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REVIEW

Primary inguinal hernia: systematic review and Bayesian network meta-analysis comparing open, laparoscopic transabdominal preperitoneal, totally extraperitoneal, and robotic preperitoneal repair

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Abstract

Purpose The Open Lichtenstein technique, the Laparoscopic Trans-Abdominal PrePeritoneal (TAPP), the Totally Extra Peritoneal (TEP), and the robotic TAPP (rTAPP) are commonly performed. The aim of the present network meta-analysis was to globally compare short-term outcomes within these major surgical techniques for primary unilateral inguinal hernia repair.

Methods PubMed, EMBASE, and Web of Science were consulted. A fully Bayesian network meta-analysis was performed.

Results Sixteen studies (51.037 patients) were included. Overall, 35.5% underwent Open, 33.5% TAPP, 30.7% TEP, and 0.3% rTAPP. The postoperative seroma risk ratio (RR) was comparable considering TAPP vs. Open (RR 0.91; 95% CrI 0.50–1.62), TEP vs. Open (RR 0.64; 95% CrI 0.32–1.33), TEP vs. TAPP (RR 0.70; 95% CrI 0.39–1.31), and rTAPP vs. Open (RR 0.98; 95% CrI 0.37–2.51). The postoperative chronic pain RR was similar for TAPP vs. Open (RR 0.53; 95% CrI 0.27–1.20), TEP vs. Open (RR 0.86; 95% CrI 0.48–1.16), and TEP vs. TAPP (RR 1.70; 95% CrI 0.63–3.20). The recurrence RR was comparable when comparing TAPP vs. Open (RR 0.96; 95% CrI 0.57–1.51), TEP vs. Open (RR 1.0; 95% CrI 0.65–1.61), TEP vs. TAPP (RR 1.10; 95% CrI 0.63–2.10), and rTAPP vs. Open (RR 0.98; 95% CrI 0.45–2.10). No differences were found in term of postoperative hematoma, surgical site infection, urinary retention, and hospital length of stay.

Conclusions This study suggests that Open, TAPP, TEP, and rTAPP seem comparable in the short term. The surgical management of inguinal hernia is evolving and the effect of the adoption of innovative minimally invasive techniques should be further investigated in the long term. Ultimately, the choice of the most suitable treatment should be based on individual surgeon expertise and tailored on each patient.

Keywords Inguinal hernia repair · Mesh · Lichtenstein technique · Laparoscopic Trans-Abdominal PrePeritoneal (TAPP) · Totally Extra Peritoneal (TEP) · Robotic Trans-Abdominal PrePeritoneal (rTAPP)

Introduction

Worldwide, more than 20 million patients undergo groin hernia repair every year [1]. Primary unilateral inguinal hernias account for 75% of abdominal wall hernias, in which there is a lifetime risk of 27% for men and 3% for women [2]. Operative techniques have continuously evolved over the past decades to provide the best management for inguinal hernias [3]. The Open tension-free Lichtenstein technique is the most commonly worldwide performed procedure with optimal outcomes and low recurrence rate [1]. After the introduction of laparoscopy, new techniques such as the transabdominal preperitoneal (TAPP) repair and the totally extraperitoneal repair (TEP) gained progressive acceptance with promising results and comparable outcomes to the Open approach [4]. Afterward, the introduction of robotic platforms opened new horizons and the robotic TAPP (rTAPP) arouses progressive enthusiasm with growing popularity and presumed advantages [5]. The previous

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meta-analysis analysed these techniques in a pairwise comparison (Open vs. TAPP or TAPP vs. TEP or Open vs. TEP), but a comprehensive review is lacking.

The aim of the present network meta-analysis was to globally compare short-term and recovery outcomes within these four major surgical approaches for primary unilateral inguinal hernia repair.

Materials and methods

A systematic review was performed according to the guidelines from the Preferred Reporting Items for Systematic Reviews and network meta-analyses' checklist (PRISMA-NMA) [6]. Institutional review board approval was not required.

PubMed, EMBASE, and Web of Science databases were used for systematic search. The last date of search was the February 28st, 2019. We searched for papers using the following search strategy: "primary unilateral inguinal hernia", "open inguinal hernia repair", "transabdominal preperitoneal repair", "totally extraperitoneal endoscopic repair", and "robotic hernia repair". All titles were initially evaluated and suitable abstracts extracted. The reference list of included articles was also screened. The study protocol was registered at PROSPERO (International prospective register of systematic reviews) (Registration number: CRD42019130852).

Inclusion and exclusion criteria

Eligible studies for the present meta-analysis included RCT and observational retrospective and prospective clinical studies. To be included in the analysis: (a) studies comparing surgical outcomes in primary unilateral inguinal hernia repair for either Open, TAPP, TEP, and rTAPP; (b) articles written in English; (c) articles with the longest follow-up or the largest sample size when two or more papers were published by the same institution, study group, or used the same data set; (d) published after the year 2000; (e) in case of duplicate studies with accumulating numbers of patients, only the most complete reports were included for quantitative assessment. Studies were excluded if (a) they were not written in English; (b) the methodology was not clearly reported; (c) the surgical technique was not clearly reported; (d) the inguinal hernia repair was performed without mesh or plug; (e) studies that did not contain a comparative group report primary unilateral inguinal hernias.

