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Cyanoacrylate mesh fixation for laparoscopic inguinal hernia repair: a prospective, multicenter, single-arm study

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Abstract

Background Inguinal hernia repair is among the most frequently performed surgical procedures. Alternatives to penetrating mesh fixation, such as surgical glue, are being investigated for their potential benefit in reducing chronic pain. The aim of this study was to assess the efficacy of the *n*-hexyl cyanoacrylate glue Ifabond™ for mesh fixation in laparoscopic inguinal hernia repair.

Methods This prospective, multicenter, single-arm study collected data from laparoscopic inguinal hernia repairs using Ifabond™ (Peters Surgical, Boulogne-Billancourt Cedex, France) and a standard [Promesh® SURG ST (Peters Surgical)/Biomesh® P1 (Cousin Biotech, Wervicq-Sud, France)] or lightweight [Promesh® SURG LI (Peters Surgical)/Premium® Implant (Cousin Biotech)] polypropylene mesh. The primary endpoint was postoperative pain [100-scale Visual Analog Scale (VAS)]. Secondary endpoints were complications, hernia recurrences, and quality of life (QoL) (EQ-5D-3L health index and EQ-VAS). Patients were followed up at 5 weeks and 12 months after surgery.

Results Six-hundred and thirteen patients underwent laparoscopic inguinal hernia repair. Postoperative pain decreased at 5-week (3.97 ± 10.04; $p < 0.0001$) and 12-month (3.83 ± 11.26; $p < 0.0001$) follow-up compared with before surgery (26.96 ± 19.42). One hundred and fifteen patients (13.74%) experienced chronic pain in the groin at 12-month follow-up, of whom 14 (2.67%) required analgesics. There were 6 patients with major morbidities and one patient died of an unrelated cause. Two hernia recurrences occurred within 12-month follow-up. Patients' QoL increased from an EQ-5D-3L index score of 0.82 ± 0.19 preoperatively to 0.90 ± 0.15 at 5 weeks ($p < 0.0001$) and 0.92 ± 0.15 at 12 months after surgery ($p < 0.0001$). The EQ-VAS general health scoring increased from 79.03 ± 12.69 preoperatively to 84.31 ± 9.97 at 5-week ($p < 0.0001$) and 84.16 ± 14.48 at 12-month follow-up ($p < 0.0001$).

Conclusions Ifabond™ (Peters Surgical) is a safe, reliable, and feasible fixation method for laparoscopic inguinal hernia repair with a very high surgeon satisfaction score, improved patients' QoL, and comparable risk of developing chronic pain and postoperative complications as described in the literature.

Keywords Inguinal hernia repair · *n*-hexyl cyanoacrylate glue fixation · Polypropylene mesh · Laparoscopy · Pain

Inguinal hernia repair is one of the most common surgical procedures. More than 20 million inguinal hernias are treated annually worldwide accounting for 10% to 15% of all general surgical procedures [1, 2]. Multiple treatment

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options exist, including open and laparoscopic techniques. Minimal-invasive laparoscopic inguinal hernia repair has become a well-established treatment option [3], with the two approaches being transabdominal preperitoneal (TAPP) and totally extraperitoneal (TEP). TAPP and TEP have demonstrated comparable recurrence and complication rates [4]. Although laparoscopic inguinal hernia repair is technically more challenging, potential benefits compared with open repair include faster postoperative recovery, decreased postoperative pain, earlier return to normal daily activities, and better cosmetic results [5–8]. Unfortunately, chronic postoperative inguinal pain remains a known complication of inguinal hernia repair, both open and laparoscopic, with reported rates ranging from 0.5 to 16% [9–12].

A common consideration in TAPP and TEP procedures is whether mesh fixation should be used. If necessary, several different fixation options are available. In the early 1990s, first-generation non-absorbable tacks and staples were used for mesh fixation. In rare instances, non-absorbable titanium tacks have been associated with complications such as nerve entrapment, erosion into the bowel and other hollow viscera, and formation of dense adhesions and so-called tack hernias [13]. Attempts at further improvement resulted in the development of alternative fixation methods such as sutures, absorbable tacks/staples, and biologic (fibrin) or synthetic (cyanoacrylate) surgical glues. Many clinical studies and meta-analyses have been conducted to establish the best method for mesh fixation in laparoscopic inguinal hernia repair. However, the benefit of one technique over another is unclear when considering chronic postoperative pain, hernia recurrences, and procedure-related complications. It is believed that nonpenetrating glue-based techniques for mesh fixation result in less acute and early postoperative pain, less chronic postoperative pain, less occurrence of hematoma, and better early postoperative activity levels compared with penetrating fixation methods [14–23]. Cyanoacrylate is the generic name of a group of fast-acting adhesives that provide secure and quick adhesion through high polymerization rates, and have proven histocompatibility, good epithelization, and negligible local inflammatory reaction [24]. Cyanoacrylate glue was first evaluated as an alternative fixation method in inguinal hernia surgery in 1998 [25].

