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SCIENTIFIC REVIEW

Outcomes of Laparoscopic Splenectomy for Treatment of Splenomegaly: A Systematic Review and Meta-analysis

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Abstract

Objectives To review the evidence regarding the outcomes of laparoscopic techniques in cases of splenomegaly.
Background Endoscopic approaches such as laparoscopic, hand-assisted laparoscopic, and robotic surgery are commonly used for splenectomy, but the advantages in cases of splenomegaly are controversial.
Review methods We conducted a systematic review using PRISMA guidelines. PubMed/MEDLINE, ScienceDirect, Scopus, Cochrane Library, and Web of Science were searched up to February 2020.
Results Nineteen studies were included for meta-analysis. In relation to laparoscopic splenectomy (LS) versus open splenectomy (OS), 12 studies revealed a significant reduction in length of hospital stay (LOS) of 3.3 days ($p = <0.01$) in the LS subgroup. Operative time was higher by 44.4 min ($p < 0.01$) in the LS group. Blood loss was higher in OS 146.2 cc ($p = <0.01$). No differences were found regarding morbimortality. The global conversion rate was 19.56%. Five studies compared LS and hand-assisted laparosocpic splenectomy (HALS), but no differences were observed in LOS, blood loss, or complications. HALS had a significantly reduced conversion rate ($p < 0.01$). In two studies that compared HALS and OS ($n = 66$), HALS showed a decrease in LOS of 4.5 days ($p < 0.01$) and increase of 44 min in operative time ($p < 0.01$), while OS had a significantly higher blood loss of 448 cc ($p = 0.01$). No differences were found in the complication rate.
Conclusion LS is a safe approach for splenomegaly, with clear clinical benefits. HALS has a lower conversion rate. Higher-quality confirmatory trials with standardized splenomegaly grading are needed before definitive recommendations can be provided.
Prospero registration number: CRD42019125251.

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Introduction

The laparoscopic approach is considered the gold standard surgical technique for diseases requiring removal of the spleen [1, 2]. Since the first laparoscopic splenectomy (LS) was performed by Delaitre et al. [3] in 1991, laparoscopy has proven to be especially useful for surgical treatment of diseases associated with a normal-sized or slightly enlarged spleen, but some diseases requiring splenectomy are associated with a marked increase in the organ's volume. Splenomegaly entails a significant technical difficulty due to the complex maneuvers involved with potential intraoperative complications and a high conversion rate.

The definition of splenomegaly varies. Some authors have categorized spleen weights below 600 g as "non-massive," weights between 600 and 1600 g and between 17 and 22 cm in length as "massive, and weights over 1600 g or 22 cm as "supramassive" [4, 5].

Splenomegaly was initially considered a contraindication for a minimal invasive approach. In a series of 108 patients, Patel et al. reported that spleen weight was the most powerful predictor of morbidity during LS [6]. In 1999, Targarona et al. found that the morbidity rate after LS was higher for patients with spleens weighing more than 400 g, that LS in spleen weight exceeding 1 kg had a 23% conversion rate, and that all spleens over 3.2 kg required conversion. These findings questioned the potential advantages of LS for splenomegaly [4]. According to the clinical practice guidelines of the European Association for Endoscopic Surgery (EAES), LS is the standard of care in children and in adults, but its recommendation in patients with splenomegaly is still under discussion [7]. Nevertheless, with the implementation of new technological devices and increasing experience, recent trials have shown that LS can be performed safely in enlarged spleens [4, 8]. We conducted the present study to analyze and clarify the best evidence in relation to the minimal invasive approach in splenomegaly and to evaluate relevant clinical outcomes. To our knowledge, this is the first meta-analysis to compare endoscopic techniques in the splenomegaly setting.

Objective

The objective was to systematically evaluate the evidence and the potential advantages of laparoscopy splenectomy (LS), hand-assisted laparoscopic splenectomy (HALS), and robotic splenectomy (RS) as the approach for treatment of splenomegaly in comparison with open splenectomy (OS). We also compared these three minimally invasive techniques.

Methods

The methods of analysis and inclusion criteria were specified in advance (Prospero registration number CRD42019125251). Studies were searched in PubMed/MEDLINE, ScienceDirect, Scopus, Cochrane Library, and Web of Science from the inception of LS in 1992 to February 2020 to identify potential eligible studies in which the primary objective was to describe efficacy, safety, and complications. Searches used the following Medical Subject Headings (MeSH) terms in combination with Boolean operators (AND, OR, NOT): "laparoscopy" [MeSH Terms] OR "minimal invasive" [All Fields] OR "hand assisted" [All Fields] OR "laparoscop*" [All Fields] OR "robotic surgical procedures" [All Fields] OR "robot*" [All Fields] OR "Vinci" [All Fields] OR "hand" [MeSH Terms] AND "splenectomy" [MeSH Terms] OR "splenectomy" [All Fields] OR "splenectomies" [All Fields] OR "splenomegalies" [All Fields] OR "splenomegaly" [MeSH Terms] OR "splenomegaly" [All Fields] NOT "paediatrics" [All Fields] OR "pediatrics" [MeSH Terms] OR "pediatrics" [All Fields] OR "paediatric" [All Fields] OR "pediatric" [All Fields] OR "animals" [MeSH Terms:noexp] OR "animals" [All Fields] OR "injuries" [MeSH Subheading] OR "injuries" [All Fields] OR "trauma" [All Fields] OR "wounds and injuries" [MeSH Terms] OR "wounds" [All Fields] AND "injuries" [All Fields] OR "wounds and injuries" [All Fields] OR "traumas" [All Fields].

The research was restricted to full-text studies published in English. Reference lists were also screened in order to find potential articles. Previous meta-analyses were identified and cross-checked to compare included studies.

The groups were constructed based on the surgical approach. The primary aim of the study was LS versus OS, LS versus HALS, HALS versus OS, RS versus LS, and RS versus OS or HALS as the secondary aims.

The review was carried out in accordance with the PRISMA statement [9]. Studies were considered eligible if they met the following criteria: (1) observational, retrospective, prospective, randomized, and non-randomized clinical studies that included laparoscopic, open, hand-assisted laparoscopic, or robotic splenectomy; (2) a clear defined comparator group; (3) data concerning (operative time, excess blood loss, length of hospital stay, conversion rate, morbidity, and mortality); and (4) grade of splenomegaly reported either by spleen weight or spleen size. Reviews, conference abstracts, editorials, and pediatrics journal were excluded. Studies that include patients <18 years were excluded and trauma as an indication for splenectomy. Studies that include merged information with splenomegaly and any other abdominal condition such as previous abdominal surgery were also excluded.

