




	Outcome	D1	D2	D3	D4	D5	Overall
de-Madaria et al. (2017)	MSAP	+	+	+	+	+	+
Lee et al. (2021)	MSAP	+	+	+	+	+	+
Kayhan et al. (2021)	MSAP	+	!	+	!	!	!
Choosakul et al. (2018)	mortality	+	+	+	+	+	+
de-Madaria et al. (2017)	mortality	+	+	+	+	+	+
Karki et al. (2022)	mortality	+	+	+	+	+	+
Lee et al. (2021)	mortality	+	+	+	+	+	+
Wu et al. (2011)	mortality	+	+	+	+	+	+
Choosakul et al. (2018)	LoH	+	+	+	+	+	+
de-Madaria et al. (2017)	LoH	+	+	+	+	+	+
Karki et al. (2022)	LoH	+	+	+	+	+	+
Lee et al. (2021)	LoH	+	+	+	+	+	+
Wu et al. (2011)	LoH	+	+	+	+	+	+
Farrell et al. (2022)	LoH	+	+	+	+	+	+
Kayhan et al. (2021)	LoH	+	!	+	+	!	!
Reddy/vasudevan et al. (2014)	LoH	!	-	!	+	!	-
de-Madaria et al. (2017)	ICU	+	+	+	+	+	+
Lee et al. (2021)	ICU	+	+	+	+	+	+
Wu et al. (2011)	ICU	+	+	+	+	+	+
Reddy/Vasudevan et al. (2014)	ICU	!	-	+	!	!	-
Choosakul et al. (2018)	OF	+	+	+	+	+	+
de-Madaria et al. (2017)	OF	+	+	+	+	+	+
Lee et al. (2021)	OF	+	+	+	+	+	+
Wu et al. (2011)	OF	+	+	+	!	+	!
Kayhan et al. (2021)	OF	+	!	+	+	!	!
Reddy/Vasudevan et al. (2014)	OF	!	-	+	!	!	-
Choosakul et al. (2018)	Local compl.	+	+	+	+	+	+
Karki et al. (2022)	Local compl.	+	+	+	+	+	+
Lee et al. (2021)	Local compl.	+	+	+	+	+	+
Kayhan et al. (2021)	Local compl.	+	!	+	+	!	!
Choosakul et al. (2018)	Necrosis	+	+	+	+	+	+
de-Madaria et al. (2017)	Necrosis	+	+	+	+	+	+
Karki et al. (2022)	Necrosis	+	+	+	+	+	+
Wu et al. (2011)	Necrosis	+	+	+	+	+	+
Farrell et al. (2022)	Necrosis	+	+	+	+	+	+
Kayhan et al. (2021)	Necrosis	+	!	+	+	!	!
Reddy/vasudevan et al. (2014)	Necrosis	!	-	!	+	!	-
Choosakul et al. (2018)	Pseudocyst	+	+	+	+	+	+
Karki et al. (2022)	Pseudocyst	+	+	+	+	+	+
Farrell et al. (2022)	Pseudocyst	+	+	+	+	+	+
Choosakul et al. (2018)	CRP	+	+	+	-	+	-
de-Madaria et al. (2017)	CRP	+	+	+	+	+	+
Wu et al. (2011)	CRP	+	+	+	+	!	!
Farrell et al. (2022)	CRP	+	+	+	+	+	+
Kayhan et al. (2021)	CRP	+	!	+	+	!	!
Choosakul et al. (2018)	SIRS	+	+	+	+	+	+
de-Madaria et al. (2017)	SIRS	+	+	+	+	+	+
Karki et al. (2022)	SIRS	+	+	+	+	+	+

 Low risk
 Some concerns
 High risk

D1 Randomisation process

D2 Deviations from the intended interventions

Figure S1. Results of risk of bias assessment with RoB2 tool. MSAP: moderate-to-severe acute pancreatitis; LoH: length of hospitalization; ICU: intensive care unite admission; OF: organ failure; CRP: C-reactive protein; SIRS: systemic inflammatory response syndrome.