We hereby present the 12-month follow-up data of 613 patients who underwent laparoscopic inguinal hernia repair with *n*-hexyl cyanoacrylate glue fixation [Ifabond™ (Peters Surgical, Boulogne-Billancourt Cedex, France)] and a standard [Promesh® SURG ST (Peters Surgical)/Biomesh® P1 (Cousin Biotech, Wervicq-Sud, France)] or lightweight [Promesh® SURG LI (Peters Surgical)/Premium® Implant (Cousin Biotech)] polypropylene mesh.

Materials and methods

Study design

A prospective, multicenter, single-arm, observational registry was conducted in five Belgian hospitals. The aim of this postmarket study was to assess the efficacy of the *n*-hexyl cyanoacrylate glue Ifabond™ for mesh fixation in laparoscopic inguinal hernia repair. Enrollment began on October 5, 2012, and the last follow-up was registered on March 13, 2020. Appropriate local ethics committee approval and informed consent were obtained prior to patient enrollment. The study protocol was registered in clinicaltrials.gov (NCT01669837). Pseudonymized data were collected in a prospectively maintained electronic database. Patients with a life expectancy of less than one year, recurrent hernias, and known allergy to the components of the surgical tissue glue were excluded from the registry. Patients were scheduled for laparoscopic TAPP or TEP with a standard [Promesh® SURG ST (Peters Surgical)/Biomesh® P1 (Cousin Biotech)] or lightweight [Promesh® SURG LI (Peters Surgical)/Premium® Implant (Cousin Biotech)] polypropylene mesh and surgical tissue glue fixation [Ifabond™ (Peters Surgical)]. Intraoperatively, the anatomic location of the hernia [lateral or indirect (L), medial or direct (M), or femoral (F)] and size of the hernia orifice [< 1.5 cm (one finger) (1), 1.5 cm to 3 cm (two fingers) (2)), or > 3 cm (more than two fingers) (3)] were evaluated according to the European Hernia Society (EHS) classification [26]. Follow-up occurred at 5 weeks and 12 months after the operation.

Study endpoints

The primary endpoint of this registry was to determine the prevalence of chronic pain at 12 months postoperatively. Pain was scored at baseline and during follow-up at 5 weeks and 12 months using the 100-scale Visual Analogue Scale (VAS). The VAS contains a 0–100 grading with 0 corresponding to no pain and 100 corresponding to the worst conceivable pain. Patients were asked to select the number on the scale that corresponded to the worst level of pain they experienced. Pain was classified into mild (1–30 mm), moderate (31–60 mm), and severe (61–100 mm). Secondary endpoints of this study were intraoperative complications, postoperative complications, analgesic intake during follow-up, quality of life (QoL) at baseline and during follow-up using the EuroQol questionnaire (EQ-5D-3L health index and EQ-VAS), hernia recurrences, and re-interventions during follow-up. Additional endpoints were operating time, intraoperative usability of

the glue, and length of hospital stay. All procedures were prospectively scored for quality of Ifabond™ mesh fixation using a scoring system ranging from 1 (bad) to 3 (moderate) to 5 (excellent) recorded by the participating surgeons. QoL was measured with a validated instrument consisting of two components. The first was a descriptive scale with five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each with three levels of assessment (no problems, some problems, and extreme problems) (EQ-5D-3L). The second component was based on an EQ Visual Analogue Scale (EQ-VAS) that recorded the patients' self-rated QoL on a scale of 0–100 and was useful for measuring patients' responses to their health status.

Surgery

All patients underwent general anesthesia and 91.84% received a single dose of prophylactic antibiotics before surgery. TAPP or TEP procedures were performed according to the investigators' standard of care. TAPP involves entering the peritoneal cavity to place the mesh through a peritoneal incision over the potential hernia sites. In brief, a pneumoperitoneum was created by introducing CO^2 gas in the abdominal cavity through a supraumbilical port. One 10-mm telescope port was placed in the supraumbilical region and the remaining two 5-mm ports were held in the bilateral mid-clavicular line at the level of the umbilicus. After inspection of the abdomen by a telescope, a 5-cm peritoneal incision was made from the cranial to inguinal defect. The Cooper's ligament was identified medially during preperitoneal dissection (Fig. 1a). The medial limit of dissection was Cooper's ligament of the opposite side. Cord structures were identified and the hernia sac was separated from cord structures. The anterior superior iliac spine (ASIS) of the ipsilateral side was the lateral limit of dissection. The lower limit of dissection was where vas deferens turn medially. After proper dissection, polypropylene mesh was positioned over the defect in the preperitoneal space and fixed with Ifabond™ (Peters Surgical) (Fig. 1b). Finally, the peritoneum was closed with a running suture or glue (Fig. 1c). What makes TEP different is that the peritoneal cavity is not entered and mesh is used to seal the hernia from outside the peritoneum. In TEP, a small access point was made by the umbilicus between the peritoneum and the abdominal wall layer to create the pneumoperitoneum by introducing CO^2 gas. A preperitoneal space was created with the help of telescopic blunt dissection until the pubic symphysis was seen in the midline. The dissection was continued with another two 5-mm working ports, one just above the pubic symphysis and the other in the midline between the umbilical port and pubic symphysis. The lateral limit of preperitoneal flap dissection corresponded to the anterior superior iliac spine. The peritoneum was excised as low as possible with careful dissection to expose the psoas major muscle, the nerves, deep ring, and triangle of doom. After reduction of the hernial sac, polypropylene mesh was positioned over the defect in the preperitoneal space and fixed with Ifabond™ (Peters Surgical). The pneumoperitoneum was released. No complementary mechanical mesh fixation (sutures/tacks/staples) was used during the TEP and TAPP procedures. After surgery, all patients were treated according to the hospitals' standard of care.

