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Research Article

Reinforcement of Intestinal anastomosis with tissue adhesive glue modified cyanoacrylate (Glubran 2) after elective colorectal cancer surgery

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Abstract

Background: Each year, millions of gastrointestinal (GIT) anastomoses are created worldwide. Anastomotic leakage (AL) after the creation of a GIT anastomosis remains an important complication in GIT surgery. **Aim:** To compare between intestinal resection reanastmosis with use of tissue adhesive modified cyanoacrylate (Glubran 2) in Group B or without in Group A as regard intestinal leakage , operative time , hospital stay. **Patients and methods:** This prospective controlled clinical study was carried out on 40 patients of intestinal resection reanastmosis with use of tissue adhesive (Glubran 2) in Group B or without adhesive material in Group A. **Results:** Postoperative outcomes show some variations between two groups, but most differences do not reach statistical significance $p<0.05$. Group B had a higher rate of ICU admissions (25% vs 15% in Group A). More patients in Group A required blood transfusions (70% vs 50% in Group B), but this difference does not reach statistical significance, Group A had a notably longer median hospital stay of 10 days compared to 7 days for Group B, and this difference shows statistical significance ($p=0.05$), Regarding the incidence of leakage between studied groups, the result was not statistically significant as only 3 cases in group A compared to only 1 case in group B had leakage. **Conclusion:** We concluded that there was a difference in postoperative leakage between groups A and B, without statistically significant difference. However, no statistically significant differences were found in ICU admission, postoperative blood transfusion operation, hospital stay, DVT, pulmonary embolism, chest infection, wound infection, quality of surgical specimen.

Key words: Reinforcement, Intestinal anastomosis, Elective surgery, Adhesive glue modified cyanoacrylate

Introduction

Millions of gastrointestinal (GIT) anastomoses are made globally each year. After a GIT anastomosis is created, anastomotic leakage (AL) is still a significant risk in GIT surgery. The prevalence of AL is still significant despite years of investigation, particularly after esophageal and colorectal anastomosis [(1-3)]. The cause of aseptic leakage is known to be complex, mostly due to ischemia of the bowel endings and/or technical failure. Numerous risk variables are well-known and may be divided into two categories: operative factors (such as the surgeon's expertise, anastomotic site, and operating time) and patient-related risk factors (comorbidity, BMI, drug usage) [(4)].

Tissue adhesives have become more and more common in several surgical specialties. Tissue adhesives come in a variety of forms, each with unique adhesive mechanisms and applications [(5)]. Tissue adhesives work by basically

creating connections with the material they adhere to these ties can be physical, such as hydrogen bonds or van der Waals forces [6], or chemical, of which covalent bonds are the strongest. Furthermore, the total strength of the glue bond depends on the balance between interaction within the tissue adhesive (cohesion) and between the tissue adhesive–substrate interfaces (adhesion). Tissue adhesives can be classified as sealants, which are used to cover and shield an anastomosis, or as glues, which are designed to attach different structures (such as wound margins) separately.

Tissue adhesives can be utilized intracor-poreally in addition to externally. Cardiovascular, plastic, and increasingly gastrointestinal (GIT) tract surgeries are using different tissue adhesives [7, 8]. One potential tool for closing wounds is tissue adhesive. They are robust and flexible, do not impede the wound-healing process, and transfer stresses throughout the wound more uniformly and noninvasively than sutures and staples. Furthermore, there is less variety in approach across surgeons due to the ease of use and standardization of the tissue adhesive administration technique.

The purpose of this research was to evaluate intestinal resection and reanast-mosis procedures with and without the use of tissue adhesive modified cyanoacrylate (Glubran 2) in terms of complications including intestinal leakage, operating time, and hospital stay.

Patients and methods

This prospective controlled clinical study was carried out on 40 patients of intestinal resection reanastmosis with use of tissue adhesive (Glubran 2) or without adhesive material. The patients were divided into 2 groups: Group A: 20 patients were managed by resection anastomosis by only hand sewing and Group B: 20 patients were managed by resection anastomosis by hand sewing with glubran 2.

Inclusion criteria:
Age >15 and <80 years old, Patients with elective colorectal cancer.
Exclusion criteria: Liver cirrhosis, Irresectable mass and colonic malinancy with distant metastasis.

Methods

All patients were subjected to the following:
Preoperative evaluation including:
Personal data, medical history, and date of admission in hospital, Careful clinical examination, Laboratory and Radiological investiationa**.Colonic preparatient** will be on oral fluids 3 days before operation till 12 hour before day of operation, Mechanical preparation: Enemas for 1 days before operation every 6 hour, chemical prepa-ration in form of IV metronidazole 500 mg every 8 hour.

