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ORIGINAL ARTICLE

Comparison of glue versus suture mesh fixation for primary open inguinal hernia mesh repair by Lichtenstein technique: a systematic review and meta-analysis

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Abstract

Background The use of glue as a mesh fixator in open Lichtenstein inguinal hernia repair (IHR) has gained popularity to reduce recurrence and postoperative complications. This meta-analysis aims to provide an up-to-date review to compare glue versus suture fixation in primary open Lichtenstein IHR.

Methods PubMed, Embase, The Cochrane Library, Web of Science, and Springer were systematically searched till June 2021 for randomized controlled trials (RCTs) comparing glue versus suture fixation in open Lichtenstein IHR. Primary outcomes were early (at 1 year) and late recurrence (5 years or more). Secondary outcomes were the length of operation, postoperative haematoma and seroma, and chronic pain at 1 year.

Results A total of 17 RCTs with 3150 hernias (glue $n=1582$, suture $n=1568$) were included. Only three studies reported late recurrence. Glue fixation was associated with shorter operative duration (MD − 4.17, 95% CI − 4.82, − 3.52; $p<0.001$ and a lower incidence of haematoma formation (OR 0.51, 95% CI 0.32, 0.81; $p=0.004$). There was no significant difference in postoperative seroma (OR 0.72, 95% CI 0.35, 1.49; $p=0.38$), chronic pain after 1 year (OR 1.10, 95% CI 0.73, 1.65; $p=0.65$), early recurrence (OR 1.11, 95% CI 0.45, 2.76; $p=0.81$, $I^2=0\%$), and late recurrence (OR 1.23, 95% CI 0.59, 2.59; $p=0.59$, $I^2=0\%$).

Conclusion Early and late recurrence were comparable between glue and suture fixation in open Lichtenstein IHR patients. Glue fixation had shorter operating time and lower haematoma formation than suture fixation. Chronic pain and seroma formation were comparable. More RCTs should report long-term outcomes.

keywords inguinal hernia repair · Lichtenstein · recurrence · tension-free · open · mesh

Introduction

Inguinal hernias are the most common type of abdominal hernias, carrying a lifetime risk of 27% in males and 3% in females [1]. Globally, more than 20 million patients undergo inguinal hernia repair (IHR) every year [2]. The Lichtenstein tension-free mesh repair is the gold standard for open IHR with lower recurrence rates than non-mesh techniques such as Shouldice and Bassini's repair [2, 3]. One-year recurrence following Lichtenstein repair is reported to be 1–2% [4]. The initial study by Lichtenstein et al. advocated for non-absorbable sutures for mesh fixation [5]. However, complications such as recurrence and chronic pain remain a cause of concern, with an alarmingly high incidence of chronic pain in 15–40% of patients [6]. Reasons for early recurrence at 1-year include the surgeon's expertise, presence of tension, postoperative infection, choice of suture material, and suturing technique [7]. Pathophysiology of chronic pain is attributed to nerve entrapment from the mechanical fixation of the mesh [6]. It is, therefore, theoretically possible to reduce these risks through variation in mesh fixation techniques.

New mesh fixation techniques such as self-fixing meshes, and glue fixation have been introduced to reduce postoperative complications and chronic pain. These techniques

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are feasible, but their utility in reducing postoperative outcomes remains inconclusive [8–12]. Glue fixation techniques include synthetic glue such as *N*-butyl-cyanoacrylate (NBCA) or biological glue such as fibrin. The use of NBCA was first introduced in 1993 but concerns over presumed inflammatory reaction and cytotoxicity limited widespread adoption [13, 14]. Biological glue such as fibrin is more tolerable but was not cost-effective [9]. Differences in outcomes between synthetic versus biological glue fixation have also not been demonstrated [15].

The most recent meta-analysis addressing mesh fixation through glue versus suture in open Lichtenstein IHR was reported by Lin et al. [12]. They included 13 randomized controlled trials (RCTs) (8 using synthetic glue, 5 using biological glue) with 2320 patients and 2375 hernias (glue fixation $n=1168$, suture fixation $n=1207$), and demonstrated that glue fixation have shorter operative time and lower incidence of early postoperative pain persisting beyond 3 months in synthetic glue. However, early recurrence (defined as 1-year recurrence) and late recurrence (defined as recurrence after 5 years) were comparable between glue and suture fixation. The lack of significant difference may be due to the small number of RCTs ($n=2$) reporting on late recurrence. In addition, a study by Köckerling et al. reported that only 13.6% and 57.5% of all IHR recur at 1-year and 10-year following initial repair [16]. Although reporting recurrence after 5-years is uncommon, it is an important outcome that must be included in hernia surgery outcomes. Since the report by Lin et al., there have been more studies published on this topic. Hence, the purpose of this study is to provide an updated systematic review and meta-analysis to assess differences in the incidence of recurrence and other postoperative complications between glue and suture for mesh fixation in open Lichtenstein IHR.

Materials and methods

Study selection and search strategy

This systematic review and meta-analysis were performed according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines [17]. The protocol for this systematic review and meta-analysis was registered at PROSPERO (Ref no. CRD42021227348). A systemic search of the following databases (PubMed, Embase, The Cochrane Library, Web of Science, and Springer) was conducted for studies published from January 2000 to June 2021. A combination of the following search terms was used: "inguinal hernia", "suture", "glue", "cyanoacrylate", "fibrin tissue adhesive" and "Lichtenstein". The search was restricted to title and abstract. The complete search strategy used in PubMed is appended in Supplementary Table S1; search strategies for other databases were modified accordingly from the initial search strategy based on the database requirements. The complete search strategy was designed under the guidance of an experienced librarian and is made publicly available on PROSPERO at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021227348.

Included studies were randomized controlled trials (RCTs) on adult population (≥ 18 years old) with primary inguinal hernia and underwent open Lichtenstein tension-free mesh repair, and compared the use of glue versus suture fixation of mesh. Exclusion criteria were non-English studies, conference abstracts, studies that did not follow a RCT design, studies that have incomplete information (e.g., type of surgical technique, type of suture or glue used), studies that only included other types of hernia repair (such as minimally invasive surgery, or other types of open hernia repair such as Shouldice or Bassini's repair), studies which report only recurrent inguinal hernias, or did not have a comparator group (only reporting of glue fixation or suture fixation). All cross-references were screened for potentially relevant studies not identified by the initial literature search. After removing duplicates, abstracts were screened for potential inclusion screening independently by two authors (SP and SHL). Full-texts of included studies were subsequently reviewed in entirety and selected based on the inclusion and exclusion criteria. If two or more studies reported on the same patient cohort, only the latest study was included in the meta-analysis. Any discrepancies were resolved by consensus and review by the senior author (VGS).

