# Reconstruction After Distal Gastrectomy for Gastric Cancer: Billroth 2 or Roux-En-Y Procedure?

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**Abstract.** Background/Aim: Distal gastrectomy (DG) represents the only curative treatment for most mid-lower gastric cancers (GCs). As of 2017, however, no reconstructive modality to conduct after DG has gained unanimous consensus. Additionally, most authors have investigated Billroth 1 and Roux-en-Y (RY) rather than Billroth 2 (B2) reconstruction. We analyzed B2 and RY gastrojejunostomy to identify the preferable technique and augment the available information on B2 restoration. Patients and Methods: We retrospectively selected 132 GC patients who were consecutively submitted to DG at our institution between April 2005 and February 2016. B2 and RY anastomosis were accomplished as methods of reconstruction (respectively 36 and 96 cases). We compared these techniques in terms of clinicopathological, surgical, postoperative and oncologic outcomes. Results: Compared to RY gastrojejunostomy, B2 reconstruction was significantly associated with a greater mean number of harvested lymph nodes (26.03 vs. 21.65, p=0.045) but also with a longer hospital stay (22.8 vs. 15.7 days) (p=0.022) and higher readmission rate (28.57% vs. 3.1%, p<0.0001). On multivariate analysis, reconstruction method was the most significant independent prognostic factor for hospital readmission. Conclusion: In light of our results, we propose that B2 gastrojejunostomy deserves more study in order to better identify the best post-DG anastomosis.

Presently, despite significant advances in early diagnosis and postoperative management, gastric cancer (GC) remains the

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fifth most common malignancy and the third leading cause of cancer-related deaths worldwide (1). As of 2017, excluding some precociously selected cases (early GC, EGC), surgery represents the only possible curative treatment for most GCs including distal gastrectomy (DG) for middle-lower tumors (2). Billroth 1 (B1), Billroth 2 (B2) and Roux-en-Y (RY) are the reconstructive procedures of gastrointestinal tract continuity most frequently performed following DG throughout the world; to date, however, no technique has been considerably advocated more than others (3). In fact, although many authors have dealt with this subject in a profusion of works including randomized controlled trials, retrospective observational studies, metaanalyses and multi-institutional questionnaires, no approach resulted in clearly superior to others intra- and post-operative outcomes (1-26). Furthermore, the majority of the relative literature published in PubMed from 2010 through 2017 focused on B1 and RY, whether by open or laparoscopic surgery (in total 15 papers), rather than B2 reconstruction (5 articles comparing B1, B2 and RY among themselves, only 4 for B2 and RY and barely 2 entertaining the two Billroth procedures) (1, 2, 4-26). Hence it arises that more investigations on B2 anastomosis are needed in order to elucidate its advantages and downsides. To this intent, we herein present a retrospective analysis of DGs fashioned with B2 and RY procedures at our multi-surgical units' institution and offer a systematic literature review of the three leading reconstructions.

### **Patients and Methods**

Study population. Between April 2005 and February 2016, 132 patients affected with middle or lower GC were consecutively submitted to elective DG at five different surgical departments (General Surgery Unit 1, 2, A, C and Emergency Surgery) of our Institution, St. Andrea's Hospital, Faculty of Medicine and Psychology, University of Sapienza, Rome, Italy. B2 and RY were the only adopted reconstruction methods. Medical records were obtained from the charts of each surgical division. Preoperative

features, operative information and postoperative outcomes were investigated retrospectively (Table I). All histopathologic features were defined and analyzed in keeping with the American Joint Committee on Cancer (AJCC) staging system 7th edition, published in 2010 (27). Postoperative morbidity was assessed according to the Clavien-Dindo classification (28). Median follow-up time was 40.75 months (range=2-130 months): patients were surveilled by abdominal ultrasound, computed tomography, upper endoscopy and serum tumor markers.

Neoadjuvant/adjuvant therapy. A total of 4 patients (3%) were given neoadjuvant chemotherapy. A total of 71 patients (53.7%) received adjuvant therapy (chemo +/- radiotherapy). The regimen most frequently administered was ECF (epirubicin, cisplatin and 5-fluorouracil).

Surgical techniques. Altogether, 16 different surgeons attending our institution performed all the cases of DG according to their own attitude. All DGs were made through open surgery and accomplished along with omentectomy, complete mesogastrium excision (29) and D1.5 lymph node dissection (that is perigastric lymphadenectomy extended to splenopancreatic nodes without performing splenopancreatectomy). Gastric lavage and peritoneal washing were performed before the manipulation of the tumor in all cases. All resected primary lesions and dissected lymph nodes were sent for definitive histological examination. Intraoperative esophagogastroscopy was performed in selected cases (when the tumor could not be macroscopically visualized and palpated using the fingers of both hands). Depending on early or advanced GC, the stomach was dissected by a linear stapling device respectively 3 and 5 cm proximally to the tumor site; the amount of stomach or the margin taken in DG made no difference in the type of reconstruction. In B2 reconstruction, a mechanical gastrojejunostomy was arranged with a linear stapler connecting part of the gastric remnant to the second jejunal loop (Finsterer's technique). Entering into surgical details, the resulting anastomosis involved the posterior wall of the gastric racket and was side-to-side, anisoperistaltic and infracolic (Figure 1a). A silicone drain was placed in the proximity of duodenal stump and gastrojejunostomy in all cases. In RY restoration, the jejunum was divided 20 cm distal to the ligament of Treitz. The jejunal loop (Roux limb) was brought up through the mesocolic route and gastrojejunostomy was confectioned by side-to-end isoperistaltic anastomosis (between cul de sac on the greater curvature side of the stomach and terminal margin of Roux limb) using a circular stapling device. In closing, the jejunal biliopancreatic limb was anastomosed to Roux limb 60 cm distal from the jejunal division: this anastomosis was end-to-side and hand-sewn in most cases, though some surgeons performed a side-to-side jejunojejunostomy with linear stapling device (Figure 1b). Two silicone drains were positioned in right and left subphrenic space in all cases.

