



## LAPAROSCOPY/ROBOTICS

### ORIGINAL ARTICLE

# Use of fibrin glue as a sealant at the anastomotic line in laparoscopic pyeloplasty: A randomised controlled trial



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#### KEYWORDS

Laparoscopic pyeloplasty;  
Fibrin glue;  
PUJ obstruction;  
Stentless pyeloplasty

#### ABBREVIATIONS

CONSORT, Consolidated Standards of Reporting Trials;  
DTPA, diethylene-triamine-penta-acetic acid;  
LPP, laparoscopic pyeloplasty;

**Abstract Objective:** To assess the effectiveness of fibrin glue as a sealant at the anastomotic line of a stentless laparoscopic pyeloplasty (LPP) repair instead of JJ stent insertion.

**Patients and methods:** In all, 46 patients with pelvi-ureteric junction obstruction scheduled for LPP were randomised into two groups each containing 23 patients. Group A underwent stented repair, while group B had a stentless repair together with sealing of the anastomotic line with fibrin glue.

**Results:** There was no statistically significant difference between the groups for the postoperative improvement in the renal scan and intravenous urography. However, there was a statistically significant decrease in early postoperative adverse events in group B. In group A, all the patients had irritative lower urinary tract symptoms (LUTS) and 16 (72.7%) had postoperative urinary tract infections (UTIs). In group B, no patient had a UTI or irritative LUTS. In all, 21 patients (95.4%) in group A had minimal terminal painful haematuria; while in group B, only one patient (4.3%) had minimal total painless haematuria. Also, patients in group B were spared the need for a second anaesthesia exposure for stent removal.

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PUJO, PUJ obstruction;  
T<sub>1/2</sub>, clearance half-time (renogram)

**Conclusion:** The use of fibrin glue is a valid alternative to stenting in LPP with the same excellent outcome but with markedly lower short-term postoperative adverse events.

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## Introduction

Recently, laparoscopic pyeloplasty (LPP) has become the standard treatment for PUJ obstruction (PUJO). Open pyeloplasty should only be performed after failed LPP [1]. The success rates of LPP vary between 87% and 100% and are comparable to open pyeloplasty success rates, but with the requisite advantages of being minimally invasive [2].

There has been an ongoing debate on intubated (stented) vs non-intubated (stentless) repair of the PUJ. The use of ureteric stents has several advantages as they ensure adequate drainage, especially in the presence of postoperative oedema [3], lowering the risk of urinary leak and urinoma formation, thereby reducing periureteric fibrosis and re-stenosis [4], and providing support and alignment of the fresh suture line [5]. However, ureteric stents have several disadvantages, such as irritative urinary symptoms, flank pain and increased risk of infection [6], migration, encrustation, retained or forgotten fragments [7], and the need for an additional procedure for removal.

There is a trend towards stentless repair in LPP, especially where a water-tight closure can be achieved [8]. Due to the fact that there is prolonged leakage and thus hospital stay in stentless LPPs [4], adding fibrin glue maybe an option to decrease this leakage.

Fibrin glue is a mixture of coagulation factors. It is used for three major reasons in urological surgery: as a urinary tract sealant in urological anastomosis like pyeloplasty, haemostatic agent, and as a tissue adhesive [9].

To our knowledge, there are no published studies in humans in which fibrin glue has been used as a sealant of the anastomotic line in LPP and compared with stented LPP. There are a few studies where fibrin glue has been used in ureteric repair and in pyeloplasty. In 1989, Kram et al. [10] used fibrin glue in ureteric trauma, as a bolster over the ureteric anastomosis to decrease urinary leakage. Edgen et al. [11] assessed the results of fibrin-glued dismembered pyeloplasty in patients with PUJO, but only in eight patients.

In the present study, we aimed to assess the efficacy of fibrin glue as a sealant of the anastomotic line in a stentless LPP repair and to compare it to a stented LPP for operative and postoperative outcomes. The primary endpoint of the present study was early postoperative complications, as they are the main disadvantage

of stented pyeloplasty. The secondary endpoint was the early outcome of both groups at the 3-month follow-up visit.

## Patients and methods

Between January 2012 and June 2014, 106 patients presented to the Urology Department, Ain Shams University hospitals with PUJO and were scheduled for pyeloplasty. Of these, 46 patients underwent transperitoneal dismembered Anderson–Hynes LPP based on the following inclusion and exclusion criteria:

Inclusion criteria:

- Persistent significant loin pain.
- Delayed excretion in IVU with significant pelvicalyceal dilatation.
- clearance half-time (T<sub>1/2</sub>) > 20 min in diuretic renogram.

