Double-Layered Hand-Sewn versus Stapled Intestinal Anastomosis in Patients Who Underwent Ileal Urinary Diversion in Radical Cystectomy: A Comparative and Cost Effective Study

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Keywords
Anastomosis · Bladder cancer · Radical cystectomy · Outcomes

Abstract
Introduction: Intestinal anastomosis can be performed by hand suturing (single layer or double layer) or by a mechanical suturing machine. The aim of the study was to compare complications, operative time, and costs of the intestinal anastomosis techniques. ***Methods:*** A retrospective comparative study was conducted including patients who underwent radical cystectomy and uretero-ileo-cutaneostomy or vescica ileale Padovana orthotopic neobladder. Double-layered hand-sewn intestinal anastomosis (HS-IA) were performed using Vicryl stitches. Mechanical-stapled intestinal anastomosis (MS-IA) were performed with a mechanical stapler. ***Results:*** Data of 195 patients who underwent were collected. 100 (51.3%) patients underwent HS-IA and 95 (48.7%) patients underwent MS-IA. Considering the complications classified according to Clavien-Dindo, a statistical difference with higher incidence for grade one in the HS-IA both in the ileal conduit group and in the neobladder one than the MS-IA (15.8% and 8.7%, respectively, in HS-IA vs. 1.7% and none in MS-IA). There is not a significant difference in time to flatus and time to defecation. Difference is recorded in the ileal conduit groups for the length of stay (10 days, range 9–12 with HS-IA vs. 13 days range 12–16 days with MS-IA ($p < 0.001$). The cost of the suture thread used for a single operation was 0.40 euros, whereas the overall cost of a disposable mechanical stapler and one refill was 350.00 €. ***Conclusion:*** Both HS-IA and MS-IA are safe and effective for patients. The cost for the stapling device is 350 €, in contrast, the cost for Vicryl sutures is negligible.

Introduction

The gold standard in patients with muscle-invasive bladder cancer is the radical cystectomy (RC). This surgery is still regarded as a high-risk procedure despite several improvements in surgical technique and perioperative care.

Reconstruction of the urinary tract is required after the demolition step of RC with an extended radical resection or pelvic exenteration for more advanced malignancies of the pelvis [1–3]. In both men and women, sound oncologic principles should always supersede the choice of diversion, and this includes the achievement of negative surgical margins at the site of the neo-anastomosis [4, 5].

RC consists of delicate steps, whether it is performed with the open technique or whether it is performed laparoscopic or robot-assisted. Intestinal anastomosis is a very important procedure and can be performed using a variety of techniques and suture materials. Generally, techniques are divided into two categories, stapled anastomosis and hand-sewn anastomosis, which include interrupted or running sutures and single- or double-layer sutures. Cost evaluation has a relevant role in the surgery choice of staples use in ileo-ileal anastomoses since it is. No differences in outcome between hand-sewn and stapled anastomoses were found in open surgery [6]. The aim of the study was to compare gastrointestinal (GI) complications, operative time, and costs of the double-layer intestinal anastomosis performed with the two techniques.

Materials and Methods

A retrospective comparative study is conducted including consecutive patients who underwent RC and uretero-ileo-cutaneostomy or vescica ileale Padovana orthotopic neobladder in three urological centers. The choice of urinary diversion (UD) was dependent on surgeon and patient preference after the evaluation of patient health, previous intestinal and abdomen surgery. We collected clinical records of patients who underwent RC and ileal UD from January 2016 to May 2021. All procedures were performed by surgeons experienced in the field of UD. Operations were performed with curative intent.

Selected patients were stratified into two groups according to the different techniques used to perform ileal anastomosis. In particular, cases receiving a manual ileal anastomosis were compared with those performed a mechanical anastomosis with staplers devices. For each patient, all the preoperative characteristics such as age, sex, co-morbidities, blood tests, American Society of Anesthesiologists (ASA), and Charlson Comorbidity Index (CCI) have been extracted from the databases of each participant center. We compared postoperative parameters of the two groups analyzing the different intestinal anastomosis operative time, the global operative time, length of stay (LOS), intra-, and 3-mo postoperative complications using Clavien-Dindo (CD) score. We focused our attention above all on GI subgroup complication: presence of ileus and bowel obstruction, anastomotic bowel leak, bowel perforation. In postoperative time, the time for the correct intestinal canalization, time to flatus (TTF), and the time to defecation (TTD) were considered. We also evaluate the different costs between the two techniques. The study was conducted on available retrospective data and was approved to our Ethical Committee.

