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A meta-analysis of randomized control trials assessing mesh fixation with glue versus suture in Lichtenstein inguinal hernia repair

Hongwei Lin, MD[a], Zhuonan Zhuang, MD[a], Tianyi Ma, MD[a], Xiaowen Sun, MD[a], Xin Huang, MD[b], Yuanxin Li, MD[a,*]

Abstract

Background: The use of glue to fix mesh instead of sutures in Lichtenstein inguinal hernia repair has been accepted worldwide, with the increasing worries about postoperative chronic groin pain and recurrence. The aim of this meta-analysis was to clarify which mesh fixation method was more suitable in Lichtenstein inguinal hernia repair.

Methods: Articles published up to July 2017 were searched using MEDLINE, the Cochrane Library, Embase, and the Web of Science. Randomized controlled trials (RCTs) comparing glue versus suture mesh fixation in Lichtenstein inguinal hernia repair were included in the review. The quality assessment and data extraction of included studies were applied by 2 independent authors. Statistical analysis was performed using RevMan 5.2 software.

Results: Thirteen RCTs with 2375 patients were eligible for inclusion. Eight trials compared synthetic glue with suture fixation and 5 compared biological glue with suture fixation. The results showed that there was a lower incidence of early chronic pain (subgroup analysis, biological glue versus sutures, odds ratio (OR) = 0.41; 95% confidence interval (CI), 0.19–0.90; $P = .03$), and hematoma (subgroup analysis, synthetic glue versus sutures, OR = 0.56; 95% CI, 0.34–0.95; $P = .03$) in the glue fixation group. Suture mesh fixation method cost more time in operation than glue (mean difference = −4.60, 95% CI −7.60 to −1.60; $P = .003$). There was no evidence of an increase in chronic pain or recurrence rates with glue fixation method in the long-term follow-up.

Conclusions: Mesh fixation with glue compared with sutures in Lichtenstein repair inguinal hernia is faster and less painful, without an increasing in terms of recurrence rates in the long term.

Abbreviations: CI = confidence interval, M-H = Mantel–Hansel method, OR = odds ratio, RCT = randomized controlled trial, WMD = weighted mean difference.

Keywords: glue, Lichtenstein inguinal hernia repair, mesh fixation, meta-analysis, suture

1. Introduction

The Lichtenstein technique is a common surgical procedure for inguinal hernia repair in general surgery, with very good results in terms of complications and a low rate of recurrence.[1,2] The original approach of fixing the mesh in Lichtenstein herniorrhaphy used nonabsorbable synthetic sutures but may contribute to an increased incidence of complications, such as chronic pain, numbness and hematoma formation.[3,4] It is reported that a large number of patients suffer chronic groin pain after Lichtenstein hernia repair.[5] Bay-Nielsen et al[6] designed a nationwide questionnaire study with 1166 patients and found that 17% of them described restrictions during work, sport or leisure as a result of chronic groin pain at 1 year after repair of inguinal hernia. Any strategy to reduce chronic groin pain would help patients to improve daily activities.

Several causes have been regarded as contributing to chronic groin pain, including irritation or damage to the inguinal nerves by sutures or mesh, inflammatory reaction to the mesh or scar tissue.[7–9] Subsequently, studies have proved that the problem of chronic groin pain is not due to topical nerve preservation or division, but rather due to the type of mesh or mesh fixation method.[2,3,5] With the aim of reducing chronic groin pain, some researchers have described using absorbable sutures, various tissue glues or novel self-gripping mesh in tension-free herniorrhaphy and have achieved excellent results.[10–12]

As the use of glue instead of sutures to fix mesh has become widespread, worries about an increased risk of postoperative hernia recurrence after glue fixation emerged. Several randomized controlled trials (RCTs) comparing glue versus sutures for mesh fixation in Lichtenstein inguinal hernia repair have reported satisfactory results in terms of hernia recurrence.[2,11,13] However, comparing with suture fixation, the efficacy of glue for Lichtenstein inguinal herniorrhaphy is still a controversial issue, because discrepancies exist between synthetic and biological glues and long-term results on chronic groin pain and hernia

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[a] Department of Gastrointestinal Surgery, [b] Department of Hepatopancreatobiliary Surgery, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing, China.

[*] Correspondence: Yuanxin Li, Department of Gastrointestinal Surgery, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, No. 168 Litang Road, Changping District, Beijing 102218, China (e-mail: surgeon_lyx@sina.com).

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recurrence are not clear. The aim of this systematic review is thus to evaluate whether the surgical outcomes differ between glue and suture for mesh fixation in Lichtenstein inguinal herniorrhaphy.

2. Methods

2.1. Identification of trials

A systematic literature search was performed using the following databases: MEDLINE, the Cochrane Library, Embase, and the Web of Science for studies published until July 2017. Search terms used for the final search were "inguinal hernia," "glue," "suture," "mesh," "herniorrhaphy," "tension-free," and "Lichtenstein." The reference lists of relevant articles were also searched for additional trials. Only randomized controlled trials comparing glue versus sutures for mesh fixation in Lichtenstein inguinal hernia repair were included in this review. Data from editorials, review, case report, and observational studies were excluded from analysis. Ethical approval and patient consent were not applicable for meta-analysis.

2.2. Quality assessment and data extraction

Two authors independently evaluated all included trials for quality assessment and data extraction according to the criteria recommended by handbook of Cochrane Collaboration. Each included trial was assessed to ascertain the methodological qualities. Data extraction was performed using a standard form: author(s), publication year, country, enrolment dates, sample size, age, gender, follow-up period, type of mesh, type of glue, type of suture, type of anesthesia and antibiotic use, as well as the following outcomes: chronic pain, recurrence; operating time, hematomas, wound infection, and mesh infection. Chronic groin pain was defined as postoperative pain persisting beyond 3 months (early chronic pain) or 60 months (late chronic pain). Recurrence was defined as clinically or radiologically diagnosed hernia recurrence within 12 months (early recurrence) or 60 months (late recurrence). Differences between authors were resolved by consensus discussion.