Surgical technique
Anasethia:
All patients received general anesthesia with endotracheal tube. Elastic stockings on both legs, a nasogastric tube to decompress the stomach, and a Foley catheter were implanted to monitor urinary output. To reduce the risk of wound infection, each patient received a single intraoperative dose of a wide spectrum antibiotic (IV ceftriaxone 1 gm).

Intraoperative
Technique
Patient is placed supine position, skin sterilization with betadine. midline abdominal incision, Peritoneal cavity is explored including liver for metastasis , omentum and malignant ascites, Dissection , kocerization and vascular ligation this facilitated resection ensures tension-free anastomosis, The specimen was removed with clamps in situ, avoiding enteric contents spillage during bowel division and then anastomosis was done.

Technique of Anastomosis:
Reconstruction after colorectal anasto-mosis can be done end-to-end or side-to-

end, with side-to-end techniques like Baker anastomosis preferred for size discrep-ancies between bowel ends. Anastomosis is performed using 3/0 vicryl, posterior interrupted full-thickness sutures, and hemostat for accurate placement. Full-thickness interrupted anterior-layer sutures are taken, as in figure (9)

- **After Resection anastomosis by hand sewing use glubran 2:**

The blister pack was opened and Glubran 2 was released into a sterile environment.

the Glubran 2 out of the single-dose vial using a sterile syringe then put the syringe into applicator Glubran 2 was applied into anastomosis by applicator in spraying manner .

Excess product was removed within 5-6 seconds and not touched until polymeri-zation reaction completes, as it may detach or not produce the desired effect as in figure (10, 11) .

Postoperative follow up

Patient was given medical treatment in the form of IV metronidazole, IV 3rd generation cephalosporin , IV controloc 40 mg every 24 hour perflgan every 8 hours on ceftriaxone 1 gm. SC clexane half of body weight for obese patients every 24 hour as a prophylactic dose starting 12h post-operative to prevent DVT or PE.

Frequent checkup of drains for amount and contents to exclude leakage.

Strict follow up of symptoms like vomiting, fever and tachycardia.

Check of vital data and blood glucose level regularly especially if diabetic.

Checking of serum albumin, Hemoglobin and electrolytes daily and correct affected labs also total leucocytic count to exclude leakage and sepsis.

Abdominal ultrasound to detect intra peritoneal collection or pocket and x ray in erect position to detect ileus.

Removal of nasogastric tube and, allow clear fluids after 6 hours post-operative then semisolid after 2 days after operation and encourage early ambulation after operation

He was allowed to leave the hospital provided she could handle semisolid food and had sufficient pain relief from oral analgesics.

Follow up:

-During first month

They were examined in the outpatient clinic after 1 weeks (post-operative) for leakage, DVT, PE then after 2 week histo-pathological outcome of the specimen and wound infection, removal sutures then after 4 weeks to check patient return to normal life (regular diet , no pain , no wound infection and return to his work)

--Every 6 months

Clinically checked and abdominal CT, colonoscopy is ordered for recurrence or organ deposits.

Results

The demographic and clinical charac-teristics of the two groups show remarkable similarities.as mean age of group A was 61.8±10 years compared to 60.6±10 years, While Group A has a higher proportion of males (60%) compared to Group B, which has more females, this difference in sex distribution is not statistically significant (p=0.11). The prevalence of chronic illnesses, including diabetes mellitus and hypertension, is comparable between the groups (p=0.877). Although. Similarly, the distribution of presenting symptoms, such as anemia, bleeding, and changes in bowel habits, is consistent across both groups (p=0.641). Overall, the demographic data shows that the two groups are well-matched, with no statistically significant differences in any of the examined variables as in table (1)

The analysis of the surgical aspects reveals continued similarities between the two groups. The distribution of colorectal lesion sites is comparable between the groups, with no statistically significant difference observed (p=0.938). This suggests that the location of the lesions is not a distinguishing factor between the groups. In terms of total operative time, Group B experienced a slightly longer mean duration at 214±25 minutes compared to Group A's 204±28 minutes.

However, this difference of 10 minutes is not statistically
significant (p=0.246), indicating that both groups underwent procedures of similar length Similarly as in table (2) & fig (1)

While Group B had a higher median total blood loss at 275 ml compared to Group A's 250 ml, this difference also fails to reach statistical significance (p=0.967). The intraoperative data suggests that the surgical procedures were comparable between the two groups, with no significant differences in lesion site, operative time, or blood loss as in table (2).

The postoperative outcomes reveal some variations between the two groups, though most differences do not reach statistical significance. Group B had a higher rate of ICU admissions (5 cases with percentage of 25% compared to 3 cases in group A with percentage of 15%, but this difference is not statistically significant (p=0.42) as in table (3).

While more patients in Group A required postoperative blood transfusions (70% vs 50% in Group B), this difference also fails to reach statistical significance (p=0.197). Group A had a notably longer median hospital stay of 10 days compared to 7 days for Group B, and this difference shows statistical significance (p=0.05 as in table (3), figure (2)

Rearding hospital stay, Group A had a notably longer median hospital stay of 10 days compared to 7 days for Group B, though this difference narrowly misses statistical significance (p=0.05) as in table (3), figure (3).