The present study protocol was reviewed and approved by the Institutional Review Board of University of Palermo (approval number: n. prot 03/2022, March 15, 2022). Informed consent was obtained by all subjects when they were enrolled. Written informed consent was obtained for participation in this study.

Surgical Technique

The surgical technique was extensively previously reported (Ficarra, 2019). Briefly, approximately 20 cm proximal to the ileocecal valve, a 20-cm long ileal segment was isolated for the ileal conduit and 30/40-cm long ileal segment in case of neobladder reconstruction. While the incision of the mesentery at the level of the distal end of the selected ileal segment is straight, the incision of the mesentery at the level of the proximal end is longer and directed in an oblique plane in order to accommodate its retrosigmoid passage with no tension. The mesentery incision was usually performed using the Harmonic Focus® Long Shears (Ethicon Endo-Surgery Inc., Cincinnati, OH, USA) or the LigaSure™ Maryland Jaw (Covidien, Mansfield, MA, USA) (Fig. 1).

A side-to-side ileo-ileal anastomosis was performed using GIA™ 80 mm and TA™ 60 mm (Covidien) staplers. Interrupted 3-0 Vicryl stitches were placed externally to reenforce the mechanical sutures anteriorly (6 stitches), posteriorly (6 stitches), and superiorly (4 stitches). The mesentery window was closed with interrupted sutures.

When hand-sewn technique is used, the ileal segment is isolated using cold scissors. The continuity of the small bowel is restored by a double-layer running suture, two 4.0 Vicryl for the mucosa layer and two 3.0 Vicryl for the serosa layer. The mesentery window is closed with a continuous suture. Care must be ensured providing sufficiently wide lumen of the completed intestinal anastomosis, with no traction on the suture (Fig. 1).

The second stage involves mobilizing the ureters. The distal portion of the ureters is cut and sent for analysis to exclude cancer extension. Care is taken to mobilize the periureteric tissue with the ureter to preserve its blood supply and prevent ischemia. The left ureter is moved to the right side of the abdomen through a window created in the mesentery behind the sigmoid colon.

In case of ileal conduit, the distal end of the ileal segment is closed with double hand-sewn technique or with linear stapler. The ureters are spatulated and anastomosed with end to side anastomosis (Bricker technique), taking interrupted full-thickness bites of both the ureter and bowel using 4.0 Vicryl. A ureteric stent are placed across the anastomosis and securely fixed to the conduit. Now the stoma is created in the right side of the abdomen in the transtubercular plane with a circular incision of skin and a cruciate incision of the anterior rectus sheath. The distal end of the conduit is delivered through the skin using a Babcock, ensuring there is no twist in the conduit. The stoma is now fixed to the sheath with Vicryl.

All orthotopic neobladder are configurated as a vescica ileale Padovana technique. The ileal segment is opened longitudinally along the true anti-mesentery board. The distal segment of bowel is then fashioned into a funnel to form the bladder neck/neourethra. The proximal segment is folded into a spiral configuration, than the pouch is folded onto itself. Using a non-tunneled anastomosis, both ureters are reimplanted on their respective sides onto the superior portion of the neobladder and the ureteric stent which are securely fixed to the ileal wall. The pouch is tested intraoperatively, with an average initial capacity of 200–400 mL [7].