2.3. Statistical analysis

Statistical analysis was performed using RevMan 5.2 from Cochrane Collaboration. For dichotomous data, results were expressed as odds ratios (ORs) with the corresponding 95% confidence intervals (CIs). The Mantel–Hansel method (M-H) was used for calculating the weighted ORs. For continuous data, weighted mean difference (WMD) with 95% CIs was calculated. Subgroup analysis was performed based on the category of glues (synthetic and biological glues). $P < .05$ was considered statistically significant difference. Heterogeneity among studies was assessed by means of the I^2 inconsistency test and chi-square test. If there was no heterogeneity between studies ($P > .1$, $I^2 < 50\%$), the fixed-effect model was used, or else, a random-effect model was instead.

3. Results

The PRISMA flowchart for systematic search and selection of article is shown in Figure 1. Twenty-three RCTs comparing glue versus sutures for Lichtenstein repair of inguinal hernia were retrieved from the electronic databases. Ten studies were excluded because 4 of them reported duplicated data and in 6 studies the intervention and control groups received different kinds of mesh. Thirteen studies were retained for final analysis.[2,13–24] The assessment of methodological quality of included trials is explained in Figure 2. The characteristics of included trials are summarized in Table 1. Five studies reported biological glue for mesh fixation while 8 studies used synthetic glue. Subgroup analysis was also introduced because of the discrepancies between synthetic and biological glues. A total of 2375 patients were enrolled in these eligible trials, with 1168 of those patients in the glue fixation group and 1207 of those patients in the suture fixation group. All of those patients were adults with primary inguinal hernia. The average follow-up period in 9 included studies was similar, at 12 to 16 months. Two studies had a follow-up less than 6 months while another 2 studies had more than 60 months.

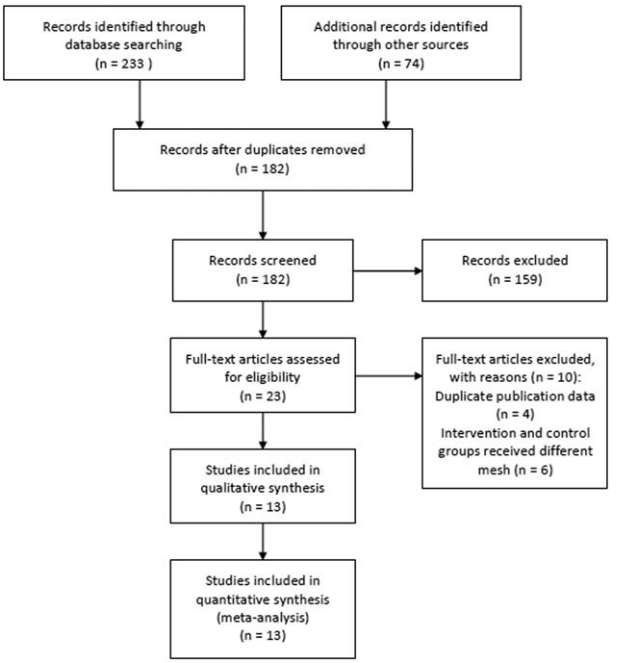

Figure 1. Flowchart of the study selection process. RCTs = randomized controlled trials.

3.1. Early chronic pain

Nine studies contributed to the combined analysis of early chronic pain (Fig. 3). There was no significant difference in terms of early chronic pain between the 2 groups (OR = 0.58; 95% CI, 0.32–1.03; $P = .06$). Subgroup analysis demonstrated that there was no significant difference between the synthetic glue fixation group and the suture fixation group (OR = 0.65; 95% CI, 0.31–1.34; $P = .24$). However, there was significant heterogeneity between these studies ($P = .06$, $I^2 = 53\%$). When comparing biological glue fixation with suture fixation, subgroup analysis showed a significant difference between the 2 groups (OR = 0.41; 95% CI, 0.19–0.90; $P = .03$). The incidence of early chronic pain was significantly lower in the biological glue fixation group than the suture fixation group.

3.2. Early recurrence

Eleven studies with a total of 2265 patients reported early hernia recurrence, with 7 studies belonged to the synthetic glue fixation