Data extraction

Data extraction was independently conducted by two authors (SP and SHL). The following variables were extracted from each study: publication details (name of the first author, publication year and study period), study characteristics (sample size, sex, age, body mass index (BMI), type of hernia, type of mesh used, type of suture or glue used, type of anaesthesia), and clinical outcomes (follow-up duration, length of operation, postoperative morbidity (seroma and haematoma), chronic pain, respective pain score, early recurrence, and late recurrence). Early and late recurrence was defined as clinical and/or radiological evidence of recurrence within 1 year and after 5 years from surgery. We defined late recurrence as after 5-years due to some studies reporting recurrence beyond 5-year intervals. Notably, the Herniamed Registry has also classified recurrence after 5-years into 5–10 year interval [16]. Wound infection was defined as either superficial skin infection involving only the skin and/or subcutaneous tissue and not extending to the fascia, or deep infection involving the mesh. Chronic pain was defined

as the presence of pain over the affected side at 1-year follow-up. Included studies reported severity of pain using the Visual Analogue Scale (VAS). Our primary outcomes were early and late recurrence. Our secondary outcomes were the length of operation, postoperative haematoma and seroma, and chronic pain at 1 year.

Assessment of study quality

Two authors (SP and SHL) independently performed a quality assessment of the finalized trials using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2.0) tool [18]. This tool considers bias arising from the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported results. Disagreements between authors were resolved by discussion with senior author (VGS).

Statistical analysis

Meta-analysis was performed using RevMan 5.4 (Review Manager 5.4, The Nordic Cochrane Centre, Copenhagen, Denmark). Most of the outcome variables were expressed based on the number of hernias: early recurrence, late recurrence, incidence of seroma and haematoma, incidence of chronic pain, and respective pain score. The length of operation was expressed based on the number of patients. Studies including bilateral hernia repair were excluded from the analysis of length of operation [10, 15]. Outcomes with dichotomous outcomes were expressed as odds ratios (ORs) with 95% confidence interval (CI), which were calculated using the Mantel-Haenszel method. Continuous outcomes were expressed as mean difference (MD) with 95% CI, pooled with the inverse-variance method. The level of statistical significance was set at $p < 0.05$. To assess the heterogeneity between the studies, I^2 was calculated to estimate the inter-study variability. Heterogeneity was defined by $I^2 > 50\%$. A random-effect model was used when $I^2 > 50\%$ and a fixed-effect model was used when $I^2 \leq 50\%$.

Results

The systematic search identified 407 articles from the databases, with an additional 3 articles identified from a systematic review by Lin et al. [12, 19–21]. Thus, there were 324 articles after the removal of duplicates. Titles and abstracts of all the identified articles were screened. Subsequently, 22 full-text articles were reviewed in entirety for inclusion in the study. Two studies did not report on recurrence, which is our primary outcome [22, 23]. Three studies were outdated data with newer studies reporting on the same patient cohort [13, 24, 25]; hence only the latest studies by Matikainen et al. (year 2020) (trial number: NCT01592942) and Matikainen et al. (year 2017) (trial number: NCT00659542) were included [21, 26]. A total of 17 articles were included in the final analysis [8–10, 15, 19–21, 26–35]. While the study by Matikainen et al. (year 2020) included recurrent inguinal hernias ($n = 13/347$ (3.7%), this study was included after discussion with the senior author (VGS) because of the small sample size of the recurrent hernia and the benefits of the study reporting 5-year recurrence rates [26]. The decision to include this study was also supported by co-author (AMO) who is a regional hernia expert. Figure 1 shows the PRISMA diagram for the study selection process. The risk of bias assessment is summarised in Fig. 2. Four studies were graded as having a high risk of bias: three studies had incomplete outcome data [20, 28, 33], and one study did not blind the patients nor the investigators [10].

Study characteristics

A total of 17 studies including 3084 patients with 3150 hernias (glue $n = 1582$, suture $n = 1568$) [8–10, 15, 19–21, 26–35]. One study only included bilateral inguinal hernia with 55 patients (110 hernias) [10]. Another study included both unilateral and bilateral inguinal hernia with 156 patients (167 hernias) [15]. Eleven studies with 1901 hernias reported on the type of hernia: direct ($n = 504$), indirect ($n = 1290$), and combined (both direct and indirect hernia on the ipsilateral side $n = 96$) [8, 15, 19, 21, 26, 27, 30–32, 34, 35]; the study by Testini et al. did not specify the type of hernia for patients with a bilateral hernia ($n = 11$) [15]. All the studies have a common follow-up duration of 12 months. The overall study characteristics are summarised in Table 1.

Early and late recurrence

All 17 studies including 3150 hernias (glue 1582, suture 1568) reported early recurrence (defined as recurrence at 1 year) [8–10, 15, 19–21, 25–35]. Three studies, including 989 hernias (glue 498, suture 491), reported late recurrence (defined as recurrence after 5 years) [21, 26, 28]. This includes one study that defined recurrence as 7-year recurrence instead of 5-year recurrence [21]. Overall early recurrence rate was 0.54% ($n = 17/3150$ hernias), and late recurrence rate was 2.93% ($n = 29/989$ hernias). There was no significant difference between glue and suture fixation in early recurrence (OR 1.11, 95% CI 0.45, 2.76; $p = 0{\cdot}81$) (Fig. 3a) and late recurrence (OR 1.23, 95% CI 0.59, 2.59; $p = 0.59$) (Fig. 3b). There was no heterogeneity between studies for both early and late recurrence ($I^2 = 0\%$).