Data collection and outcome definition

Titles and abstracts were screened independently by two authors (R.R. and E.T). After screening for title and abstract, we assessed the full-text versions of each study for eligibility. Data on the study were extracted independently by two authors (R.R and E.T). Study characteristics included author, date of publication, study design, study period, and number of patients in each group. Patient

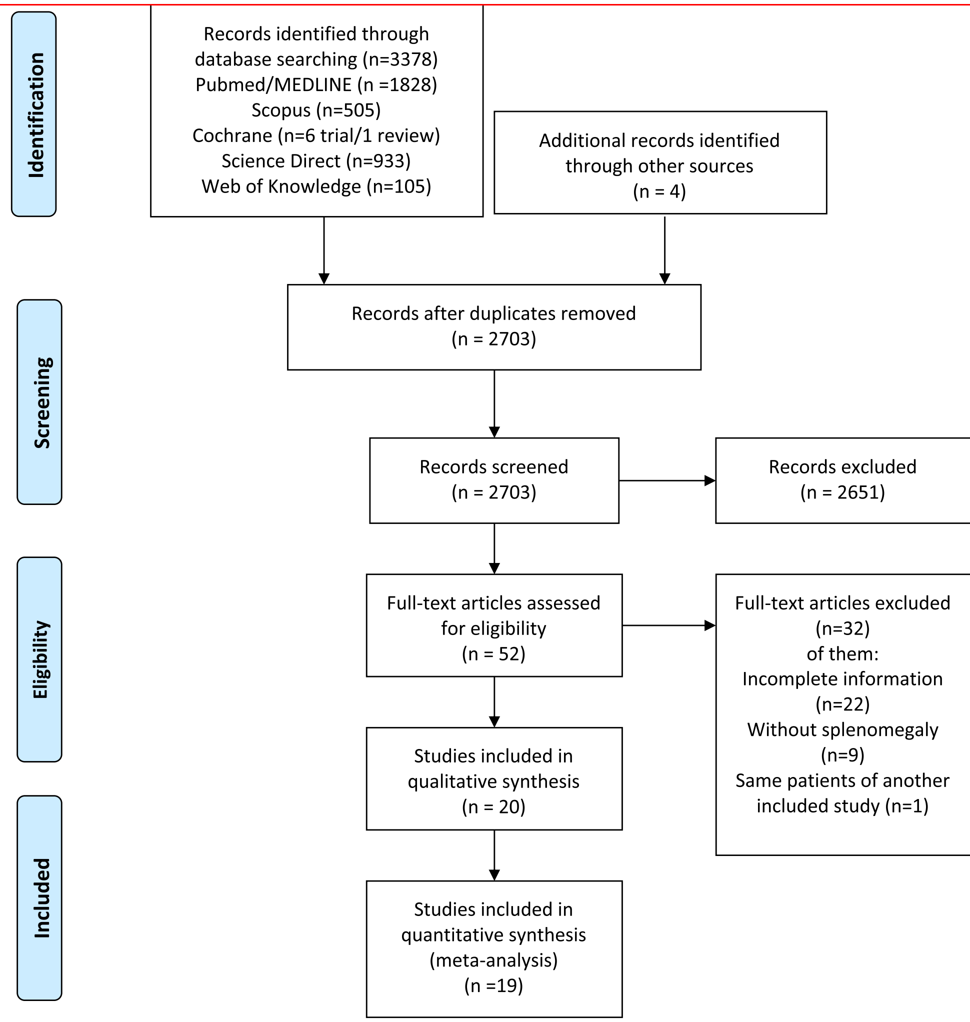

Fig. 1 PRISMA diagram detailing the study selection and exclusion process. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta- Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. https://doi.org/10.1371/journal.pmed1000097. For more information, visit https://www.prisma-statement.org

characteristics were age, sex, body mass index (BMI), malignant rate, spleen weight, and spleen size. Outcomes evaluated were length of hospital stay, excess blood loss, conversion rate, morbidity, and mortality. Disagreements between reviewers were resolved by consensus.

The authors Rosen M, Pietrabissa A, Zhong W, and Grahn S were contacted by e-mail in order to clarify information and decide whether or not to include their studies for the analysis.

Methodological quality of included studies

All studies were assessed for methodological quality using the Newcastle–Ottawa Scale (NOS) [10]. This scale evaluates the methodology quality in three domains: patient selection, comparability, and outcome, with the maximal grade being nine points. Studies with a score of 8 or higher were classified as high quality, 4–8 as moderate, and less than 4 as low. To evaluate the randomized control trial, we used the revised tool to assess risk of bias in randomized trials (RoB 2.0) [11].

Statistical analysis

Meta-analyses were conducted on each continuous and binary outcome. For each criterion, the heterogeneity between all studies was studied and measured. Statistical heterogeneity between the studies was assessed using the I^2 value and Chi-square test. If the I^2 was less than 50% or the p value was >0.05, heterogeneity was not taken into account, and a model with a fixed effect was used. If I^2 was >50% or if $p < 0.05$, the heterogeneity between studies

Table 1 Overview of the studies included

Author	N	Mean age	Gender M/F	BMI	Malignant %	Spleen weight	Spleen size	Operative time	Excess blood loss	Length of hospital stay	Conversion%	Complication%	Mortality %
A. Laparoscopic versus open splenectomy in splenomegaly													
Terrosou [12]	8	50 (21–60)	4 (50)	–	75	1762 ± 1150 (500–3680)	–	197 ± 65)110–300)	393 ± 239 (100–800)	6 ± 3 (4–12)	0	1 (12.5)	0
Laparoscopic													
Open	15	50 (31–64)	11 (73.33)	–	100	27,138 ± 1097 (800–3850)	–	110 ± 21 (85–150)	393 ± 239 (100–800)	9 ± 3 (6–14)	–	5 (33)	0
Targarona et al. [13]	21	58 (12)	9 (42.85)	–	80.95	1600 (586)	–	176 (56)	–	6 (3)	23	28	0
Laparoscopic													
Open	20	56 (12)	10 (50)	–	80	1973 (713)	–	111 (19)	–	12 (5)	–	55	0
Boody et al. [14]	11	64 (43–76)	10 (90.9)	–	–	2000 (1000–3530)	–	90 (45–225)	800 (20–5120)	6 (2–8)	6 (54.5)	2 (18.2 5)	1 (9.1)
Laparoscopic													
Open	18	67 (29–81)	10 (55.5)	–	–	2447.5 (1025–6000)	–	45 (25–85)	65 (0–1635)	7 (5–44)	–	2 (11.1)	0
Owera et al. [15]	15	63 (53–67)	10 (66.7%)	–	66.66	1300 (1000–3600)	–	175 (120–270)	–	2 (2–40)	6.6	2 (13.3)	0
Laparoscopic													
Open	13	53 (31–65)	4 (30.8%)	–	61.4	1100 (100–3800)	–	90 (70–120)	–	10 (6–20)	–	4 (30.76)	1 (7.7)
Feldman et al.[16]	18	64 (55–71)	6 (33.33)	25 (24–28)	77.77	1051 (833–1325)	20 (18–22)	135 (116–145)	350 (163–750)	3 (3–5)	6	7 (39)	0
Laparoscopic													
Open	11	52 (44–63)	8 (72.72)	26 (24–28)	72.72	1645 (940–2250)	20 (18–23)	100 (116–145)	375 (100–863)	6 (5–7)	–	6 (55)	0
Zhou et al. [17]	33	48.2 (14.8)	17 (51.51)	–	–	1450.8 (345.7)	22.5 (4.8)	219.9 (43.3)	163 (56.2)	7.5 (.17)	1 (3.03)	3 (9.1)	0
Laparoscopic													
Open	29	44.5 (13.0)	16 (55.17)	–	–	1554.6 (283.8)	21.5 (4.8)	182.3 (66.8)	420 (177.3)	10.1 (2.4)	–	10 (34.5)	0
Koshenkov et al. [5]	10	48	3 (30)	–	30	611 (277–1268)	19 (17–20)	160 (115–315)	425 (59–1500)	3 (1–6)	30	20	0
Massive laparoscopic													
Open	7	53	6 (85.71)	–	43	624 (470–1459)	17 (15–20)	140 (45–245)	500 (100–800)	6 (4–14)	–	43	0
Koshenkov et al. [5]	12	64	9 (75)	–	92	1808 (988–2681)	25 (24–30)	195 (120–350)	308 (150–1000)	1 (1–13)	25	17	0
Supramassive laparoscopic													
Open	14	61	7 (50)	–	79	1712 (660–5039)	28 (22–40)	105 (45–310)	400 (100–6000)	4.5 (2–7)	–	14	0
Wu et al. [18]	18	46.6 (10.6)	12 (66.6)	–	–	–	23.7 (4.8)	203.6 (48.3)	70.3 (36.9)	6.3 (1.3)	0	2 (11.1)	0
Laparoscopic													
Open	16	45.7 (7.9)	11 (68.75)	–	–	–	26.3 (3.7)	162.8 (56.9)	300 (254.2)	8.8 (1.9)	–	3 (18.75)	0
Bo et al. [19]	40	38.8 (15.6)	25 (62.5)	–	–	–	22.4 (3)	150 (30)	150 (110)	6.1 (2.2)	2 (5)	8 (20)	0
Laparoscopic													
Open	40	40.3 (17.2)	27 (67.5)	–	–	–	23.8 (3.7)	100 (30)	140 (50)	11.3 (2.3)	0	7 (17.5)	0
Tsamalaidze et al. [6]	27	60.3 ± 15.42 (22–85)	20 (74.1)	28.7 ± 6.51 (18.7–48.4)	16	–	33 ± 2 (31–359	153 ± 70–58 (76–328)	100 ± 110.77 (10–400)	3.2 ± 1.63 (1–7)	3 (11.1)	9 (33.33)	0
Laparoscopic													