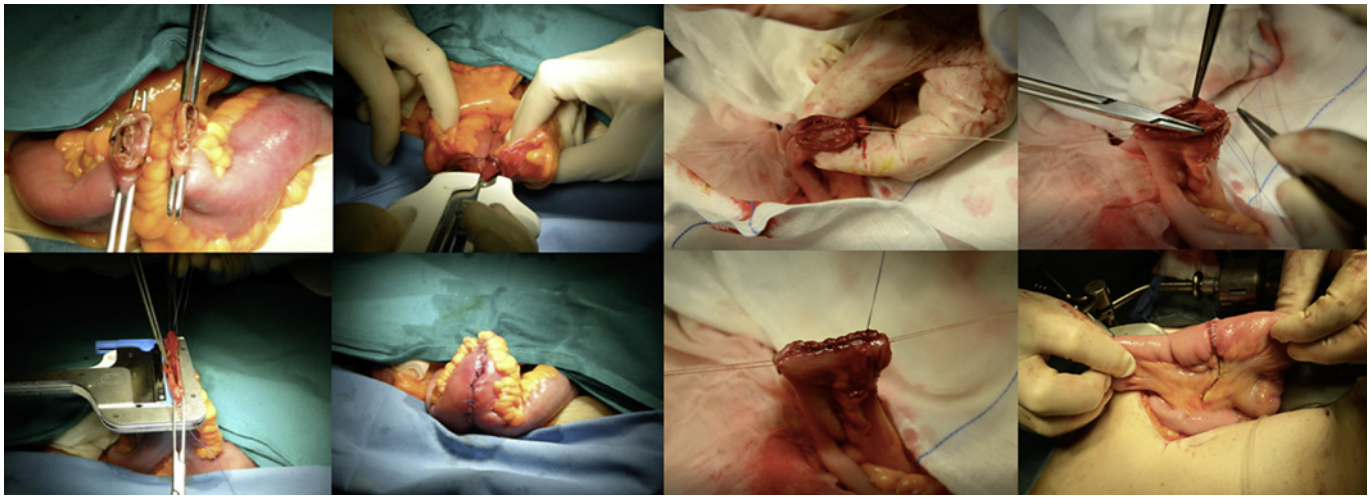

Fig. 1. Stapled intestinal anastomosis versus double-layered hand-sewn anastomosis.

Statistical Analysis

Descriptive analysis included frequencies and proportions for categorical variables. Medians and interquartile range (IQR) were reported for continuous coded variables. The Mann-Whitney U test or Kruskal-Wallis was used for comparison of the continuous data and the χ^2 or Fisher's exact test for categorical data. All tests were two-sided with a level of significance set at $p < 0.05$. Univariable and multivariable binomial logistic regression models were used to assess the odds ratio with 95% confidence intervals, testing the risk of both any-grade and major complications according to the Clavien-Dindo classification (cit.) after adjusting for preoperative and surgical covariates. Preoperative factors included age at RC, BMI, Charlson Comorbidity Index (CCI), American Society of Anesthesiologists (ASA) score, prior pelvic or abdominal surgery, preoperative parameters such us anemia, hydronephrosis, and estimated glomerular filtration rate, and neoadjuvant chemotherapy administration. Preoperative anemia was defined as hemoglobin <12.0 g/dL or <13.0 g/dL in female and male patients, respectively. Surgical determinants included estimated blood loss, type of UD, presence of intraoperative complications, number of lymph nodes removed, and operative time considering each phase of the procedure: RC, IA, and UD. After univariable analysis, factors with $p < 0.2$ were entered into the multivariable model, followed by backward elimination to determine the factors most associated with any-grade and major complications' occurrence. Statistical analyses were performed using RStudio Version February 1, 5001 (RStudio: Integrated Development for R. RStudio, Inc., Boston, MA URL http://www.rstudio.com/).

Results

We analyzed clinical records of 195 consecutive patients who underwent RC and ileal UD in the three participant academic centers. In details, 100 (51.3%) of them received a double-layered hand-sewn intestinal anastomosis (HS-IA) and the remaining 95 (48.7%), a mechanical-stapled intestinal anastomosis (MS-IA). Baseline data of the study population are reported in Table 1. The mean age of patients is 71 years (range 67–77 years). The performance status has been evaluated with CCI and ASA score. There is a statistically significant difference between the incidence of comorbidities with an higher rate in the HS-IA group both for ilea conduit and orthotopic neobladder, 33.6% and 60.9%, respectively, had CCI >3 in the HS-IA versus 20% and 20% for the MS-IA. ASA score was similar higher in the HS-IA groups (Table 1). Only 3 patients performed a neoadjuvant chemotherapy in the first group and 6 in the second.

Ileal conduit was performed in 137 patients (70.3%) and the orthotopic neobladder in 58 patients (23.7%). The operative times of ileal anastomosis performed with the hand-sewn technique were compared with the use of the mechanical stapler and we noticed that there are no substantial differences. Total operating time and estimated blood loss are also reported in Table 2.