Regarding the postoperative complications that the most significant difference is in the incidence of leakage, which was significantly higher in Group A (15%) vs (5%) in group B, (p=0.03), which show no statistically significant differences between the groups, Other complications such as deep vein thrombosis, pulmonary embolism, chest infection, and wound infection showed no statistically significant differences between the groups as in table (4), figure (4)

Regarding the incidence of leakage between studied groups, the result was not statistically significant as only 3 cases in group A compared to only 1 case in group B had leakage.
For time of diagnosis and method of diagnosis, it was found that, mean time of diagnosis in group A was 3.1days ranged from 2 to 4 days with fever positive in 2 cases, tachycardia positive in 2 cases and tachypnea was positive in only 1 case, for the case that had leakage in group B, the diagnosis was done after 6 days with positive fever, tachycardia and tachypnea as in table (5), figure (5).

Regarding drains, 2 cases in group A had low output less than 200 cc enteric discharge and the remaining 1 case had high output in drain more than 500 cc enteric discharge, on other hand, the only 1 case who had leakage in group B, had low output in drain less than 200 cc enteric discharge as in table (5), figure (6).

The histopathological analysis and surgical outcomes reveal some differences between the two groups, although most do not reach statistical significance. The distribution of cancer types varies between the groups, but this difference is not statistically significant (p=0.56), suggesting that the overall histopathological profile is relatively similar. Regarding resection margins, Group B showed a very slight higher percentage of free margins at 95% compared to 90% in Group A. and also this small difference is not significant(p=0.54). Similarly, the lymph node status appears more favorable in Group B, with 95% of patients having free lymph nodes compared to 85% in Group A. This 10% difference also don’t reach statistical significance (p=0.29) as in table (6), in figure (8).

Table 1: Demographic data

		Group A N=20	Group B N=20	P value
Age	***Range*** ***Mean ± SD***	(43-78) 61.8±10	(38-70) 60.6±10	***0.70***
Sex	***Male*** ***Female***	12(60%) 8(40%)	7(35%) 13(65%)	***0.11***
Chronic illness	***No*** ***DM*** ***HTN*** ***Both***	6(30%) 6(30%) 4(20%) 4(20%)	4(20%) 8(40%) 4(20%) 4(20%)	***0.87***
presenting symptoms	***Anemia*** ***Bleeding per rectum*** ***Change bowel habit***	8(40%) 10(50%) 2(10%)	8(40%) 8(40%) 4(20%)	***0.64***

Table 2: Intraoperative data

		Group A N=20	Group B N=20	P value
Site of colorectal cancer	ceacum Asecending colon Transverse colon Descending colon Sigmoid	4(20%) 6(30%) 6(30%) 2(10%) 2(10%)	6(30%) 6(30%) 4(20%) 2(10%) 2(10%)	*0.938*
Total operative time (min)	*Range* *Mean ± SD*	(180-280) 204±28	(200-250) 214±25	*0.24*
Total blood loss	*Median* *IQR*	250 (200-387.5)	275 (125-400)	*0.967*

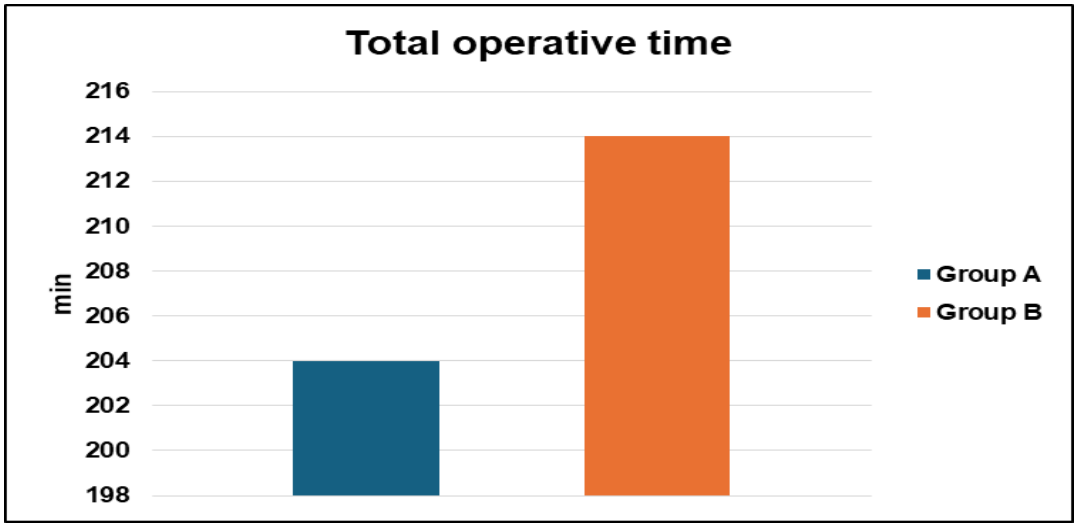

Fig. (1) bar chart represent compariosn between studied groups regarding total operative time finding