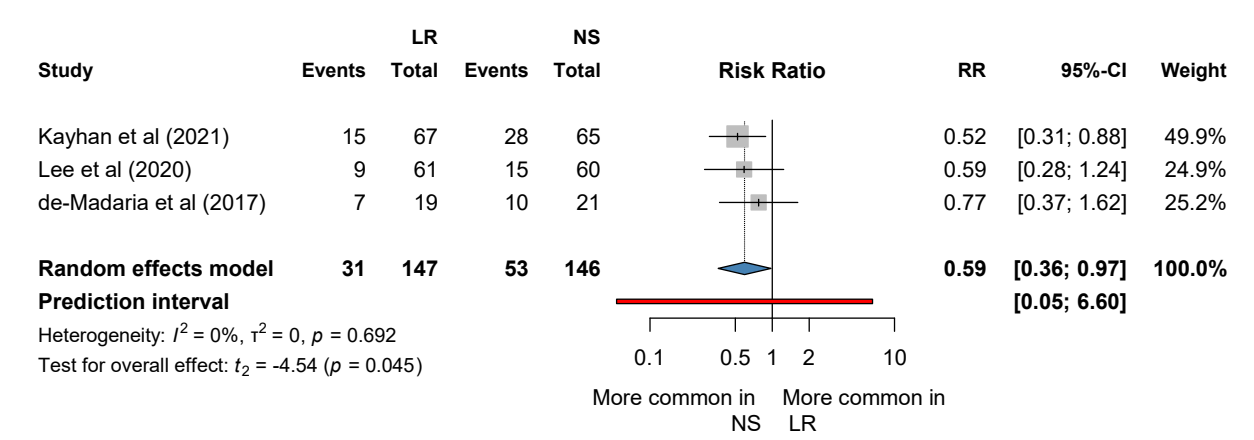


Figure S2. Moderate-to-severe acute pancreatitis. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

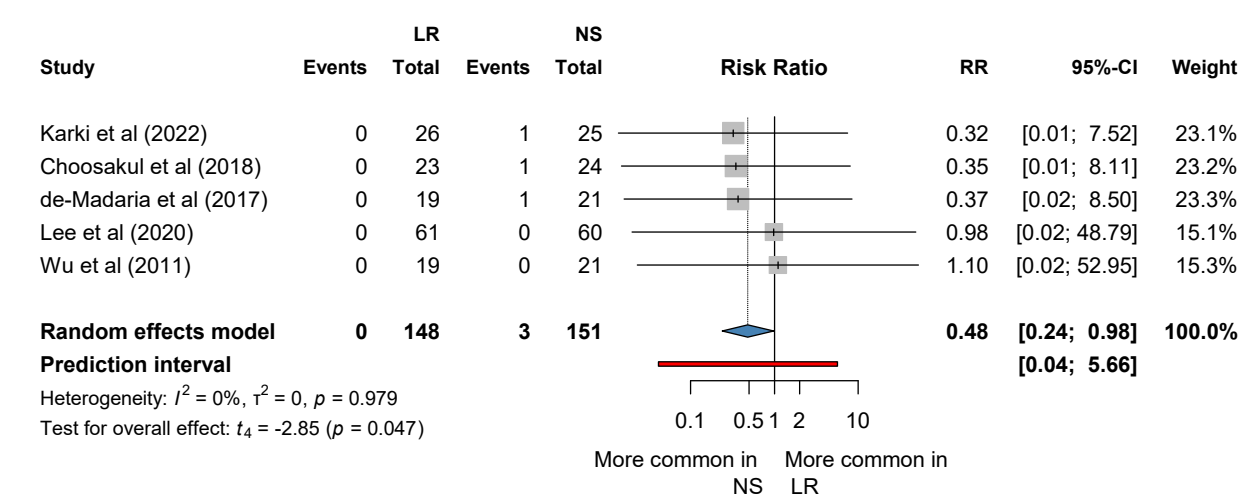


Figure S3. In-hospital mortality. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