Tables 2 and 3 report the rate of postoperative complications according to CD classification. No differences were reported in the specific subgroup recording on the gastrointestinal early complication (ileus, anastomotic bowel leak, and other intestinal complication). Considering the complications classified according to Clavien-Dindo, a statistical difference with higher incidence for grade one in the HS-IA both in the ileal conduit group and in the neobladder one than the MS-IA (15.8% and 8.7%, respectively, in HS-IA vs. 1.7% and none in MS-IA). The most common complications are fever and anemia.

Table 1. Descriptive baseline characteristics and clinicopathological features of 195 patients who underwent RC and UD according to intestinal anastomosis technique and type of UD performed

Variables	Overall	Ileal Conduit		*p* value	Orthotopic neobladder		*p* value
		HS-IA	MS-IA		HS-IA	MS-IA	
Patients, *n* (%)	195 (100.0)	77 (39.5)	60 (30.8)		23 (11.8)	35 (17.9)	
Age, years, median (IQR)	71 (65–77)	74 (69–79)	75 (65–78)	0.76	65 (59–71)	66 (59–70)	0.9
BMI, kg/m^2, median (IQR)	26 (23.6–29.0)	26 (23–39)	26 (23–29)	0.59	26 (22–27)	26 (24–28)	0.56
CCI, *n* (%)							
0	37 (19.0)	1 (1.3)	17 (28.3)	<0.001	3 (13.0)	16 (45.7)	0.01
1	25 (12.8)	2 (2.6)	17 (28.3)		2 (8.7)	4 (11.4)	
2	41 (21.0)	15 (19.5)	14 (23.3)		4 (17.4)	8 (22.9)	
≥3	92 (47.2)	59 (33.6)	12 (20.0)		14 (60.9)	7 (20.0)	
ASA score, *n* (%)							
1, 2	48 (24.6)	9 (11.7)	16 (26.7)	0.01	4 (17.4)	17 (48.6)	0.03
3, 4	147 (75.4)	68 (8.3)	44 (73.3)		19 (82.6)	18 (51.4)	
Prior pelvic or abdominal surgery, *n* (%)	62 (31.8)	15 (19.5)	32 (53.3)	<0.001	6 (26.1)	9 (25.5)	0.9
Preoperative anemia, *n* (%)	100 (51.3)	41 (53.2)	38 (63.3)	0.31	5 (21.7)	16 (45.7)	0.11
Preoperative hemoglobin, g/dL, median (IQR)	12.9 (11.3–14.4)	12.8 (11.5–14.2)	11.8 (10.6–13.5)	0.04	14.4 (13.5–15.2)	13.3 (11.9–14.7)	0.04
Preoperative hydronephrosis, *n* (%)							
Unilateral	40 (20.5)	15 (19.5)	12 (20.0)	0.65	4 (17.4)	9 (35.7)	0.27
Bilateral	13 (6.7)	7 (9.1)	5 (8.3)		1 (4.3)	0 (0.0)	
Preoperative eGFR (mL/min/1.73 m^2), median (IQR)	70.6 (52.0–87.9)	64.0 (52.0–83.8)	64.0 (43.3–82.8)	0.59	91.0 (85.0–100.0)	75.9 (59.3–90.3)	0.002
NAC[a], *n* (%)	9 (5.4)	2 (2.6)	4 (6.7)	0.47	1 (4.3)	2 (5.7)	0.9
pT-stage[a], *n* (%)	1 (0.6)	0 (0.0)	0 (0.0)	0.1	0 (0.0)	1 (2.9)	0.1
pT0	46 (27.7)	22 (28.6)	8 (13.3)		9 (39.1)	7 (20.0)	
NMIBC (pTa/is/1) pT2	36 (21.7)	11 (14.3)	14 (23.3)		3 (13.0)	8 (22.9)	
pT3	45 (27.1)	13 (16.9)	18 (30.0)		2 (8.7)	12 (34.3)	
pT4	38 (22.9)	19 (24.7)	16 (26.7)		3 (13.0)	0 (0.0)	
pN-positive[a], *n* (%)	53 (31.9)	20 (26.0)	23 (38.3)	0.15	5 (21.7)	5 (14.3)	0.22
Number of LNs removed[a], median (IQR)	17 (12–21)	17 (13–22)	17 (10–20)	0.43	14 (12–19)	19 (12–23)	0.17
LVI[a], *n* (%)	57 (34.3)	10 (13.0)	31 (51.7)	0.01	0 (0.0)	16 (45.7)	0.02
Positive soft-tissue SMs[a], *n* (%)	22 (13.3)	11 (14.3)	7 (11.7)	0.77	3 (13.0)	1 (2.9)	0.29
VHs[a], *n* (%)							
UC with squamous divergent differentiation	12 (7.2)	3 (3.9)	7 (11.7)	0.01	0 (0.0)	2 (5.7)	0.16
Micropapillary	5 (3.0)	0 (0.0)	4 (6.7)		1 (4.3)	0 (0.0)	
Microcystic	1 (0.6)	0 (0.0)	1 (1.7)		0 (0.0)	0 (0.0)	
Nested	13 (7.8)	2 (2.6)	7 (11.7)		0 (0.0)	4 (11.4)	
Plasmacytoid	3 (1.8)	0 (0.0)	2 (3.4)		0 (0.0)	1 (2.9)	
Sarcomatoid	3 (1.8)	2 (2.6)	1 (1.7)		0 (0.0)	0 (0.0)	
Neuroendocrine/small cell	2 (1.2)	1 (1.3)	0 (0.0)		1 (4.3)	0 (0.0)	