Table 3: Postoperative data

		Group A N=20	Group B N=20	P value
ICU admission after operation	*No* *Yes*	17(85%) 3(15%)	15(75%) 5(25%)	*0.42*
Need for Post. Operative Blood Transfusion	*No* *Yes*	6(30%) 14(70%)	10(50%) 10(50%)	*0.197*
Hospital stay	*Median* *IQR*	10 (7-14)	7 (4-12)	*0.05**

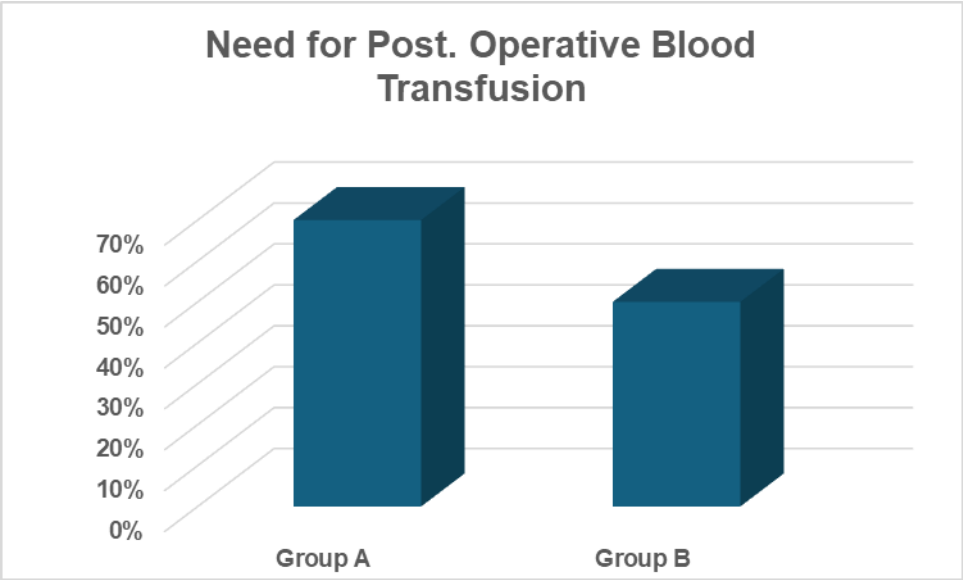

Fig (2) bar chart represent compariosn between studied groups regarding need for post operative blood tranfusion

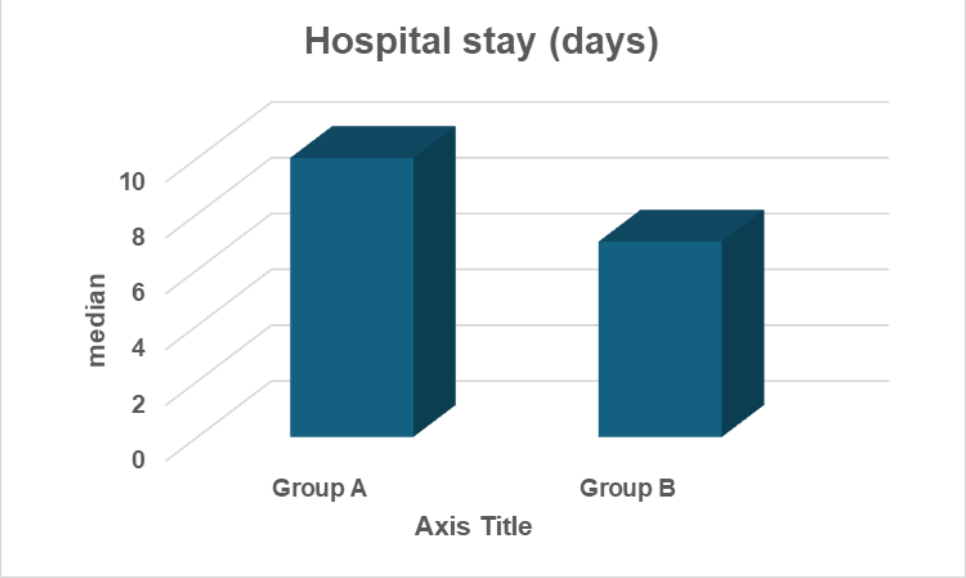

Fig (3) bar chart represent compariosn between studied groups regarding hospital stay