Glue

Ifabond™ (Peters Surgical) is a CE-marked, Class III, sterile, non-toxic, biocompatible, and biodegradable synthetic (*n*-hexyl cyanoacrylate) surgical tissue glue. It is a fast-acting adhesive monomer that instantly polymerizes in the presence of body fluids (proteins), with a limited exothermic reaction (< 2 °C), reaching its adhesive effect after only 30 s. Mesh attachment is based on very fine, drop-by-drop application of the glue. Ifabond™ glue applicators consist of a polycarbonate Luer lock adapter and two hollow PVC tubes: a transparent external tube with a diameter that enables the use of the applicators with a 5-mm trocar and a transparent internal tube with an internal diameter of 0.4 mm for drop-by-drop application of the glue. The syringe is first filled with the glue and then locked on the Luer lock adapter. The glue is applied directly to the desired areas by gently pressing on the plunger of the syringe.

Fig. 1 Surgical procedure

Surgical mesh

Promesh® SURG ST (Peters Surgical)/Biomesh® P1 (Cousin Biotech) and Promesh® SURG LI (Peters Surgical)/Premium® Implant (Cousin Biotech) are Class IIb sterile medical devices, biocompatible and non-resorbable surgical meshes made of polypropylene monofilament. These meshes are manufactured by Cousin Biotech. Promesh® SURG ST (Peters Surgical)/Biomesh® P1 (Cousin Biotech) is a standard polypropylene 100 g/m^2 mesh with a pore area of 1.114 mm^2. Promesh® SURG LI (Peters Surgical)/Premium® Implant (Cousin Biotech) is a lightweight polypropylene 37.8 g/m^2 mesh with a pore area of 1.770 mm^2. These parietal reinforcement implants are all intended for extraperitoneal implantation.

Statistics

Continuous variables are presented as mean and standard deviation (SD). Categorical variables are presented as percentage, number, and denominator. As this is a single-arm study, no statistical inferences were made with regard to comparison of treatment arms or subgroups. *p*-value for pain-VAS, EQ-5D index scores, and EQ-VAS were calculated using the paired T-test for change from baseline at the timepoint. As per Bonferroni correction, the *p*-value was compared vs the value 0.025 to maintain alpha-level of 0.05 for the overall endpoint (2 comparisons: value = alpha/2). *p*-values for the EQ-5D dimensions were calculated using the paired McNemar test for change from baseline at the timepoint, for the category 'no problems' vs. 'some' or 'extreme problems.' As per Bonferroni correction, the *p*-value was compared vs the value 0.025 to maintain alpha-level of 0.05 for each EQ-5D dimension (2 comparisons: value = alpha/2). All datasets, table and figures, and statistical analyses were created using the SAS Statistical Software packages (SAS V9.4, The SAS Institute, Cary NC).

Results

A total of 613 patients with 978 hernias (unilateral and bilateral) underwent laparoscopic repair with polypropylene mesh and Ifabond™ surgical glue from October 5, 2012, until August 08, 2019, at 5 Belgian centers by 9 surgeons/operators. The last follow-up was registered on March 13, 2020. Descriptive characteristics of the patients are listed in Table 1. The majority (87.93%) of patients were men (74 females and 539 males), and the mean age was 58.03 ± 13.65 years ranging from 18 to 85 years (Table 1). The mean Body Mass Index (BMI) at surgery was 25.46 ± 3.59. Of the total number of procedures, 585 (95.43%) TAPP and 28 (4.57%) TEP procedures were performed. A total of 262 (42.74%) patients had unilateral inguinal hernias, and 351 (57.26%) patients were treated for bilateral inguinal hernias. Of the 978 repaired inguinal hernias, 423 (43.25%) were lateral (indirect), 547 (55.93%) were medial (direct), 4 (0.41%) were femoral, and 4 were not classified as such. The mean number of hernia subtypes treated during one procedure was 1.6 ± 0.53 ranging from 1 to 4 hernias. A standard polypropylene Promesh® SURG ST (Peters Surgical)/Biomesh® P1 (Cousin Biotech) mesh was used in 88.10% of surgeries, while a lightweight polypropylene Promesh® SURG LI (Peters Surgical)/Premium® Implant (Cousin Biotech) mesh was used in 11.90%. The mean operating time was 35.05 ± 15.14 min. Most patients were discharged the same day (80.91%) (Table 2). Seven perioperative complications were recorded (1.14%), one of which was major urine retention resulting in placement of a urinary catheter and overnight stay (Table 3). There were no conversions to open surgery. Surgeons' assessment of the intraoperative usability of the Ifabond™ surgical glue was 4.76/5.