Data extraction

The following data were retrieved: author, year of publication, country, study design, number of patients, sex, age, body mass index (BMI), surgical approach, and early postoperative outcomes. All data were entered independently by three investigators (FL, AA, and AM) and compared only at the end of the reviewing process. A fourth author (GC) eventually reviewed the database. Discrepancies were clarified.

Quality assessment

Two authors (AA and FL) independently assessed the methodologic quality of the selected trials using the Cochrane risk of bias tool [7]. This tool evaluates the following criteria: (1) method of randomization; (2) allocation concealment; (3) baseline comparability of study groups; and (4) blinding and completeness of follow-up. Trials were graded as follows: A adequate, B unclear, and C inadequate on each criterion. Thus, each RCT was graded as having low, moderate, or high risk of bias. Two authors (FL and AA) independently assessed the quality of observational studies using the ROBINS-I tool [8]. The following domains were considered: confounding bias, selection bias, classification bias, intervention bias, missing data bias, outcomes measurement bias, and reporting bias. Each domain is evaluated with one of the following: "yes", "probably yes", "probably no", and "no". The categories of judgement for each study are low, moderate, serious, and critical risk of bias. Disagreements were solved by discussion.

Outcomes of interest

Primary outcomes: haematoma, seroma, post-operative chronic pain, and recurrence. Secondary outcomes: surgical site infection (SSI), urinary retention, operative time (minutes), and postoperative hospital length of stay (HLOS).

Statistical analysis

We performed fully Bayesian arm-based random effect network meta-analysis, in particular, mixed treatment comparison (MTC). Briefly, the MTC simultaneously synthesizes data from all available trials within a consistent network and combines direct evidence (comparison of treatments within head-to-head trials) with indirect evidence (comparison of treatments across trials against a common comparator) [9]. Compared with the frequentist meta-analysis, the Bayesian approach takes into account all sources of variations, reflects these variations in the pooled result, can provide accurate estimates for small samples, and allows computation of predictive distribution [10]. Furthermore, Bayesian posterior analysis should yield exact coverages, independent of sample size. An ordinary consistency model was adopted with the binomial/log model [11]. We used risk ratio (RR) as a pooled effect size measure. For RR on log scale, we applied two different prior distributions to the model: a "sceptical"

and "vague" prior distribution. In particular, we assigned a Normal with zero mean and scale 0.4 as sceptical distribution (10% of the distribution is contained within the clinically unimportant null interval); we assigned Normal with zero mean and scale 100 as vague prior distribution, and we used it as prior distribution into prior sensitivity analysis. For the between-study variability (τ), we used an informative half-normal prior with zero mean and scale 0.5 [12] assuming a common heterogeneity parameter across the various treatment comparisons. Sensitivity analysis regarding the choice of prior distribution for τ was also considered [13]. For continuous outcomes, mean difference was adopted using Normal prior distribution with mean 0 and scale 10, and uniform distribution (0.5) as τ prior. To evaluate statistical heterogeneity, we calculated I2 index: value of 25% was defined as low heterogeneity, 50% as moderate heterogeneity, and 75% as high heterogeneity [14]. The inference was performed using mean and relative 95% credible intervals (CrI), based on draws from marginal posterior distribution in Monte Carlo Markov chain (MCMC), simulating 300,000 iterations after a burn-in period of 30,000 iterations. We consider the estimated parameter statistical significant when its 95% CrI encompasses null-hypothesis value. The accuracy of the inference was assessed by convergence of MCMC algorithm, checked using graphical inspection of running means, MCMC error, and diagnostic statistics included into R/Boa package [15]. The plot of Leverage values vs. the square root of the residual deviance (mean per data point for each study) was used to identify potentially study outlier. The transitivity assumption (i.e., studies comparing different sets of interventions needed to be sufficiently similar) was considered to provide valid indirect inferences. To assess transitivity, we generated descriptive statistics and we compared the distributions of baseline participant characteristics across studies and treatment comparisons. To assess local inconsistencies, we used the node-splitting method [16], which was not possible to conduct a formal assessment of the consistency of the direct and indirect evidence where the evidence network included open loops. We plotted rank probabilities against the possible ranks for all competing treatments. The confidence in estimates of the outcome was assessed using Confidence in Network Meta-Analysis (CINeMA) [17]. In accordance with Cochrane guidelines, we did not investigate publication bias as our search consider less than ten studies for each data comparison [18]. Statistical analyses were carried out using JAGS and R-Cran 3.4.3 (Distributed Statistical Computing; Vienna, Austria) [19, 20].

Review of network geometry

We appraised the geometry of the networks for each outcome separately, and provided network graphs for primary outcomes with nodes reflecting the surgical approaches and two nodes linked together by an edge, if at least one study compared the two corresponding surgical techniques. The connection between surgical approaches was analysed (Fig. 1).

Results

Systematic review

Sixteen studies met the inclusion criteria. The flowchart selection process is reported in Fig. 2. Twelve articles were RCT, three were prospective clinical studies, and one was retrospective clinical study. Overall, 51.037 patients were included in the analysis. Of these, 18.135 (35.5%) underwent Open, 17.112 (33.5%) TAPP, 15.687 (30.7%) TEP, and 103 (0.3%) rTAPP repair (Table 1). The age range from 18 to 65 years and the majority were males (81.5%). Body mass index (BMI) ranged from 24 to 52 kg/m^2 (Table 1). The hernia site was reported in six studies, the type of hernia, according to the Nyhus or European Hernia Society (EHS) classification, was reported in seven studies, and the hernia size was reported in three studies. The American Society of Anesthesiologists (ASA) classification was reported in seven studies. Three studies reported the cost analysis. All studies reported the postoperative follow-up that ranged from 1 to 60 months. Quality of life according to the Short-Form 36 (SF-36) questionnaire was accomplished in two studies. We tried out to ensure transitivity by applying narrow inclusion criteria and making populations as similar as possible within and across treatment comparisons. The quality of all included studies is depicted in Fig. 3 and Table 2.

