downstaging: Residual tumor size and diameter within Milan criteria (1 lesion <5 cm, 2-3 lesions <3 cm) 1. Only viable tumor(s) are considered; tumor diameter measurements should not include the area of necrosis from tumor directed therapy 2. If there is more than one area of residual tumor enhancement, then the diameter of the entire lesion should be counted towards the overall tumor burden	**Criteria for successful downstaging:** Residual tumor size and diameter within Milan criteria (1 lesion <5 cm, 2-3 lesions <3 cm) 1. Only viable tumor(s) are considered; tumor diameter measurements includes the area of necrosis from tumor directed therapy 2. If there is more than one area of residual tumor enhancement, then the diameter of the entire lesion should be counted towards the overall tumor burden
Additional guidelin 1. A minimal ... and liver tr...	...s between successful down-staging ...emain <400 ng/mL during the

25 estudios
- Criterios UNOS: 5 estudios
- Criterios Bolonia: 2 estudios
- Sin límite de carga tumoral: 18 estudios

n=3997 pacientes

Hun Jao Tan D et al. UNOS Down staging criteria for liver transplantation of hepatocellular carcinoma: systematic review and meta-análisis of 25 studies. Clin Gastroenterol Hepatol 2023: 1475-84
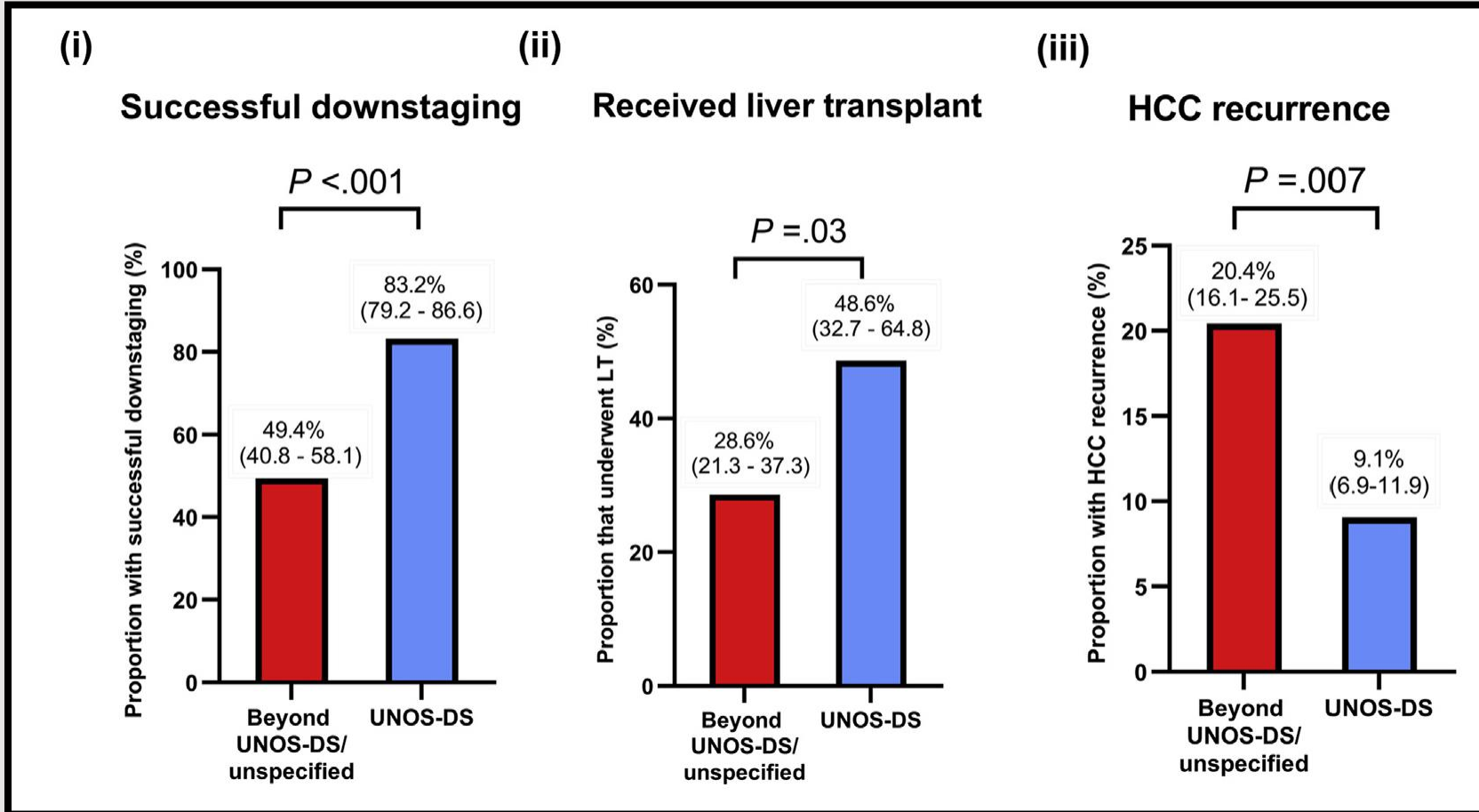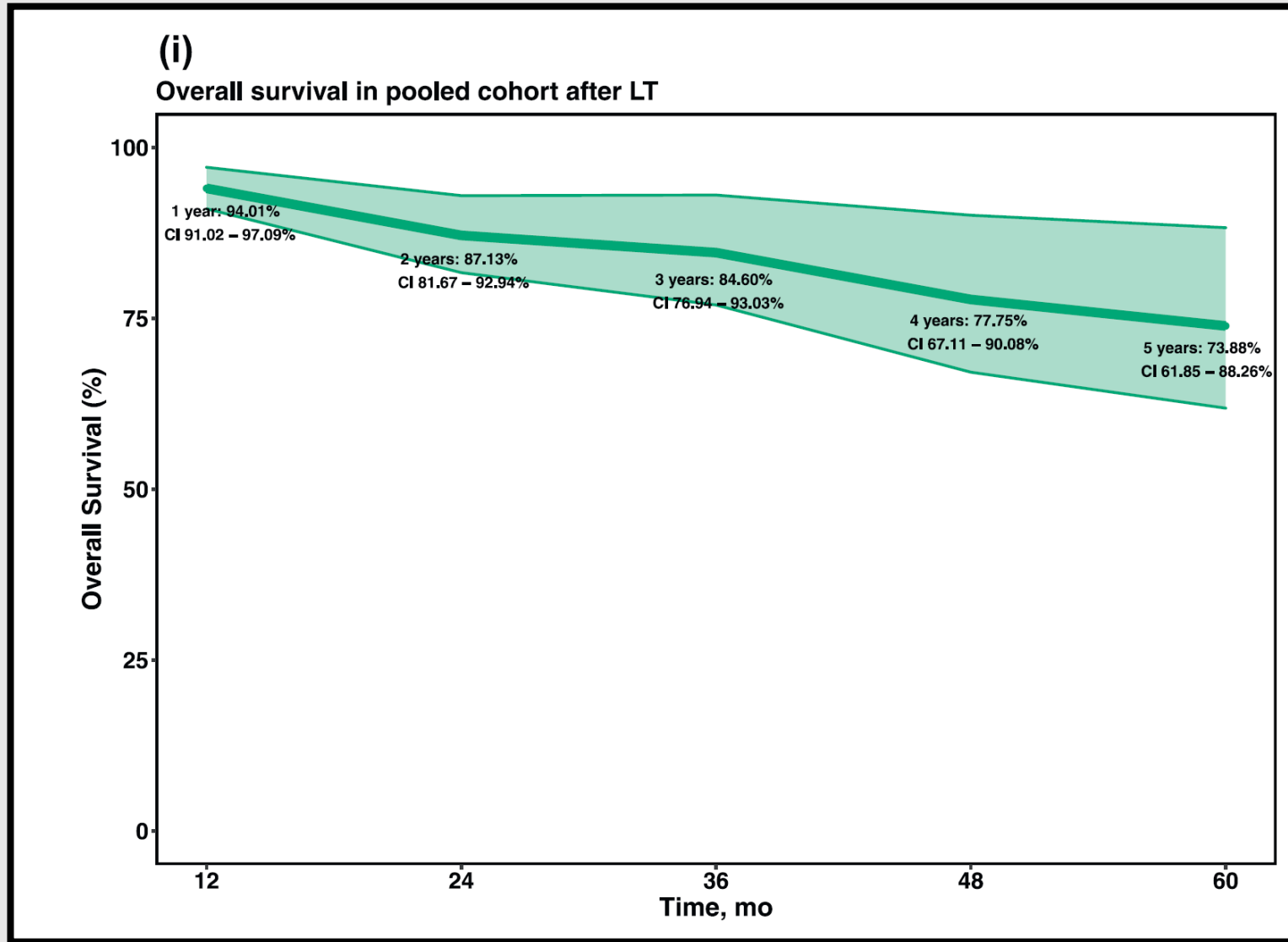
Risk factor	No. of studies	OR (95% CI)	*p*
Age (years)	16	0.971 (0.883 - 1.068)	0.512
Female	16	0.947 (0.879 - 1.021)	0.140
MELD score	9	0.773 (0.615 - 0.973)	**0.033**
Child-Pugh grade			
A	13	1.007 (0.968 - 1.046)	0.727
B	13	0.983 (0.941 - 1.028)	0.421
C	10	1.038 (0.934 - 1.153)	0.438
AFP at listing (ng/mL)	11	1.000 (0.999 - 1.001)	0.871
AFP >100ng/mL at listing	5	0.910 (0.809 - 0.979)	**0.042**
Uninodular HCC	11	0.980 (0.948 - 1.013)	0.200
Etiology of liver disease			
HBV	13	1.034 (0.989 - 1.082)	0.125
HCV	14	1.011 (0.981 - 1.042)	0.437
ALD	9	0.958 (0.886 - 1.035)	0.229
NASH	5	0.978 (0.915 - 1.045)	0.364