Exclusion criteria:

- Previous renal surgery.
- Pyonephrosis.
- Children aged < 10 years.
- Bleeding tendency.

The sample size calculation was done using Power and Sample Size Calculation Program version 3.1.2. Prior data indicate that the complication rate among controls is ~0.7. If the true complication rate for experimental subjects is 0.3, then 23 experimental subjects and 23 control subjects are needed to be able to reject the null hypothesis that the complication rates for experimental and control subjects are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

Patients were randomised by simple 1:1 randomisation by alternating patients between the treatment groups once they were included in the study. Randomisation was done by the first author. Patients in group A underwent a stented repair, while those in group B had a stentless repair with fibrin glue sealing of the anastomotic line.

All patients were assessed preoperatively by history and physical examination, pelvi-abdominal ultrasonography, IVU with delayed films as needed, (F-15) diuretic renogram diethylene-triamine-penta-acetic acid (DTPA)

with furosemide, urine analysis and culture, in addition to the standard preoperative evaluation. The study design and work flow is summarised in a Consolidated Standards of Reporting Trials (CONSORT) flow chart (Fig. 1).

The patients were placed in a lateral position for transperitoneal laparoscopic access. After Kocherisation of the colon, the renal pelvis and upper ureter were identified and dissected. The ureter was divided just distal to the PUJ and spatulated posteriorly for 2–3 cm. The pelvi-ureteric segment and redundant pelvis were excised. The posterior lip of the spatulated ureter was anastomosed with the renal pelvis with 4/0 polyglactin 910 (Vicryl) in a running fashion. In group A, a 6-F JJ-stent is passed antegrade to the bladder under fluoroscopic guidance over a guidewire, while the superior coil of the JJ-pigtail stent is placed in the renal pelvis, then the anterior lip of the spatulated ureter is anastomosed with the renal pelvis using 4/0 polyglactin 910 in a run-

ning fashion. In group B, no stent was left and after the anastomosis was completed the fibrin glue was delivered through one of the laparoscopic ports and injected through a 16-F Nelaton catheter on the anastomotic line.

In both groups, a 16-F tube drain was inserted from one of the ports and left parallel to the ureter under laparoscopic guidance. The drain was removed when drainage was < 50 mL in 24 h. In all patients in group A the JJ stent was removed 6 weeks later.

The following data were recorded: patient age, gender, operative time, intraoperative complications and difficulties, amount and duration of urinary leakage, incidence of UTI, hospital stay, and postoperative pain determined using an analogue scale of 0–10 and the need for analgesic. At the 3-month follow-up IVU and a DTPA diuretic renogram were performed and compared to the preoperative ones.