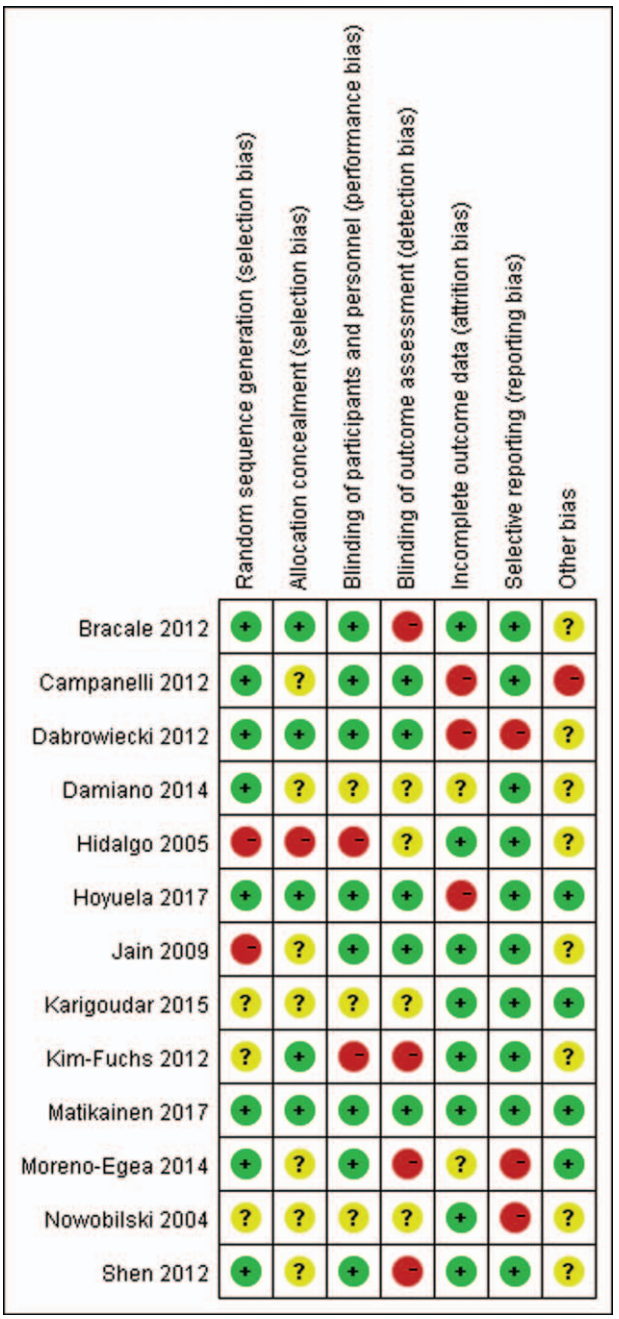

Figure 2. The risk of bias summary for the included studies.

group and 4 studies to the biological glue fixation group. No significant difference was found between the glue and suture fixation groups, either in the combined or subgroup analysis (Fig. 4).

3.3. Late chronic pain and recurrence

Only 2 studies had a follow-up period more than 60 months. Both studies have applied synthetic glue in their trials. No significant difference was found between the 2 groups in terms of late chronic pain (OR = 0.62; 95% CI, 0.32–1.19; $P = .15$; Fig. 5), as well as late recurrence (OR = 1.54; 95% CI, 0.62–3.83; $P = .35$; Fig. 6).

3.4. Operating time

Eleven studies reported this outcome. The operating time was significantly longer in the suture fixation group compared with the glue fixation group in Lichtenstein inguinal hernia repair (Fig. 7). The results of subgroup analysis were similar in accordance with total effects. However, there was significant heterogeneity among included trials (Total: $P < .01$, $I^2 = 95\%$).

3.5. Hematoma

Nine studies reported the incidence of postoperative hematomas, with 6 studies belonged to the synthetic glue fixation group and 3 studies to the biological glue fixation group (Fig. 8). The incidence of postoperative hematomas was significantly higher in the suture fixation group compared with the glue fixation group in combined analysis (OR = 0.54; 95% CI, 0.33–0.89; $P = .02$). Subgroup analysis demonstrated that there was a significant difference between the synthetic glue and suture fixation groups (OR = 0.56; 95% CI, 0.34–0.95; $P = .03$). When comparing biological glue fixation with suture fixation, subgroup analysis showed no significant difference between the 2 groups (OR = 0.33; 95% CI, 0.05–2.13; $P = .25$).

3.6. Wound infection

Seven studies contributed to the analysis of wound infection, 4 studies reported no events and the remaining 3 were in the synthetic glue fixation group (Fig. 9). No significant difference was found between the 2 groups in terms of wound infection (OR = 0.56; 95% CI, 0.34–0.95; $P = .03$).

3.7. Mesh infection

Eight studies reported the incidence of mesh infection in Lichtenstein inguinal hernia repair (Fig. 10). Five of those studies reported no events. The meta-analysis showed no significant difference between the glue and suture fixation groups, either in the combined or subgroup analysis.

4. Discussion

This meta-analysis was based on 13 RCTs comparing glue versus sutures for mesh fixation in Lichtenstein inguinal hernia repair. The results of the current meta-analysis showed that early chronic pain was reduced when biological glue fixation of mesh was used for inguinal hernia repair compared to suture fixation. The incidence of hematomas was significantly higher in the suture fixation group than the glue fixation group. There was no significant difference between the 2 groups in terms of early recurrence, late chronic pain, late recurrence, wound infection, and mesh infection. The main disadvantage of suture fixation was the duration of operation as the mean operating time was significantly longer than glue fixation. Although there was significant heterogeneity demonstrated among the studies in terms of operating time and early chronic pain, the results were in accordance with other similar articles.

Till now, several meta-analyses have compared the outcomes of glue versus sutures for mesh fixation in Lichtenstein inguinal hernia repair.[25–29] The meta-analysis by de Goede et al[27] included 7 RCTs comprising 1185 patients and concluded that inguinal hernia repair using glue mesh fixation compared with sutures was faster and less painful, with comparable hernia recurrence rates.[27] Liu et al[28] analyzed 4 RCTs and 5

Table 1

The basic characteristics of included trials.

Included trials	Year of publication	Country	Enrolment dates	Type of intervention	No. of patients	Mean age, years	Men (%)	Anesthesia	Antibiotic	Follow-up, months
Nowobilski et al[19]	2004	Poland	2003.05– 2003.11	Glue	22	60.5	100	Local	Yes	3
				Suture	24	52.6	100			
Hidalgo et al[20]	2005	Spain	2001.01– 2003.07	Glue	55	–	100	Regional or epidural	Yes	12
				Suture	55	–	100			
Jain and Vindal[15]	2009	India	–	Glue	40	45.6	100	Spinal	Yes	12
				Suture	40	51.9	100			
Dabrowiecki et al[16]	2012	Poland	2008.07– 2010.11	Glue	20	47.4	100	General, local, or subarachnoid	No	16
				Suture	21	45.4	100			
Bracale et al[14]	2012	Italy	2009.01– 2010.06	Glue	50	59	96	Spinal	–	12
				Suture	52	56	94			
Campanelli et al[13]	2012	7 European countries	2006.01– 2007.04	Glue	158	58	100	Local, regional or general	Yes	12
				Suture	158	59	100			
Kim-Fuchs et al[2]	2012	Switzerland	2001.01– 2004.12	Glue	131	55.1	100	Local, spinal, or general	–	60
				Suture	133	56.8	100			
Shen et al[21]	2012	China	2010.01– 2010.04	Glue	55	63	81.8	Local	–	13
				Suture	55	60	85.5			
Moreno-Egea[18]	2014	Spain	2008.01– 2011.01	Glue	50	57	68	Local	Yes	15
				Suture	52	55	71.2			
Damiano et al[17]	2014	Italy	2004.01– 2010.02	Glue	216	52.9	–	Local	–	12
				Suture	252	55.1	–			
Karigoudar et al[22]	2015	India	–	Glue	32	44.5	–	–	–	3
				Suture	32	44.2	–			
Hoyuela et al[24]	2017	Spain	2013.11– 2015.11	Glue	188	60.6	90.4	Local, spinal, or general	Yes	12
				Suture	182	59.0	89			
Matikainen et al[23]	2017	Finland	2007.06– 2009.05	Glue	151	53	86.8	Local	No	84
				Suture	151	53	89.4			