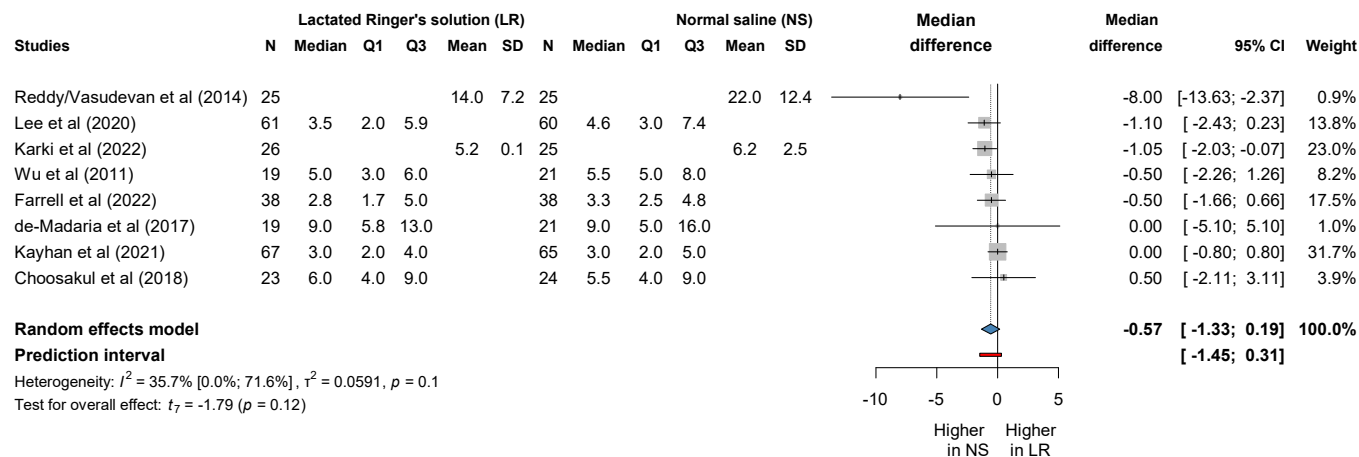


Figure S4. Length of hospital stay. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

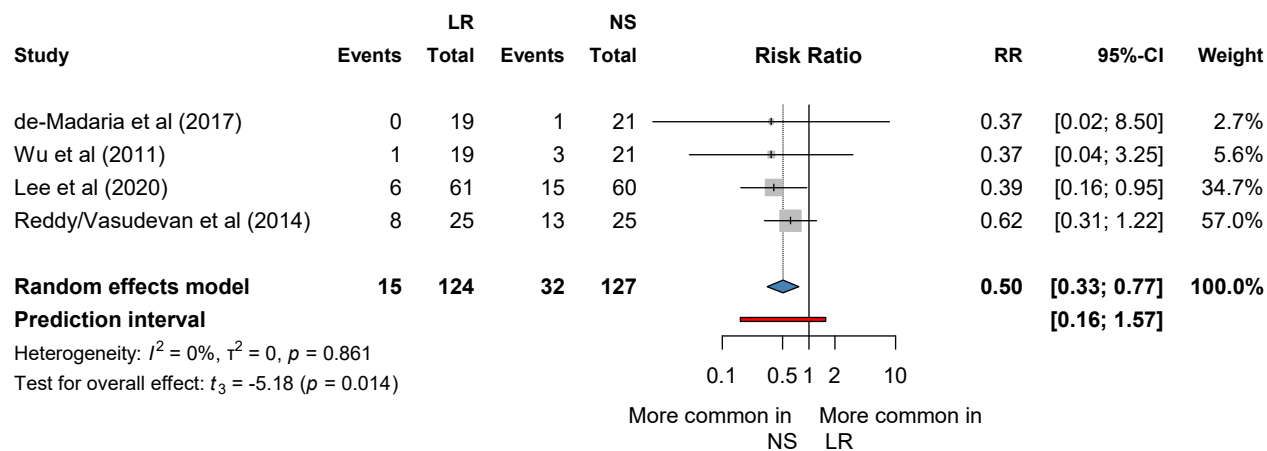


Figure S5. Need for intensive care. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