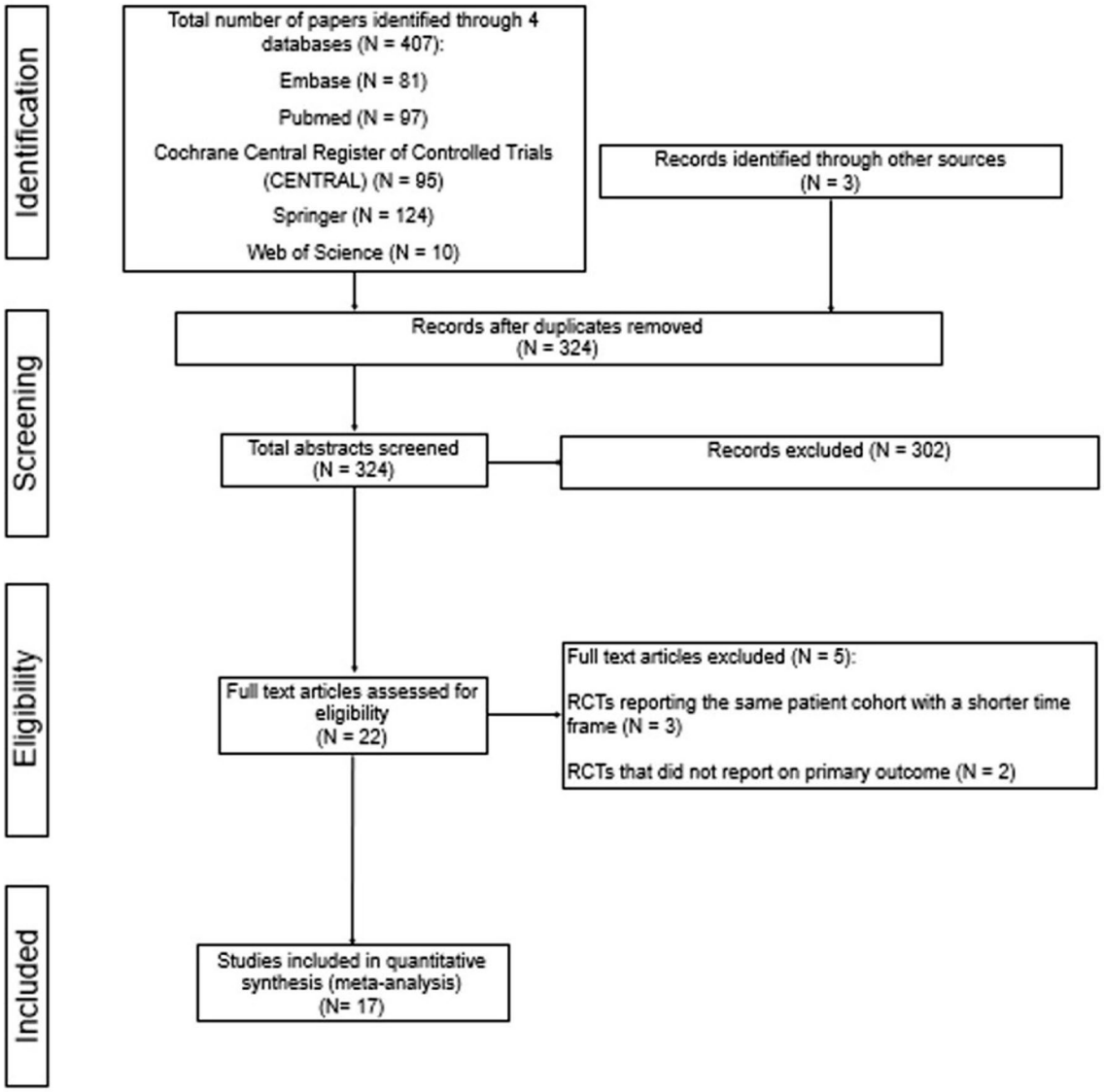

Fig. 1 PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) flowchart for study selection

Length of operation

Thirteen studies including 2409 patients (glue 1183, suture 1226) reported on length of operation [8, 9, 19–21, 27–32, 34, 35]. The abovementioned studies did not include the study by Testini et al. as the length of operation included patients who underwent both unilateral and bilateral hernia repair and may not be representative [15]. Length of operation was significantly shorter in the glue group compared to the suture group (MD − 4.17, 95% CI − 4.82, − 3.52; $p < 0.001$) (Fig. 4). There was considerable heterogeneity between studies ($I^2 = 94\%$).

Postoperative morbidity (seroma and haematoma formation)

Nine studies including 1993 hernias (glue 1008, suture 985) reported on the incidence of postoperative seroma formation [8, 15, 20, 26, 27, 29–31, 34]. The overall incidence of postoperative seroma formation was 1.51% ($n = 30/1993$ hernias). The incidence of postoperative seroma after glue fixation and suture fixation was 1.19% ($n = 12/1008$ hernias) and 1.83% ($n = 18/985$ hernias), respectively. There was no significant difference in the incidence of seroma formation in the glue group compared to the suture group (OR 0.72, 95% CI 0.35, 1.49; $p = 0.38$) (Fig. 5a). There was no heterogeneity between the studies ($I^2 = 0\%$).

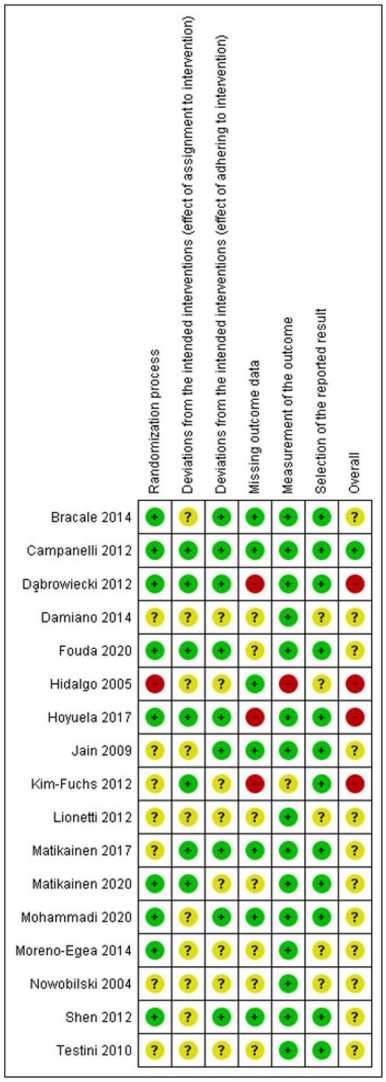

Fig. 2 Risk of bias summary for included studies ($n=17$); green (+): low risk of bias; yellow (?): unclear risk of bias; red (−): high risk of bias (Color figure online)

Twelve studies including 2092 hernias (glue 1068, suture 1024) reported on the incidence of postoperative haematoma formation [8–10, 15, 20, 21, 28, 29, 31, 32, 34, 35]. Overall incidence of post-operative haematoma formation was 3.82% ($n=80/2092$ hernias). Incidence of postoperative haematoma was significantly lower in the glue group ($n=28/1068$ hernias (2.62%)) compared to the suture group ($n=52/1024$ hernias (5.08%)) (OR 0.51, 95% CI 0.32, 0.81; $p=0.004$) (Fig. 5b). No heterogeneity was observed between studies ($I^2=0\%$).

Subgroup analysis was performed to compare incidence of postoperative haematoma in synthetic glue and biologic glue subgroups. Eight studies including 1364 hernias (synthetic glue $n=681$, suture $=683$) compared synthetic glue versus suture [8, 15, 20, 21, 28, 32, 34, 35]. Five studies including 787 hernias (biologic glue $n=387$, suture $n=400$) compared biologic glue versus suture [9, 10, 15, 29, 31]. Testini et al. studied both the use of synthetic glue and biologic glue [15]. Overall incidence of postoperative haematoma with synthetic glue and biologic glue was 3.67% ($n=25/681$) and 0.78% ($n=3/387$) respectively. Incidence of postoperative haematoma was significantly lower in the synthetic glue group compared to the suture group (OR 0.53, 95% CI 0.32, 0.87; $p=0.01$, $I^2=0\%$) (Fig. 5c). When comparing biologic glue versus suture fixation, incidence of postoperative haematoma was comparable (OR 0.42, 95% CI 0.13, 1.23, $p=0.11$, $I^2=0\%$) (Fig. 5d).

Chronic pain and respective pain scores

Six studies including 1151 patients and 1206 hernias (glue 603, suture 603) reported the incidence of chronic pain after 1 year [8, 10, 20, 21, 28, 31]. One study included bilateral hernias ($n=55$ patients, 110 hernias), which did not report any incidence of chronic pain [15]. The overall incidence of chronic pain after 1 year was 8.96% ($n=108/1206$ hernias); incidence of chronic pain was 9.29% ($n=56/603$ hernias) following glue fixation and 8.62% ($n=52/603$ hernias) following suture fixation. There was no significant difference in the incidence of chronic pain between the suture and glue groups (OR 1.10, 95% CI 0.73, 1.65; $p=0.65$) (Fig. 6a). There was low heterogeneity between studies ($I^2=24\%$).