prospective observational clinical studies and reported that there was a lower incidence of chronic pain and hematomas in the fibrin glue mesh fixation group in open inguinal hernia repair. The meta-analysis from Cochrane Library by Sun et al[29] included twelve RCTs for a total of 1932 patients and concluded that glue might reduce postoperative chronic pain and not simultaneously increase the recurrence rate compared with sutures for mesh fixation in Lichtenstein hernia repair. However,

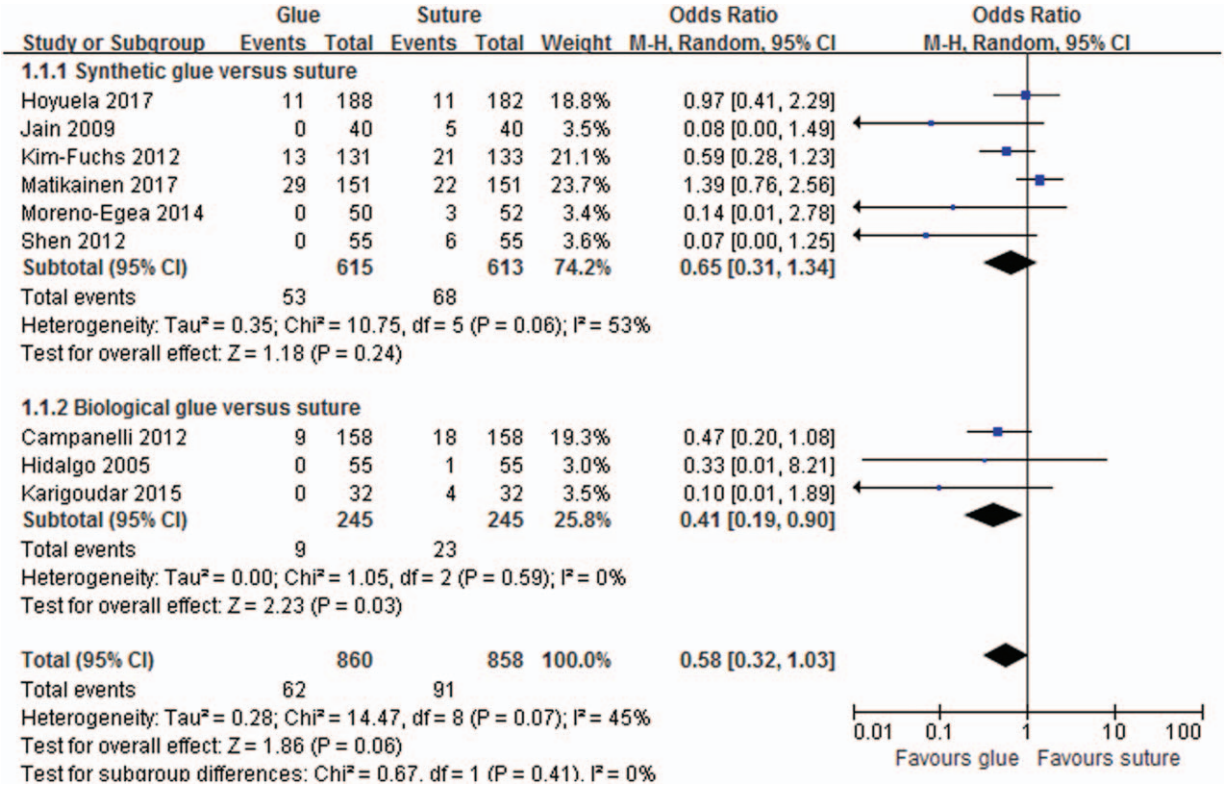

Figure 3. The Forest plot for early chronic pain.