Meta-analysis

Haematoma

Nine studies for a total of 54.044 patients reported the incidence of postoperative haematoma. Pooled network meta-analysis shows similar RR when comparing TAPP vs. Open (RR 0.68; 95% CrI 0.40–1.30), TEP vs. Open (RR 0.67; 95% CrI 0.43–1.20), and TEP vs. TAPP (RR 1.01; 95% CrI 0.51–1.80) (Fig. 4a). Node splitting revealed no statistical difference between the direct and indirect comparison (TAPP vs. Open $p = 0.242$; TEP vs. Open $p = 0.202$; TEP vs. TAPP $p = 0.232$). The prior sensitivity analysis yields robust results for TAPP vs. Open (RR 0.68; 95% CrI 0.40–1.30) and TEP vs. Open (RR 0.67; 95% CrI 0.42–1.21). The global heterogeneity is low ($I^2 = 24\%$). The SUCRA ranking was 91% for Open, 31% for TEP, and 27% for TAPP.

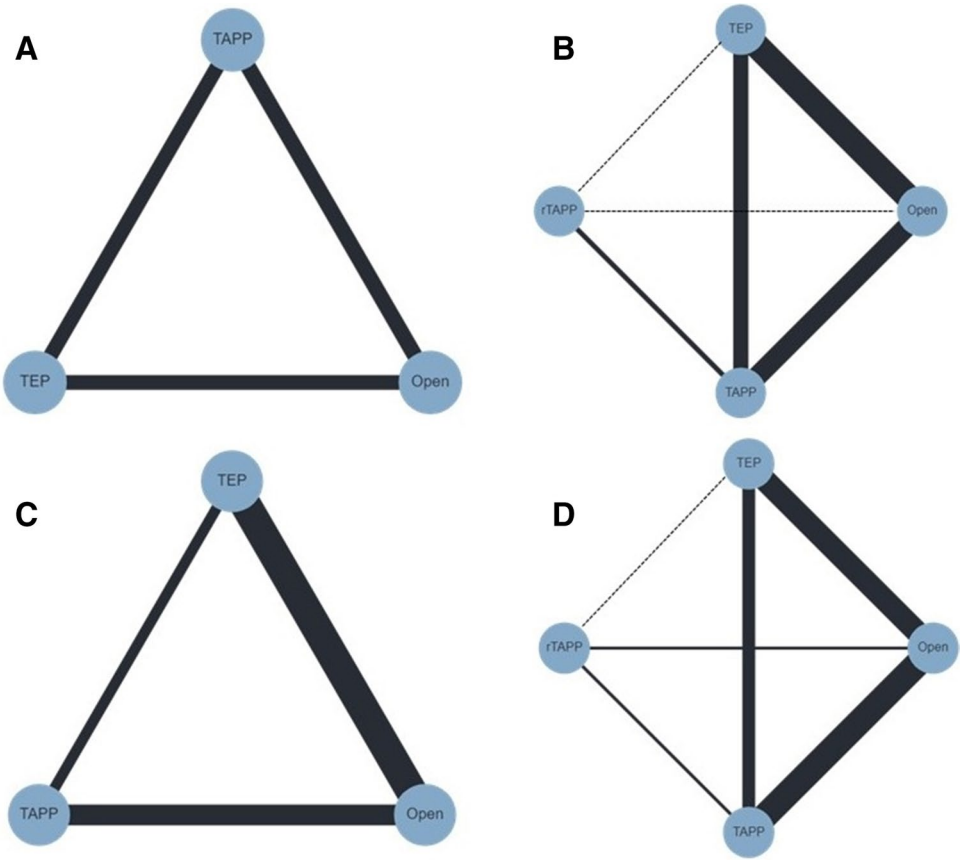

Fig. 1 Network geometry for studies reporting: **a** hematoma, **b** seroma, **c** postoperative chronic pain, and **d** hernia recurrence

Seroma

Nine studies for a total of 54.138 patients reported the incidence of postoperative seroma. Pooled network meta-analysis shows similar RR when comparing TAPP vs. Open (RR 0.91; 95% CrI 0.50–1.62), TEP vs. Open (RR 0.64; 95% CrI 0.32–1.33), TEP vs. TAPP (RR 0.70; 95% CrI 0.39–1.31), and rTAPP vs. Open (RR 0.98; 95% CrI 0.37–2.51) (Fig. 4b). Node splitting revealed no statistical difference between the direct and indirect comparison (TAPP vs. Open $p=0.885$; TEP vs. Open $p=0.899$; TEP vs. TAPP $p=0.917$). The prior sensitivity analysis yields robust results for TAPP vs. Open (RR 0.91; 95% CrI 0.49–1.60), TEP vs. Open (RR 0.63; 95% CrI 0.32–1.31), and rTAPP vs. Open (RR 0.98; 95% CrI 0.37–2.61). The global heterogeneity is moderate ($I^2=39\%$). The SUCRA ranking was 68% for Open, 62% for rTAPP, 55% for TAPP, and 14% for TEP.