RC, radical cystectomy; UD, urinary diversion; MIBC, muscle-invasive bladder cancer; HS-IA, hand-sewn intestinal anastomosis; MS-IA, mechanical-stapled intestinal anastomosis; BMI, body mass index; IQR, interquartile range; CCI, Charlson Comorbidity Index; ASA, American Society of Anesthesiologists; eGFR, estimated glomerular filtration rate; NAC, neoadjuvant chemotherapy; pT-stage, pathological tumor stage; pN-stage, pathological nodal stage; LNs, lymph nodes; LVI, lymphovascular invasion; SMs, surgical margins, VHs, variant histologies. [a]Refers to 166 RCs due to MIBC (82 with HS-IA and 84 with MS-IA).

In the 3 centers, all patients followed the Enhanced Recovery After Surgery (ERAS) protocol (Table 4). Although there is not a significant difference in TTF and TTD, an important difference is recorded in the ileal conduit groups for the LOS, (10 days, range 9–12 with HS-IA vs. 13 days range 12–16 days with MS-IA

Table 2. Intraoperative and postoperative features of 195 patients who underwent RC and UD according to intestinal anastomosis technique and type of UD performed

Variables	Overall	Ileal conduit		*p* value	Orthotopic neobladder		*p* value
		HS-IA	MS-IA		HS-IA	MS-IA	
Patients, *n* (%)	195 (100.0)	77 (39.5)	60 (30.8)		23 (11.8)	35 (17.9)	
EBL, mL, median (IQR)	350.0 (250.0–500.0)	300.0 (250.0–500.0)	400.0 (300.0–450.0)	0.44	400.0 (275.0–500.0)	325.0 (200.0–500.0)	0.25
RC operative time, min, median (IQR)	187.8 (160.1–224.3)	185.0 (162.7–224.5)	180.0 (150.0–216.2)	0.40	206.7 (184.8–251.1)	180.0 (132.5–220.0)	0.03
IA operative time, min, median (IQR)	18.4 (16.3–20.0)	16.3 (15.0–17.4)	20.0 (20.0–20.0)	<0.001	16.4 (15.2–18.1)	20.0 (20.0–20.0)	<0.001
UD operative time, min, median (IQR)	80.0 (70.0–110.0)	70.0 (70.0–70.0)	80.0 (80.0–110.0)	<0.001	90.0 (90.0–90.0)	120.0 (117.0–195.0)	<0.001
Intraoperative complications, *n* (%)	12 (6.2)	9 (11.7)	3 (5.0)	0.28	0 (0.0)	0 (0.0)	-
Intraoperative blood transfusion, *n* (%)	15 (7.7)	5 (6.5)	8 (13.3)	0.29	0 (0.0)	2 (5.7)	0.67
Clavien complications grade, *n* (%)							
1	15 (7.7)	12 (15.6)	1 (1.7)	0.001	2 (8.7)	0 (0.0)	0.19
2	22 (11.3)	5 (6.5)	8 (13.3)		4 (17.4)	5 (14.3)	
3	18 (9.2)	2 (2.6)	9 (15.0)		2 (8.7)	5 (14.3)	