Table 4: Postoperative complications

		Group A N=20	Group B N=20	P value
Leakage	*No* *Yes*	17(85%) 3(15%)	19(95%) 1(5%)	***0.29***
DVT	*No* *Yes*	19(95%) 1(5%)	20(100%) 0(0%)	*0.99*
Chest infection	*No* *Yes*	18(85%) 2(10%)	19(95%) 1(5%)	*0.54*
Wound infection				
Superficial wound infection	*No* *Yes*	18(90%) 2(10%)	19(95%) 1(5%)	*0.54*
Deep wound infection	*No* *Yes*	19(95%) 1(5%)	20(100%) 0(0 %)	*0.99*
Organ infection	*No* *Yes*	20(100%) 0(0%)	20(100%) 0(0%)	*1*

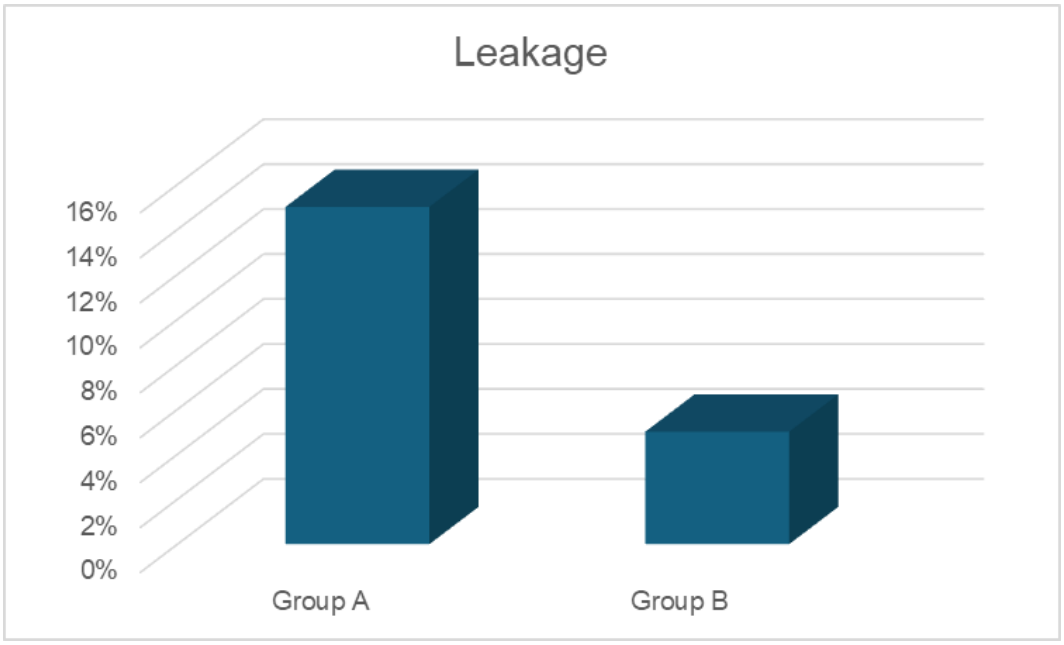

Fig. (4) bar chart represent compariosn between studied groups regarding incidence of leakage

Table (5): leakage data between studied groups

		Group A	Group B
		N=3	N=1
Time of diagnosis	*Mean ±SD* *Range*	3±1 2-4	6±0 6-6
Method of diagnosis	*Fever* *Tachypnea* *Tachycardia*	2(66.7%) 1(33.3%) 2(66.7%)	1(100%) 1(100%) 1(100%)
Drain	*Low output <200 cc enteric* *High output >500 cc enetric*	2(66.7%) 1(33.3%)	1(100%) 0(0%)
wound	*Clean* *Eenetric discharge*	2(66.7%) 1(33.3%)	1(100%) 0(0%)
Hospital stay	*Mean ±SD* *Range*	17.6±2.1 14-20	12±0 12-12