Postoperative chronic pain

Six studies for a total of 36.724 patients reported the incidence of postoperative chronic pain. Pooled network meta-analysis shows similar RR when comparing TAPP vs. Open (RR 0.53; 95% CrI 0.27–1.20), TEP vs. Open (RR 0.86; 95% CrI 0.48–1.16), and TEP vs. TAPP (RR 1.70; 95% CrI 0.63–3.20) (Fig. 4c). Node splitting revealed no statistical difference between the direct and indirect comparison (TAPP vs. Open $p=0.872$; TEP vs. Open $p=0.894$; TEP vs. TAPP $p=0.974$). The prior sensitivity analysis yields robust results for TAPP vs. Open (RR 0.54; 95% CrI 0.28–1.12) and TEP vs. Open (RR 0.86; 95% CrI 0.48–1.70). The global heterogeneity is moderate ($I^2=63\%$). The SUCRA ranking was 81% for Open, 59% for TEP, and 10% for TAPP.

Recurrence

Nine studies for a total of 111.197 patients reported the postoperative early recurrence. Pooled network meta-analysis shows similar RR when comparing TAPP vs. Open (RR 0.96; 95% CrI 0.57–1.51), TEP vs. Open (RR 1.0; 95% CrI 0.65–1.61), TEP vs. TAPP (RR 1.10; 95% CrI 0.63–2.10), and rTAPP vs. Open (RR 0.98; 95% CrI 0.45–2.10) (Fig. 4d). Node splitting revealed no statistical difference between the direct and indirect comparison (TAPP vs. Open $p=0.81$; TEP vs. Open $p=0.707$; TEP vs. TAPP $p=0.675$). The prior sensitivity analysis yields robust results for TAPP vs. Open (RR 0.96; 95% CrI 0.58–1.50), TEP vs. Open (RR 1.0; 95% CrI 0.65–1.62), and rTAPP vs. Open (RR 0.98; 95% CrI 0.45–2.10). The global heterogeneity is zero ($I^2=0.0\%$). The SUCRA ranking was TEP 56%, 52% for Open, 49% for

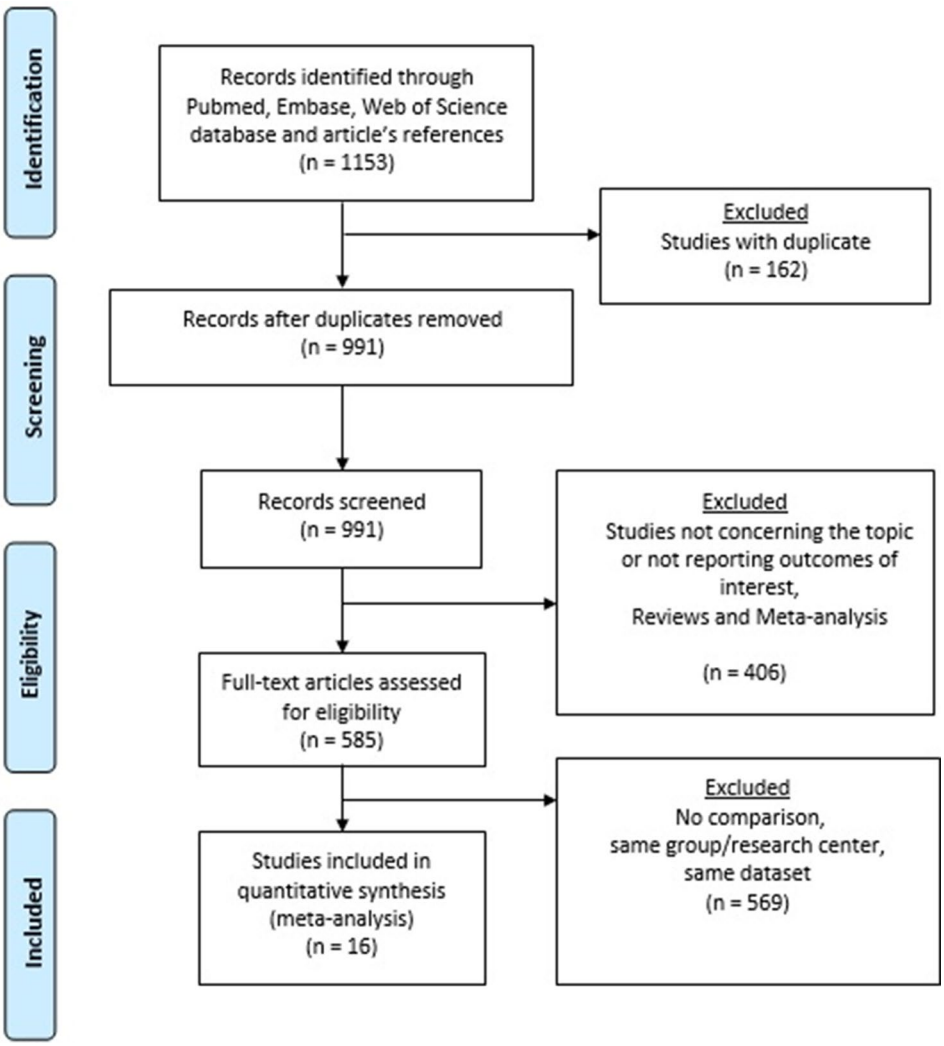

Fig. 2 The Preferred Reporting Items for Systematic Reviews and network meta-analyses checklist (PRISMA-NMA) diagram

rTAPP, and 44% for TAPP. The League table for primary outcomes is depicted in Table 3.

