A Meta-Analysis Examining the Use of Fibrin Glue Mesh Fixation versus Suture Mesh Fixation in Open Inguinal Hernia Repair

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Key Words
Inguinal hernia · Fibrin glue · Mesh fixation · Open tension-free repair

Introduction
The incidence of inguinal hernia is about 16% in adult men [1], making this disease a major public health issue. In general surgery, it is very common to perform the procedures of inguinal hernia surgical repair and is one of the top three surgical operations in the western world [2]. In the past few years the guidelines and teaching for the treatment of hernia proved that open tension-free repair is a widely accepted technique for primary, secondary, unilateral and bilateral inguinal hernia. Nowadays, open mesh repair of inguinal hernia has been shown to be an effective and safe method of hernia repair [3].

Tension-free hernioplasty using a variety of techniques and synthetic meshes has become a widely accepted method of management, and has been found to reduce the incidence of recurrence. However, surgeons and patients are currently concentrating on other postoperative measures of the quality of hernia repair. At present, chronic pain is the main problem with a reported rate of 15 to 40% [4], which is attributed to nerve entrapment syndromes and osteitis pubis because of the mechanical fixation of mesh. Thus, it may be possible to reduce the incidence of postoperative inguinal pain by limiting the use of sutures and staples as fixation devices. The cyanoacrylate glue was first used by Helbling and Schlumpf in the Lichtenstein mesh repair in the year of 1993 [5]. However, concerns about the cyanoacrylate glue, which are the presumed inflammatory reactions and its cytotoxicity

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Abstract
Background: The aim of this study was to systematically analyze the randomized trials comparing fibrin glue mesh fixation with suture mesh fixation in open inguinal hernia repair.

Methods: Information was collected from a literature search using PubMed, Springer, Cochrane Library database and reference lists. The methodological quality of included publications was evaluated. Statistical analysis was performed using Review Manager Version 5.2.5 software.

Results: Nine articles were identified for inclusion: four randomized controlled trials (RCTs) and five prospective observational clinical studies. All the trials were considered to be of fair quality. The results showed that there was a lower incidence of chronic pain (RR 0.42, 95% CI 0.22–0.79, I² 11%; p < 0.01), and hematoma/seroma (RR 0.43, 95% CI 0.21–0.87, I² 0%; p < 0.05) in the fibrin glue mesh fixation group. However, the results of meta-analysis revealed that the incidence of recurrence or urinary problems between the two procedures were similar.

Conclusions: During the 6–15 months follow-up, fibrin glue mesh fixation is a feasible alternative for mesh fixation with sutures in open inguinal hernia repair. However, the poor quality of the included trials limits the evidence; rigorously designed trials are warranted to confirm this conclusion.

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Table 1. Characteristics of the trials included in this study

<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>Type of hernia</th>
<th>Sample size (FG/suture)</th>
<th>Experimental group</th>
<th>Control group</th>
<th>Parameters compared</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testini et al.</td>
<td>RCT</td>
<td>Unilateral/bilateral</td>
<td>52/59</td>
<td>Tissucol</td>
<td>Prolene sutures</td>
<td>①②③④⑤⑥⑦⑧⑨⑩</td>
<td>12</td>
</tr>
<tr>
<td>Campanelli et al.</td>
<td>RCT</td>
<td>Unilateral/bilateral</td>
<td>158/158</td>
<td>Tissucol/tisseele</td>
<td>Prolene sutures</td>
<td>①②③④⑤⑥⑦⑧⑨⑩</td>
<td>12</td>
</tr>
<tr>
<td>Lionetti et al.</td>
<td>Prospective study</td>
<td>Unilateral/bilateral</td>
<td>72/76</td>
<td>Quixil</td>
<td>Prolene sutures</td>
<td>①②③④⑤⑥⑦⑧⑨⑩</td>
<td>12</td>
</tr>
<tr>
<td>Negro et al.</td>
<td>Prospective study</td>
<td>Unilateral/bilateral</td>
<td>349/171</td>
<td>Tissucol/tisseele</td>
<td>Prolene sutures</td>
<td>①②③④⑤⑥⑦⑧⑨⑩</td>
<td>12</td>
</tr>
<tr>
<td>Bracale et al.</td>
<td>RCT</td>
<td>Unilateral</td>
<td>50/52</td>
<td>Quixil</td>
<td>Prolene sutures</td>
<td>①②③④⑤⑥⑦⑧⑨⑩</td>
<td>15</td>
</tr>
<tr>
<td>Sozen et al.</td>
<td>Prospective study</td>
<td>Unilateral/bilateral</td>
<td>64/56</td>
<td>Tisseele</td>
<td>Prolene sutures</td>
<td>①②③④⑤⑥⑦⑧⑨⑩</td>
<td>12</td>
</tr>
<tr>
<td>Wong et al.</td>
<td>RCT</td>
<td>Unilateral</td>
<td>30/26</td>
<td>Tissucol/tisseele</td>
<td>Prolene sutures</td>
<td>①②③④⑤⑥⑦⑧⑨⑩</td>
<td>6</td>
</tr>
<tr>
<td>Hidalgo et al.</td>
<td>Prospective study</td>
<td>Bilateral</td>
<td>55/55</td>
<td>Tissucol</td>
<td>Prolene sutures</td>
<td>①②③④⑤⑥⑦⑧⑨⑩</td>
<td>12</td>
</tr>
<tr>
<td>Benizzi et al.</td>
<td>Prospective study</td>
<td>Unilateral/bilateral</td>
<td>70/70</td>
<td>Tissucol</td>
<td>Prolene sutures</td>
<td>①②③④⑤⑥⑦⑧⑨⑩</td>
<td>&gt;12</td>
</tr>
</tbody>
</table>