Subgroup analysis was performed to compare the incidence of chronic pain at the 1-year interval. The overall incidence of chronic pain in synthetic glue and biologic glue groups was 11.2% and nil, respectively. Four studies including 994 patients and 994 hernias (synthetic glue $n=498$, suture $n=496$) compared synthetic glue versus suture fixation [8, 20, 21, 28]; no significant difference was observed in incidence of chronic pain (OR 1.10, 95% CI 0.73, 1.65; $p=0.65$, $I^2=24\%$) (Fig. 6b). Two studies including 212 patients and 212 hernias (biologic glue $n=105$, suture $n=107$) compared biologic glue versus suture fixation [10, 31]. We could not compare biologic glue versus suture fixation as there was no incidence of chronic pain (Fig. 6c).

Five studies, including 972 patients and 972 hernias (glue 489, suture 483), utilized the Visual Analog Scale (VAS) to report the severity of chronic pain after 1 year [21, 26, 31, 34, 35]. There was no significant difference in the VAS between the glue and suture groups after a year (MD − 0.08, 95% CI − 0.29, 0.13; $p=0.45$) (Fig. 6d). There was considerable heterogeneity between studies ($I^2=95\%$).

Table 1 Study characteristics of the included 17 randomized controlled trials

First author	Publication year	Study period	Number of patients (Glue/Suture)	M:F ratio	Age		Type of mesh	Type of glue	Type of suture	Type of anaesthesia	Follow up duration	Type of hernia		
					Glue	Suture						Unilateral/bilateral	Direct/indirect/combined	
													Glue	Suture
Hidalgo [10]	2005	January 2001–July 2003	55 (55/55)[a]	55:0	Range 49–71		Polypropylene	Fibrin	Prolene 2-0	Regional or epidural	1, 3, 6, 12 months	Bilateral	NR	
Nowobilski [27]	2004	May 2003–November 2003	46 (22/24)	46:0	60.5 (30–76)	52.6 (20–78)	Polypropylene	Butyl 2-Cyanoacrylate	Dexon 3-0	Local	1 week, 1, 3 months	Unilateral	9/13/0	8/16/0
Jain [19]	2009	NR	80 (40/40)	80:0	45.65[c]	51.98[c]	Polypropylene	Gelatin–resorcin–formalin (GRF)	Prolene 3-0	Spinal	1 week, 1, 6, 12 months	Unilateral	10/30/0	12/28/0
Kim-Fuchs [28]	2012	January 2001–December 2004	264 (131/133)	264:0	55.1 (28–85)	56.8 (25–83)	Vipro II	N-Butyl 2-Cyanoacrylate	PDS 2-0	Local, spinal or general	3, 12 months, 5 years	Unilateral	NR	
Campanelli [29]	2012	January 2006–April 2007	316 (158/158)	NR	58/0 (46;65)	59.0 (48;66)	Polypropylene	Fibrin	Prolene 2-0	Local, regional or general	12 months	Unilateral	NR	
Testini [15]	2010	January 2003–December 2007	156 (108/59)[a]	144:12	58.0 (17–85)[b]		Polypropylene	*N*-Butyl 2 cyanoacrylate ($n=56$), fibrin ($n=52$)	Prolene 3-0	Epidural	3, 7, 15 days, 1, 3, 6, 12 months	145 Unilateral, 11 bilateral[d]	45/53/5	31/18/4
Lionetti [9]	2012	July 2006–July 2009	148 (72/76)	148:0	55.7 (18–82)[b]		Ultrapro, polypropylene	Fibrin	Prolene	Local or spinal	7 days, 1, 6, 12 months	Unilateral	NR	
Matikainen [21]	2017	June 2007–May 2009	302 (151/151)	266:36	53 ± 15	53 ± 15	Optilene	Butyl 2-cyanoacrylate	Dexon 3-0	Local	1, 7, 30 days, 12 months	Unilateral	41/104/6	55/90/6
Damiano [30]	2014	January 2004–February 2010	468 (216/252)	NR	52.9 ± 4.9	55.1 ± 5.4	NR	Fibrin	Prolene 3-0, Dexon 3-0	Local	1 week, 6, 12 months	Unilateral	32/160/24	50/186/16
Bracale [31]	2014	January 2009–June 2010	102 (50/52)	97:5	59 (50;67)	56 (46;67)	Ultrapro	Fibrin	Prolene 3-0	Spinal	1 week, 1, 6, 12 months	Unilateral	15/35/0	22/30/0
Shen [32]	2012	January 2010–April 2010	110 (55/55)	92:18	63 ± 10	60 ± 12	ProLite Ultra	*N*-Butyl 2 cyanoacrylate	Prolene 2-0	Local	1 week, 1, 3, 6, 9, 12, 15 months	Unilateral	8/47/0	6/49/0
Dąbrowiecki [33]	2012	July 2008–November 2010	41 (20/21)	41:0	47.4 ± 13.4	45.4 ± 14.8	Polypropylene	*N*-Butyl 2-cyanoacrylate	Prolene	Local, subarachnoid or general	2, 7 days, 1, 2, 6, 12 months	Unilateral	NR	
Moreno-Egea [35]	2014	January 2008–January 2011	102 (50/52)	71:31	57 ± 16	55 ± 14	Polypropylene	*N*-Hexyl cyanoacrylate	Prolene 2-0	Local	1 week, 1, 3, 6, 12, 24 months	Unilateral	10/40/0	9/43/0

Table 1 (continued)

First author	Publication year	Study period	Number of patients (Glue/Suture)	M:F ratio	Age		Type of mesh	Type of glue	Type of suture	Type of anaesthesia	Follow up duration	Type of hernia		
					Glue	Suture						Unilateral/bilateral	Direct/indirect/combined	
													Glue	Suture
Matikainen [26]	2020	January 2012–December 2013	423 (216/207)	NR	64 ± 14	61 ± 14	Ultrapro, Optilene	*N*-Butyl 2-cyanoacrylate	Prolene 2-0	Local	1, 5 years	Unilateral	74/125/17	67/122/18
Hoyuela [20]	2017	November 2013–November 2015	370 (188/182)	332:38	60.6 ± 14.9	59.0 ± 13.5	Polypropylene	*N*-Butyl 2-cyanoacrylate	Prolene 2-0	Local, spinal or general	1 week, 1, 6, 12 months	Unilateral	NR	
Fouda [34]	2020	March 2018–September 2018	43 (22/21)	NR	47.9 ± 13	49 ± 11.6	Polypropylene	*N*-Butyl 2-cyanoacrylate	Prolene 2-0	Spinal	1 week, 6, 12 months	Unilateral	0/22/0	0/21/0
Mohammadi [8]	2020	September 2018–March 2019	58 (28/30)	58:0	53.1 ± 10.9	55.8 ± 6.9	Polypropylene	*N*-Hexyl cyanoacrylate	Prolene 3-0, Vicryl, 2-0 and Monocryl 3-0	Spinal	12 months	Unilateral	0/28/0	0/30/0