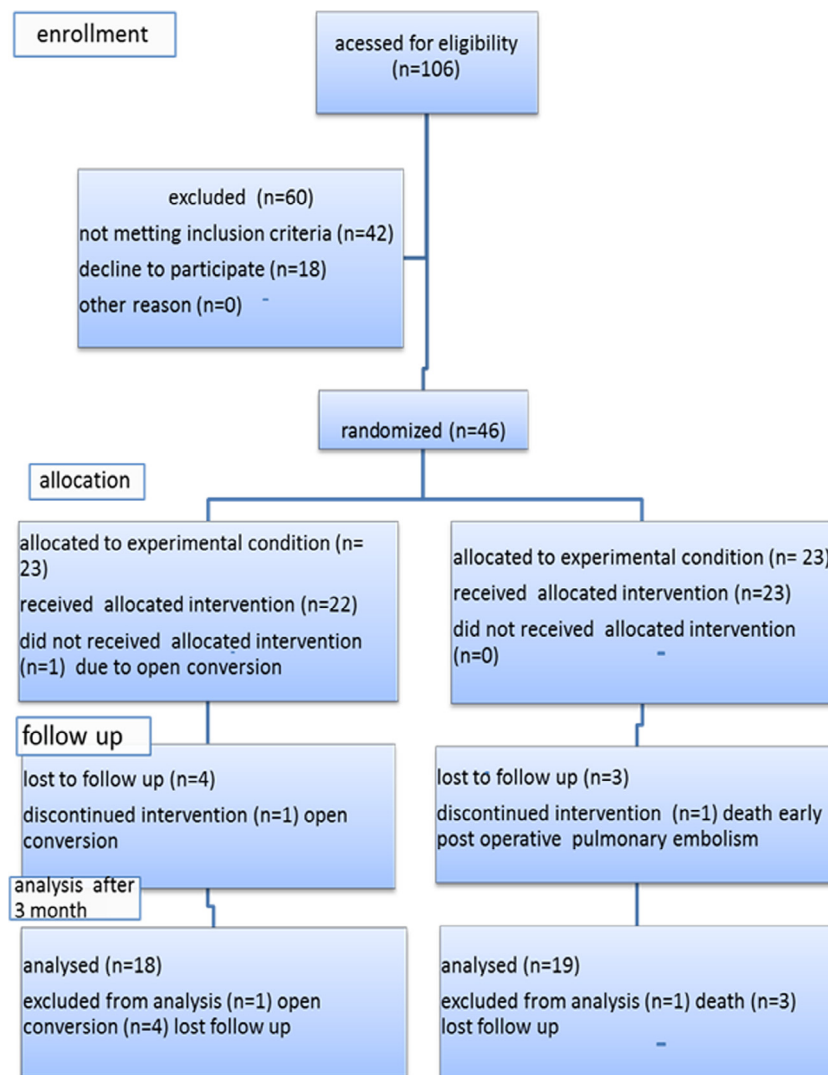


Figure 1 CONSORT flow chart.

The fibrin glue was prepared from autologous blood as follows: two different components of the fibrin glue were prepared and kept separate until the time of usage. The first component was prepared as follows: 100 mL of patients' blood was drawn on 10% sodium citrate. This blood was centrifuged for 8 min at 3200g. The plasma was then removed. Ethanol (100%) was added to portion of the plasma in a ratio of 1:7. This mixture was then refrigerated at  $-18^{\circ}\text{C}$  for 20 min and then centrifuged for 8 min at 3200g. The supernatant was discarded leaving the fibrinogen pellets. The rest of the plasma was used to dissolve the fibrinogen pellets by incubating them at  $37^{\circ}\text{C}$  for 15 min. The second component of the adhesive was prepared by adding 9.2 mL calcium chloride solution (40 mmol/L) to thrombin. This was kept at  $37^{\circ}\text{C}$  and ready to be used. At the time of surgery, the two components were mixed together to yield a gelatinous substance.

The collected data were analysed using SPSS statistical package version 18. All continuous variables are presented as means with standard deviations (SDs). Comparisons between the two groups were done using Student's *t*-test for parametric quantitative variables and Wilcoxon Mann–Whitney test for non-parametric continuous variables. The chi-square test was used for qualitative variables. A  $P < 0.05$  was considered significant and highly statistically significant if  $< 0.001$ .

The present study was approved by Faculty of Medicine, Ain Shams University Ethical Committee. Written informed consent was obtained from all patients. The study group patients (group A) were not exposed to any increased risk compared to those of the control group (group B), as the new technique has the same success rate with less postoperative complications.

## Results

There were no statistically significant differences in the patients' demographics between the groups (Table 1) and no difference in presentation of both groups; all patients had loin pain with pelvicalyceal dilatation and a  $T_{1/2} \geq 20$  min (Table 2).

**Table 1** The patients' demographics.

Variable	Group A ( $n = 23$ )	Group B ( $n = 23$ )	<i>P</i>
Age, years			
Range	14–56	11–51	
Mean (SD)	39.8 (10.7)	35.7 (11.7)	0.2
Median	42	39.5	
Gender, n (%)			
Males	16 (69.6)	15 (65.2)	0.7
Females	7 (30.4)	8 (34.8)	

No statistically significant difference was found between both groups.

**Table 2** Indication for surgery.

Indication	Group A ( $n = 23$ )	Group B ( $n = 23$ )
Significant loin pain, <i>n</i> (%)	23 (100)	23 (100)
Significant pelvicalyceal dilatation by IVU, <i>n</i> (%)	21 (91.3)	22 (95.7)
Non-secreting kidney in IVU, <i>n</i> (%)	2 (8.7)	1 (4.3)
$T_{1/2}$ , min		
Range	20–26	20–25
Mean (SD)	22.6 (1.4)	22.4 (1.3)
Split renal function, %		
Range	12–38	13–38
Mean (SD)	23.6 (7)	23.5 (7)

There was no difference in presentation of both groups.

There was no statistically significant difference between the groups for operative time and blood loss. As regards conversion to open, we had only one case in group A. This was the first case in the whole study and was converted to open due to markedly attenuated ureter with very difficult handling and suturing. No visceral injury occurred in either group, but we had one case of injury to the gonadal vessels during dissection of the upper ureter in each group, which was managed by clipping of the vessel (Table 3).