The subgroup analysis including 12 RCT studies showed comparable non-statistically significant results in term of postoperative hematoma, seroma, chronic pain, and recurrence comparing Open, TAPP, and TEP.

Secondary outcomes

Pooled network meta-analysis does not show statistically significant RR comparing TAPP vs. Open, TEP vs. Open, TEP vs. TAPP, and rTAPP vs. Open in term of SSI (RR 0.65; 95% CrI 0.34–1.43, RR 0.59; 95% CrI 0.31–1.34, RR 0.90; 95% CrI 0.39–2.21, RR 1.10; 95% CrI 0.53–2.46, respectively). The global heterogeneity is zero ($I^2 = 0.0\%$). Similarly, the pooled network meta-analysis does not show statistically significant RR comparing TAPP vs. Open, TEP vs. Open, TEP vs. TAPP, and rTAPP vs. Open in term of urinary retention (RR 0.92; 95% CrI 0.49–1.78, RR 1.0; 95% CrI 0.55–1.91, RR 1.10; 95% CrI 0.49–2.57, RR 0.96; 95% CrI 0.45–2.14, respectively). The global heterogeneity is zero ($I^2 = 0.0\%$). Again, the pooled network meta-analysis does not show statistically significant difference comparing TAPP vs. Open, TEP vs. Open, and TEP vs. TAPP in term of operative time (smd = 2.20; 95% CrI − 1.60 to 5.90, smd = − 1.40; 95% CrI − 5.10 to 2.30, smd = − 3.60; 95% CrI − 7.70 to 0.58, respectively). By contrast, rTAPP was associated with a statistically significant longer operative time compared to Open (smd = 30.0; 95% CrI 21.01–39.02). The global heterogeneity is high ($I^2 = 89.4\%$). The pooled network meta-analysis does not show statistically significant differences comparing TAPP vs. Open, TEP vs. Open, and TEP vs. TAPP in term of postoperative length of stay (smd = − 0.73; 95% CrI − 1.70 to 0.20, smd = − 0.47; 95% CrI − 1.70 to 0.69, smd = 0.27; 95% CrI − 0.84 to 1.30, respectively).

The Leverage plots do not show the evidence of study outliers into this network meta-analysis. For all outcomes, there was no evidence of non-MCMC convergence using the diagnostic tools described in the Statistical analysis section. The assessments of confidence in the estimates using

Table 1 Demographic and clinical characteristics of patients undergoing Open Lichtenstein repair (Open), Laparoscopic Trans-Abdominal PrePeritoneal (TAPP), Totally Extra Peritoneal (TEP), and robotic TAPP (rTAPP)

Author, year, country	Study design	Surgical procedure	No. patient	Age (years)	Gender (M/F)	BMI (kg/m^2)	OR time (min)	HLOS (days)	Hernia side R/L	Medial	Lateral	Femoral
Anadol (2004), Turkey [21]	RCT	TAPP	25	41.8 ± 10.9	nr	nr	57.4 ± 12.2	1.5 ± 0.5	14/11	nr	nr	nr
		Lichtenstein	25	41.2 ± 10.9			54.2 ± 14.8	2.2 ± 0.9	14/11			
Lau (2006), China [21]	RCT	TEP	100	55 ± 15.5	100/0	nr	50 ± 13.2	nr	nr	27	73	0
		Lichtenstein	100	56 ± 13.1	100/0		58 ± 17.6			25	75	
Butters (2007), Germany [22]	RCT	Lichtenstein	76	56 ± 8.33	nr	25.2 ± 3.16	nr	nr	nr	nr	nr	nr
		TAPP	81	53 ± 7.33		25.4 ± 1.61						
Pokorny (2008), Austria [23]	RCT	Lichtenstein	69	52 (19–84)	5/64	25 (19–33)	48 ± 4.5	5 ± 0.5	42/27	nr	nr	nr
		TEP	36	48 (19–73)	1/35	25 (17–35)	78 ± 8	5 ± 0.3	20/16			
		TAPP	93	49 (21–78)	7/86	25 (19–33)	66 ± 5	4 ± 0.4	58/35			
Eklund (2009), Sweden [24]	RCT	TEP	665	53 ± 9.6	nr	nr	nr	nr	nr	222	436	2
		Lichtenstein	705	52 ± 10.1						237	457	3
Hamza (2009), Egypt [25]	RCT	Lichtenstein	25	35.1 ± 10.1	nr	24.3 ± 14.2	34.2 ± 23.5	nr	nr	nr	nr	nr
		TAPP	25	36.7 ± 12.1		22.4 ± 1.2	96.1 ± 22.5					
		TEP	25	34.9 ± 13		23.2 ± 5.3	77.4 ± 43.2					
Gong (2010), China [26]	RCT	TAPP	50	56 ± 10	50/0	nr	76 ± 16	3.4 ± 1.7	nr	12	38	0
		TEP	52	57 ± 9	52/0		79 ± 13	3.6 ± 1.6		13	39	0
		Lichtenstein	62	56 ± 10	62/0		66 ± 19	5 ± 2.5		15	48	0
Abbas (2012), Egypt [27]	RCT	TAPP	88	35.8 (18–65)	2.3	nr	46.2 ± 8.9	1.2 ± 1.2	60/28	nr	nr	nr
		Lichtenstein	97	34.6 (18–63)	3.1		45.3 ± 9.8	1.3 ± 0.8	59/38			
Dhankhar (2014), India [28]	RCT	TEP	29	38.1 ± 11.5	nr	nr	75.9 ± 13.7	nr	nr	nr	nr	nr
		Lichtenstein	30	43.2 ± 13.6			64.8 ± 12.7					
Wang (2013), China [29]	RCT	TAPP	84	48.2 ± 13.2	70/14	nr	47.2 ± 16.6	nr	nr	6	77	1
		TEP	84	48.2 ± 17.1	71/13		50.5 ± 14			8	73	3
		Lichtenstein	84	52.1 ± 17.4	69/15		46.2 ± 4.5			10	70	4
Dahlstrand, (2013) NY [30]	RCT	TEP	193	52.8 ± 9.3	nr	26.5	60 ± 3.7	nr	nr	nr	nr	nr
		Lichtenstein	191	53.1 ± 8.3		24.8	70 ± 3.3					
Aigner (2013), Austria [31]	RCT	TEP	77	44.3	nr	nr	61	nr	42/35	13	43	nr
		Lichtenstein	77	53.1			56		35/42	16	51	
Pedroso (2017), Brazil [32]	Pros	TAPP	28	50.5	25/3	27.3	nr	nr	15/13	12	16	0
		Lichtenstein	28	59	26/2	25.8			13/15	11	17	0
Charles, (2018), USA [33]	Ret	TAPP	241	57 ± 5.5	214/27	25.8 ± 1.3	81 ± 7	nr	nr	nr	nr	nr
		rTAPP	69	52 ± 3.8	59/10	24.9 ± 0.9	105 ± 17.5					
		Lichtenstein	191	56 ± 3.1	175/16	25.1 ± 0.7	71 ± 5.3					
Muysoms, (2018), Belgium [34]	Pros	TAPP	22	59 ± 11.8	20/2	24 ± 3	45 ± 11	nr	14/8	32	64	5
		rTAPP	34	60.4 ± 16.5	33/1	25 ± 3.4	54 ± 16		18/16	18	79	3