Table 1 continued

Author	N	Mean age	Gender M/F	BMI	Malignant %	Spleen weight	Spleen size	Operative time	Excess blood loss	Length of hospital stay	Conversion%	Complication%	Mortality %
Open	47	60.5 ± 13.58 (19–82)	27 (57.44)	26.3 ± 4.41 (17.6–36.2)	26	–	33.3 ± 4.68 (30–45)	131 ± 58.38 (38–346)	278 ± 563 (29–2300)	5.4 ± 3.09 (2–21)	–	6/17.02)	1 (2.1)
HALS	12	56 ± 22.25 (16–80)	8 (66.7)	27.6 ± 8.43 (17.8–49.5)	7	–	23.7 ± 4.08 (20–29)	168 ± 92.86 (55–418)	162 ± 297 (20–1000)	4.9 ± 3.14 (2–12)	1 (8.3)	1 (8.3)	0
Shin et al. [20]	22	60.8 (37–82)	11 (59)	27.1 (14.8–39.7)	–	677.6 (570–984)	–	178.4 (114–296)	–	5.5 (2–25)	3 (14)	9 (41)	1 (5)
Moderate laparoscopic													
Open	44	52.2 (25–77)	23 (52.2)	26.4 (17.9–36.9)	–	689 (508–1000)	–	107.21 (38–288)	367 (50–2200)	6.5 (3–48)	–	10 (23)	2 (5)
Shin et al. [20]	26	58.5 (25–87)	9 (40.9)	27.9 (20.4–39.3)	–	1754.9 (1032–3800)	–	170.8 (70–291)	606.6 (5–2400)	4.6 (2–12)	9 (35)	11 (42)	0
Massive laparoscopic													
Open	52	60.6 (29.3–83)	14 (26.92)	25.4 (18.8–30.9)	–	1755.6 (10,434–3850)	–	112.1 (45–322)	588.5 (5–9500)	5.7 (3–27)	–	14 (27)	1 (2)
Cassacia et al. [21]	25	53 (15)	9 (76)	24.8 (2.9)	–	–	24 (3.3)	143 (31)	278 (302)	6 (3)	0	4 (16%)	0
Laparoscopic													
Open	40	58 (11)	27 (67.5)	23 (3.4)	–	–	27.9 (5.3)	112 (40)	574 (583)	9 (4)	–	9 (22.5)	4 (10)
B. HALS versus laparoscopic splenectomy in splenomegaly													
Targarona et al. [26]	36	58 (13) 19–82	24 (66.6)	–	66.66	1425 (884) 400–700	25 (5) 19–34	177 (52) 95–300	–	6.3 (3.3) 3–14	7 (20)	13 (36)	0
Laparoscopic													
HALS	20	58 (16) 16–84	10 (50)	–	85	1753 (1124) 720–4500	26 (8) 16–42	135 (52) 85–270	–	4 (1.2) 2–5	1 (5)	2 (10)	0
Rosen et al. [25]	31	54	22 (70.96)	28	54.83	1031	–	186	376	4.2	7 (23)	6 (19.35)	0
Laparoscopic													
HALS	14	57	7 (50)	25	71.42	1516	–	177	602	5.4	1 (7)	5 (35.71)	0
Ke-Xin et al. [27]	16	38 (12) 15–61	7 (43.75)	–	18.75	1185 (536) 720–3900	24 (5) 16–31	195 (71) 110–320	138 (80) 60–550	5.3 (3.8) 3–13	4 (25)	2 (12.5)	0
Laparoscopic													
HALS	20	43 (14) 17–65	12 (60)	–	5	1346 (735) 750–4800	27 (7) 18–40	141 (64) 95–280	86 (45) 30–350	7.4 (1.6) 5–9	0	0	0
Wang et al. [32] Massive	8	51 (10)	4 (50)	–	–	–	21 (1)	94 (19)	63 (26)	7.9 (3.8)	0	1 (13)	0
laparoscopic													
HALS	10	47 (11)	2 (25)	–	–	–	20 (1)	162 (24)	66 (20)	7.7 (1.7)	0	2 (20)	0
Wang et al. [32] Supramassive	11	45 (12)	4 (36.36)	–	–	–	32 (6)	146 (40)	113 (78)	7.5 (1.8)	0	3 (27)	0
laparoscopic													
HALS	10	48 (12)	7 (70)	–	–	–	28 (3)	229 (29)	272 (122)	9.3 (2.5)	0	7 (70)	0
Tsamalaidze et al. [6]	27	60.3 (15.42) 22–85	20 (74.1)	28.7 (6.51) 18.7–48.4	59.3	–	24.2 (3.92) 20–35	153 (70.58) 76–328	100 (110.77) 10–400	3.2 (1.63) 1–7	3 (11.1)	9 (33.33)	0
Laparoscopic													
Open	47	60.5 (13.58) 19–82	27 (20)	26.3 (4.41) 17.6–36.2	55.3	–	26.6 (5.58) 20–45	131 (58.38) 38–346	278 (563.06) 20–2300	5.4 (3.09) 2–21	–	28 (59.57)	1 (2.1)