Hun Jao Tan D et al. UNOS Down staging criteria for liver transplantation of hepatocellular carcinoma: systematic review and meta-análisis of 25 studies.
Clin Gastroenterol Hepatol 2023: 1475-84

CRITERIOS UNOS

(i)

Overall survival in pooled cohort after LT

1 year: 94.01%
CI 91.02 – 97.09%

2 years: 87.13%
CI 81.67 – 92.94%

3 years: 84.60%
CI 76.94 – 93.03%

4 years: 77.75%
CI 67.11 – 90.08%

5 years: 73.88%
CI 61.85 – 88.26%

Overall Survival (%)

Time, mo

Hun Jao Tan D et al. UNOS Down staging criteria for liver transplantation of hepatocellular carcinoma: systematic review and meta-análisis of 25 studies. Clin Gastroenterol Hepatol 2023: 1475-84

Conclusiones

■ Criterios UNOS-DS:

– *Down staging 83% de los pacientes.*

– *Probabilidad de trasplante: 49%*

– *Excelentes tasas de supervivencia post-trasplante si se consigue down-staging*

– *SE REQUIEREN ESTUDIOS PROSPECTIVOS*

Hun Jao Tan D et al. UNOS Down staging criteria for liver transplantation of hepatocellular carcinoma: systematic review and meta-análisis of 25 studies.
Clin Gastroenterol Hepatol 2023: 1475-84

Downstaging hepatocellular carcinoma before liver transplantation: A multicenter analysis of the "all-comers" protocol in the Multicenter Evaluation of Reduction in Tumor Size before Liver Transplantation (MERITS-LT) consortium

Brahma Natarajan [1] iD, Parissa Tabrizian [2] iD, Maarouf Hoteit [3] iD, Catherine Frenette [4] iD, Neehar Parikh [5] iD, Tara Ghaziani [6] iD, Renu Dhanasekaran [6] iD, Jennifer Guy [7] iD, Amy Shui [1] iD, Sander Florman [2] iD, Francis Y. Yao [1] iD, Neil Mehta [1,*] iD

All-comers and united network for organ sharing (UNOS) downstaging (DS) protocols.

UNOS-DS protocol N=229	All-Comers protocol N=82

Inclusion criteria

Hepatocellular carcinoma (HCC) exceeds Milan criteria but meets one of the following:

1. Single lesions 5.1 to 8 cm

2. 2 to 3 lesions each $\leq$ 5 cm with the sum of the maximal tumor diameters $\leq$ 8 cm

3. 4 to 5 lesions each $\leq$ 3 cm with the sum of the maximal tumor diameters $\leq$ 8 cm

HCC exceeding UNOS-DS protocol by any of the following:

1. HCC tumor number

2. HCC tumor size

3. Total HCC tumor diameter

Criteria for successful downstaging

Residual tumor size and diameter within Milan criteria (1 lesion $\leq$ 5 cm, 2 to 3 lesions $\leq$ 3 cm)