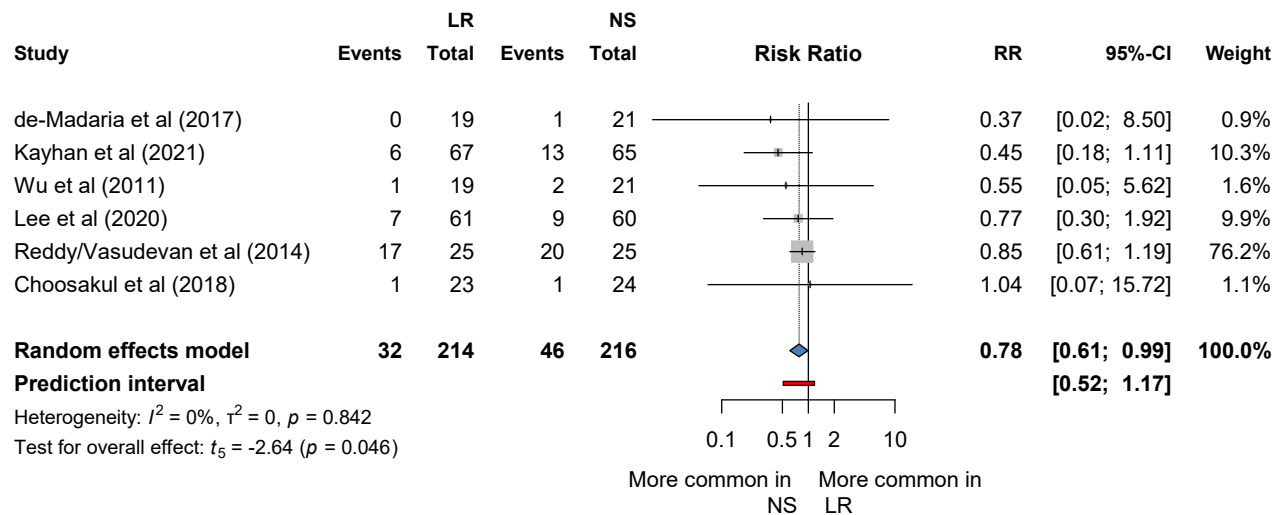


Figure S6. Organ failure. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

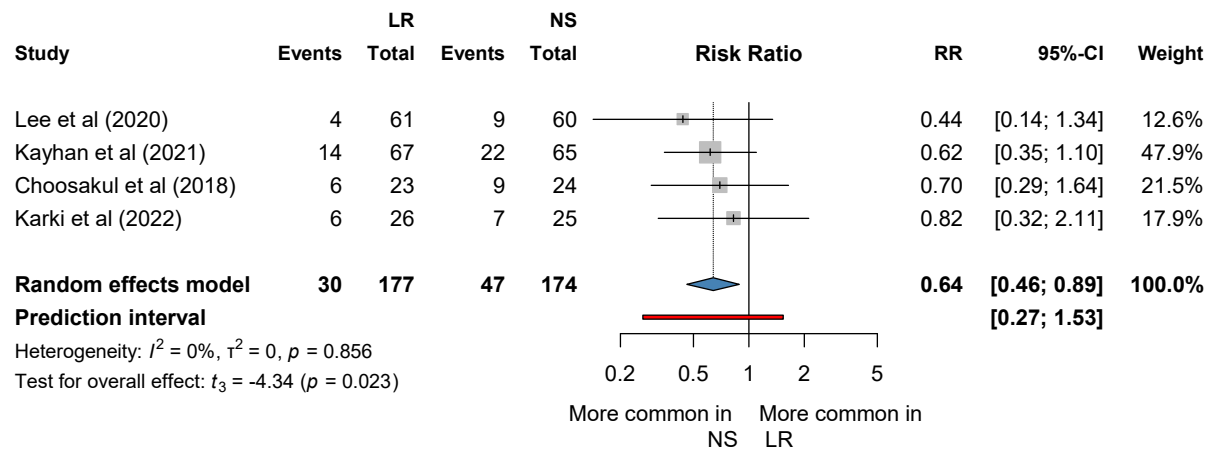


Figure S7. Local complications. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