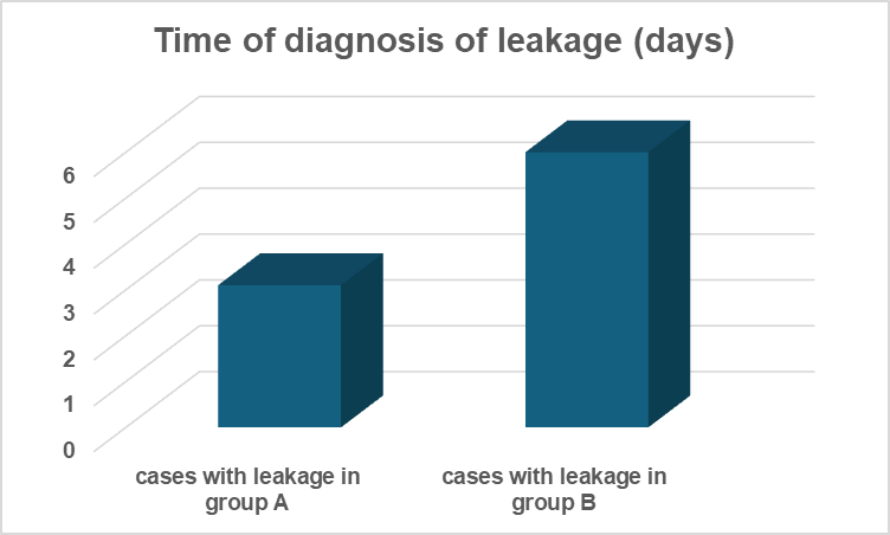

Fig. (5): comparison of time of diagnosis for leakage between studied groups

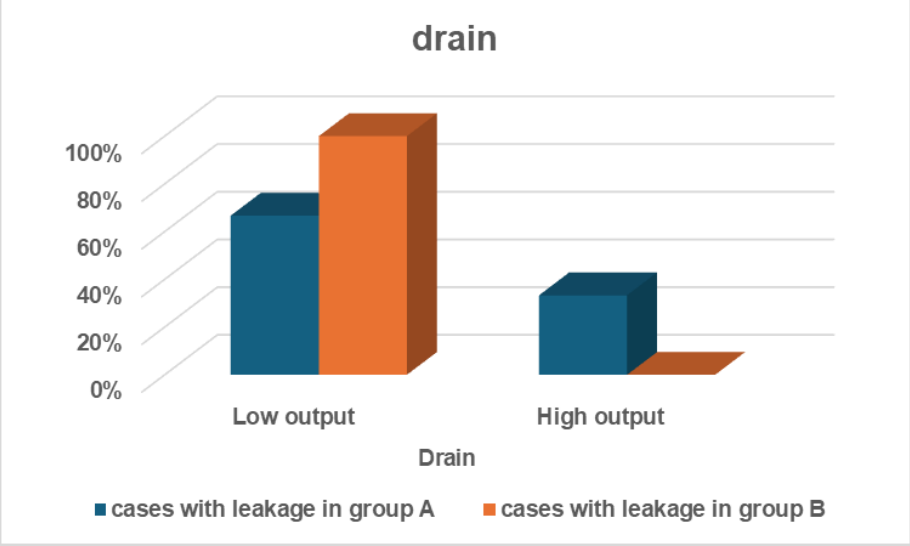

Fig. (6): comparison of drain finding for leakage between studied groups

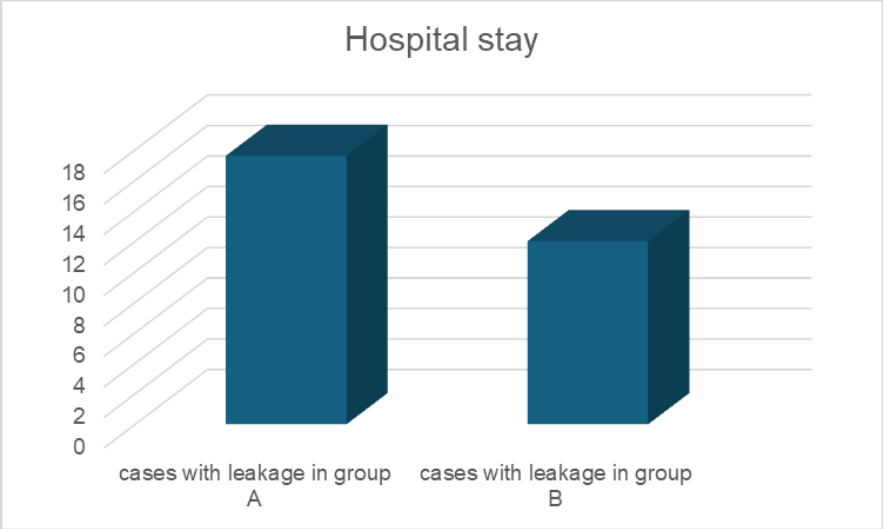

Fig. (7): comparison of hospital stay for leakage between studied groups

Table 6: Quality Of surgical specimen

		Group A N=20	Group B N=20	P value
Histopathology	*Adenocarcinoma* *Signet ring cell* *Medullary*	12(60%) 6(30%) 2(10%)	14(70%) 6(30%) 0(0%)	*0.56*
Resection margins	*Free* *Infiltrated*	18(90%) 2(10%)	19(95%) 1(5%)	*0.54*
Total number of LN removed	*Mean ±SD* *Range*	15±*3.5* 12-22	16.2±*3.1* *12-20*	*0.25*
Lymph Nodes Status	*-ve* *+ve*	17(85%) 3(15%)	19(95%) 1(5%)	*0.29*
Number of positive LN	*Mean ±SD* *Range*	5±*1* 4-6	6±*0* 6-6	*0.35*