Table 1 continued

Author	N	Mean age	Gender M/F	BMI	Malignant %	Spleen weight	Spleen size	Operative time	Excess blood loss	Length of hospital stay	Conversion%	Complication%	Mortality %
HALS	12	56 (22.25) 16–80	8 (66.7)	27.6 (8.43) 17.8–49.5	58.3	–	23.7 (4.08) 20–29	168 (92.86) 55–418	162 (297) 20–1000	4.9 (3.14) 2–12	1 (8.3)	5 (41.66)	0
Sun et al. [24]	46	57 (17)	38 (82.6)	–	–	–	22.7 (4.8)	172 (43)	230 (130–740)	6.7 (3)	9 (19.56)	12 (26.08)	1 (2.17)
Laparoscopic													
HALS	45	55 (16)	34 (75.5)	–	–	–	23.5 (5.4)	141 (46)	215 122–332	6.4 (2.8)	1 (2.22)	15 (33.33)	0
C. HALS versus open splenectomy in splenomegaly													
Barbaros et al. [23] HALS	13	48 (13–68)	7 (53.84)	24 (20–29)	46.15	1200 (480–2110)	–	90 (30–150)	200 (200–800)	3 (2–10)	0	1 (7.69)	0
Open	14	50 (24–75)	8 (57.14)	23 (19–28)	78.57	1800 (600–3050)	–	97 (80–150)	300 (100–900)	6 (4–12)	–	1 (7.14)	0
Swanson et al. [22] HALS	20	55.2 (15.9)	15 (75)	–	60	–	22.9 (2.5)	163 (50)	375 (227)	4.2 (3)	1	7 (35)	0
Open	19	53.8 (12)	15 (78.94)	–	68.4	–	25.3 (3.7)	115 (40)	935 (877)	8.9 (5)	–	6 (32)	0
D. Robotic versus laparoscopic splenectomy in splenomegaly													
Cavalier et al. [28]	27	56 (42–64)	–	24.1 (21.8–27.7)	66.6	–	20 (18–23)	180 (146–238)	350 (100–800)	6 (4–8)	4 (14.8)	3 (11.1)	1 (3.7)
Laparoscopic													
Robotic	12	54 (46–60)	–	26 (23.9–32.1)	66.6	–	21 (17–23)	270 (190–300)	100 (100–250)	6 (5–6)	0	0	0

N indicates number of patients; *BMI* body mass index, *HALS* hand-assisted laparoscopic splenectomy

was taken into account for the modelization. We then added a random effect to model a supplementary variance source that we called an inter-study variation. For continuous variables, the mean difference between two groups was measured and estimated (using the inverse variance weighting correction) and the 95% confidence intervals were calculated. For binary variables, odds ratios were evaluated in their 95% asymptotic confidence interval. The adjusted results and the associated forest plot for each criterion are given. We set the first risk error alpha at 5%, and a p value <0.05 was then considered statistically significant. The statistical analysis was performed using R Software version 3.6.1, with all the packages necessary to perform the meta-analysis.

Results

Literature search

A total of 3382 papers were identified through the literature research. After removing duplicated articles, 2703 were retained for screening and 52 were potentially eligible for full-text evaluation. Thirty-two of these were excluded. The systematic review therefore included 20 studies, 19 of which were finally pooled into the meta-analysis (Fig. 1).

Study characteristic and quality assessment

The LS versus OS group included 12 studies [5, 8, 12–21] (one ambidirectional cohort, five prospective cohorts, and six retrospective cohorts, with a total of 652 patients). The HALS versus OS [22, 23] group included two studies (one retrospective cohort and one prospective randomized control trial with a total of 398 patients), and the LS versus HALS [8, 24–27] group included five studies (four retrospective cohorts and one prospective cohort, with a total of 306 patients). The RS versus LS [28] group included only one retrospective cohort. We found no studies comparing RS versus OS or RS versus HALS (Tables 1a, b, c, d, 2).

Synthesis of results

Primary aim: comparison between LS and OS

A comparison of LS versus OS showed that LOS was significantly shorter after LS: − 3.3 days [− 4.2; − 2.4] ($p < 0.01$). However, operative time was shorter for OS: 44.4 min [36.4; 52.5] ($p < 0.01$). Blood loss was significantly lower in LS − 146.2 cc [− 276.4; − 16.1] ($p < 0.01$) than in OS, with a global OR of 0.66 [0.19; 2.27]. Differences between the two groups regarding mortality and complications were not significant OR = 0.95 [0.65; 1.39] (p = 0.8) (Fig. 2a–e).

Subanalysis according to the splenic weight and size The meta-analysis of spleen weight and size showed no differences between the LS and OS groups : − 121.2 g [− 250.6; 8.1] (p = <0.05), − 0.9 cm [− 2.5; 0.6] (p = 0.2485), respectively.

In the LS subgroup, the median of weights was 1450.8 g (611; 2000), SD 644.2 g (345; 4293). In the OS subgroup, the median of weights was 1554.6 g (624; 2738), SD 3780 g (283; 6716.25).

In the LS subgroup, the median of sizes was 22.5 cm (19.0; 33.0), SD 4.8 cm (3.0–10.8). In the OS subgroup, the median of sizes was 23.8 cm (17.0; 33.3), SD 5.3 cm (3.7; 24.3) (Fig. 2f, g).

Secondary aim: comparison between LS and HALS

The model did not identify any statistically significant difference between LS and HALS regarding LOS mean difference: − 0.4 days [− 1.9; 1.2] (p = 0.9), operative time mean difference − 7.1 min [− 57.3; 43.1] ($p > 0.05$), or excess blood loss − 35.9 cc [− 106.3; 34.4] (p = 0.32). Neither did we find any difference in the complication rate: OR 0.78 [0.44; 1.37] (p = 0.38). The conversion rate was significantly reduced OR 4.92 [1.75; 13.89] ($p < 0.01$) in the HALS group. We were unable to analyze mortality as only one event was reported among all the studies (Fig. 3a–f).

Subanalysis of splenic weight and size The meta-analysis revealed no statistically significant differences between the groups in spleen weight − 218.8 g [− 554.9; 117.2] ($p > 0.05$) or spleen size 0.6 cm [− 0.2; 1.4] (p = 0.123). In the LS subgroup, the median of weights was 1425 g (1185; 1425), SD 884 g (536; 884). In the HALS subgroup, the median of weights was 1549.5 g (1346.0; 1753.0), SD 929.5 g (735.0; 1124.0).

The median of sizes was 24.2 cm (21.0; 32.0), SD 4.8 cm (1.0; 6.0). In the HALS subgroup, the median of sizes was 23.7 cm (20.0; 28.0), SD 5.4 cm (1.0; 8.0) (Fig. 3 g, h).

Secondary aim: comparison between HALS and OS

LOS was significantly lower after HALS than after OS, with a mean difference of 4.5 days [2.1; 7] ($p < 0.01$). Operative time was significantly lower after OS, with a mean difference of 44 min [− 71.3; − 16.7] ($p < 0.01$). Moreover, excess blood loss was lower after HALS: 448 cc [94.3; 801.7] (p = 0.01). The model did not find any significant difference in the complication rate OR = 0.87 [0.26; 2.91] (p = 0.82) (Fig. 4a–d).