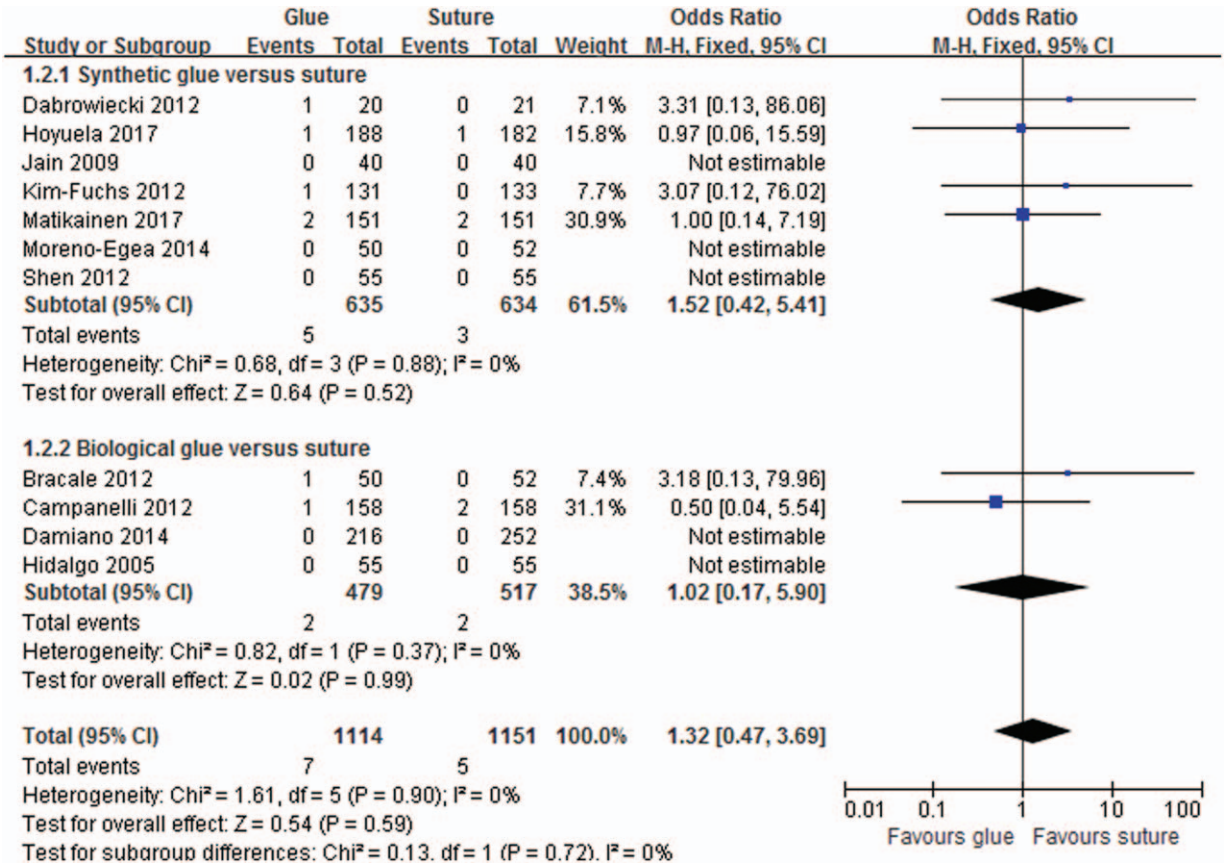

Figure 4. The Forest plot for early recurrence.

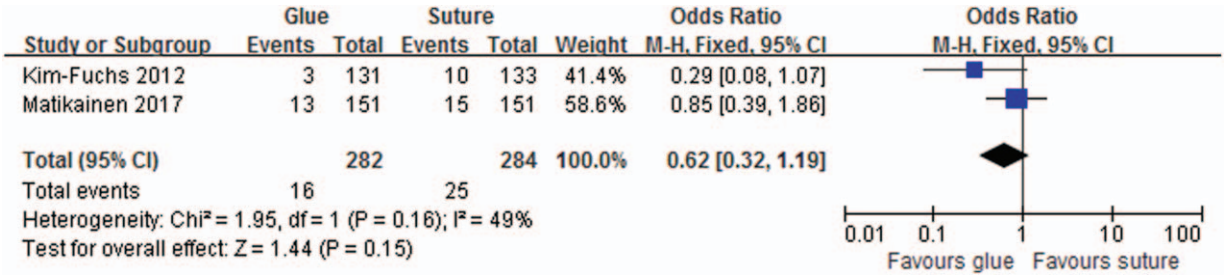

Figure 5. The Forest plot for late chronic pain.

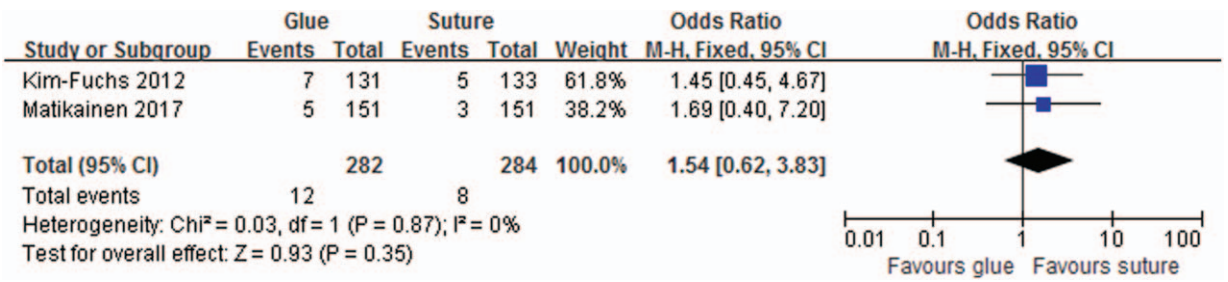

Figure 6. The Forest plot for late recurrence.