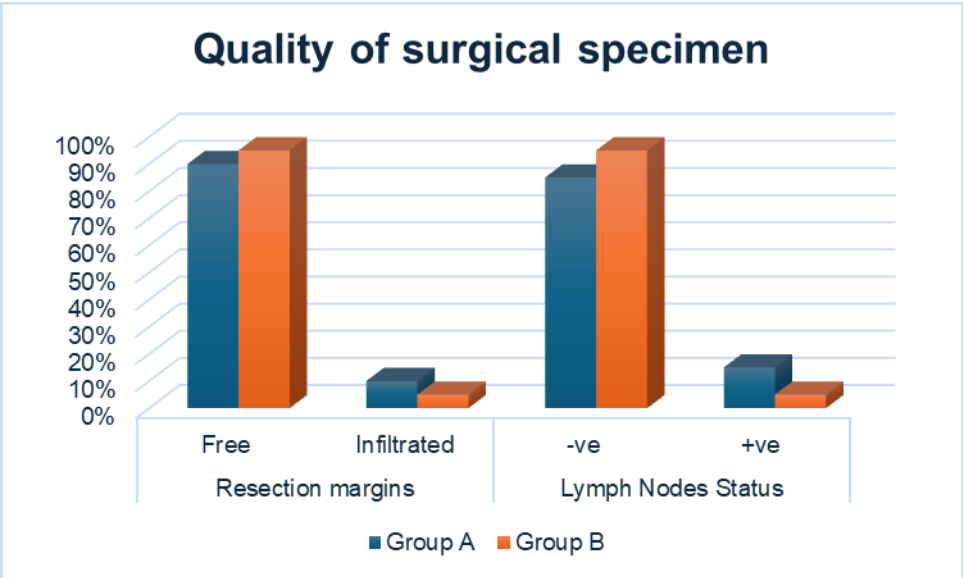

Fig. (8): bar chart represent compariosn between tudied groups regarding Quality of surgical specimen