Table 1 Demographic and preoperative characteristics

	Population (*N* = 613)
Age (years)	58.03 ± 13.65
Sex ratio (M:F)	539:74
ASA I	53.67% (329)
ASA II	39.15% (240)
ASA III	7.01% (43)
ASA IV	0.16% (1)
Length (cm) (*N* = 612)	1.74 ± 0.08
Weight (kg)	77.68 ± 12.91
BMI (kg/m^2) (*N* = 612)	25.46 ± 3.59

ASA American Society of Anesthetists score, *BMI* body mass index

Of the 613 eligible patients recruited for laparoscopic inguinal hernia repair, 84 patients were lost for follow-up, of which 25 immediately after the procedure. One patient died at 12 months (not related to the procedure), leaving 588 (95.92%) and 528 (86.13%) patients available for evaluation at 5-week and 12-month follow-up, respectively.

The mean pain-VAS was significantly lower at 5 weeks (3.97 ± 10.04; $p < 0.0001$) and 12 months (3.83 ± 11.26; $p < 0.0001$) postoperatively compared with preoperatively (26.96 ± 19.42) (Fig. 2). At 12-month follow-up, 3.66% (19/519) of patients reported a pain level of VAS > 30 (Table 4). Upon discharge, 99.51% of patients required analgesic medication, with continued intake after discharge in 70.77% of patients for a mean duration of 5.68 ± 6.09 days. Pain medication was used by 2.67% of the patients at 12-month follow-up (Table 5).

Patient's QoL increased significantly from an EQ-5D-3L index score of 0.82 ± 0.19 at baseline to 0.90 ± 0.15 at

Table 2 Procedural and hernia characteristics

	Population ($N=613$)
Unilateral hernia	42.74% (262)
Bilateral hernia	57.26% (351)
Mean number of hernias treated	1.60 ± 0.53
Number of hernias treated per patient	
1	42.09% (258)
2	56.44% (346)
3	1.31% (8)
4	0.16% (1)
Number of hernias treated	978
EHS classification ($N=978$)	
L1	7.26% (71)
L2	12.07% (118)
L3	23.93% (234)
M1	10.22% (100)
M2	19.73% (193)
M3	25.97% (254)
F1	0.31% (3)
F2	0.10% (1)
Unknown	0.41% (4)
Laparoscopic technique	
TAPP	95.43% (585)
TEP	4.57% (28)
Prophylactic antibiotics	91.84% (563)
Anesthesia ($N=612$)	
General	100.00% (612)
Volume of surgical glue (mL) ($N=609$)	1.57 ± 0.50
Usability of the glue ($N=604$)	4.76 ± 0.76
Type of mesh	
Polypropylene	88.10% (540)
Lightweight polypropylene	11.90% (73)
Operating time (min) ($N=586$)	35.05 ± 15.14
Period of hospitalization (days)	
Ambulant	80.91% (496)
23 h observation	17.46% (107)
> 48 h stay	1.63% (10)

EHS European Hernia Society, *TAPP* transabdominal preperitoneal repair, *TEP* totally extraperitoneal repair

5-week follow-up ($p<0.0001$) and 0.92 ± 0.15 at 12-month follow-up ($p<0.0001$) (Fig. 3). Significant improvement was reported for the dimensions of mobility ($p<0.0001$), self-care ($p<0.0001$), usual activities ($p<0.0001$), and pain/discomfort ($p<0.0001$) for both the 5-week and 12-month follow-up. Anxiety/depression was significantly reduced at 5-week follow-up ($p=0.0236$) compared to preoperatively (Table 6). The EQ-VAS general health scoring increased significantly from 79.03 ± 12.69 at baseline to 84.31 ± 9.97 at 5-week ($p<0.0001$) and 84.16 ± 14.48 at 12-month follow-up ($p<0.0001$) (Fig. 4).

Table 3 Intraoperative and postoperative complications

	Population
Intra-operative complications ($N=613$)	1.14% (7)
Minor	85.71% (6)
Major	14.29% (1)
Postoperative complications at 5 weeks ($N=588$)	16.33% (96)
Minor	94.79% (91)
Major	5.21% (5)
Hematoma	7.82% (46)
Ecchymosis	1.19% (7)
Seroma	1.36% (8)
Local numbness	1.87% (11)
Urinary retention	2.21% (13)
Wound infection	0.00% (0)
Mesh infection	0.00% (0)
Hernia recurrence	0.34% (2)
Death	0.00% (0)
Postoperative complications at 12 months	
Annoying sensation at the groin ($N=519$)	22.16% (115)
Pain at the groin ($N=524$)	13.74% (72)
Intake of analgesics	19.44% (14)
Death ($N=529$)	0.19% (1/529)