Table 1 (continued)

Author, year, country	Study design	Surgical procedure	No. patient	Age (years)	Gender (M/F)	BMI (kg/m^2)	OR time (min)	HLOS (days)	Hernia side R/L	Medial	Lateral	Femoral
Kockerling (2019), Germany [35]	Ret PS	TEP	14,426	nr	nr	nr	nr	nr	nr	nr	nr	nr
		TAPP	16,375									
		Lichtenstein	16,375									

Data are reported as numbers, mean ± standard deviation, median (range)

RCT randomized-controlled trial, *Pros* prospective, *Ret* retrospective, *PS* Propensity Score matching, *BMI* body mass index, *OR* time operative time (minutes), *HLOS* hospital length of stay (days), *nr* not reported

CINeMA show moderate-to-very low confidence, essentially due to study limitation, imprecision, and inconsistence.

Discussion

The aim of the present network meta-analysis was to globally compare short-term outcome of the main surgical approaches for primary unilateral inguinal hernia repair. No significant differences were found in term of postoperative hematoma, seroma, chronic pain, and early recurrence. Similarly, no differences were found in term of postoperative surgical site infections, urinary retention, and postoperative hospital length of stay. rTAPP was found to have a statistically significant longer operative time compared to the Open approach.

While the Open approach is considered the gold standard treatment for non-complicated primary inguinal hernia repair, different minimally invasive techniques have been progressively proposed with the introduction of advanced technologies [21]. In the European Hernia Society's guidelines, the Lichtenstein procedure and the minimally invasive techniques are recommended as the best evidence-based options in experts' hands [1]. The *pros* and *cons* have been largely discussed, but, to date, results are contrasting and a robust evidence favouring one treatment over another is lacking. The previous observational, RCT studies, and pairwise meta-analyses have been published with discordant results. These were mainly related to the heterogeneity of the included populations, surgical techniques, and indications [22–37]. We performed a fully Bayesian network meta-analysis to globally compare outcomes of the main surgical approaches to inguinal hernia. To reduce background heterogeneity, we mainly focused on mesh-reinforced tension-free techniques for primary non-complicated unilateral inguinal hernia.

Postoperative seroma and hematoma represent the most common surgery-related complications [38]. The method for mesh fixations, large hernia size, and medial hernia represent independent risk factors for seroma formation [39]. Kockerling et al. in a recently published data set-based retrospective study reported a significantly lower incidence of overall postoperative complications and seroma in patients that underwent TEP compared to Open and TAPP procedures [37]. Our study showed that Open, TAPP, TEP, and rTAPP seem associated with similar results in term of postoperative hematoma and seroma. The related-global heterogeneity was moderate and low (39% and 21%, respectively). The meta-regression analysis was not possible, because data were reported as aggregated and individual-patient comorbidity was lacking. These results are in accordance with the study by Wu et al. showing no differences comparing TAPP vs. Open [3]. This may be the result of a rigorous