Continuous variables are expressed in mean ± SD or median (range), or median (*Q*1; *Q*3)

NR not reported; *M:F* Male:Female

[a]Values in parenthesis are expressed as number of hernias in each group as these studies included bilateral hernias

[b]Value expressed as mean (range) instead

[c]Values are reported as mean. No standard deviation, range or interquartile range was reported

[d]Number expressed based on number of patients, rather than number of hernias. Overall, the study included 156 patients with 167 hernias

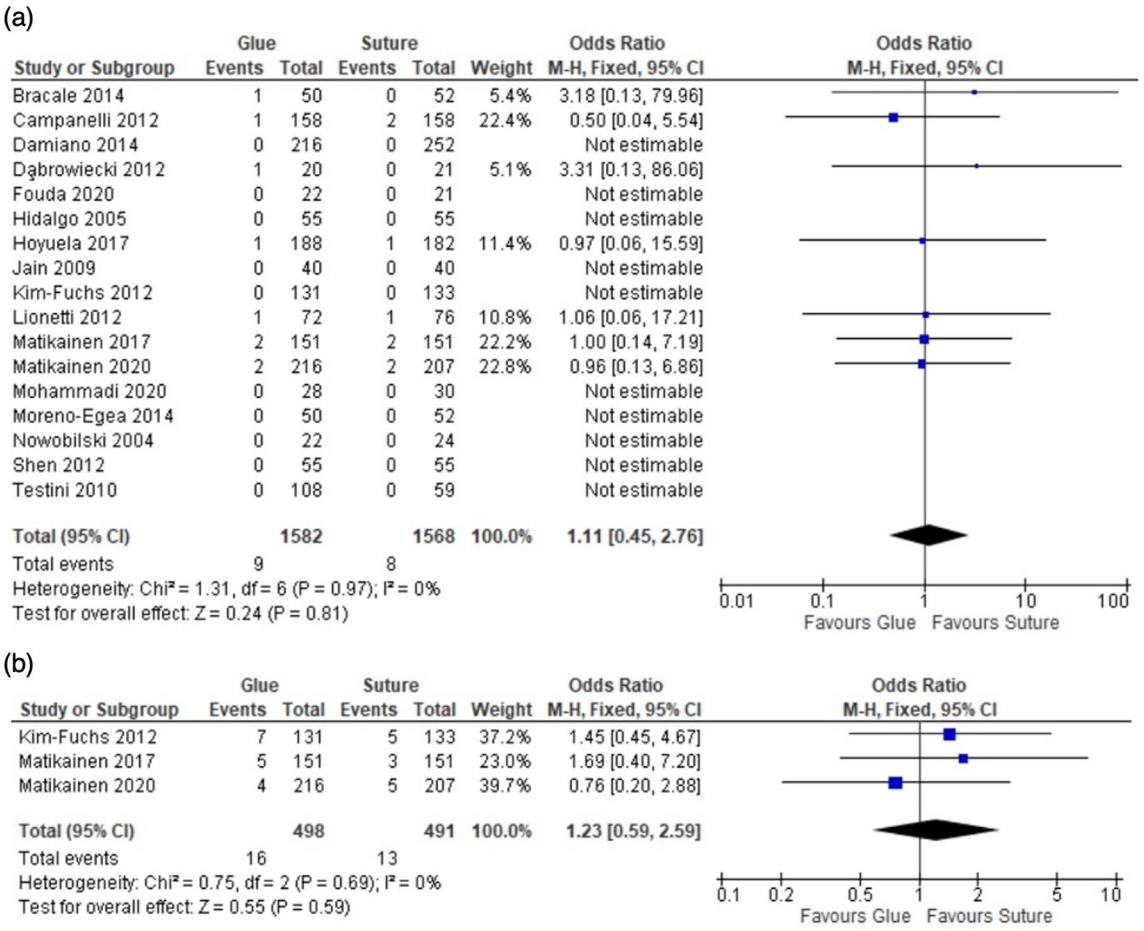

Fig. 3 Forest plot showing **a** early recurrence (at 1-year) and **b** late recurrence (after 5 years), comparing glue versus suture fixation in primary open Lichtenstein inguinal hernia repair

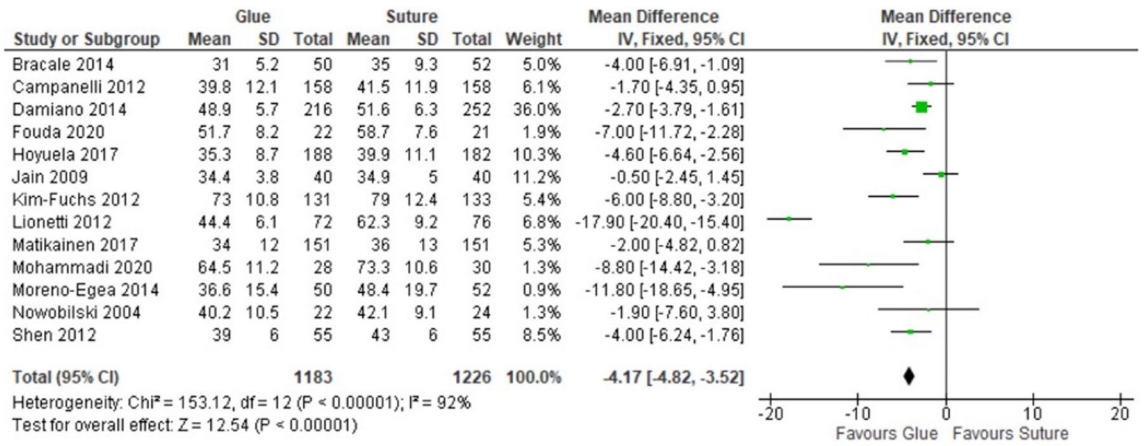

Fig. 4 Forest plot on length of operation comparing glue versus suture fixation in primary open Lichtenstein inguinal hernia repair