The early postoperative data also showed no statistically significant difference between the groups. In group B we had three patients who had a hospital stay of  $> 7$  days. One of them had persistent urinary leakage of about 700 mL/day for 14 days and was managed by JJ stent insertion and the remaining two patients became dry after 10 days (Table 3).

For short-term postoperative adverse events (Table 4), all patients in group A had irritative LUTS in the form of burning micturition, frequency, and urgency, which were relieved by oral analgesic and anticholinergics. In all, 16 patients (72.7%) in group A had a postoperative UTI confirmed by urine culture and sensitivity tests that were treated with oral antibiotic for 7 days. In contrast, in group B no patient had a UTI or irritative LUTS. For haematuria, 21 patients (95.4%) in group A had minimal terminal painful haematuria, which did not necessitate any treatment; while in group B, only one patient (4.3%) had minimal totally painless haematuria, which resolved spontaneously. In group A, two patients (9.09%) had reflux pyelonephritis; they were managed by oral antibiotic for 14 days. We had one case of sudden death in group B (4.3%). This was a 49-year-old female patient with above average body build and had no medical comorbidities. Her operative time was 240 min and she suddenly died on the fifth postoperative day due to a massive pulmonary embolism (Table 4).

At the 3-month follow-up IVU and diuretic DTPA renal scan, there was significant postoperative improvement in the  $T_{1/2}$  and split renal function in both groups.

**Table 3** Operative and early postoperative data.

Variable	Group A (n = 23)	Group B (n = 23)	Z value	P
<b>Operative</b>				
Operation time, min				
Range	120–420	120–240		
Mean (SD)	169.6 (65)	157.8 (35)		0.45
Blood loss, mL				
Range	10–30	15–30		
Mean (SD)	20 (8)	23 (5.8)	–1.300	0.193
Open conversion	1	0		
Vascular injury	1	1		
<b>Early postoperative</b>				
Amount of leakage, mL/day				
Range	30–300	20–700		
Mean (SD)	149.6 (96.7)	145 (146)	–0.901	0.368
Median	150	100		
Duration of leakage, days				
Range	2–5 days	2–15		
Mean (SD)	3.6 (1.2)	4 (2.8)	–0.104	0.907
Median	4	4		
Postoperative pain by analogue scale 0–10				
Range	4–10	4–10		
Mean (SD)	6 (2)	5.7 (2)	–0.147	0.883
Hospital stay, days				
Range	5–7	4–17		
Mean (SD)	5.6 (0.6)	5.7 (2.7)	1.071	0.284
Median	6	6		

There was no statistically significant difference between the groups for operative and early postoperative variables.

**Table 4** Early postoperative adverse events.

Adverse event	Group A (n = 22, n (%))	Group B (n = 23, n (%))	P
Irritative LUTS	22 (100)	0	<0.001
Haematuria	21 (95.4)	1 (4.3)	<0.001
Pyuria	16 (72.7)	0	<0.001
Reflux pyelonephritis	2 (9.09)	0	0.1
Death	0	1 (4.3)	

There were statistically significant differences between the groups for early postoperative adverse events.

In group A, 17 patients (77.2%) had downgrading of pelvicalyceal dilatation, and improved mean T½ and mean split renal function. Only one patient in group A showed deterioration of pelvicalyceal dilatation where the T½ became 27 min compared with 22 min and split function became 17% compared with 21% preoperatively. Five patients in group A missed their follow-up appointment. In group B, 18 patients (78.3%) had downgrading of pelvicalyceal dilatation, with mean T½ and mean split function improvement. The patient who needed JJ stent insertion due to persistent leakage showed deterioration of pelvicalyceal dilatation with a T½ of 27 min compared to 23 min preoperatively, and split function of 16% compared to 19% preoperatively.

The other two patients with persistent urinary leakage showed improvement as T½ became 12 and 15 min compared to 22 and 25 min preoperatively and split function became 40% and 35% compared to 27% and 22% preoperatively. Three patients missed their follow-up in group B (Table 5).

There was no statistically significant difference between both groups in postoperative IVU, mean split function, mean T½ (Table 5). The postoperative complications are summarised according to Clavien–Dindo classifications in Table 6.

## Discussion

Open dismembered pyeloplasty is the ‘gold standard’ for PUJO in children and adults, with high success rates ranging between 90% and 100%. LPP is a viable alternative and has the requisite advantages of a minimally invasive procedure, i.e. improved cosmesis, reduced analgesic requirement, and short hospital stay, and has high success rates similar to those of the open approach [12].