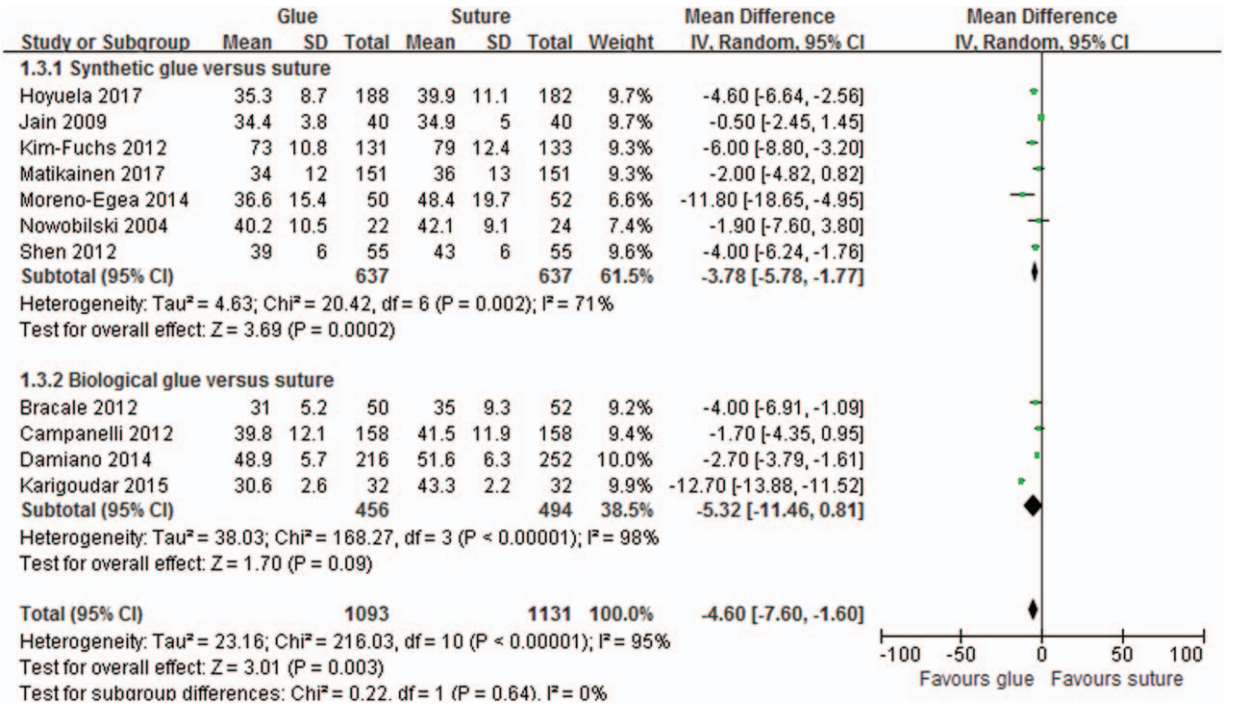

Figure 7. The Forest plot for operating time.

there are some limitations within these meta-analyses, such as low quality evidence, duplicated trials and different kinds of mesh applied in the intervention and control groups in a single trial. The most important, none of these studies has reported long-term results. In our systematic research, only 2 controlled trials comparing synthetic glue versus suture fixation have reported long-term results of Lichtenstein inguinal herniorrhaphy.[2,23] We showed that there was no significant difference in terms of late

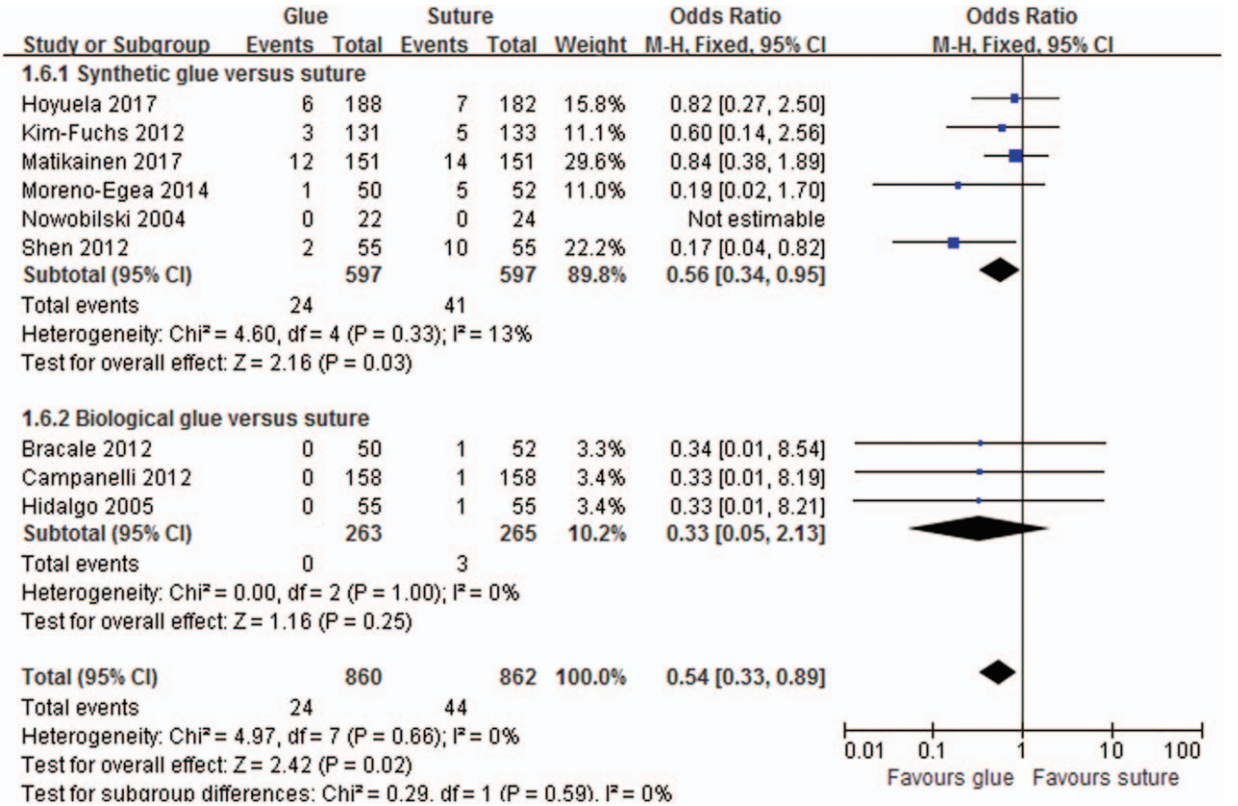

Figure 8. The Forest plot for hematoma.