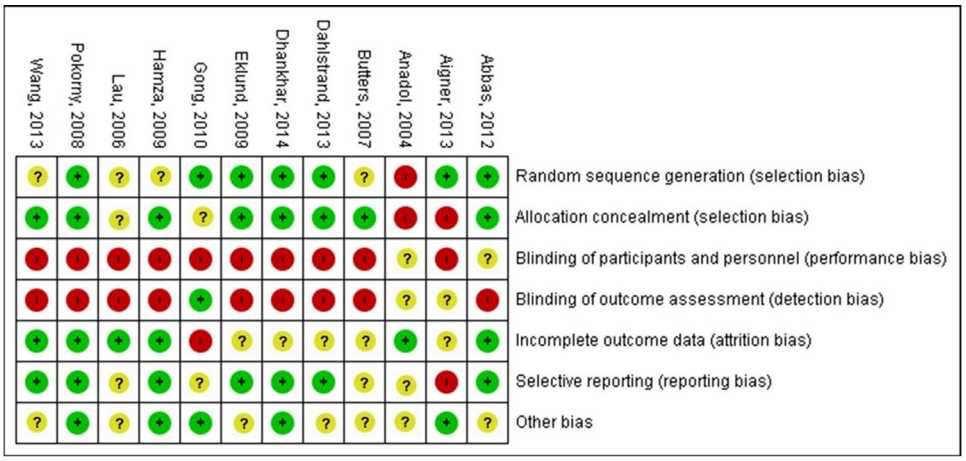

Fig. 3 Risk of bias for randomized-controlled trials was assessed with the Cochrane risk-of-bias tool

Table 2 Quality assessment of the included observational studies (ROBINS-I tool)

Author	Confounding bias	Selection bias	Classification bias	Intervention bias	Missing data bias	Measurement bias	Reporting bias	Bias
Pedroso (2017), Brazil	pn	py	pn	pn	py	n	pn	Serious
Charles (2018), USA	py	py	pn	pn	y	py	py	Moderate
Muysoms (2018), Belgium	pn	y	pn	n	py	pn	py	Serious
Kockerling (2019), Germany	py	y	n	py	y	pn	pn	Moderate

The categories of judgement for each study are low, moderate, serious, and critical risk of bias

Each domain is evaluated with one of the following: *y* "yes", *py* "probably yes", *pn* "probably no", and *n* "no"

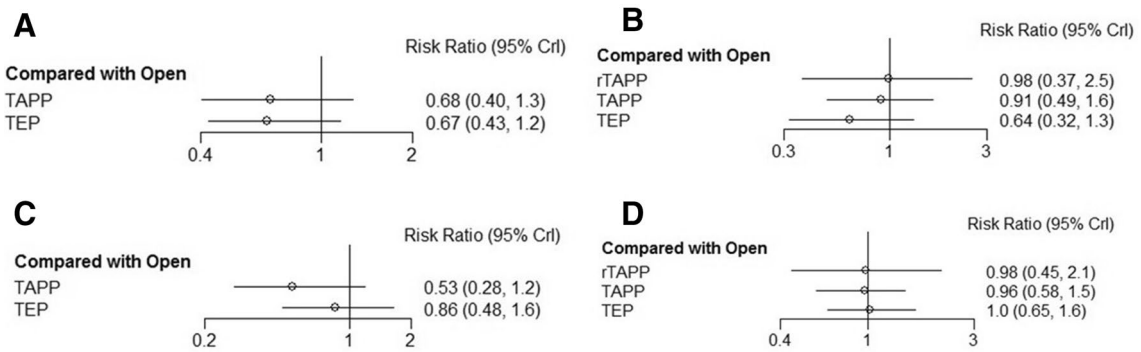

Fig. 4 Forest plots of network meta-analysis estimates the RR for **a** hematoma, **b** seroma, **c** postoperative chronic pain, and **d** hernia recurrence

surgical technique and careful anatomical planes dissection performed in the experienced hands [40]. It should be noted, however, that despite the lack of statistically significance the Open approach was ranked in the SUCRA as the treatment having a higher likelihood of postoperative hematoma and seroma.

Postoperative chronic pain has been shown to be associated with perioperative nerves injury or entrapment [38]. Nerves can also be trapped in a shrinked mesh or by periprosthesis inflammatory processes. In addition, the type of the mesh, the weight of the mesh (g/m^2), and fixation method may be contributing factors for the development of postoperative chronic pain [41]. In the present analysis, none of the studies evaluating the robotic approach reported this outcome, and the Open, TAPP, and TEP approaches seem comparable in term of postoperative chronic pain. The global heterogeneity was moderate ($I^2 = 63\%$) probably reflecting the lack of a globally accepted and standardized definition of postoperative pain. Notably, the Open approach was classified in the SUCRA ranking as the treatment with

Table 3 League table

Open	0.68 (0.41–1.27)	0.67 (0.43–1.15)		A
1.46 (0.79–2.47)	**TAPP**	0.99 (0.51–1.78)		
1.50 (0.87–2.35)	1.01 (0.56–1.98)	**TEP**		
Open	0.98 (0.37–2.51)	0.90 (0.49–1.63)	0.63 (0.32–1.30)	B
1.02 (0.39–2.68)	**rTAPP**	0.92 (0.44–1.94)	0.65 (0.25–1.72)	
1.10 (0.61–2.03)	1.08 (0.51–2.23)	**TAPP**	0.70 (0.39–1.31)	
1.57 (0.77–3.13)	1.54 (0.58–3.94)	1.42 (0.76–2.54)	**TEP**	
Open	0.53 (0.28–1.19)	0.86 (0.48–1.64)		C
1.88 (0.83–3.57)	**TAPP**	1.67 (0.63–3.23)		
1.16 (0.61–2.09)	0.59 (0.31–1.57)	**TEP**		
Open	0.97 (0.45–2.11)	0.96 (0.58–1.46)	1.02 (0.65–1.63)	D
1.04 (0.68–1.72)	**rTAPP**	0.97 (0.39–2.36)	1.05 (0.43–2.57)	
1.04 (0.68–1.72)	1.03 (0.42–2.53)	**TAPP**	1.06 (0.63–1.99)	
0.98 (0.61–1.53)	0.95 (0.39–2.31)	0.94 (0.50–1.57)	**TEP**	