4	3 (1.5)	1 (1.3)	1 (1.7)		1 (4.3)	0 (0.0)	
5	5 (2.6)	1 (1.3)	2 (3.3)		0 (0.0)	2 (5.7)	
Major complications, *n* (%)	26 (13.3)	4 (5.2)	12 (20.0)	0.01	3 (13.0)	7 (20.0)	0.6
Detailed GI complications, *n* (%)							
Ileus (paralytic)	3 (1.5)	1 (1.3)	1 (1.7)	0.43	1 (4.3)	0 (0.0)	0.26
Constipation	2 (1.0)	1 (1.3)	0 (0.0)		1 (4.3)	0 (0.0)	
Small bowel obstruction (mechanical)	2 (1.0)	0 (0.0)	1 (1.7)		1 (4.3)	0 (0.0)	
GI bleeding	1 (0.5)	0 (0.0)	1 (1.7)		0 (0.0)	0 (0.0)	
Emesis	1 (0.5)	1 (1.3)	0 (0.0)		0 (0.0)	0 (0.0)	
Anastomotic bowel leak	1 (0.5)	1 (1.3)	0 (0.0)		0 (0.0)	0 (0.0)	
Bowel perforation	2 (1.0)	0 (0.0)	1 (1.7)		0 (0.0)	1 (2.9)	
Peritonitis	1 (0.5)	1 (1.3)	0 (0.0)		0 (0.0)	0 (0.0)	
TTF, days, median (IQR)	2 (2–3)	2 (2–3)	3 (2–3)	0.65	2 (1–3)	2 (2–3)	0.50
TTD, days, median (IQR)	5 (4–6)	5 (4–6)	5 (4–7)	0.23	5 (4–6)	5 (4–6)	0.49
LOS, days, median (IQR)	13 (10–17)	10 (9–12)	13 (12–16)	<0.001	16 (14–18)	17 (15–21)	0.12

RC, radical cystectomy; UD, urinary diversion; HS-IA, hand-sewn intestinal anastomosis; MS-IA, mechanical-stapled intestinal anastomosis; IQR, interquartile range; CCI, Charlson Comorbidity Index; EBL, estimated blood loss; GI, gastrointestinal.

[$p < 0.001$]). No differences are present in LOS in the orthotopic neobladder groups (Table 2). There are no differences in histological variants (Table 1).

An important objective of our study was to assess the economic impact of the two different techniques. Cost-effectiveness has a great impact in all surgical areas. The cost of MS-IA device is 350 € for the ileo-ileal anastomosis using two 55 mm cartridges. The cost of the HS-IA is about 0.40 € (Table 5).

Discussion

One of the most delicate steps of RC is the urinary derivation and the ileo-ileal anastomosis. The two methods used in open surgery for the creation of ileo-ileal anastomoses include hand suturing and stapling. Both techniques are not free from complications. The choice of the technique used depends on the greater confidence and experience of the surgeon.

Table 3. Univariable and multivariable binomial logistic regression analysis for prediction of any-grade postoperative complications and major postoperative complications