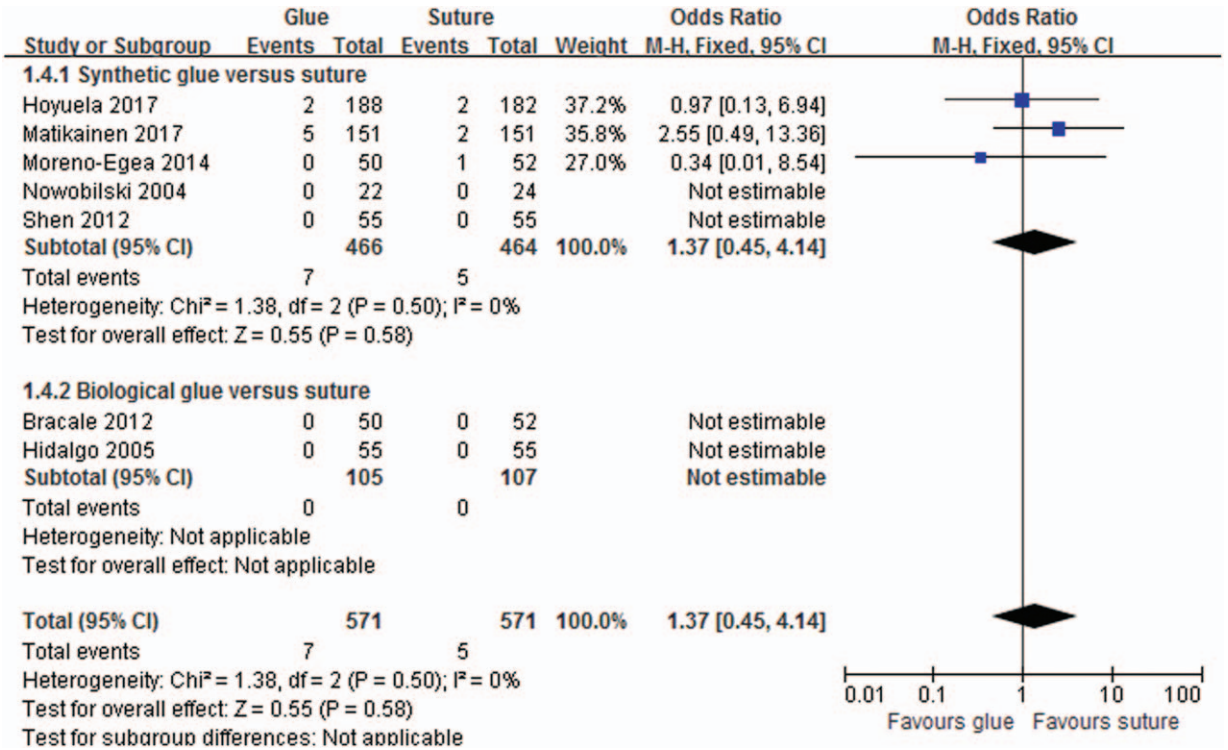

Figure 9. The Forest plot for wound infection.

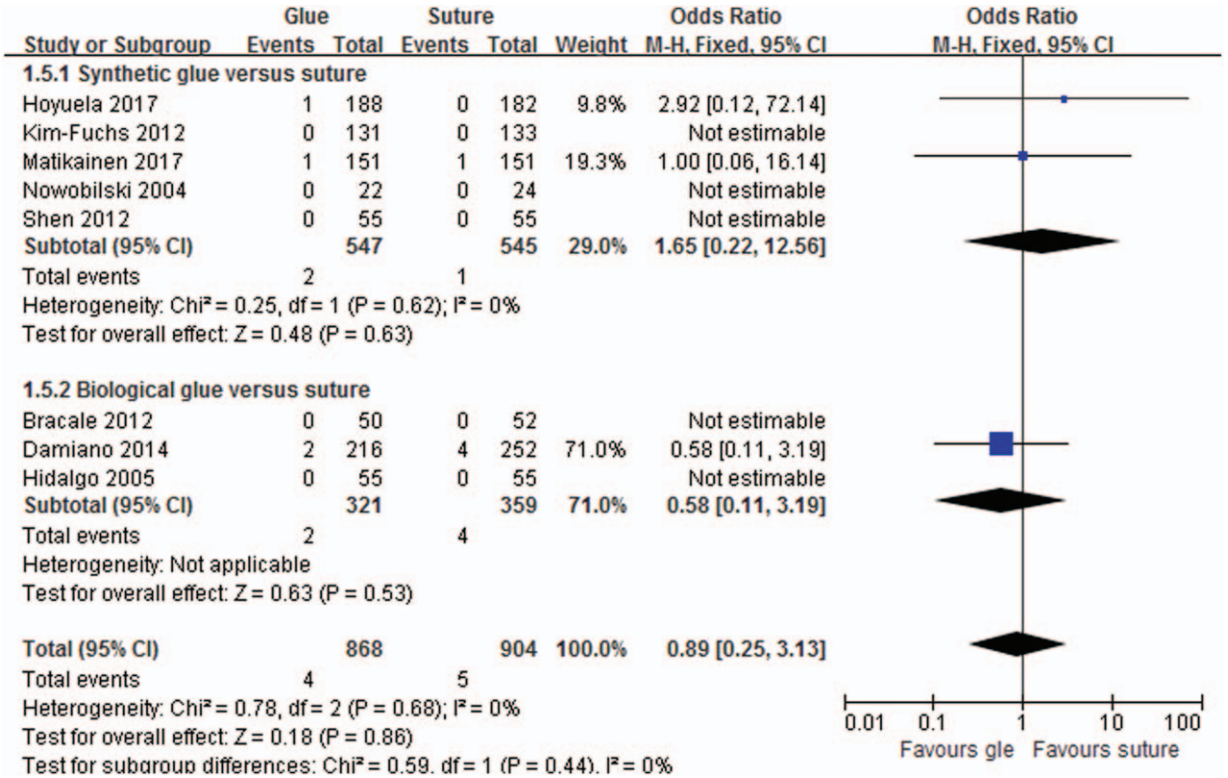

Figure 10. The Forest plot for mesh infection.

chronic pain or recurrence between the 2 groups in the long-term follow-up.