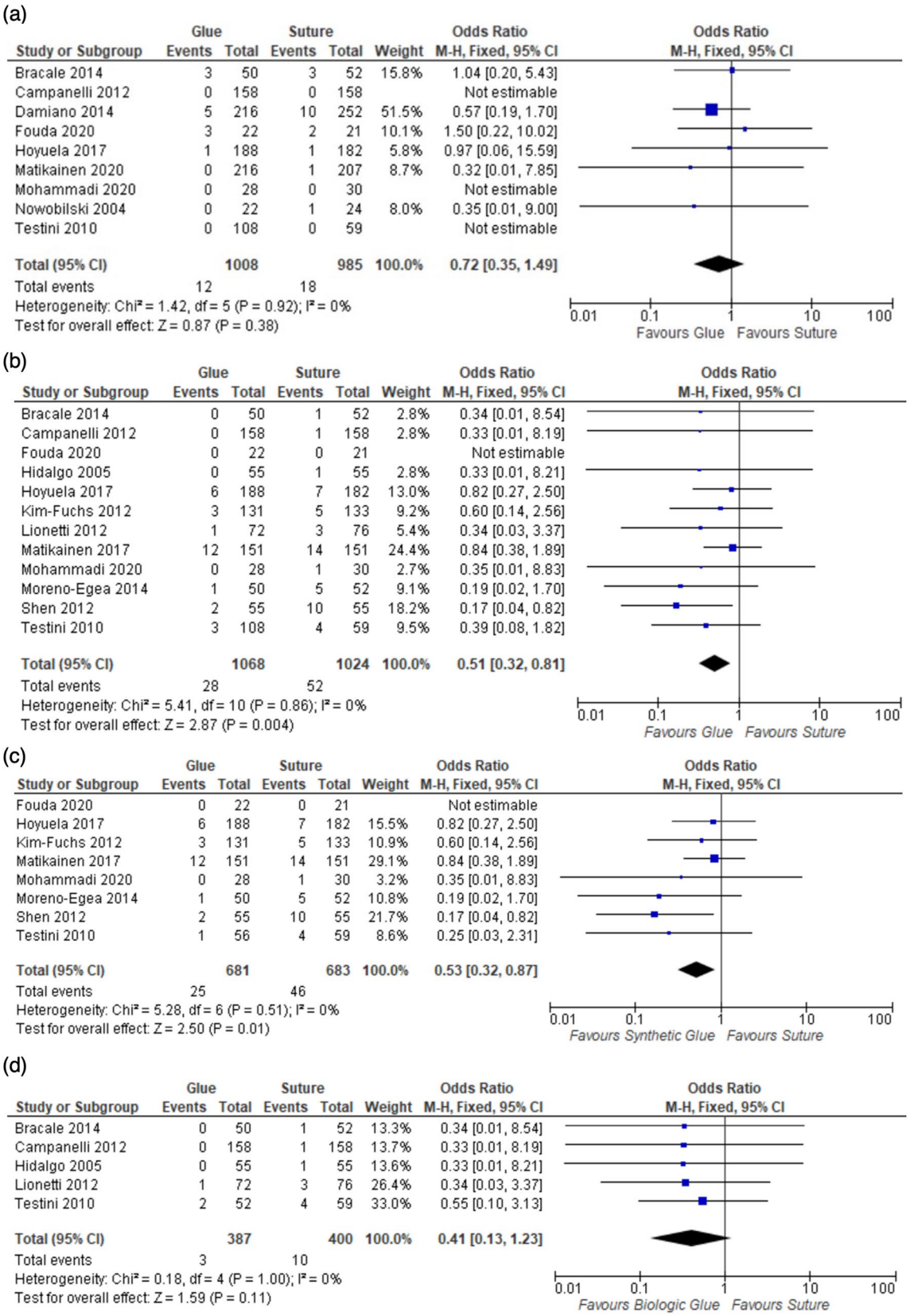

Fig. 5 Forest plot on post-operative complications: **a** seroma, **b** haematoma comparing glue versus suture fixation in primary open Lichtenstein inguinal hernia repair; and subgroup analysis of incidence of postoperative haematoma in **c** synthetic glue, and **d** biological glue versus suture fixation

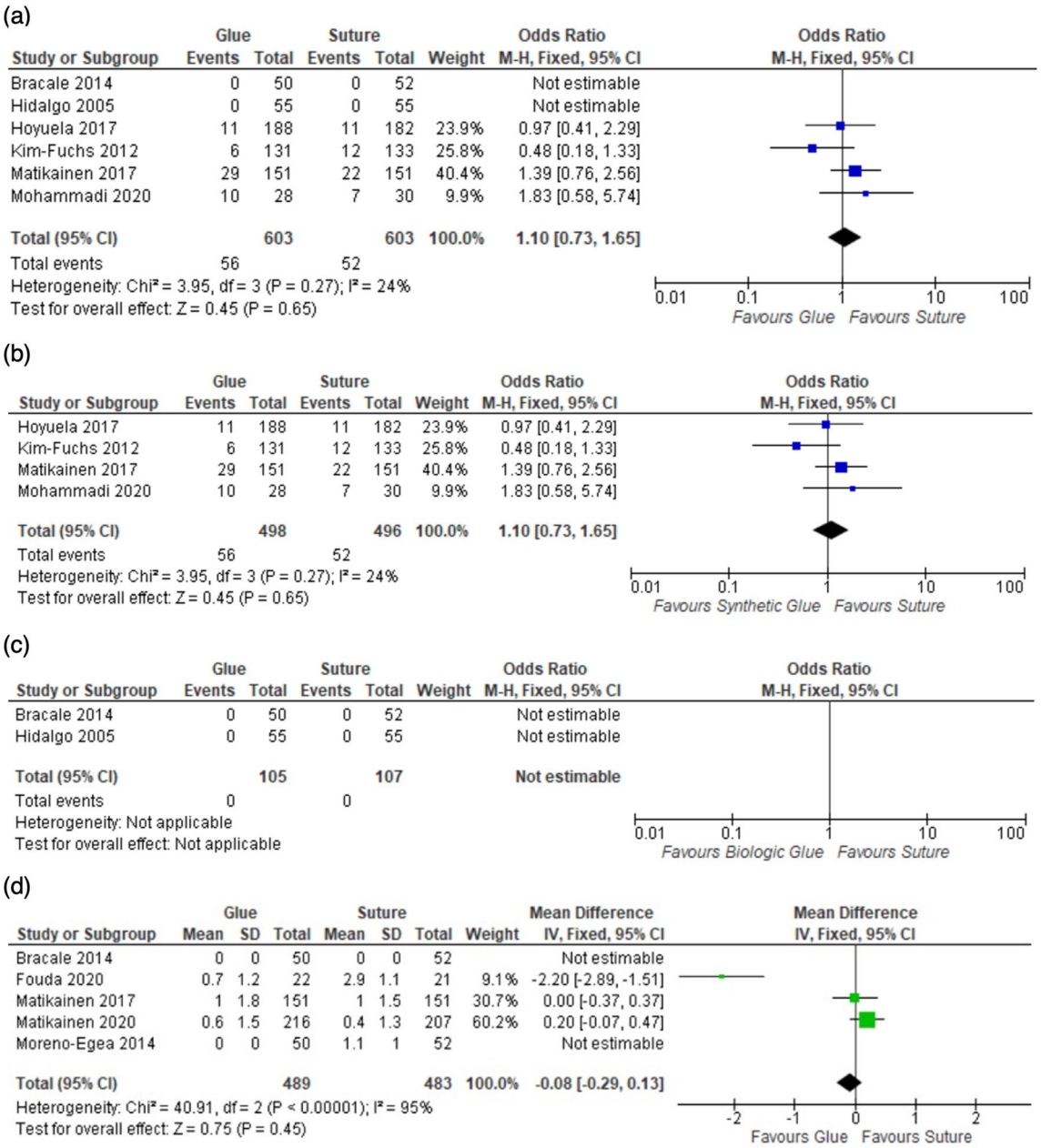

Fig. 6 Forest plot on chronic pain at 1-year follow up: **a** incidence of chronic pain comparing glue versus suture fixation in primary open Lichtenstein inguinal hernia repair and subgroup analysis of incidence of chronic pain in **b** synthetic glue, and **c** biological glue versus suture fixation; **d** comparison of severity of chronic pain using the Visual Analogue Scale

Discussion

This study is an updated meta-analysis from the previous meta-analysis and includes 709 more patients with an estimated 30% increase in sample size [12]. This study reported similar early and late recurrence between glue and suture fixation in open Lichtenstein IHR. Glue fixation has shorter operating time and lower postoperative haematoma incidence than suture fixation. Chronic pain and seroma were comparable between glue and suture fixation.