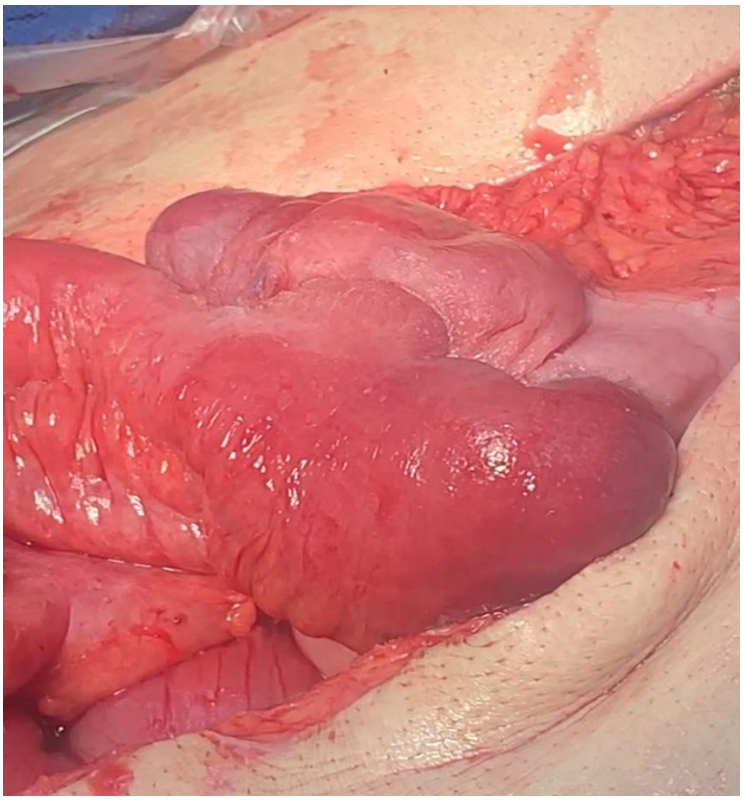

Fig. (9): shows anastomosis between transverse colon and sigmoid

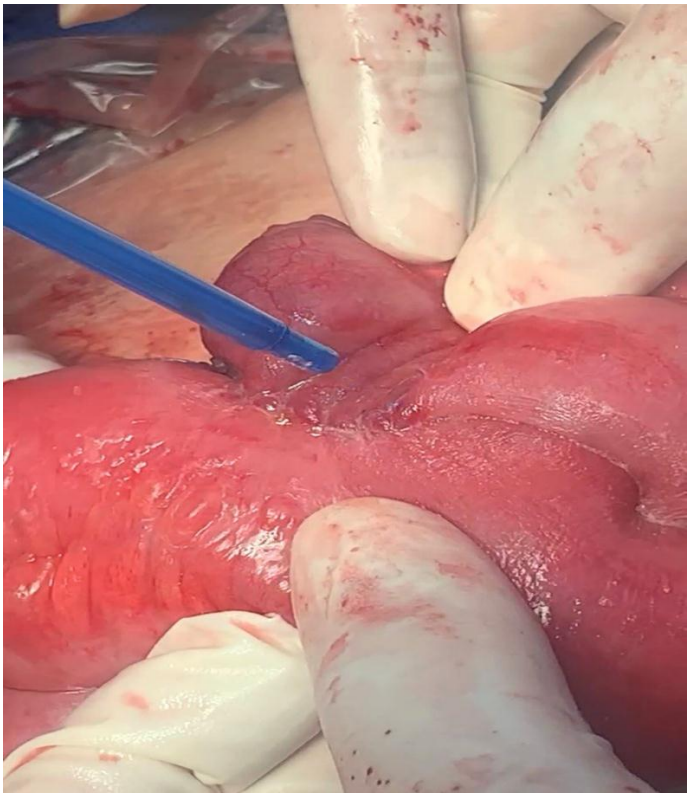

Fig. (10): shows: addition of glue in spraying manner

Fig. (11): shows applicator of glubran & glubran

Discussion

Our results showed that the demographic and clinical characteristics of the two groups show remarkable similarities. Although Group A had a higher proportion of males, this difference in sex was not statistically significant (p=0.206). Symptoms like anemia, bleeding per rectum, and bowel habits were consistent across both groups.

The postoperative complications in our study revealed that the most significant difference is the incidence of leakage, which was significantly higher in Group A (15%) vs (5%), p=0.29), 3 cases in group A compared to only 1 case in group B had leakage with mean of hospital stay 17.6±2.1 in group A and mean of hospital stay 12±0 in group B as in table (5), figure (7)..Other complications such as deep vein thrombosis, pulmonary embolism, chest infection, and wound infection showed no statistically significant differences between the groups .

In Cira, K., et al., Patients having intestinal anastomoses covered by fibrin sealants or collagen-based laminar biomaterials showed a substantial reduction in AL and reoperation rate. Patients in the intervention group seemed to stay in the hospital for a much shorter period of time [9].

In Sieda et al., over the course of 2.5 years, they performed surgery on 70 patients in the emergency department. They condu-cted resection anastomosis utilizing single-layer continuous anastomosis on 35 patients, and single-layer reinforced with fibrin glue on another 35 patients. In their trial, fibrin

sealant—which surgeons are beginning to embrace more and more—was used to strengthen a single layer. In the case of postoperative problems, we found that the single layer group experienced a higher incidence of leakage (20%) and fistula formation (14.2%) compared to the reinforced anastomosis group, which saw a lower incidence of leakage (8.5%) and fistula (5.7%)[10].

In a scoping review of Valsamidis, T.N., et al., Out of the 846 studies that were examined, seven were included. The rate of AL in each author's intervention group was disclosed. In five of the investigations, the rate of AL was shown to be lower than in the control group. In one research, there were no cases of AL, while in the final study, there was a low-looking incidence of AL but no comparison group. There was little information provided on secondary outcomes, while the findings suggested a favorable outcome. The healing of colorectal anastomosis may benefit from the use of tissue adhesives and sealants. [11]

In a systematic review of Pommergaard et al, **Out** of the twenty coating materials that have been studied in forty research, only three have been utilized in humans: hyaluronic acid/carboxymethylcellulose, fibrin sealant, and omental pedicle graft. Fibrin sealant has produced encouraging but unremarkable outcomes. Although omental pedicle grafts are safe and have no side effects, hyaluronic acid and carboxymethylcellulose should be avoided since they increase the risk of problems. The only way to assess the remaining coating materials has been on experimental animals, with mostly negative and inconsistent findings. Colonic anastomoses coated externally has not yet shown results that are compelling. To ascertain the efficacy of fibrin sealant, omental pedicle graft, and other coating materials for the prevention of colon anastomotic leakage, randomized clinical trials and high-quality experimental research are necessary. [12]

The histopathological analysis and surgical outcomes reveal some differences between the two groups, although most do not reach statistical significance. The distribution of cancer types varies between the groups, but this difference is not statistically significant (p=0.56), suggesting that the overall histopathological profile is relatively similar. Regarding resection margins, Group B showed a very slight higher percentage of free margins at 95% compared to 90% in Group A. and also this small difference is not significant(p=0.54). Similarly, the lymph node status appears more favorable in Group B, with 95% of patients having free lymph nodes compared to 85% in Group A. This 10% difference also don’t reach statistical significance (p=0.29)

Conclusion

Based on our findings, we came to the conclusion that group A differed from group B in terms of leakage following resection anastomosis.

Nevertheless, in terms of ICU admission following surgery, hemoglobin, albumin post, post-operative blood transfusion, hospital stay, deep vein thrombosis, pulmonary embolism, chest infection, and wound infection, there was no statistically significant difference between the groups under investigation. Between the groups under investigation, there was no statistically significant variation in the quality of surgical specimen (histo-pathology, resection margins, and lymph node status).

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