Criteria for DS failure and exclusion from a liver transplant

1. Tumor progression beyond inclusion/eligibility criteria above 2. Extrahepatic disease and vascular disease on cross-sectional imaging

3. Per current UNOS policy, when alpha-fetoprotein (AFP) $\geq$ 1000, then transplant cannot be performed unless AFP declines to $<$ 500 ng/mL with LRT

Transplant timing

Minimal observation period of 3 mo between successful DS and transplant demonstrating disease stability

Minimal observation period of 6 mo between DS and transplant demonstrating disease stability and approval by review board
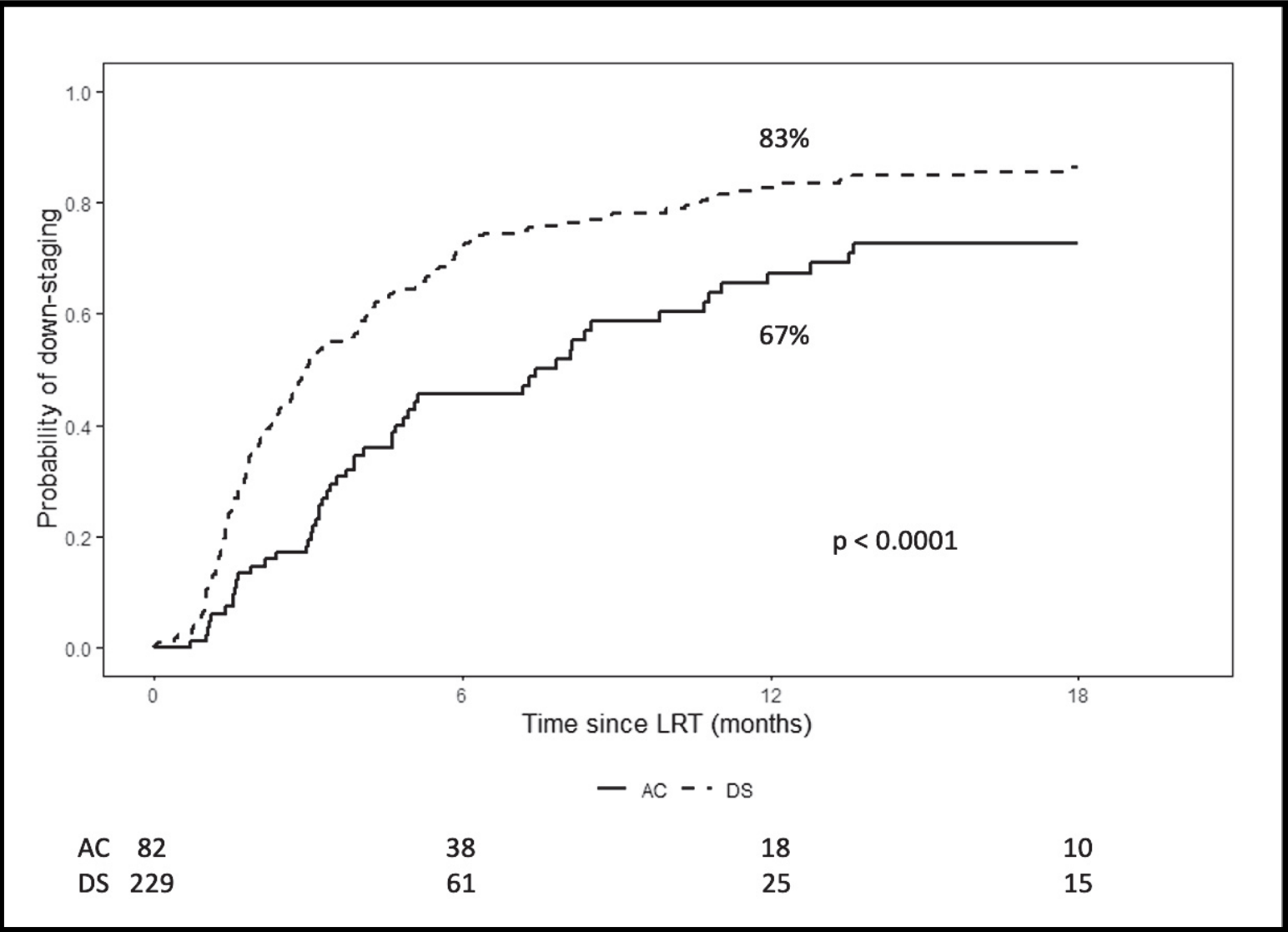