There has been an ongoing debate on the merits of intubated (stented) vs non-intubated (stentless) repair of PUJO using either a laparoscopic or open technique [14]. Many authorities recommend a tube for the fear that oedema at the anastomotic site may lead to occlusion of the lumen postoperatively. On the other hand,

**Table 5** The 3-month follow-up data.

Variable	Group A (n = 18)	Group B (n = 19)	Z value	P
Improvement on IVU, n (%)	17 (77.2)	18 (78.3)		0.7
Deterioration on IVU, n (%)	1 (5.5)	1 (5.2)		
T½, min				
Range	8–27	7–27	0.308	0.758
Mean (SD)	10.5 (4)	10.1 (4)		
Split renal function, %				
Range	17–48	16–50		0.8
Mean(SD)	34.8 (10)	34 (10.6)		
Patients missed follow-up, n/N (%)	5/23 (21.7%)	4/23 (17.4)		

No significant difference was found in the outcome of both groups after 3 months.

**Table 6** Clavien classifications of postoperative complications.

Complication grade	Group A (n = 22), n (%)	Group B (n = 23), n (%)
I	21 (95.4)	1 (4.3) haematuria
II	22 (100) LUTS 16 (72.7) UTI 2 (9.09) reflux pyelonephritis	2 (8.7) urinary leak 0
III		
IIIa		1 (4.3) urinary leak managed with JJ stenting
IIIb	0	0
IV	0	0
V		1 (4.3)

The statistical comparison is shown in [Table 4](#).

the presence of a stent acts as a foreign body leading to an increased incidence of postoperative UTI and dissolution of sutures at the anastomotic line and finally failure of the pyeloplasty [15].

Urinary leakage and hospital stay are important issues to be discussed. In our present series, although the mean values in both groups were almost equal, three patients (13%) in the stentless group had prolonged urinary leakage and therefore a longer hospital stays (> 7 days) than the stented-group patients. Elmalik et al. [16] reported that a significant number of stentless patients had marked and persistent urinary leakage, which necessitated JJ stent insertion and therefore had a significantly longer hospital stay. These finding of Elmalik et al. [16] correspond with the results of Smith et al. [4] who also reported a shorter hospital stay for their stented group as compared to their stentless group, at a mean (SD) of 2.1 (0.89) vs 2.6 (1.1) days. On the other hand, Khawaja et al. [14] and Bilen et al. [17] showed no statistically significant differences between the two groups as regards urinary leakage and hospital stay. Others concluded that, stentless LPP is an ideal solution for repair of PUJO in adults but that the success rate was lower for the paediatric age group [13]. In contrast to the previous studies, Meisheri et al. [15]

reported a markedly shorter hospital stay in their stentless group (8 days) than in their stented group (16 days).

For early postoperative adverse events, they were markedly higher in group A than in group B. These findings agree with those of Khawaja et al. [14] who showed significant bothersome irritative LUTS and haematuria in stented-group patients. Conversely, Elmalik et al. [16] reported minimal incidence of UTI as a stent-related complication [16].

In our present series, there was no statistically significant difference between the two groups for postoperative T½, split renal function, improvement of pelvicalyceal dilatation, and the overall success rate of the LPP. Khawaja et al. [14], Bilen et al. [17] and Smith et al. [4] reported equivalent outcomes when they compared stented vs stentless LPP. By contrast, Meisheri et al. [15] reported better outcomes for stentless pyeloplasty when they compared 31 stentless to 39 stented pyeloplasties, with three failures in the stented group and 100% success in the stentless group. Ariei et al. [18] concluded that, stentless LPP is an efficient method for PUJO repair when done by an experienced surgeon, but they included only five patients with PUJO their series. Similarly, Sethi et al. [19] concluded that stentless robot-assisted pyeloplasty is a safe and effective option for surgical treatment of PUJO. In contrast to Meisheri et al. [15], Bilen et al. [17], and Khawaja et al. [14], Elmalik et al. [16] recommended the use of a stent when they compared stented vs stentless repair. Elmalik et al. [16] demonstrated that the adjunct use of a ureteric stent was significantly favourable for earlier resolution of hydronephrosis at a mean (SD) of 3.0 (0.46) months postoperatively in stented patients vs 15.1 (3.05) months in stentless patients.

The presence of two confounding factors in group B, namely fibrin glue and being stentless, means that the results cannot be confidently attributed to one factor alone or both together.

## Conclusion

Omitting stenting during LPP together with the application of fibrin glue decreases postoperative complications

significantly and has similar excellent outcomes when compared to stented LPP.

### Conflicts of interest

We did not have any funds or conflict of interest.

### Source of Funding

None.

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