Variable	Any-grade complications				Major complications			
	univariable		multivariable		univariable		multivariable	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age (years), as cont	1.03 (0.99–1.06)	0.2	1.02 (0.99–1.06)	0.2	1.07 (1.02–1.14)	0.02	1.08 (1.02–1.16)	0.02
BMI (kg/m^2), as cont	1.04 (0.96–1.12)	0.4			1.14 (1.02–1.27)	0.02	1.18 (1.05–1.36)	0.01
CCI (points), as cont	0.98 (0.86–1.08)	0.7			0.92 (0.72–1.07)	0.4		
ASA score								
1, 2	1.00 (Ref.)	–			1.00 (Ref.)	–		
3, 4	1.44 (0.67–3.28)	0.4			1.57 (0.55–5.66)	0.4		
Prior pelvic or abdominal surgery								
No	1.00 (Ref.)	–			1.00 (Ref.)	–		
Yes	0.97 (0.50–1.86)	0.9			0.79 (0.30–1.88)	0.6		
Preoperative anemia								
No	1.00 (Ref.)	–	1.00 (Ref.)	–	1.00 (Ref.)	–		
Yes	1.62 (0.87–3.06)	0.13	1.54 (0.80–2.99)	0.2	1.65 (0.71–3.98)	0.3		
Preoperative eGFR (ml/min/1.73m^2), as cont	1.01 (0.99–1.02)	0.4			0.99 (0.97–1.01)	0.4		
Preoperative hydronephrosis								
No	1.00 (Ref.)	–			1.00 (Ref.)	–		
Unilateral	0.87 (0.40–1.82)	0.7			0.64 (0.20–1.71)	0.5		
Bilateral	0.72 (0.19–2.35)	0.6			0.87 (0.32–1.97)	0.6		
NAC administration								
No	1.00 (Ref.)	-	1.00 (Ref.)	-	1.00 (Ref.)	-		
Yes	0.23 (0.01–1.34)	0.2	0.21 (0.01–1.23)	0.15	0.78 (0.04–4.67)	0.8		
UD								
Ileal conduit	1.00 (Ref.)	–			1.00 (Ref.)	–		
Orthotopic neobladder	0.97 (0.49–1.89)	0.9			1.01 (0.39–2.43)	0.9		
EBL (mL), as cont	1.00 (1.00–1.00)	0.9			1.00 (1.00–1.00)	0.8		
IA technique								
Hand-sewn	1.00 (Ref.)	–			1.00 (Ref.)	–	1.00 (Ref.)	–
Mechanical-stapled	0.92 (0.49–1.72)	0.8			3.15 (1.26–9.04)	0.02	2.60 (0.88–8.45)	0.1
Intraoperative complications								
No	1.00 (Ref.)	–			1.00 (Ref.)	–		
Yes	1.23 (0.35–4.03)	0.7			1.12 (0.16–4.58)	0.9		
RC operative time (min), as cont	1.00 (1.00–1.01)	0.3			1.00 (0.99–1.01)	0.6		
IA operative time (min), as cont	0.94 (0.82–1.03)	0.3			1.03 (0.92–1.14)	0.5		

Table 3 (continued)

Variable	Any-grade complications				Major complications			
	univariable		multivariable		univariable		multivariable	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
UD operative time (min), as cont	1.00 (1.00–1.01)	0.2	1.00 (1.00–1.01)	0.2	1.01 (1.00–1.01)	0.003	1.01 (1.00–1.01)	0.03
LNs removed, as cont	0.99 (0.95–1.04)	0.8			1.03 (0.97–1.09)	0.3		

RC, radical cystectomy; UD, urinary diversion; IA, intestinal anastomisis; OR: odds ratio; CI, confidence interval; BMI, body mass index; CCI, Charlson Comorbidity Index; ASA, American Society of Anesthesiologists; NAC, neoadjuvant chemotherapy; LN, lymph node.

Table 4. ERAS items

ERAS items	
Preoperative items	Preoperative counseling Omitting oral bowel preparation
Intraoperative items	Avoidance of long-term sedatives Optimized fluid management Prevention of PONV
Postoperative items	Prevention of postoperative ileus – medical stimulation Early mobilization Early oral diet Non-opioid analgesia

The most intriguing and worrisome factors associated with ileo-ileal anastomosis are for sure the risk of anastomotic leak, intra-abdominal abscesses, bleeding, strictures, wound infections, and overall morbidity and mortality. All these factors have been investigated in the Cochrane review by Choy et al. [8]. Anastomotic leak remains a significant cause of morbidity and mortality after intestinal resections [9]. An ideal anastomosis requires an adequate blood supply, tension-free serosal apposition, and an uncompromised lumen with a watertight seal [9–11].

Both sutured and stapled anastomoses involve the introduction of foreign materials that penetrate and injure the bowel wall thus potentiating a localized inflammatory response [12]. Hand-sewn anastomoses are technically challenging, while stapled anastomoses are more expensive and are associated with a higher rate of technical mishap in the operating room [9, 13].