Natarajan B et al. Downstaging hepatocellular carcinoma before liver transplantation: A multicenter análisis of the "all-comers" protocol in the Multicenter Evaluation of Reduction in Tumor Size before Liver Transplantation (MERITS-LT consortium. Am J Transplantation 2023: 1771-80
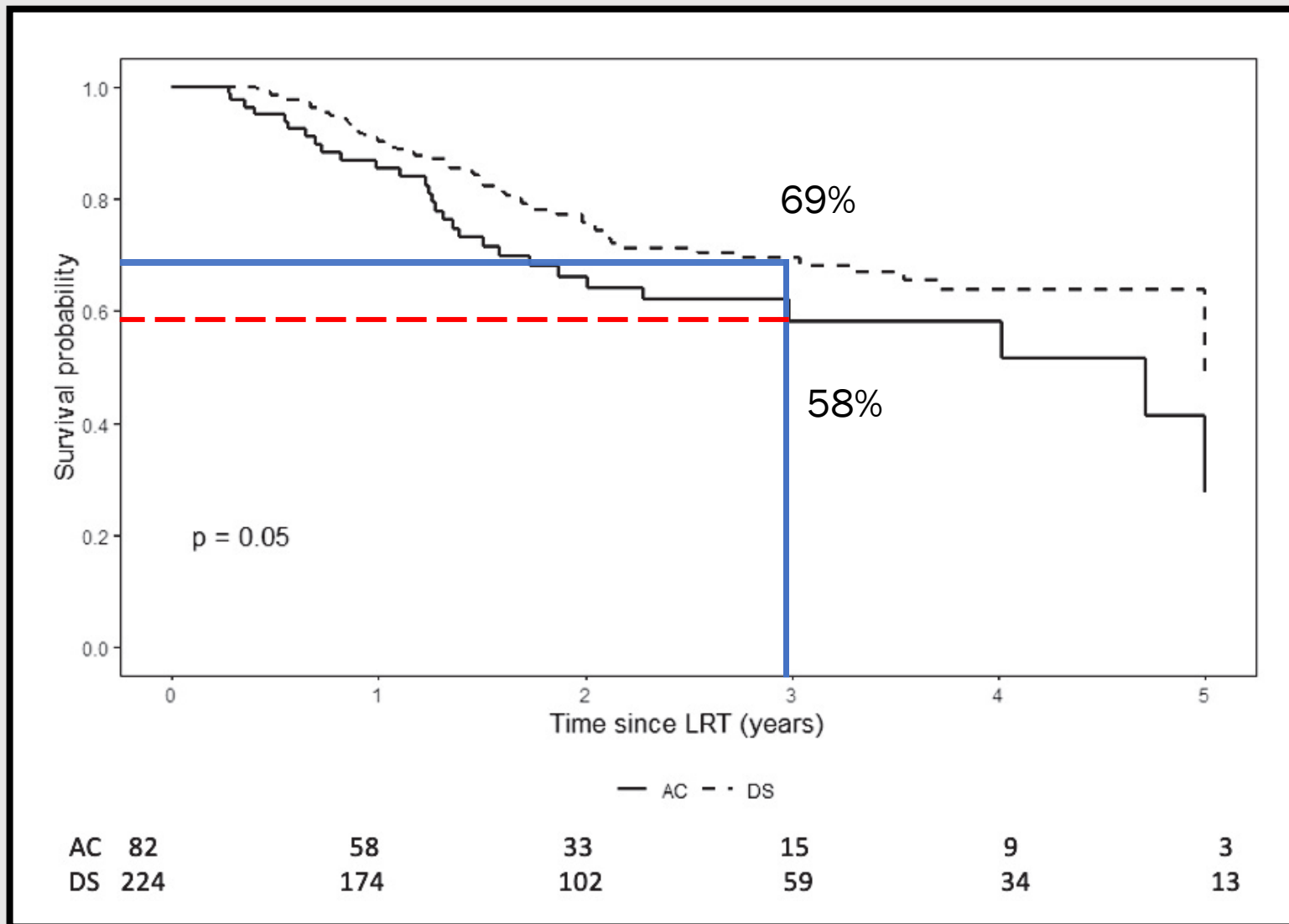
Natarajan B et al. Downstaging hepatocellular carcinoma before liver transplantation: A multicenter análisis of the "all-comers" protocol in the Multicenter Evaluation of Reduction in Tumor Size before Liver Transplantation (MERITS-LT consortium. Am J Transplantation 2023: 1771-80