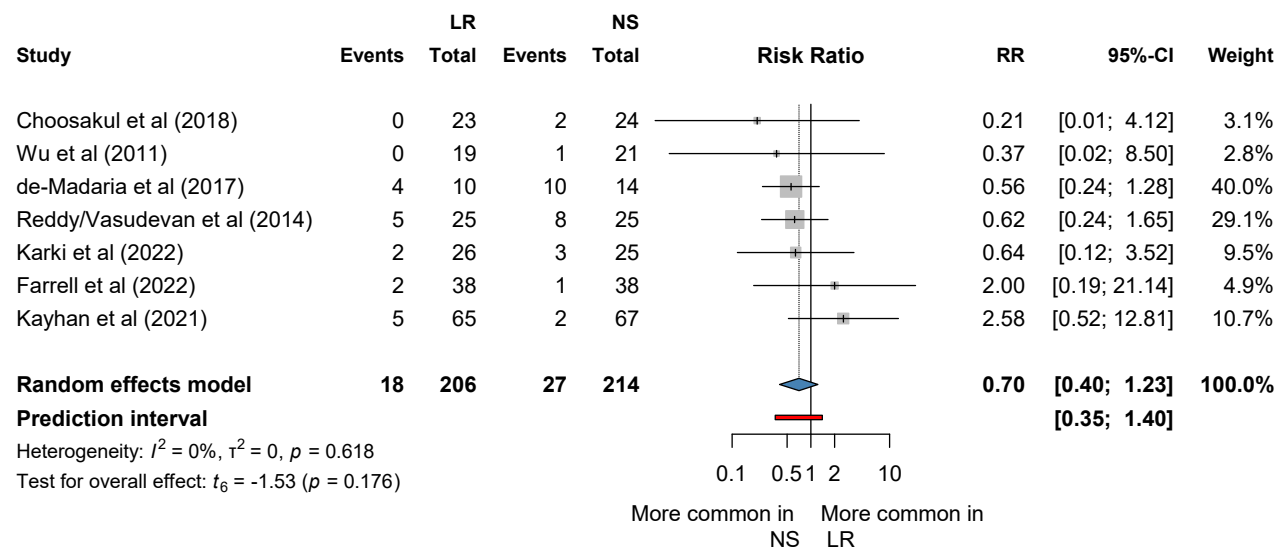


Figure S8. Necrosis. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

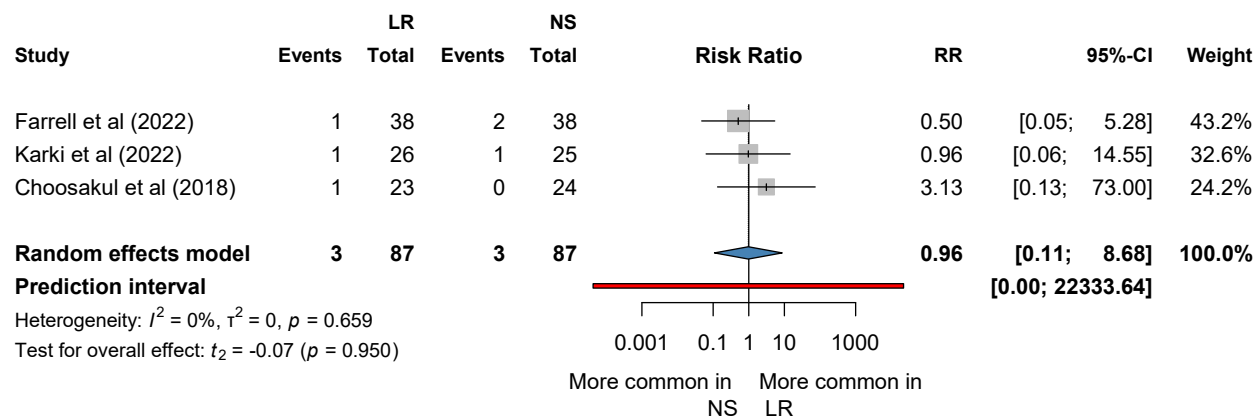


Figure S9. Pseudocyst. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

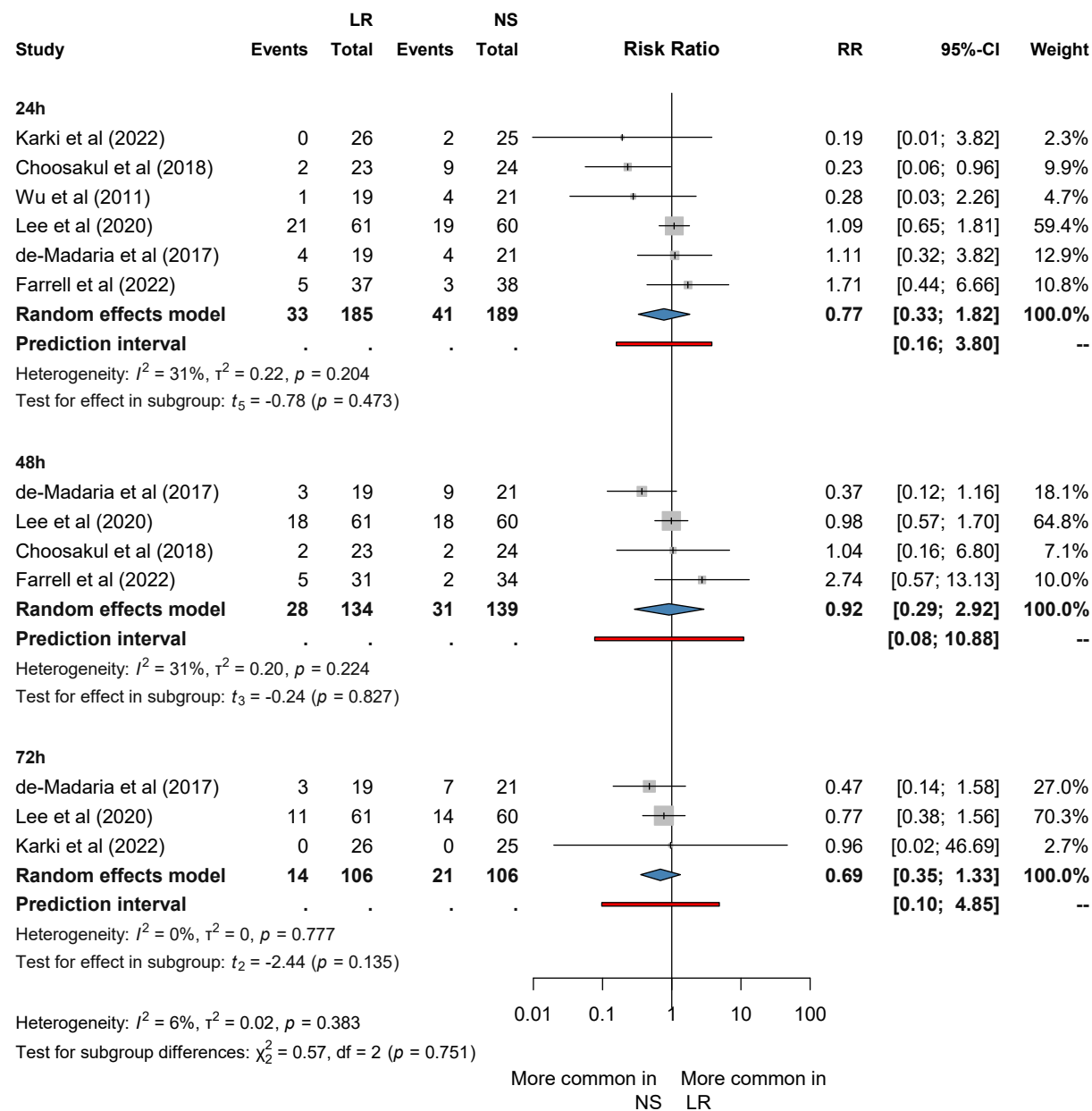


Figure S10. Systemic inflammatory response syndrome. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