Values are expressed as risk ratio (RR) and 95% credible intervals (95% CrI)

A hematoma, *B* seroma, *C* postoperative chronic pain, *D* hernia recurrence

major probability for postoperative chronic pain. In the previous studies, the comparison of Lichtenstein vs. TAPP showed a significantly lower chronic pain for TAPP, whereas there was insufficient evidence to determine the best treatment comparing Open vs. TEP and TAPP vs. TEP [42]. Wu et al. revealed that, compared to the Open approach, TAPP was associated with a lower rate of paresthesia with similar chronic pain [3]. In the Open technique, the prophylactic ilioinguinal neurectomy has been proposed to avoid nerve entrapment, thus, reducing postoperative pain [43]. However, it seems that the intraoperative identification and preservation of all three inguinal nerves during open surgery reduces significantly the incidence of postoperative chronic incapacitating groin pain (< 1%) [38, 44, 45].

Age > 50 years, smoking history, BMI > 30, and medial vs. lateral hernia are independent risk factors for hernia recurrence [46, 47]. The pooled network meta-analysis showed that the four surgical approaches seem comparable in term of hernia recurrence. Therefore, this result may not be generalized and the variability in operative technique should be taken into account. Notably, the global heterogeneity was zero ($I^2 = 0.0\%$) indicating a low degree of inconsistence across studies and ultimately giving robustness to the result. No significant differences were found in term of surgical site infections, urinary retention, and postoperative length of stay.

After the introduction of robot-assisted minimally invasive surgery, the number of rTAPP has progressively increased worldwide [48, 47]. The robot-assisted approach offers increased range of instruments motion and improved surgeon ergonomics [5]. However, some concerns exist including operative time, surgeon learning curve, real patient-effectiveness, and global costs [49, 50]. In the present review, the rTAPP was associated with an estimated longer operative time compared to the Open approach, probably attributable to instruments positioning and surgeons' learning curve. The cost analysis was reported in only three studies with a trend toward higher expenses in minimally invasive rTAPP. The pooled analysis was not performed, because the heterogeneity in cost reporting, but this seems imputable to instrument maintenance and equipment costs.

We acknowledge some limitations to the present meta-analysis, because the publication bias related to the heterogeneity of the included studies. Both RCT and observational design studies were considered. The intrinsic bias of observational studies could be considered a study limitation; however, the a priori exclusion of observational studies in systematic reviews is inappropriate and inconsistent with a comprehensive evidence-based approach [51]. Furthermore, the quality and quantity of RCT for surgical techniques comparison is acknowledged to be limited [52]. The imprecision must be considered for some of the outcomes, because the credible interval crosses null value or includes values favouring either treatment. The treatment ranking should be cautiously interpreted, because the treatment ranking does not consider the magnitude of differences in effects, and therefore, chance may explain any apparent difference between treatments. Therefore, surgeons should choose the most suitable surgical approach appraising the treatment ranking, costs, and personal expertise. Finally, the postoperative follow-up was heterogeneous across studies, thus, adding further background bias and the rTAPP was performed in a limited number of patients.

To our knowledge, this is the first network meta-analysis that globally compare outcomes within the major surgical approaches for primary unilateral inguinal hernia. Using

network meta-analytical techniques, we were able to globally synthesize data from numerous studies and, therefore, rank the treatments according to our studied outcomes. The study was planned in agreements with the PRISMA guidelines, and followed a sound methodology that was a priori stated in the PROSPERO protocol. This included comprehensive outcome measures and the evaluation of quality at study level (risk of bias) and confidence in results at outcome level (CINeMA). The selection criteria led to a homogenous population for some of the primary outcomes, as confirmed by low heterogeneity. This makes us confident that the results of this study are robust. Finally, we conducted the study accounting for single-study effect performing the prior sensitivity analysis.

In conclusion, this network meta-analysis suggests that Open, TAPP, TEP, and rTAPP seem comparable in term of postoperative hematoma, seroma, postoperative chronic pain, recurrence, infectious complications, urinary retention, and hospital length of stay. The surgical management of inguinal hernia is evolving and the effect of the adoption of innovative minimally invasive techniques should be further investigated in the long term. Ultimately, the choice of the most suitable treatment should be based on individual surgeon expertise and tailored on each patient.

Author contributions AA, FL, AM, and GC did the literature search; AA, FL, and GC formed the study design; Data collection was done by AA, FL, MC, and AM. AA, GB, and DB analysed the data; AA, GM, and DB interpreted the data; AA, GB, and DB wrote the manuscript; AA, DB, and GC critically reviewed the manuscript.

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Compliance with ethical standards

Conflict of interest AA, MC, GM, FL, GB, AM, PGB, GC, and Db declare no conflicts of interest.

Ethical approval Approval from the Institutional review board was not required for this study.

Human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this systematic review and meta-analysis, formal consent is not required.

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