To date, several meta-analyses have been conducted on the use of glue versus suture fixation of mesh in open Lichtenstein IHR [11, 12, 36–40]. The latest meta-analysis by Lin et al. in 2018 included 13 RCTs (8 using synthetic glue, 5 using biological glue) with 2375 patients (glue fixation $n = 1168$, suture fixation $n = 1207$) [12], while a network meta-analysis by Rausa et al. included 28 RCTs with 5495 patients comparing self-gripping mesh, glue fixation and suture fixation [40]. Our meta-analysis is an update from the review by Lin et al. [12]; we excluded one study originally

included in their meta-analysis as the authors did not report recurrence, which is our primary outcome [22]. We also included 5 additional studies with 828 patients and 839 hernias [8, 9, 15, 26, 34], of which there was an additional study reporting late recurrence [26]. Thus, this updated meta-analysis should not be considered a replication of the previous report but an updated piece of evidence.

Hernia recurrence rate is an important measure of the success of IHR. From a patient's perspective, this translates into mental burden from a "failed surgery" and physical burden from the need to adjust the personal schedule and additional costs of repeat surgery [41]. Repair of recurrent inguinal hernia is more technically challenging because of anatomy distortion from scar tissue formation, and deviation from guideline recommendations is not uncommon [42]. Existing meta-analyses have yet to demonstrate any benefit on recurrence rates conferred by glue fixation following open Lichtenstein repair of primary inguinal hernia [11, 12, 36–40]. Our study is consistent with their findings: early recurrence (OR 1.11, 95% CI 0.45, 2.76; $p = 0{\cdot}81$) and late recurrence (OR 1.23, 95% CI 0.59, 2.59; $p = 0.59$). A network meta-analysis by Rausa et al. in 2019 including 28 RCTs with 5495 patients comparing self-gripping mesh, suture fixation and glue fixation similarly showed comparable recurrence rates between each modality [40]. Advantages of tissue adhesives over traditional suture fixation include the reduced risk of nerve entrapment and ease of application with reduced operating time. However, there are concerns over the use of glue on recurrence rates; biological glue such as fibrin is fully absorbed within 2 weeks of application [43]. Early recurrence following open IHR is attributed to faults in operative technique and postoperative infection, while late recurrences are attributed to collagen defects, age, and medical morbidities [7]. Many surgeons define this as a technical failure and tissue failure, respectively. Operative techniques and materials include the type of mesh and suture used and suturing technique. Suture materials that do not hold the tissues for at least 6 weeks are unsuitable for hernia repair as the surgical wound requires 3 months before regaining 80% of its original strength, which is the maximum amount [7, 44]. Though biological glue is fully absorbed within 2 weeks, the fibrinogen component provides tensile strength, adhesive properties and promotes fibroblast proliferation [45, 46]. While we have data to support the non-inferiority of glue fixation on 1-year recurrence, whether the use of glue will lead to long-term recurrence is still a question to be addressed as only 3 studies report late recurrence [21, 26, 28]. This is an important question that needs to be addressed as most hernia recurrence occurs beyond the 1-year mark. Recurrence is a function of follow-up, i.e., the longer the follow-up, the higher the recurrence. Köckerling et al. reported a fourfold increase in recurrence at 10 years following repair compared to 1 year (1-year recurrence 13.6%, 10-year recurrence 57.5%) [16]. Existing 3 studies reporting recurrence after 5 years demonstrate comparable recurrence between glue and suture fixation [21, 26, 28]. However, a lack of statistical significance does not equate to a lack of clinical significance. For example, 5-year recurrence was 10% in glue fixation and 5.8% in suture fixation in the study by Kim-Fuchs et al. [28], 2.2% in glue fixation, and 2.9% in suture fixation by Matikainen et al. (year 2020) [26], and 4.5% in glue fixation and 2.6% in suture fixation by Matikainen et al. (year 2017) [21]. These studies appear to suggest that late recurrence is clinically higher in glue fixation with a close to twofold increase [21, 28]. However, these recurrence rates reported account for patients lost to follow-up and were assessed using per-protocol analysis [47]. Per-protocol analysis results in a biased assessment of intervention, and meta-analysis should analyse data based on intention-to-treat. Our limited data on late recurrence shows comparable results between glue fixation and suture fixation.

Open Lichtenstein repair of primary inguinal hernia is a relatively common and "straightforward" surgery performed by general surgeons with a median operating time of 50 min [48]. Our study demonstrated a shorter operating time for glue fixation compared to suture fixation (MD − 4.17, 95% CI − 4.82, − 3.52, $p < 0.001$). This is an expected finding; suture fixation requires running a continuous suture from the pubic tubercle along the inguinal ligament to the deep inguinal ring. General benefits conferred by shorter operating time are reduced anaesthesia time, lower postoperative morbidity, and length of hospitalisation stay [49]. Reduced anaesthesia time may benefit patients with poor co-morbidities and are at risk of cardiopulmonary complications [50]. In addition, reduced anaesthesia time could reduce intravenous fluid infusion and potentially reduce the risk of urinary retention. Nevertheless, while statistical significance is obtained for the shorter operating time in glue fixation, caution is required in its interpretation with a mean difference of − 4.17 min (95% CI − 4.82, − 3.52). The significance of 5 min reduction in operating time may not be clinically meaningful. Most studies that demonstrated worse outcomes following surgery reported prolonged anaesthesia time of more than 2–6 h [49, 51]. Studies on IHR showed that shorter operating time is associated with an increased risk of repeat surgery and recurrence [48, 52], while prolonged operating time has been associated with worse outcomes in other surgeries, such as increased revision rate in total hip replacements [53]. While these studies did not consider the size of hernia defect and whether the presence of scrotal extension may have confounded recurrence rate, it is imperative to know that shorter operating time may compromise the diligence in surgical technique that may predispose patients to recurrence risk. In patients with large inguinal hernias, identification of indirect sac is easy, and recurrence is likely a direct recurrence. In patients with small inguinal hernias,

identification of indirect sac may be difficult. We advocate that surgeons should always search for an indirect sac, as essentially it means identifying the peritoneal layer at the level of the deep inguinal ring. Thus, a diligent search for indirect hernia sac by meticulous high dissection with identification of inferior epigastric artery and preperitoneal fat is essential before concluding that indirect sac is absent. Despite the shorter operating time with glue fixation, our study showed that early and late recurrence incidence was similar to suture fixation. This reinforces that the statistically significant reduction in operating time in glue fixation may not be clinically significant.