Parameters compared are as follows: ① (recurrence); ② (hematoma); ③ (seroma); ④ (chronic pain); ⑤ (infection); ⑥ (paresthesia); ⑦ (return to activity); ⑧ (urinary retention).

[6] such as quick hardening and indiscriminate binding to body surfaces and instruments, hampered its success in widespread use. The cyanoacrylate glue, the characteristic of fibrin glue such as efficacy, excellent local tolerability, and less of adverse effects makes it an optimal choice for the atraumatic mesh fixation [7]. It has been used in a variety of surgical fields for its effectiveness, excellent local tolerability and relative lack of adverse effects and contraindications. However, the hospital costs were increased by the use of fibrin glue instead of the sutures [8]. The efficacy of fibrin glue compared to sutures in open tension-free inguinal hernioplasty is an ongoing debate. To the best of our knowledge, no meta-analysis has specially compared mesh fixation using fibrin glue with suture fixation, in open tension-free repair of inguinal hernia. The objective of the present meta-analysis is to pool the existing literature to determine whether fibrin glue is a safe and effective means over traditional suture fixation methods with regard to chronic pain, recurrence and any other postoperative complications.

Methods

Study Selection

All studies of open inguinal hernia repairs performed with mesh were identified by conducting an intensive search of the literatures in the PubMed, Springer and Cochrane Library database. The search terms were inguinal AND (hernia OR hernioplasty) AND (fibrin glue OR fibrin sealant OR Quixil OR Tisseel OR Tissucol). We identified all trials published up to and including August 2013. The electronic search was supplemented by a manual search of reference lists in the articles and the ‘related articles’ function, revealing no additional studies. The reference lists and relevant articles referenced in these primary studies were downloaded from the databases. The relevance function of these articles was used to widen the search results. All abstracts, comparative studies, nonrandomized trials, and citations scanned were searched comprehensively. At last, nine trials were summarized in a formal meta-analysis [1, 8–15].

Inclusion and Exclusion Criteria

The trials, in which the hernia repair was done using open tension-free technique, with fibrin glue compared to the sutured mesh fixation, were included. However, the studies were excluded during the initial review phase; if the hernioplasty was done by the laparoscopic approach, the suture-less technique with cyanoacrylate glue or staple, case reports, non-comparative trials or reviews were excluded.

Data Extraction and Quality Assessment

Two independent researchers (Huihui Liu and Xiao Zheng) read the abstracts and used a standardized data extraction form to identify potentially eligible articles. At least one of the following outcomes should be included in the eligible trials: chronic pain, recurrence, hematoma, infection, parenthesis, seroma, testicular problem or urinary problem (table 1). Disagreements were resolved by a discussion with a third investigator (Shanyu Guo). The methods of Jadad et al. [16] and Chalmers et al. [17] were used to assess the methodological quality of the included studies. On the basis of the quality of the included trials, the strength and summary of the evidence were further evaluated using GradePro (Cochrane Collaboration).

Statistical Analysis

For this study, the random-effect model was used, which takes into account both the methodological variations between studies and the variance within a study [18]. We used the chi-square statistic to assess the heterogeneity between trials and the I² statistic to assess the extent of inconsistency. The level of statistical significance was set at p < 0.05. Heterogeneity was quantified by calculating I² where p < 0.10 was determined to be significant. Risk ratio (RR) with 95% confidence intervals (CIs) were estimated for binary data; otherwise, continuous data were calculated by the mean differences with 95% CIs. Publication bias was evaluated using a
funnel plot. Forest plots were used for the graphic display of results from the meta-analysis. Statistical analysis was conducted by RevMan 5.2.5 software (Cochrane-Information and Management System, Cochrane Collaboration, Copenhagen).