Chronic groin pain is a serious complication following Lichtenstein hernia repair and has significant impact on the patient's quality of life.[30] It is described as "groin pain reported by the patient at or beyond 3 months following inguinal hernia repair" by the International Association for the Study of Pain.[31] The incidence of chronic groin pain ranges from 16% to 53% and that of severe, unbearable pain from 2% to 5% after 2 years, with one-third of these patients presented an obvious impact on daily activities.[32,33] Two factors have been considered major underlying factors in chronic groin pain, the type of mesh implanted and its method of fixation.

There is still a controversial issue about whether the type of mesh influences the results in patients with tension-free hernia repair. Lightweight meshes have less polypropylene volume and have been supposed to make less inflammation in the abdominal wall compared with heavyweight meshes.[34] Using lightweight mesh instead of heavyweight mesh has been reported may reduce the incidence of chronic groin pain.[35] Previous study by O'Dwyer et al[36] reported that the use of lightweight mesh was associated with less chronic groin pain but an increase in hernia recurrence rate after inguinal hernia repair. In contrast, a meta-analysis comparing the influence of lightweight and heavyweight meshes on inguinal hernia showed that the long and short term postoperative outcomes, such as chronic groin pain, time to return to work and recurrence, were similar between the 2 meshes.[37] Over the last decades, biologic mesh was introduced as an alternative to synthetic mesh. Fang et al[38] analyzed 5 RCTs and found that biologic mesh had no superiority to synthetic mesh in open inguinal hernia repair with similar recurrence rates and incidence of chronic groin pain, but higher rate of seroma and longer operating time. Because discrepancies exist between different meshes in inguinal hernia repair, the present meta-analysis excluded some trials in which intervention and control groups received different kinds of mesh. This could help to reduce the risk of bias.

The approaches for mesh fixation can be classified into suture and sutureless techniques. Suture fixation may cause tissue ischemia, nerve damage, and muscle contracture. The change may be the source of postoperative groin pain. Some clinical trials attempted to replace nonabsorbable with absorbable sutures, but the results did not show any significant differences.[2,3] Therefore, sutureless mesh fixation technique with glue has been developed for the purpose of reducing chronic groin pain rate. Glues are classified into synthetic and biological tissue adhesives. Cyanoacrylic adhesives are synthetic glues firstly employed in medicine. There are many cyanoacrylate-derived tissue adhesives available for clinical uses. The properties of cyanoacrylic adhesives vary depending on the length of their alkyl chain which controls their degradation speed.[18] Fibrin adhesive has been used as biological glue in the included trials of current meta-analysis. It is a two-component material consisting of fibrinogen and thrombin. The fibrin adhesive is an effective biodegradable sealant and possesses an excellent local tolerability.[39] A study comparing *N*-butyl-2-cyanoacrylate and human fibrin glue for mesh fixation in primary inguinal hernia repair in a single-surgeon randomized trial found no significant difference between these 2 glues.[40] There is a certain doubt as to whether glue provides sufficient and necessary attachment of the mesh and whether or not its use can lead to hernia recurrence in the long term. Several studies suggested that glue fixation was not associated with an increased risk of hernia recurrence and was a feasible alternative for mesh fixation with sutures in Lichtenstein inguinal hernia repair.[2,23,29] The present meta-analysis indicated that both early and late recurrence rates between the glue and suture fixation groups were similar. For the chronic groin pain, fixation with synthetic glue or biological glue showed similar results to fixation with suture, with the exception of early chronic pain, where there was a statistical reduction of early chronic pain rate in the biological glue fixation group. However, long-term results on biological glue fixation method are still needed.

Postoperative complications were also analyzed in the present study where there was no significant difference between the suture and glue fixation groups, except for the incidence of hematomas. A recent case-control study reported that independent risk factors for the development of groin hematoma after inguinal hernia repair included warfarin use and recurrent hernia.[41] Medical adhesives have been proved to provide effective and safe hemostasis for surgical site in Lichtenstein inguinal hernia repair.[42,43] Compared to the synthetic glue fixation group, the incidence of hematoma was significantly high in the suture fixation group. Shen et al[21] reported that the local hematoma formation rate in suture fixation group was up to 18.4% which was the highest among the included trials and explained that they used a well-defined criterion of hematoma in the trial. Considering the different definitions of included trials on hematomas, conclusion on postoperative hematoma should be interpreted with caution.

There were some limitations to the present review. First, the follow-up time in most of the included trials was up to 18 months, which was not long enough with respect to late chronic pain and recurrence. Second, the definition and assessment of chronic groin pain presented varying degrees of differences among trials. The definition discrepancies may explain the significant heterogeneity among the included trials. Third, considering the different types of mesh, the present study excluded some trials in which intervention and control groups received different kinds of mesh. However, subgroup analysis should be introduced if there were enough trials. Fourth, cost-effectiveness and quality of life are not included in this review for the insufficient data of trials. Last, most of included trials showed high risk of bias in at least one of the investigated domains. Only 1 of 13 trials was assessed as having low risk of bias. However, these are common problems in hernia surgery. More RCTs with high quality and long-term follow-up data are needed to make convinced conclusions.

In conclusion, the use of glue for mesh fixation during Lichtenstein inguinal hernia repair is comparable to, and seemingly superior to suture fixation based on the present meta-analysis. Also, there is an appreciable decrease in chronic groin pain for biological glue. However, the quality of the evidence for most of the outcomes is low to moderate, and lack of stronger evidence to support glue mesh fixation is better than suture, but the use of glue can be considered an alternative.

Author contributions

Conceptualization: Y. Li.
Data curation: X. Sun, X. Huang.
Investigation: T. Ma, Z. Zhuang.
Methodology: T. Ma, Z. Zhuang.
Project administration: Y. Li.
Software: Z. Zhuang.
Supervision: H. Lin, Y. Li.
Validation: X. Sun, X. Huang.

Visualization: T. Ma.
Writing – original draft: H. Lin.
Writing – review & editing: Y. Li.

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