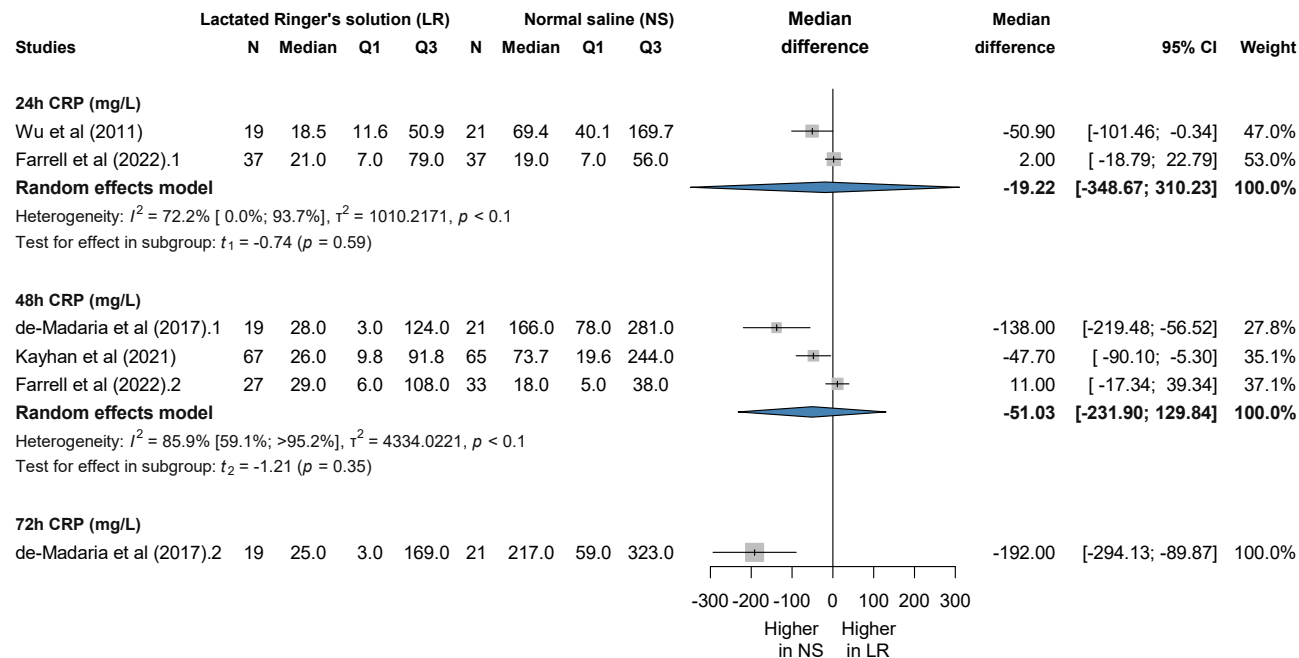


Figure S11. C-reactive protein levels (mg/dL) at 24, 48 and 72 h after randomization. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

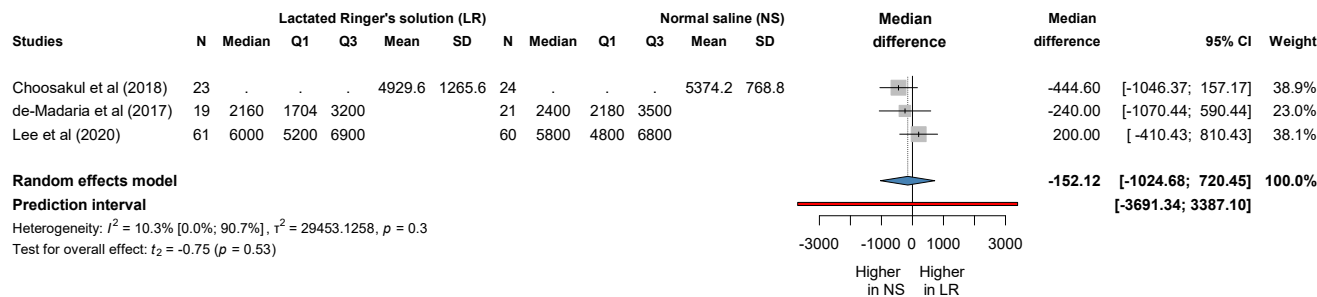


Figure S12. Amount of fluid administered in the first 24 h after randomization. Statistical heterogeneity across trials was assessed by means of the Cochrane Q test and the I^2 values.

6	RCT	very serious ^c	not serious	not serious	not serious	none	32/214 (15.0%)	46/216 (21.3%)	RR 0.78 (0.61 to 0.99)	47 fewer per 1 000 (from 83 fewer to 2 fewer)	⊕⊕○ ○ Low	critical
Local complications												
4	RCT	not serious ^g	not serious	not serious	serious ^h	none	30/177 (16.9%)	47/174 (27.0%)	RR 0.64 (0.46 to 0.89)	97 fewer per 1 000 (from 146 fewer to 30 fewer)	⊕⊕⊕ ○ Moderate	critical
Necrosis												
7	RCT	very serious ⁱ	not serious	not serious	not serious	none	16/206 (7.8%)	28/214 (13.1%)	RR 0.70 (0.40 to 1.23)	39 fewer per 1 000 (from 79 fewer to 30 more)	⊕⊕○ ○ Low	critical
Pseudocyst												
3	RCT	not serious ⁱ	not serious	not serious	very serious ^f	none	3/87 (3.4%)	3/87 (3.4%)	RR 0.96 (0.11 to 8.68)	1 fewer per 1 000 (from 31 fewer to 265 more)	⊕⊕○ ○ Low	important but not critical

a. In our cohort, moderate plus severe cases were 29%; calculating with a 50% reduction, OIS is 121 per group.

b. Mortality rate is under 5%, therefore, considering OIS more than 500.

c. One high risk and one some concerns study.

d. Heterogeneity originates from Reddy (has a small sample size, not influential).

e. Reddy/ Vasudevan with high risk of bias produced most patients with event.

f. Considering the number of patients with event, total number of patients in analysis does not reach OIS.