**Results**

**Article Search**

Figure 1 shows the flowchart of studies from the initial results of publication searches to final inclusion. After an initial search 273 studies were identified from the selected electronic databases; at last nine studies met the selection criteria in the meta-analysis.

Characteristics of each trial are shown in table 1. There are four randomized controlled trials (RCTs) and five prospective observational clinical studies. The publication dates ranged from 2005 to 2012. In total, these studies included 1,623 patients: 900 in the fibrin glue group and 723 patients in the suture group. Five of the studies were conducted in Italy, and four in Spain, Turkey, Taiwan and France. A funnel plot based on the most frequently cited outcome was broadly symmetrical, indicating minimal publication bias (fig. 2).

![Funnel plot](image-url)  
**Fig. 1.** Flowchart for selection of studies.

**Fig. 2.** A funnel plot showing no significant publication bias.

**Methodological Quality of Included Studies**

Based on the methods of Jadad et al. and Chalmers et al., all the studies were considered to be of fair quality because the intention-to-treat analysis and the allocation concealment were not adequate (table 2). To summarize,
the quality of evidence for each outcome was discussed by GradePro (fig. 3). The Mantel-Haenszel method was used for the calculation of RR under the random effect model to compute robustness and susceptibility to any outliers among these trials.

Recurrence
A total of nine trials studied the recurrence of hernia after inguinal hernia repair [1, 8–15]. However, only five trials reported the recurrence. The recurrence rate in these trials was 1.79% [11], 0.95% [9], 1.35% [8], 0.38% [14] and

**Table 2. Quality assessment of included studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Randomization</th>
<th>Power calculations</th>
<th>Blinding</th>
<th>ITT</th>
<th>Concealment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testini et al.</td>
<td>Random numbers</td>
<td>Yes</td>
<td>Double blind</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Campanelli et al.</td>
<td>Computer generated</td>
<td>Yes</td>
<td>Double blind</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Lionetti et al.</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>No</td>
<td>Unclear</td>
</tr>
<tr>
<td>Negro et al.</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>No</td>
<td>Unclear</td>
</tr>
<tr>
<td>Bracale et al.</td>
<td>Computer generated</td>
<td>Unclear</td>
<td>Single blind</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sozen et al.</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>No</td>
<td>Unclear</td>
</tr>
<tr>
<td>Wong et al.</td>
<td>Sequential numbers</td>
<td>Yes</td>
<td>Double blind</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Hidalgo et al.</td>
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<td>Unclear</td>
<td>Unclear</td>
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<tr>
<td>Benizri et al.</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>No</td>
<td>Unclear</td>
</tr>
</tbody>
</table>
0.98% [15], respectively, with the follow-up of 6 to 15 months. One trial [8] determined the recurrence by clinical examination, while others didn’t provide specific methods. Five recurrences in the fibrin group and four recurrences in the suture group were found. From the result we can see that the incidence of recurrence after reparation between the suture and fibrin glue mesh fixation groups was similar (RR 0.96, 95% CI 0.27–3.42, I² 0%; p = 0.98; fig. 4). Sensitivity analysis showed that excluding any one study from the pooled analysis did not vary the results substantially. We excluded three trials [1, 11, 13] in which the mesh dislocation was different from the others, and the result did not change (RR 1.21, 95% CI 0.30–4.86, I² 0%; p = 0.79).

Chronic Pain

We defined chronic pain as any groin pain that have an impact on the quality of life at or beyond 3 months after surgery [19]. Six studies reported the incidence of chronic pain after inguinal hernia repair [1, 8, 9, 12–14]. Five of them reported a lower percentage of chronic pain in the fibrin group, while only one study [14] reported a higher percentage of chronic pain. The pooled data showed that the suture fixed mesh group had a significant higher incidence of chronic pain when compared with the fibrin glue fixed mesh group (RR 0.42, 95% CI 0.22–0.79, I² 11%; p < 0.01; fig. 5).

Hematomas/Seromas

Seven studies [1, 9, 11–15] reported the incidence of hematomas or seromas. There were 11 patients in the fibrin group and 23 patients in the suture group who were complaining of hematoma/seroma. The result showed that the incidence of hematoma/seroma was higher in the suture fixed mesh group than in the fibrin glue fixed mesh group in the random-effects model (RR 0.43, 95% CI 0.21–0.87, I² 0%; p = 0.02; fig. 6).

Urinary Problems

Six trials [1, 8, 11–13, 15] described the occurrence of urinary problems (i.e. urinary retention/infection), but only three were included in this analysis. Bracale’s [15], Testini’s [1] and Hidalgo’s [12] study did not reveal the presence of any occurrence of urinary problems in either of these groups. The result of these studies that included information about urinary problems indicated that there is no significant difference between the fibrin glue and suture group in the incidence of urinary problems (RR 0.73, 95% CI 0.22–2.40, I² 6%; p = 0.61).