The aim of our study was to evaluate the difference of outcome in patients who underwent RC with HS-IA comparing with MS-IA, even if Clavien-Dindo classification has recorded the postoperative complications in both groups. Clavien-Dindo 4 and 5 grades were separately considered in Table 2. However, the low number of events (8) was considered merged as "Major Complications" in the univariable and multivariable logistic regression models. The number of our data is very small and overlapping. The two techniques are safe and feasible. All patients in the three centers underwent ERAS protocol, all the pre-, intra-e postoperative recommendations followed are described in Table 5. Difference in TTF, TTD are not statistically significant between the two groups. However, LOS in the ileal conduit groups is shorter in HS-IA when compared to MS-IA (10 days, IQR 9–12 with HS-IA vs. 13 days IQR 12–16 days with MS-IA [$p < 0.001$]) (Table 2).

In the literature, numerous studies on ileo-ileal anastomosis compared the two techniques, handmade and mechanical suture, in terms of safety, risk of complications. Most of these studies concluded that the two techniques where comparable in terms of safety and possible complications [14, 15] and our study confirms these findings.

In the urological field, the mechanical suture is used by surgeons during RC with the purpose of reducing operating time. However, for most of the MA performed, the suture is reinforced with an additional Vicryl stitch and despite this measure, the risk of dehiscence of the anastomosis is not

Table 5. Procedure cost

Procedure cost	
MS-IA (MA)	350 € (Ethicon Endo Surgery™ Linear Cutter Johnson & Johnson and two cartridges)
Double-layered HS-IA (HA)	0.40 € (two 3–0 Vicryl and two 4–0 Vicryl sutures)

completely canceled. Our study demonstrates that there is no advantage in terms of time and in terms of early postoperative GI complications.

A hand-sewn bowel anastomosis can be done in a single layer or double layer depending on surgeon preference: all HS-IA performed in our patients have been done in double layer. The double-layer intestinal anastomosis is seen as the conservative approach, with an extra layer to prevent against the dreaded anastomotic leak [16–18].

Another important aspect that supports the use of the HS-IA is the hemodynamic behavior of bowel anastomosis. The HS-IA is an end-to-end anastomosis while MS-IA can be an end-to-end or a side to side anastomosis. Functional end-to-end anastomosis is preferred to side-to-side anastomosis because of the lower probability of intestinal leakage. It can be noted that the functional end-to-end anastomosis technique is safer because of less turbulence, based on the data of fluid flow velocities, pressure, turbulent kinetic energy, turbulence vortex distribution, vortex viscosity, and wall shear stresses in the anastomosis [17]. End-to-end HS anastomosis is a more anatomic procedure because the natural and anatomical intestinal continuity is reestablished (Fig. 1).

Finally, but not less important aim of our study was the economic evaluation of cost versus effectiveness. The identification of the cost components that influence the total cost in this surgery is crucial. The operative time, instruments used, length of hospital stay, and the numbers of annual cases are key drivers of costs.

The cost for the stapling device is 350 € when using Ethicon Endo Surgery™ Linear Cutter Johnson & Johnson. Depending on the number of stapling cartridges, the total cost for a stapled anastomosis reaches 350 € for the ileo-ileal anastomosis using two 55 mm cartridges [9]. In contrast, the cost for the two 4-0 Vicryl and two 3-0 Vicryl sutures is negligible (Table 5).

Limitations of the Study

Our study is limited by the small sample size and the possibility of a selection bias created by the practice of an individual institution. The analysis of retrospectively collected data is subject to limitations inherent to all retrospective studies. A larger sample size would allow better analysis.

Conclusion

HS-IA and MS-IA intestinal sutures techniques are equally safe and effective for patients. No differences are reported in the postoperative course. Handmade ileo-ileal anastomosis is an important cost-saving approach compared to the stapled alternative.

Statement of Ethics

The present study protocol was reviewed and approved by the Institutional Review Board of University of Palermo (approval number: n. prot 03/2022, 15/03/2022). Informed consent was obtained by all subjects when they were enrolled. Written informed consent was obtained for participation in this study.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Study concept and design: Prof. Alchiede Simonato. Data analysis: Dr. Francesco Claps. Drafting of manuscript: Dr. Gabriele Tulone. Data acquisition Dr. Piero Mannone, Dr. Davide Baiamonte, Dr. Sofia Giannone. Critical revision of the manuscript: Dr. Nicola Pavan, Dr. Alberto Abrate, Dr. Rosa Giaimo, Dr. Marta Rossanese, Prof. Vincenzo Ficarra.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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