We were unable to perform a subanalysis for splenic weight and size in this group because values were lacking in all the studies.

We found only one study comparing RS with another technical approach [28]. The authors compared RS versus LS in a retrospective study of 12 versus 27 patients. They found a longer operative time in the RS group (p = 0.007). However, blood loss was lower (100 vs. 350 cc) (p = 0.032) in RS group. The series reported four cases of conversion from RS to LS due to intraoperative bleeding.

Our search did not identify any studies that compared RS and OS.

The quality of included studies

Twelve studies that compared LS and OS were considered high quality, and one was moderate quality according to NOS. In the HALS versus LS subgroup, five were considered high quality and one had some concerns according to the RoB 2.0 tool. One study in the HALS versus OS analysis was considered high quality, and one presented some concerns according to RoB 2.0. The RS versus LS study was of high quality according to NOS (Table 2).

Discussion

The outcome of the current meta-analysis helps us better understand the clinical impact of minimally invasive surgery (MIS) in this challenging situation of splenomegaly.

Following the pooled meta-analysis, our model did not find differences between LS and OS regarding morbimortality. The operative time was higher in the LS group, but it was also associated with a lower blood loss and a shorter hospital stay. These results, along with the well-known rapid postoperative recovery in laparoscopic procedures, can be considered as potentially cost-effective [29] despite the need for conversion to OS in some cases. The median global conversion rate in the LS subgroup was 19.56% [11.11; 25]. The highest conversion rate was that of Boddy et al. [14] with 54.55% [mean spleen weight: 2000 g (1000–3530)], followed by that of Shin et al. [20] with 34.62% in the subgroup of massive splenomegaly [mean splenic weight of 1754.9 g (1032–3800)], and Targarona et al. [13] with 23.81% [mean weight of 1616 ± 651 g (1000–2950)]. However, in a cohort with 25 patients, Cassacia et al. [21] reported a 0% conversion rate [mean splenic diameter of 24.0 ± 3.3] in cases of massive splenomegaly.

After demonstrating that spleen size was not an obstacle for successful LS despite its association with a variable and

Table 2 Quality overview of the studies included

A. Studies quality assessment for primary and secondary aims

Outcome	Author	Type of study	Quality assessment NOS/RoB 2.0
LS versus OS	1998 Terrosou [12]	Retrospective cohort	9
LS versus OS	1999 Targarona [13]	Retrospective cohort	8
LS versus OS	2006 Boddy [14]	Ambidirectional cohort	8
LS versus OS	2006 Owera [15]	Retrospective cohort	8
LS versus OS	2008 Feldman [16]	Retrospective cohort	8
LS versus OS	2011 Zhou [17]	Prospective cohort	9
LS versus OS	2012 Koshenkov [5]	Retrospective cohort	8
LS versus OS	2012 Wu [18]	Prospective cohort	8
LS versus OS	2013 Bo [19]	Prospective cohort	8
LS versus OS	2017 Tsamaliadze [6]	Retrospective cohort	7
LS versus OS	2018 Shin [20]	Retrospective cohort	8
LS versus OS	2019 Casaccia [21]	Prospective cohort	8
LS versus HALS	2001 Targarona [26]	Prospective cohort	9
LS versus HALS	2002 Rosen [25]	Retrospective cohort	8
LS versus HALS	2007 Xin [27]	Retrospective cohort	8
LS versus HALS	2012 Wang [32]	Retrospective cohort	8
LS versus HALS	2017 Tsamaliadze [6]	Retrospective cohort	8
LS versus HALS	2019 Sun [24]	Prospective randomized control trial	Some concerns (RoB 2.0)
HALS versus OS	2007 Barbaros [23]	Prospective randomized control trial	Some concerns (RoB 2.0)
HALS versus OS	2011 Swanson [22]	Retrospective cohort	8
RS versus LS	2018 Cavaliere [28]	Comparative retrospective cohort	8

B. Revised Cochrane risk of bias tool for randomized trials (RoB 2.0)

Variable	2007 Barbaros [23]	2019 Sun [24]
Random sequence generation	+	+
Allocation concealment	?	?
Blinding of participant and personal	+	+
Incomplete outcome data	+	+
Selective reporting	+	+
Other bias	+	+

high conversion rate, the logical next step was to introduce HALS in the treatment of an enlarged spleen. HALS has been described as a middle option between LS and OS. The tactile feedback allows surgical and facilitates intra-abdominal manipulation [30]. It has also been suggested that HALS can be a starting point in the advanced laparoscopic learning curve and serve as a bridge in the armamentarium for difficult cases before conversion. These advantages could explain the lower conversion rate in HALS than in LS and also the conversion rates in the literature of around 5% [26], which is similar to findings found in this systematic review [mean 5% (0–8.3)].

In our analysis, when comparing LS and HALS, seven studies met the inclusion criteria and statistical differences were found, with a significant increase in the conversion rate in the LS group. However, we did not find statistical differences in relation to the length of hospital stay, excess blood loss during surgery, or complications. Six studies reported the spleen size and only three studies reported the spleen weight, but we did not find any significant differences between groups ($p = \ > 0.05$).

Yong Huang et al. recently published a meta-analysis comparing HALS versus LS in cases of splenomegaly and splenectomy plus upper stomach devascularization. In the pure splenomegaly subanalysis, the authors included nine trials with 486 patients and they did not find differences between the groups in splenic weight (0.6, 95% CI − 0.12 to 1.32; $p = 0.1$). The operative time was significantly shorter and blood loss volume and conversion rate were significantly lower in the HALS group, with no significant differences in length of hospital stay, blood transfusion, time to food intake, or morbidity and mortality rate [31]. In