In evaluating postoperative complications at 5-week follow-up, 46 patients (7.82%) presented with hematoma, 7 patients (1.19%) with ecchymosis, and 8 patients (1.36%) with seroma. Eleven patients (1.87%) reported local numbness and thirteen patients (2.21%) urinary retention. No wound infection or mesh infection occurred (Table 3). Six major adverse events occurred. Hernia recurrence occurred in two patients (0.34%), one of which was surgically corrected. One patient suffered from chronic urinary retention treated with transurethral resection of the prostate (TURP), one patient developed a pulmonary embolism, and one patient had an intestinal obstruction due to adhesions at the site of peritoneal closure during a TAPP procedure (Table 3). Discomfort at the groin at 12-month follow-up was reported by 115 patients (22.16%); 72 patients (13.74%) experienced groin pain for which 14 patients (2.67%) used analgesics. One patient died during the study from an unrelated cause (Table 3).

These results of 613 patients represent a sub-analysis of a total study population of 1000 patients treated with Ifabond™ (Peters Surgical) and polypropylene mesh from various companies. The results of this total population are similar to the sub-analysis, showing compatibility of Ifabond™ with various polypropylene meshes. Surgeons' rating of the intraoperative usability of the Ifabond™ surgical glue was 4.76/5. Patients showed reduced pain and better QoL at follow-up compared with before surgery. Mean pain-VAS was significantly reduced at 5-week (6.64 ± 11.52 vs.

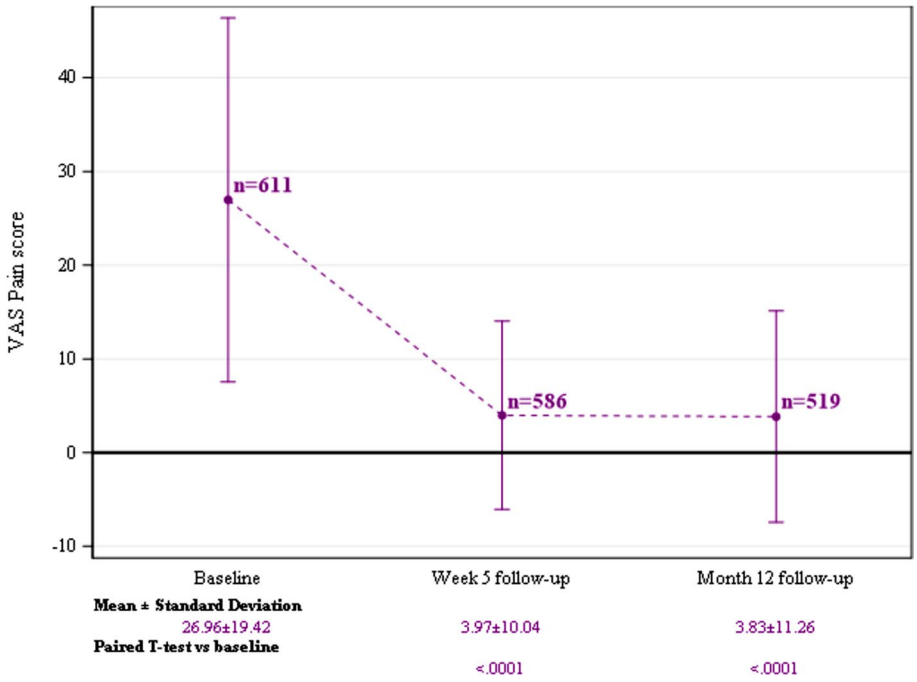

Fig. 2 Preoperative and postoperative pain scoring (VAS). *VAS* visual analog scale

Table 4 Preoperative and postoperative pain classification (VAS)

Assessment time	*N*	Pain classification
Preoperative (baseline)	611	Mild: 60.23% (368)
		Moderate: 23.40% (143)
		Severe: 5.40% (33)
5 weeks	586	Mild: 22.35% (131)
		Moderate: 1.71% (10)
		Severe: 0.51% (3)
12 months	519	Mild: 16.76% (87)
		Moderate: 2.70% (14)
		Severe: 0.96% (5)

VAS visual analog scale

Table 5 Postoperative intake of analgesic medication

	Population
Discharge ($N=613$)	99.51% (610)
Paracetamol	99.51% (610)
NSAID	13.70% (84)
COX-2 inhibitor	0.00% (0)
Opiate	0.49% (3)
After discharge ($N=585$)	70.77% (414)
Period of intake (days) ($N=404$)	5.68 ± 6.09
12-month follow-up ($N=524$)	2.67% (14)