- g. Half of the data comes from study with some concerns.
- h. A 13% incidence of local compl., OIS is not reached.
- i. Proportion of studies carrying high risk of bias or some concern is high.

Table S2. References of the included studies (as per the reference list of the manuscript).

Ref- er- ence Num- ber	Reference
17.	Wu, B.U.; Hwang, J.Q.; Gardner, T.H.; Repas, K.; Delee, R.; Yu, S.; Smith, B.; Banks, P.A.; Conwell, D.L. Lactated Ringer's Solution Reduces Systemic Inflammation Compared with Saline in Patients with Acute Pancreatitis. <i>Clin. Gastroenterol. Hepatol.</i> 2011, 9, P710–P717.e1. https://doi.org/10.1016/j.cgh.2011.04.026 .
30.	Karki, B.; Thapa, S.; Khadka, D.; Karki, S.; Shrestha, R.; Khanal, A.; Shrestha, R.; Paudel, B.N. Intravenous Ringers lactate versus normal saline for predominantly mild acute pancreatitis in a Nepalese Tertiary Hospital. <i>PLoS ONE</i> 2022, 17, e0263221. https://doi.org/10.1371/journal.pone.0263221 .
31.	Kayhan, S.; Akyol, B.S.; Ergul, M.; Baysan, C. The effect of type of fluid on disease severity in acute pancreatitis treatment. <i>Eur. Rev. Med. Pharmacol. Sci.</i> 2021, 25, 7460–7467.
42.	Reddy, Y.R.; Talukder, S.; Yadav, T.D.; Siddappa, P.K.; Kochhar, R. Effect of intravenous fluid resuscitation on inflammatory markers of acute pancreatitis and its clinical outcome. <i>United Eur. Gastroenterol. J.</i> 2014, 2, 132–135. https://doi.org/10.1177/2050640614548980 .
43.	Choosakul, S.; Harinwan, K.; Chirapongsathorn, S.; Opuchar, K.; Sanpajit, T.; Piyanirun, W.; Puttapitakpong, C. Comparison of normal saline versus Lactated Ringer's solution for fluid resuscitation in patients with mild acute pancreatitis, A randomized controlled trial. <i>Pancreatology</i> 2018, 18, 507–512. https://doi.org/10.1016/j.pan.2018.04.016 .
44.	de-Madaria, E.; Herrera-Marante, I.; Gonzalez-Camacho, V.; Bonjoch, L.; Quesada-Vazquez, N.; Almenta-Saa-vedra, I.; Miralles-Macia, C.; Acevedo-Piedra, N.G.; Roger-Ibanez, M.; Sanchez-Marin, C.; et al. Fluid resuscitation with lactated Ringer's solution vs normal saline in acute pancreatitis: A triple-blind, randomized, controlled trial. <i>United Eur. Gastroenterol. J.</i> 2018, 6, 63–72. https://doi.org/10.1177/2050640617707864 .
45.	Lee, A.; Ko, C.; Buitrago, C.; Hiramoto, B.; Hilson, L.; Buxbaum, J.; Grp, N.-L.S. Lactated Ringers vs Normal Saline Resuscitation for Mild Acute Pancreatitis: A Randomized Trial. <i>Gastroenterology</i> 2021, 160, 955. https://doi.org/10.1053/j.gastro.2020.10.044 .
46.	Vasu De Van, P.; Verma, G.R.; Bhalla, A.; Kalra, N.; Basha, J.; Appasani, S.; Chhabra, P.; Manrai, M.; Sinha, S.K.; Singh, K.; et al. Does the type of fluid used in resuscitation matter in the clinical course of acute pancreatitis? <i>Indian J. Gastroenterol.</i> 2013, 32, A110. https://doi.org/10.1007/s12664-013-0417-z .
47.	Farrell, P.R.; DesPain, A.W.; Farmer, P.F.; Farrell, L.M.; Greenfield, B.; Rogers, M.; Hornung, L.; Kim, E.; Pearman, R.; Neway, B.; et al. Mitigating the Inflammatory Response in Acute Pancreatitis; A Randomized Clinical Control Trial Comparing the Effects of Lactated Ringers and Normal Saline. <i>Gastroenterology</i> 2022, 162, S140–S141.