"All-comers"

Natarajan B et al. Downstaging hepatocellular carcinoma before liver transplantation: A multicenter análisis of the "all-comers" protocol in the Multicenter Evaluation of Reduction in Tumor Size before Liver Transplantation (MERITS-LT consortium. Am J Transplantation 2023: 1771-80

Seguimiento post-trasplante

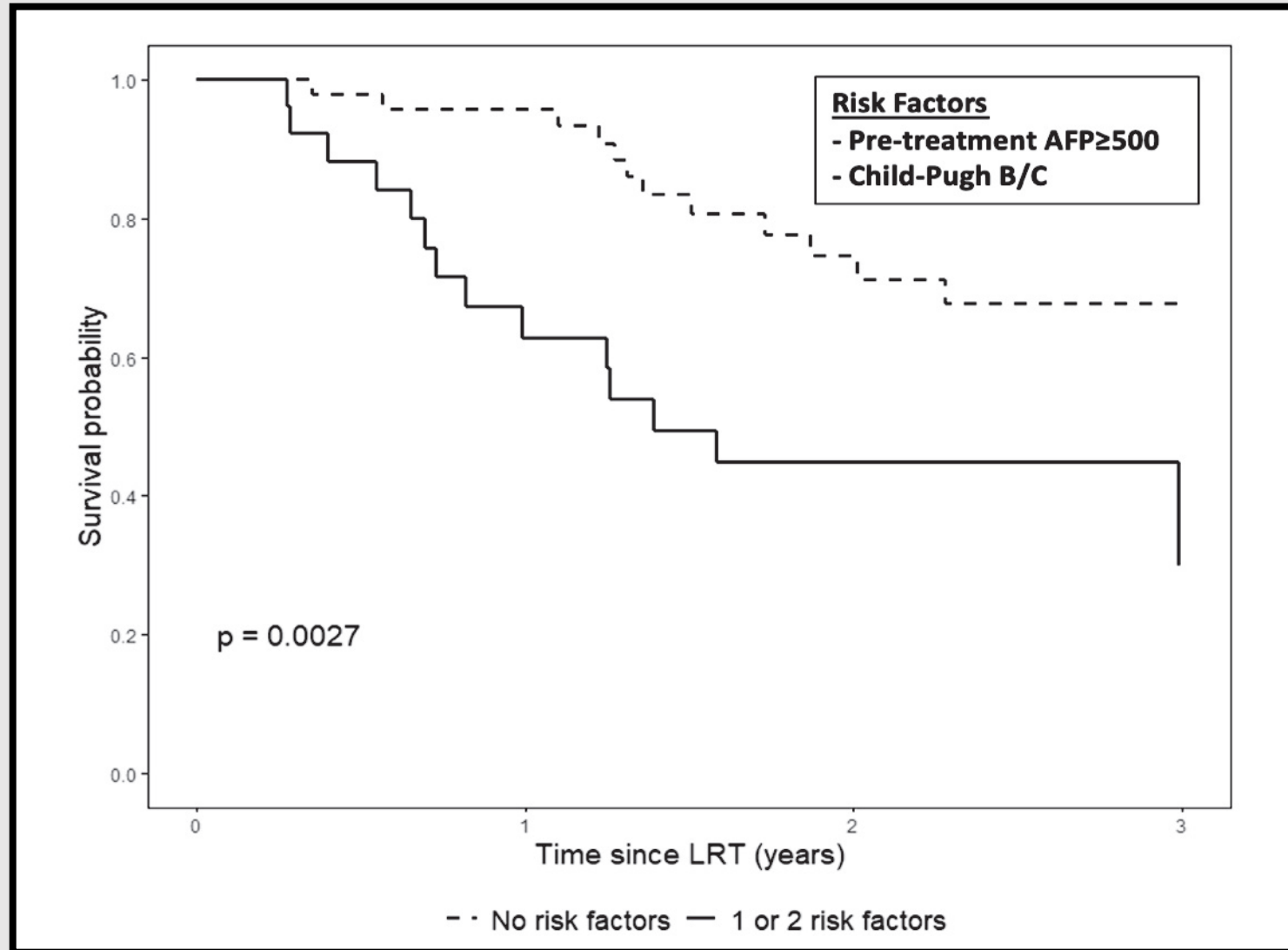|	UNOS	ALL-COMERS	P
Probabilidad trasplante a 1 año	9.8%	13%	0.1
Probabilidad trasplante a 3 años	73.6%	42.2%	0.1
Supervivencia a 3 años	80.6%	90.9%	0.66
Recurrencia tumoral	8.2%	5%	>0.99