Cost

Only one study [15] paid attention to the differences in the cost between the two methods of the mesh fixation. Although the glue is more expensive than the sutures, the cost of the two procedures is very similar. This was mainly due to decreased analgesics consumption, reduction in operative time and reduction in hospital stay.

Discussion

Open tension-free inguinal hernia repair has become a preferred method of management, and the rate of recurrence has been decreased due to the usage of prosthetic
mesh. Studies reported that the incidence of recurrence after tension-free repair was as low as 2–5% recently [20], but other complications such as postoperative pain and discomfort have gained increased attention in the recent past considering the patients’ quality of life after surgery. The commonly used mesh fixation techniques include staples, sutures, fibrin glues, and synthetic glues. Nowadays, the debate on what the preferred method is in the fixation of prosthetic mesh to improve the postoperative quality of life there is still ongoing. The purpose of this meta-analysis was to summarize the current evidences with regard to fibrin glue mesh fixation and suture mesh fixation in the management of patients with inguinal hernia repair.

Until recently, the main clinical outcome was the rate of recurrence, leading to reoperation. Hernia can recur if the mesh overlap around the hernia orifice is inadequate [21]. Meshes should be properly secured using high-quality fixation methods at insertion, which remain effective until the mesh is incorporated. The analysis revealed that recurrence outcomes were comparable between the two groups in inguinal hernia repair. Generally, sutures are
generally used to secure the prostatic mesh; however, that may lead to chronic pain and other problems such as numbness or groin discomfort, presumably through tension or nerve compression [5]. Some studies showed that chronic pain was influenced by the type of the mesh implanted and its fixation [22, 23]. For these reasons, some surgeons searched for a new type of atraumatic methods of fixation. Fibrin glue can be used as an adjuvant to hemostasis in various kinds of surgical fields for its effectiveness, excellent local tolerability, and relative lack of adverse effects and contraindications. Its adhesive and hemostatic properties have been demonstrated in a number of experimental studies and clinical trials [24, 25]. From this meta-analysis of nine trials on the use of fibrin glue for the open inguinal hernia repair, it was concluded that the use of fibrin glue reduced the risk of developing postoperative chronic groin pain. Although two studies [9, 15] reported a significant increase in recurrences, the pooled data did rule out this concern. It is equivalent to suture mesh fixation in terms of operation time and urinaiy problems. The use of glue to fix mesh during the open tension-free hernioplasty has come across another important issue, cost-benefit analysis. Only one of the included studies reported a cost-benefit analysis. Although the glue is more expensive than the sutures, the total costs of the two procedures did not change significantly. The cost of glue may be balanced against a shorter operating time, shorter time to return to daily activities and potentially reduced convalescence owing to less early postoperative pain. Further studies, dealing with the cost effectiveness of different fixation techniques, are needed to investigate this issue.

No significant heterogeneity and publication bias were observed among the trials, indicating that the results of present meta-analysis were statistically robust. However, our meta-analysis has and should be acknowledged. The main weakness of this study was the low number of randomized trials analyzed. In order to induce sufficient patient data to our study, we included both RCTs and prospective studies. It might have led to selection bias. But we considered that it was more important to have a larger number of included patients than the inclusion of RCTs only. Hernia recurrence is known to be a function of time, and around 5 years follow-up is considered adequate as most hernia recurrences appear within this time [26]. The follow-up time of these trials ranged from 6 to 15 months, with the majority of trials having a follow up of a year, which may be not consistent and not long enough to come to a definite conclusion regarding recurrence rates. Therefore, it is unclear whether hernia recurrence in the fibrin glue group becomes significantly different over this length of time. Moreover, the degrees of differences also existed among trials concerning the definitions of ‘chronic groin pain’ and ‘hematomas/seromas’. Although the reporting of chronic groin pain did not demonstrate significant heterogeneity, the definition of chronic groin pain in terms of when and how it was measured was variable among the studies, as were the types of mesh used, which can have a bearing on chronic groin pain. Furthermore, there was also a potential bias of surgeon experience, which is a major factor on the different outcomes of the patients.

In conclusion, our result about the hernia recurrence showed that mesh fixation with fibrin glue was statistically similar with the suture fixation in open tension-free hernioplasty, while the risk of developing chronic inguinal pain was decreased. However, the quality of the included studies was in some cases low, and lack of stronger evidence to support fibrin glue mesh fixation is better than suture, but it can be considered an alternative. More trials with high-quality and long-term follow-up observation are needed to ensure this conclusion.

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**Disclosure Statement**

The authors have no conflicts of interest.

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