Postoperative wound or scrotal haematoma is a common postoperative complication with an incidence of 0.3–6% [54–56]. Small haematomas are managed conservatively and resolve spontaneously. In rare circumstances, large and/or unresolving haematoma may require drainage or surgical evacuation. Risk factors for postoperative groin haematoma include anticoagulant medication, incarcerated hernia, and recurrent hernia [57]. Incarcerated and recurrent hernias were excluded from our analysis. Most of the studies did not comment on the use of antiplatelet or anticoagulant medications. Three studies excluded patients who had warfarin usage [19, 29, 30]. Hoyuela et al. included patients who used antiplatelets and/or anticoagulants (glue 13.3% versus suture 9.3%) [20]. However, they showed a comparable incidence of postoperative haematoma (glue 3.2% versus suture 3.8%, $p=0.258$) [20]. Our meta-analysis showed a lower incidence of postoperative haematoma using glue fixation (OR 0.52, 95% CI 0.32, 0.82, $p=0.005$), and this difference may truly be due to the method of mesh fixation. It has been theorized that biological glue such as fibrin is effective in haemostasis and has been used in several contexts for surgical haemostasis, such as following trauma [58–60]. The overall incidence of haematoma in our meta-analysis following biological glue was 0.78% compared to 3.67% in synthetic glue but was not significant ($p=0.11$) which may be due to the smaller sample size in the biological glue subgroup. Several meta-analyses have reported no difference in incidence of haematoma following laparoscopic versus open primary IHR [61–63], while a recent updated network meta-analysis by Aiolfi et al. in 2021 comparing open Lichtenstein IHR, laparoscopic transabdominal preperitoneal repair and totally extraperitoneal repair showed reduced haematoma following laparoscopic repair [64]. While it is theoretically possible that the use of glue, a medical adhesive, allows for reliable hemostasis and reduces the incidence of postoperative haematoma, interpretation of our results is to be taken with caution. In our opinion, a good surgical technique for suture fixation of the mesh during open surgery is necessary and sufficient. We do not advocate that based on the results of this meta-analysis, a hernia surgeon should switch his or her clinical practice. It is not the suture itself, but the person who places the suture that is relevant to haematoma risk. Further, it is obvious from the existing literature that the true incidence of haematoma is likely to be more than reported by RCTs, as RCTs' stringent inclusion and exclusion criteria are not representative of day-to-day clinical practice.

Symptomatic inguinal hernia presenting with persistent groin pain is an indication for IHR. However, chronic pain is a major cause of morbidity in patients following hernia repair, accounting for up to 54% [65]. Open repair, recurrent hernia, high intensity of preoperative pain, and history of chronic pain are risk factors that have been established to result in chronic groin pain following IHR [66]. Our study failed to demonstrate a benefit of glue fixation to reduce the incidence of chronic pain at 1-year follow-up (OR 1.10, 95% CI 0.73, 1.65, $p=0.65$). This is contrary to the findings by Lin et al., who demonstrated a lower incidence of early chronic pain (defined as beyond 3 months) following biological glue fixation compared to suture fixation (OR 0.41; 95% CI 0.19–0.90; $p=0.03$) [12]. The advent of adhesives for mesh fixation has been thought to reduce postoperative pain by reducing nerve compression and has lower tissue tension. In our opinion, early and late chronic pain terminology is unconventional and deviates from the unified term as chronic pain. While chronic pain is defined as pain lasting more than 3 months by the International Association for the Study of Pain, it has been suggested for a cut-off of at least 6 months following operation due to the possibility of inflammation around the prosthetic mesh [67–69]. Existing meta-analysis comparing laparoscopic versus open hernia repair also used 1 year as a cut-off for defining chronic pain [61]. One year is, therefore, a reasonable cut-off to define chronic pain following open inguinal hernia repair. The lack of statistical significance in chronic pain compared to the study by Lin et al. may be due to the different definitions used and the heterogeneity of studies; they used different time points ranging 3 months to 1 year to define chronic pain [12]. Therefore, it is not possible to conclude that glue fixation results in a lower incidence of chronic pain, and there is a need to standardize definitions. Similarly, in laparoscopic hernia repair (either transabdominal preperitoneal repair (TAPP) or totally extraperitoneal repair (TEP)), Antoniou et al. showed a benefit of biological glue compared to mechanical fixation in reducing chronic pain (defined as 3 months post-operatively) (OR 0.46, 95% CI 0.22–0.93, $p=0.03$) [70]. Chronic pain following IHR is multifactorial and may be attributed to the mesh type, mesh weight, mesh porosity, extent of dissection, tissue handling, nerve injury and method of fixation [38, 68, 71–73]. Presence of chronic pain at 3 months following IHR may be attributed to the initial inflammatory reaction post-operatively from trauma to tissue at suture points, or due to suturing of the iliopubic tract and periosteum of the pubic tubercle [74]. However, whether or not the method of fixation impacts incidence of

chronic pain needs to be validated by further RCTs with standardised definitions of chronic pain.

Our study has its strengths. To date, this is the most updated meta-analysis, including RCTs till June 2021, with a total of 17 studies and 3150 hernias. We also used 1 year as the cut-off for chronic pain, consistent with current recommendations following inguinal hernia repair [67, 68]. We also performed subgroup analysis for the type of glue (synthetic and biological glue) versus suture fixation. There are a few limitations to our study. Firstly, follow-up time is limited to 12 months in most of the studies, and we only had three studies reporting late recurrence. In addition, there is a lack of standardized definition of postoperative haematoma, and the true incidence of complications is underreported due to a lack of long-term results. We also did not analyse synthetic or biological glue separately for late recurrence, given the small number of studies reporting. While synthetic glue may theoretically result in a higher inflammatory reaction, foreign body sensation, and chronic pain, this has not been demonstrated in existing RCTs [15]. This meta-analysis did not assess other outcomes such as cost and quality of life due to the paucity of studies reporting these outcomes. Only one study compared the quality of life, and no statistical difference was found between glue and sutures [29]. The only study that analyzed cost observed a €24.90 reduction per patient in the fibrin glue group than the suture group [31]. In public funded hospitals, the operating theatre costs are not billed per unit of time. Further, the cost of suture is bundled with operating costs, while glue is billed as an additional consumable item, and thus cost of glue fixation is likely to be higher.

Conclusion

This updated meta-analysis shows that glue fixation in primary open Lichtenstein IHR has similar early and late recurrence compared to suture fixation. Operating time was shorter and incidence of postoperative haematoma was lower with glue compared to suture fixation. Multicentre collaborative studies with long-term follow-up reporting recurrence, cost-effectiveness analysis, and quality of life outcomes remain an unmet need in herniology.

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Declarations

Conflict of interest The authors declare no conflicts of interest.

Ethical approval This study is a systematic review and meta-analysis and does not require ethics approval. This study was approved by PROSPERO (Ref: CRD42021227348).

Human and animal rights Not applicable.

Informed consent Not applicable.

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