Natarajan B et al. Downstaging hepatocellular carcinoma before liver transplantation: A multicenter análisis of the "all-comers" protocol in the Multicenter Evaluation of Reduction in Tumor Size before Liver Transplantation (MERITS-LT consortium. Am J Transplantation 2023: 1771-80

1. Should all Eligible Patients Be Transplanted After Successful Downstaging?

Currently, given the scarcity of graft resources and competing indications for liver transplantation, patients beyond conventional pre-defined criteria are often not transplanted. Despite achieving successful downstaging to within accepted criteria, patients are not always offered the option of liver transplantation. The question remains whether they should.

Recommendation 1.1: All HCC patients achieving a successful downstaging to pre-defined transplantable criteria should be considered for liver transplantation as the benefit in terms of both recurrence-free survival and overall survival of this approach is significantly higher than any other non-transplant strategy.

2. Should all Patients Outside Transplant Criteria (All Comers) Be Considered for Downstaging?

Many patients with HCC are diagnosed at an advanced stage, falling beyond accepted transplant criteria. However, if the overall tumor burden were to decrease, they could potentially reach a stage for which liver transplantation is usually indicated. Whether this should be actively pursued, treating patients with the goal of lowering their tumor burden so that liver transplantation might become possible, regardless of their initial stage, is still up for debate.

Recommendation 2.1: All patients beyond transplant criteria, without extra-hepatic disease or macrovascular invasion, should be considered for downstaging as long as potentially eligible for transplantation, as the original HCC state has not demonstrated to significantly hamper post-transplant survival.

Claasen M et al. ESOT consensus report on downstaging, bridging and immunotherapy in liver transplantation for hepatocellular carcinoma. Transplant Int 2023: Article 11648

RECHAZO

Acute rejection after liver transplantation with machine perfusion versus static cold storage: A systematic review and meta-analysis

Marianna Maspero[1,2] | Khaled Ali[1] | Beatrice Cazzaniga[1] |
Sumeyye Yilmaz[1] | Roma Raj[1] | Qiang Liu[1] | Cristiano Quintini[1,3] |
Charles Miller[1] | Koji Hashimoto[1] | Robert L. Fairchild[4] |
Andrea Schlegel[5,6]

Study or Subgroup	Organ Perfusion Events	Total	Static Cold Storage Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
A 1.3.1 HOPE							
van Rijn 2021	9	78	16	78	32.9%	0.51 [0.21, 1.23]	
Czigany 2021	4	23	6	23	12.7%	0.60 [0.14, 2.48]	
Schlegel 2019	2	50	14	50	10.8%	0.11 [0.02, 0.50]	
Patrono 2019	4	25	6	50	13.8%	1.40 [0.36, 5.48]	
Dutkowski 2015	3	25	8	50	12.7%	0.72 [0.17, 2.97]	
Ravaioli 2020	1	10	4	30	4.8%	0.72 [0.07, 7.34]	
Subtotal (95% CI)		211		281	87.8%	0.54 [0.29, 1.01]	
Total events	23		54				

Heterogeneity: Tau² = 0.13; Chi² = 6.32, df = 5 (P = 0.28); I² = 21%
Test for overall effect: Z = 1.93 (P = 0.05)