NSAID non-steroidal anti-inflammatory drugs, *COX* cyclo-oxygenase

27.09 ± 18.71; $p < 0.0001$) and 12-month (4.11 ± 11.62 vs. 27.09 ± 18.71; $p < 0.0001$) follow-up. Patient QoL increased significantly from an EQ-5D-3L index score of 0.81 ± 0.18 at baseline to 0.91 ± 0.14 at 5-week follow-up ($p < 0.0001$) and 0.93 ± 0.13 at 12-month follow-up ($p < 0.0001$). At 5-week follow-up, hematoma (7.25%), seroma (3.21%), local numbness (1.55%), ecchymosis (0.83%), and wound infection (0.10%) were reported. Pain in the groin was reported by 94 patients (10.49%) at 12-month follow-up for which 22 patients (2.46%) used analgesics. A total of three patients experienced a hernia recurrence between discharge and 5-week follow-up. Since these were not treated during this period, the same recurrences were again reported at 12-month follow-up. One hernia recurrence was treated between the 5-week and 12-month follow-ups. In addition to the above-mentioned major complications for the subanalysis group, one mesh infection occurred that resulted in partial mesh removal.

Discussion

Inguinal hernia repair is one of the most common surgical procedures worldwide [1]. Recurrence rates appear to be similar after laparoscopic inguinal hernia repair and open mesh repair, especially with the standard Lichtenstein technique. However, TAPP and TEP have the advantage of less pain compared to Lichtenstein repair [27]. Nevertheless, chronic postoperative pain remains the most significant long-term complication of inguinal hernia repair and can be considered to be a significant burden on the global healthcare

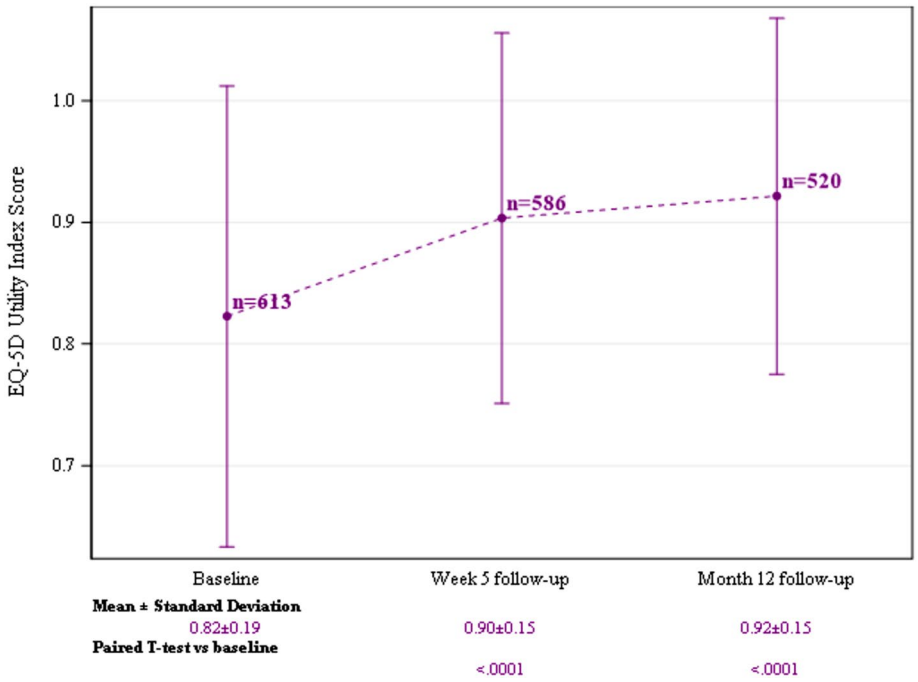

Fig. 3 Preoperative and postoperative EQ-5D index scores

Table 6 Preoperative and postoperative EQ-5D dimensions

EQ-5D dimension	Score	Preoperative (baseline)	5 weeks	12 months
Mobility	*N*	612	586	520
	No problems	77.78% (476)	93.17% (546)	93.85% (488)
	Some problems	21.73% (133)	6.66% (39)	6.15% (32)
	Extreme problems	0.49% (3)	0.17% (1)	0.00% (0)
			< 0.0001	**< 0.0001**
Self-care	*N*	612	586	520
	No problems	91.83% (562)	97.95% (574)	98.65% (513)
	Some problems	7.52% (46)	1.88% (11)	1.35% (7)
	Extreme problems	0.65% (4)	0.17% (1)	0.00% (0)
			< 0.0001	**< 0.0001**
Usual activity	*N*	611	586	520
	No problems	74.96% (458)	90.96% (533)	91.54% (476)
	Some problems	21.77% (133)	8.19% (48)	7.88% (41)
	Extreme problems	3.27% (20)	0.85% (5)	0.58% (3)
			< 0.0001	**< 0.0001**
Pain/discomfort	*N*	610	586	519
	No problems	53.61% (327)	70.48% (413)	77.26% (401)
	Some problems	45.08% (275)	28.67% (168)	21.58% (112)
	Extreme problems	1.31% (8)	0.85% (5)	1.16% (6)
			< 0.0001	**< 0.0001**
Anxiety/discomfort	*N*	612	586	519
	No problems	93.63% (573)	95.56% (560)	94.99% (493)
	Some problems	5.88% (36)	3.92% (23)	4.62% (24)
	Extreme problems	0.49% (3)	0.51% (3)	0.39% (2)
			0.0236	0.5164

p-values are indicated in bold where significant differences between baseline and follow-up QoL scores were identified