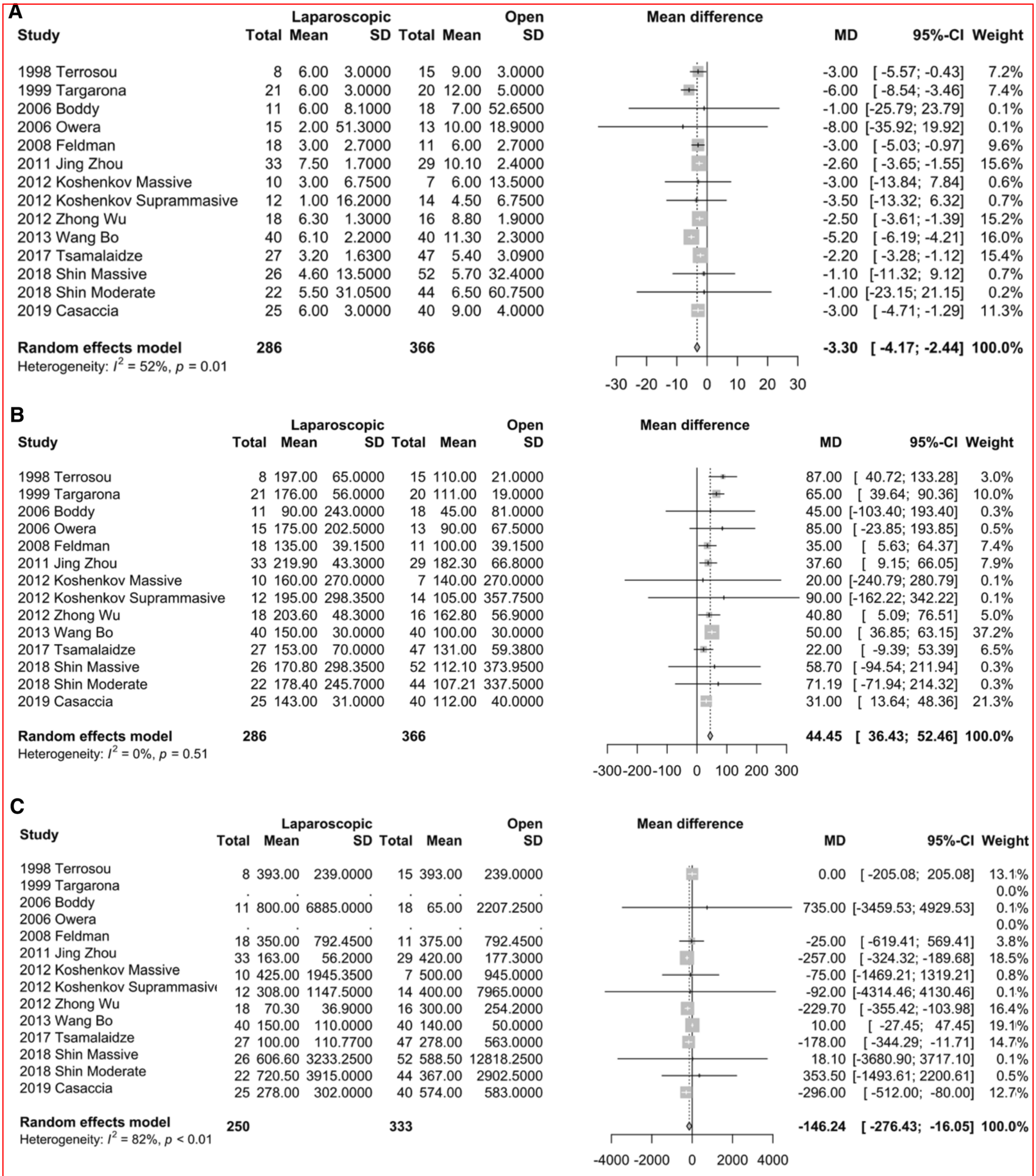

Fig. 2 Meta-analysis of main aim. LS versus OS. **a** Length of hospital stay, **b** operative time, **c** excess blood loss, **d** mortality, **e** complications, **f** spleen weight, **g** spleen size

contrast with the result from Huang et al., in our analysis the operative time was not lower in HALS than in the LS group. Regarding conversion rates, both meta-analyses found differences favoring the HALS subgroup. Ailawaidi et al. in our meta-analysis was not included because the authors mixed the results of laparoscopy in cases of