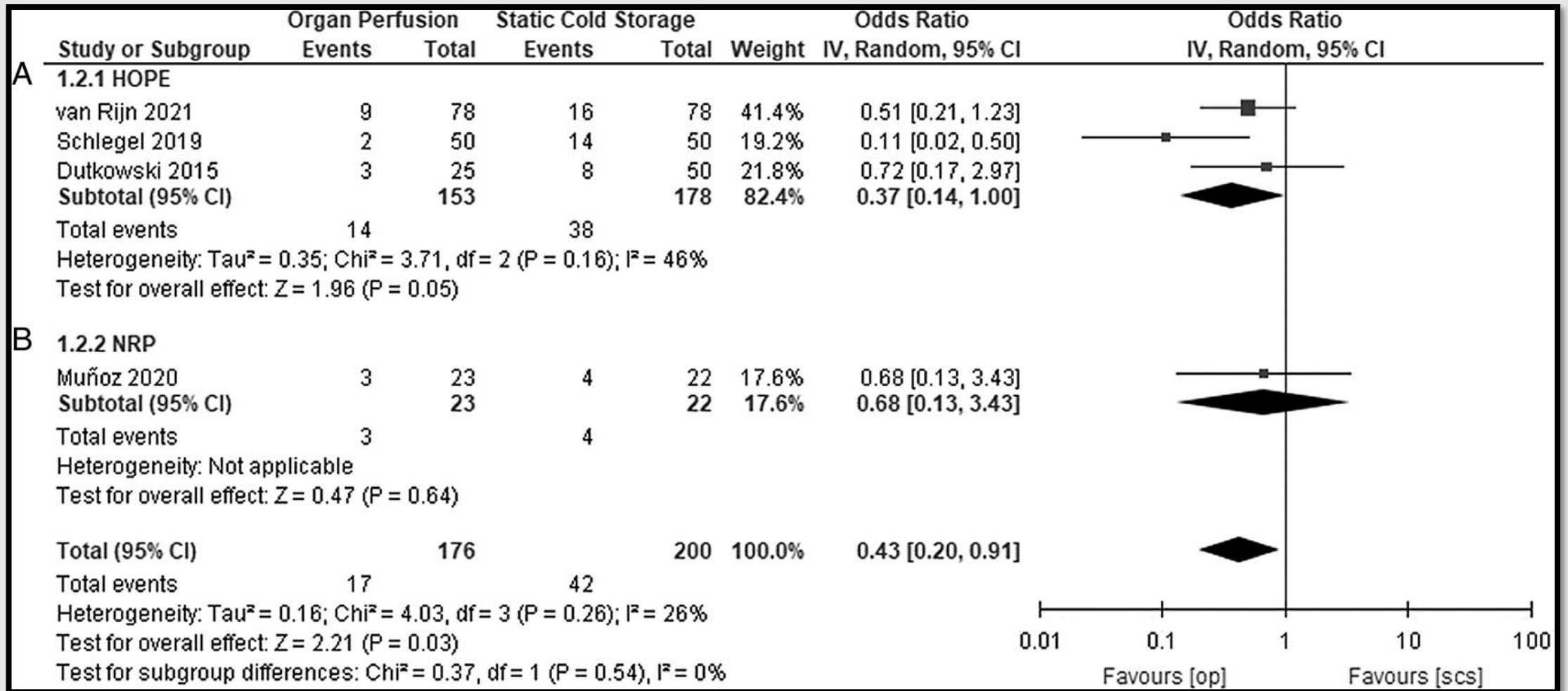|							
B 1.3.2 NMP							
Jassem 2019	0	12	1	17	2.4%	0.44 [0.02, 11.74]	
Subtotal (95% CI)		12		17	2.4%	0.44 [0.02, 11.74]	
Total events	0		1				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.49 (P = 0.62)

C 1.3.3 NRP							
Muñoz 2020	3	23	4	22	9.8%	0.68 [0.13, 3.43]	
Subtotal (95% CI)		23		22	9.8%	0.68 [0.13, 3.43]	
Total events	3		4				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.47 (P = 0.64)

Total (95% CI)		246		320	100.0%	0.55 [0.33, 0.91]	
Total events	26		59				

Heterogeneity: Tau² = 0.00; Chi² = 6.41, df = 7 (P = 0.49); I² = 0%
Test for overall effect: Z = 2.32 (P = 0.02)
Test for subgroup differences: Chi² = 0.08, df = 2 (P = 0.96), I² = 0%

0.01 0.1 1 10 100
Favours [op]   Favours [control]

11%   18%

Donantes en asistolia

Maspero M et al. *Acute rejection after liver transplantation with machine perfusion versus static cold storage: A systematic review and meta-análisis. Hepatology 2023: 835-46*

Muchas gracias