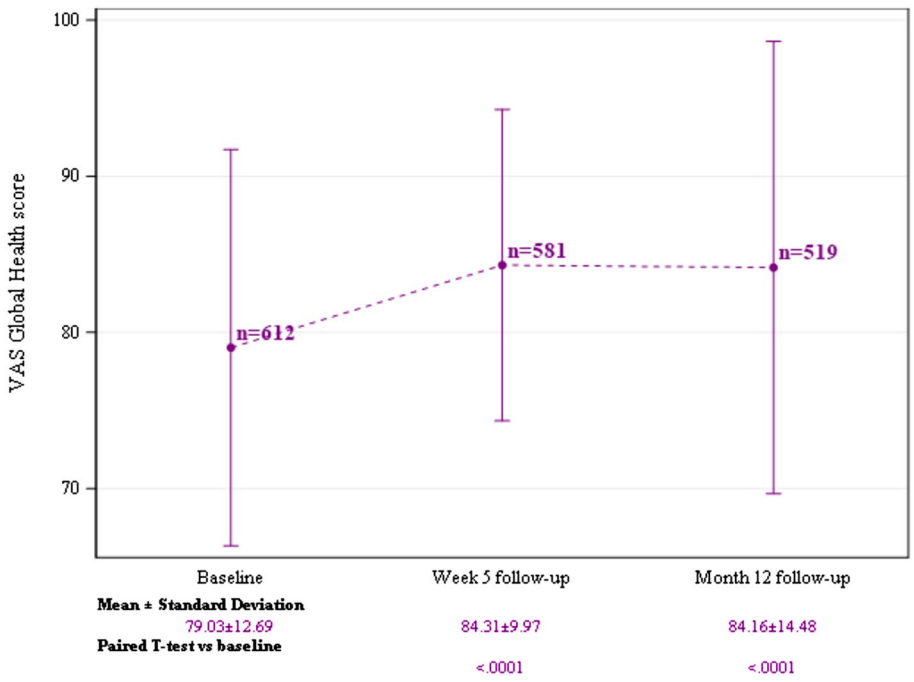

Fig. 4 Preoperative and postoperative EQ-VAS scoring. *VAS* visual analog scale

system. The frequency of chronic inguinal postoperative pain is not entirely clear, mainly because studies use different definitions to report pain [28]. To define a clinically significant level of discomfort, guidelines suggest that the threshold should be defined as "bothersome moderate pain affecting everyday activities" [3]. Based on this definition, approximately 10% to 12% of all operated patients suffer from clinically significant chronic postoperative pain [3]. Chronic postoperative pain is multifactorial and likely due to the surgical strategy, mesh composition, as well as mesh fixation method [29].

Currently, the method of mesh fixation is still open to discussion. Several techniques exist, including sutures, absorbable tacks/staples, biologic (fibrin) or synthetic (cyanoacrylate) surgical glues, self-fixating mesh, and no fixation. However, there is no consensus on a "best" method because of lack of high-quality evidence for differences between mesh fixation techniques [14, 30], and the technique used is mostly based on surgeons' preference. While penetrating fixation techniques such as tacks and staples were common in the first era of TAPP and TEP, surgical glues have become increasingly popular, with promising postoperative outcomes leading to greater surgeon and patient satisfaction [31]. According to the International Guidelines For Groin Hernia Management, no fixation is recommended for all hernia types in TAPP and TEP repair, except for large direct hernias [3]. Furthermore, considering the risk of postoperative pain due to traumatic fixation, the use of adhesive fixation should be considered in open and laparoscopic repair [3].

Mesh fixation with fibrin sealant or cyanoacrylate surgical glues has been investigated, showing similar or improved postoperative outcomes compared with penetrating fixation [14, 17, 21]. Alabi et al. recently conducted a review of existing systematic reviews of randomized controlled trials to compare the risk of chronic pain and recurrence after open and laparoscopic inguinal hernia repairs with different mesh fixation techniques [suture, self-gripping mesh, glue, no fixation, and mechanical fixation (staple, tack, strap)] [14]. With respect to laparoscopic mesh repairs, this review showed that glue fixation generally resulted in a lower rate of chronic pain compared with penetrating fixation (tack and/or staple) [15, 18–21, 32, 33]. The network meta-analysis by Techapongsatorn et al. reviewed 15 randomized controlled trials comparing metallic tack, no fixation, absorbable tack, suture, and glue in TEP and ranked glue as the best for reducing chronic pain compared with suture and no fixation, and glue and suture were ranked the highest for lowering the incidence of recurrence compared to traumatic fixation. Non-penetrating fixation such as glue and no fixation had similar risk of complications [21]. The same group recently evaluated available data of 28 systematic reviews and meta-analyses and 2 network meta-analyses in an umbrella review to assess various mesh fixation (suture, glue, self-gripping mesh, tacks, and no fixation) effects on pain, hernia recurrence, complications, operation time, hospital stay, and time to return to daily life activities [22]. They showed a reduction in pain with glue, and to some extend with self-gripping mesh, in both short- and medium-term postoperative periods. Few differences in complication rates

were detected reflecting the equivalence of the various mesh fixation techniques.