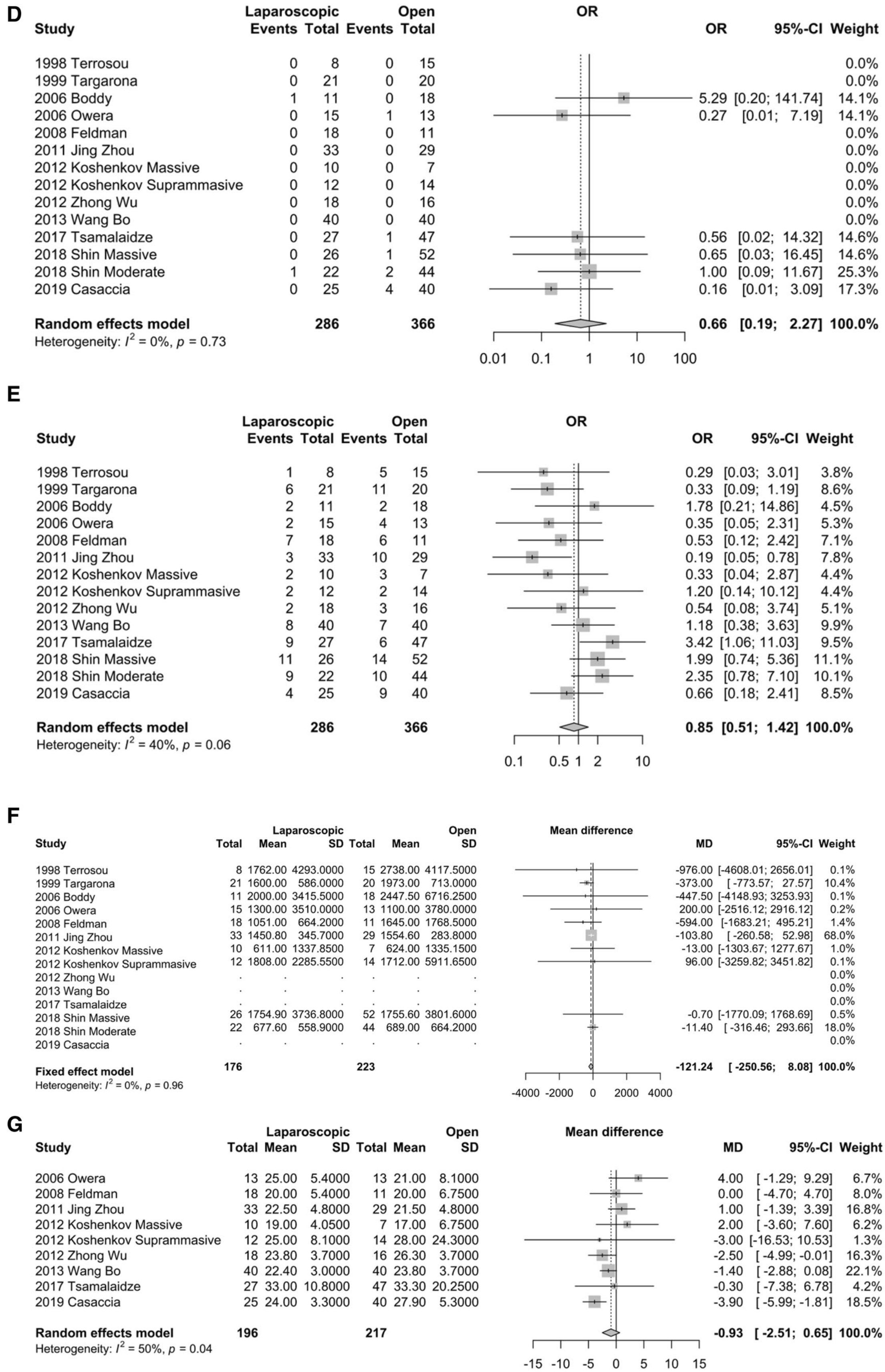

Fig. 2 continued

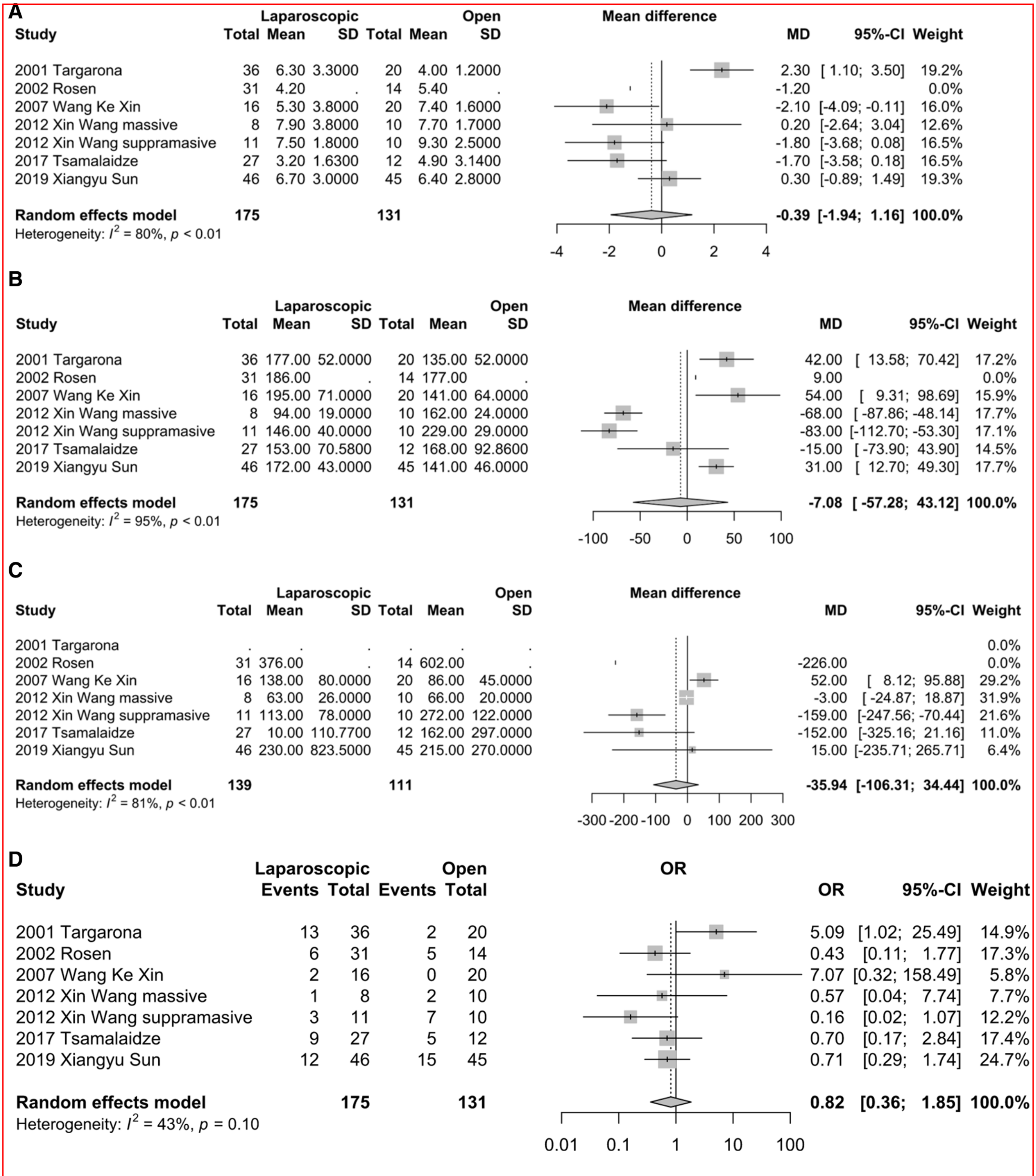

Fig. 3 Meta-analysis of secondary aim. HALS versus LS. **a** Length of hospital stay, **b** operative time, **c** excess blood loss, **d** mortality, **e** conversion, **f** complications, **g** spleen weight, **h** spleen size

splenomegaly and prior abdominal operation [32]. It should also be noted that Huang et al. meta-analysis was conducted mainly in diseases that conferred portal hypertension, such as hepatitis B and C viral infection and clinical situation that are less prevalent in Western countries and preclude definitive comparison with our study.

When OS was compared with HALS, HALS showed the obvious clinical advantages.

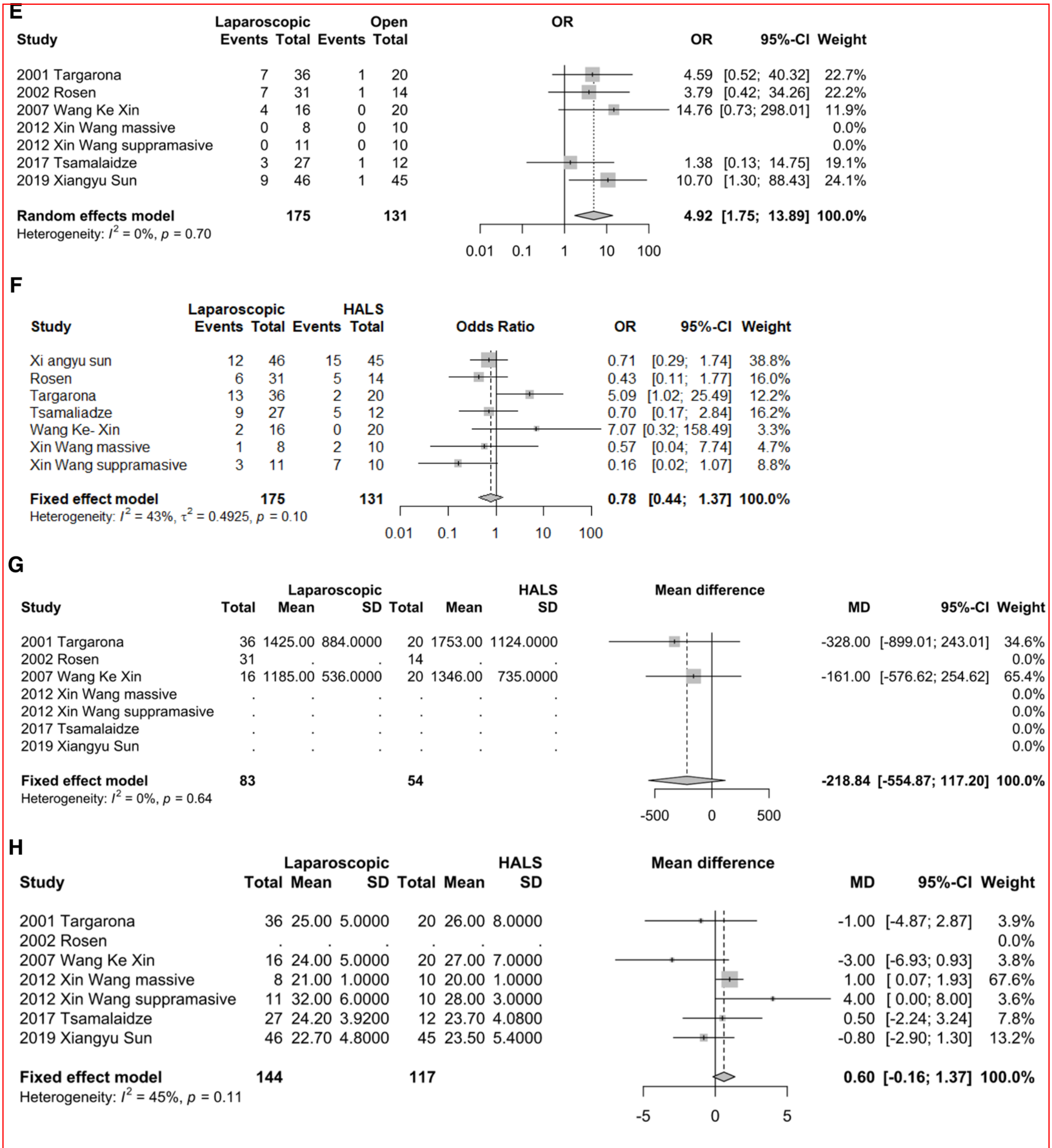

Fig. 3 continued

Robotic-assisted surgery has also been proposed in splenic surgery [33, 34], but data are scarce regarding the use of this technique in the case of splenomegaly. We found only one study that compared this approach with LS [28].