The recent review of Bedwani et al. compared the effects of glue versus traumatic mesh fixation in laparoscopic inguinal hernia repair on the incidence of chronic postoperative pain and other secondary outcomes, including acute pain, seroma, hematoma, hernia recurrence, and other postoperative complications [17]. Glue mesh fixation methods were found to be associated with a lower incidence of chronic pain and hematoma formation, with no significant difference in seroma formation and recurrence rates.

Rare randomized controlled studies report on glue fixation versus self-gripping mesh [34–36] or no fixation [37], showing no difference in operation time, pain, hospital stay, complications, and hernia recurrence.

This study collected pain and QoL data from a large number of patients undergoing inguinal hernia repair using a TAPP or TEP approach at five investigational sites. Polypropylene or lightweight polypropylene mesh was fixed exclusively with *n*-hexyl cyanoacrylate glue fixation [Ifabond™ (Peters Surgical)]. Postoperative pain was significantly reduced at 5-week (3.97 ± 10.04; $p < 0.0001$) and 12-month (3.83 ± 11.26; $p < 0.0001$) follow-up compared with before surgery (26.96 ± 19.42) on a 0–100 VAS. These results showed similar or improved pain levels compared with those reported in other studies evaluating glue for mesh fixation. Mitura et al. showed a significant reduction of pain from 4.28 preoperatively to 0.38 at 12-month follow-up, using the pain-VAS (0–10 scale) at rest ($p < 0.001$), after glue mesh fixation with Glubran®2 cyanoacrylate glue in 146 patients [38]. Mean pain-VAS scores decreased from 5.5 before surgery to 2.0 after surgery, using a 10-point VAS ($p < 0.0001$), in a study by Shah et al. evaluating fibrin glue (Tisseel™) in 92 patients [39]. The median follow-up time was 24 months (7–40 months). Pilkington et al. also reported outcomes on fibrin glue (Tisseel™) fixation in 274 patients. The median preoperative pain score of 5.0 decreased significantly to 1.0 postoperatively at 4–6 weeks follow-up ($p < 0.001$) (VAS 1–10). One patient (0.3%) experienced chronic groin pain (pain after three months) [40]. In addition, the current study showed that at 12-month follow-up 13.74% of patients experienced some groin pain for which 2.67% used analgesics. A pain level of VAS > 30 was reported by 3.66% of patients at 12 months after surgery.

QoL increased significantly. Mobility ($p < 0.0001$), self-care ($p < 0.0001$), usual activities ($p < 0.0001$), and pain/discomfort ($p < 0.0001$) improved at both 5-week and 12-month follow-up compared with before surgery. Anxiety/depression was significantly reduced at 5-week follow-up ($p = 0.0236$). Shah et al. reported a significant improvement in the two dimensions mobility ($p = 0.01$) and pain/discomfort ($p < 0.0001$) [32].

Rates of common laparoscopic inguinal hernia repair-related complications such as hematoma, seroma, hernia recurrence, urinary retention, and intestinal obstruction remained well within the reported ranges; 7.82% vs. 4.2–13.1% reported for hematoma [7], 1.36% vs. 0.5–12% reported for seroma [3], 0.34% vs. up to 2% reported for hernia recurrence [3], 2.21% vs. 1–20% reported for urinary retention, and 0.17% vs. up to 0.3% for intestinal obstruction, which is a rare complication [3].

Although fibrin and cyanoacrylate glues have different biochemical profiles, a systematic review by Tavares et al. showed no difference between glue subtypes in recurrence rates or postoperative complications [41].

A limitation of the present study is the absence of imaging to assess hernia recurrence at 12-month follow-up during a hospital visit. Data on hernia recurrences were collected as patient-reported outcome measure (PROM) via a patient letter or telephone interview. An underestimation of the recurrence rate could be expected. However, an established reason for non-retention of patients in clinical studies is that they are 'too well' to further engage in study processes in hospital, which could be expected with the inguinal hernia indication and could also lead to underestimation [42]. Furthermore, no direct comparison was made with other fixation methods.

In conclusion, our data, collected from a large number of patients and including both pain and QoL data, strongly support the safety, reliability, and feasibility of Ifabond™ mesh fixation of polypropylene mesh [standard polypropylene Promesh® SURG ST (Peters Surgical)/Biomesh® P1(Cousin Biotech) mesh and lightweight polypropylene Promesh® SURG LI (Peters Surgical)/Premium® Implant (Cousin Biotech) mesh] in laparoscopic inguinal hernia repair. High surgeon satisfaction of glue usability was reported (4.76/5). Significant improved patients' QoL and pain scores were seen at both 5-week and 12-month follow-up compared with preoperatively. All with a comparable risk of developing chronic pain and postoperative complications according to the literature.

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