Some studies report splenomegaly according to the preoperative diameter. This is an objective measure that may help to predict the outcome, but most studies report the postoperative spleen weight, which is an outcome result, and not available preoperatively. The EAES consensus thus recommends using the preoperative size rather than the postoperative weight. However, we found that spleen weight was the most commonly reported variable to define splenomegaly in most of the studies.

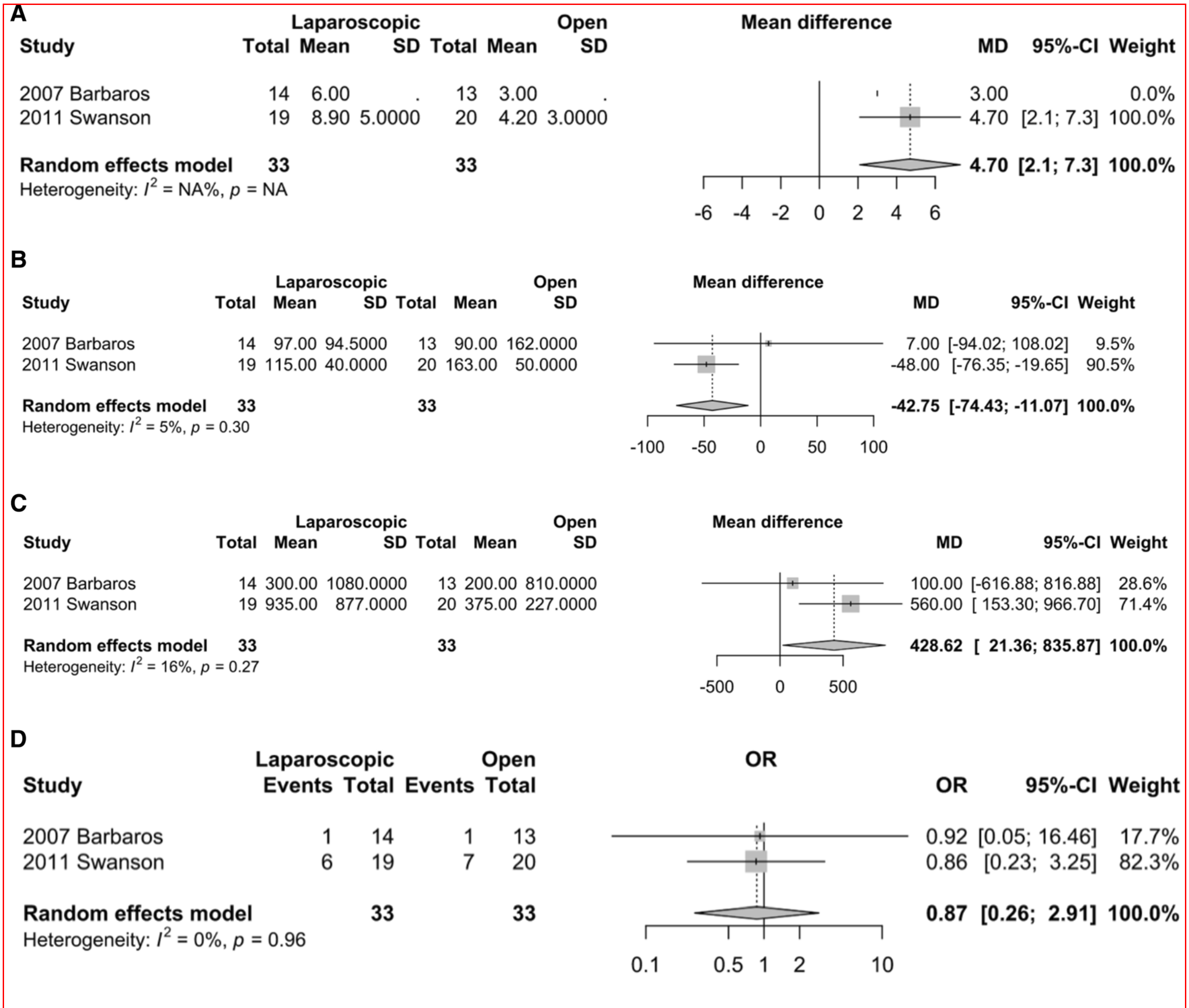

Fig. 4 Meta-analysis of secondary aim. HALS versus OS. **a** Length of hospital stay, **b** operative time, **c** excess blood loss, **d** complications

The main strength of this study is that it is the first meta-analysis to date to analyze LS in splenomegaly and compare it to classical OS. Furthermore, it analyzes other minimal invasive techniques such as HALS as secondary aims. The study also has several limitations. Most studies were graded as high quality according to NOS, but the majority were retrospective observational studies. There were only four prospective cohorts and few RCTs. An additional limitation is the lack of a standardized definition of splenomegaly (size versus weight*)*. We found great heterogeneity in splenomegaly grading and definition.

Despite our efforts to perform a subanalysis with a clear cutoff regarding values of weight or size, we were unable to achieve this due to the lack of standardized terminology and the different cutoff measures used in each study. Moreover, to assure comparability between groups either by weight or spleen size, we conducted an individual meta-analysis for these two variables. We found no statistical difference in LS versus OS or in LS versus HALS groups. An additional weak point was the difficulty in analyzing the outcomes according to the intention-to-treat principle. This subanalysis would help us better understand the outcome of cases operated purely by a minimally invasive technique and assess the additional impact of conversion to open surgery.

In conclusion, the data obtained from this meta-analysis provide an overview regarding the safety and feasibility of surgical strategies for the treatment of splenomegaly. After analyzing pooled results, we conclude that LS may be performed safely and has advantages over OS in the case of splenomegaly, despite a longer operative time. HALS shows superiority to LS, with a lower conversion rate and a clear reduction in surgical difficulty. Authors should use terminology and stratification in accordance with current guidelines in order to facilitate data synthesis. Future prospective randomized studies with standardized spleen size report are warranted to obtain stronger evidence.

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Compliance with ethical standards

Conflict of interest Drs Rodriguez-Luna R, Balagué C, Fernández-Ananín S, Vilallonga R, and Targarona Soler E. have no conflicts of interest or financial ties to disclose.

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