Statistical analysis. Statistical analysis was performed using MedCalc for Windows, version 16.2.1 (MedCalc Statistical Software, Ostend, Belgium). All values are presented as means, standard deviation or numbers. Continuous variables were calculated using the Student's *t*-test or the Mann-Whithney *U*-test, whereas categorical variables were compared with the Pearson's chi-square test or the Fischer exact probability test. The one-way analysis of variance (one-way ANOVA) was used to determine any significant differences between the means of the two unrelated

surgical techniques: all items showing significant variations were further analyzed using multiple regression analysis in order to eliminate confounding factors and assess their independency as prognostic factors. *p*-Values inferior to 0.05 were considered statistically significant.

## Results

Preoperative features. After exclusion of GC patients submitted to total gastrectomy (67 cases) or palliative interventions, 132 patients submitted to elective DG were identified meeting the inclusion criteria. The clinicopathologic features of the study population is given in Table I. There were no significant differences in age, gender, comorbidity and neoadjuvant therapy between the B2 and RY group. Most patients (60%) were in ASA class 3 (17% B2 group vs. 87% RY group, p=0.029). All interventions were conducted in elective setting.

Intraoperative, histological and cytopathological results. B2 and RY gastrojejunostomy were performed in 36 (27.3%) and 96 cases (72.7%) respectively. The choice of the type of reconstruction depended on several stochastic variables such as paternal surgeon's personal attitude, site of GC (middle or lower gastric position), size of remnant stomach and vascular variants; the stage of disease was not a criterion for deciding in favor of one modality of reconstruction. Altogether, four surgeons (25%) performed at least one technique (at least one B2 and at least one RY), whereas eleven surgeons conducted only RY (68.75%) and one surgeon executed only B2 (6.25%). B2 reconstruction was significantly associated with a greater mean number of harvested lymph nodes (26.03 vs. 21.65, p=0.045) whereas the RY group had more cytopathological analyses (performed on gastric lavage and peritoneal washing) positive for cancer cells (9/41 vs. 1/21 case, 14.5% vs. 1.6%, p<0.0001). There were no differences in mean operative time (191 min vs. 203 min, p=0.19) and mean estimated intraoperative blood loss (186 ml vs. 157 ml, p=0.24) between B2 and RY procedure respectively. There were also similar results between the groups in the AJCC staging class, T depth, N status, mean number of positive nodes, mean LNR, Lauren's classification, lymphovascular invasion, perineural invasion, presence of signet ring cells and rates of curative resection. Most patients from both groups suffered from poorly differentiated GC (58.3% for B2, 76.4% for RY group, p=0.004).

Postoperative and oncological outcomes. Postoperative and oncological outcomes following B2 and RY procedures are shown in Table I. In comparison with RY, B2 reconstruction was significantly associated with a longer hospital stay (mean 22,8 days vs. 15,7 days) (p=0.022) and higher readmission rate (10 vs. 3 cases, 27.7% vs. 3.1%, p<0.0001). There were no significant differences in terms of overall

Table I. Clinicopathologic features of patients with B2 versus RY reconstruction after open DG for GC.

	Billroth II (n=36)	Roux-en-Y (n=96)	p-Value
Preoperative features			
Mean age (yo)	67 (10a)	68 (13a)	0.732
Male gender	19 (52.7%)	57 (59.3%)	0.496
ASA class ≥3	6 (16.6%)	27 (28%)	0.029
Comorbidity	12 (35.2%)	41 (44.56%)	0.353
Neoadjuvant therapy	0	4 (4.2%)	0.270
Intraoperative, histologic and cytologic features			
Tumor depth			0.329
pT1	10 (30.3%)	26 (28.57%)	
pT2	7 (21.21%)	13 (14.28%)	
pT3	11 (33.3%)	27 (29.67%)	
pT4	5 (15.15%)	25 (27.47%)	
LN metastasis 0.952			
pN0	16 (44.4%)	43 (44.8%)	
pN1	7 (19.4%)	17 (17.7%)	
pN2	6 (16.6%)	17 (17.7%)	
pN3	7 (19.4%)	19 (19.8%)	
Mean number of harvested LNs	26.3 (14 <sup>a</sup> )	21.6 (10 <sup>a</sup> )	0.045
Mean number of metastatic LNs	4.9 (8 <sup>a</sup> )	4 (6 <sup>a</sup> )	0.534
Mean LNR	0.216	0.173	0.379
AJCC stage 0.589			
I	16 (44.4%)	29 (30.2%)	
II	8 (22.2%)	23 (23.9%)	
III	9 (25%)	33 (34.4%)	
IV	3 (8.3%)	11 (11.4%)	
Differentiation			0.016
Well	10 (27.7%)	6 (6.74%)	
Moderate	4 (11.1%)	11 (12.36%)	
Poor	21 (58.3%)	68 (76.4%)	
Undifferentiated	1 (2.7%)	4 (11.1%)	
LVI	16 (44.4%)	43 (45.74%)	0.894
PnI	8 (22.2%)	15 (16.3%)	0.434
intestinal vs diffuse type	14 vs. 10 (58.3%)	52 vs. 25 (67.53%)	0.410
signet ring cells	9 (25.7%)	14 (14.9%)	0.155
R1 vs. R0 resection	4 (11.4%)	9 (9.6%)	0.756
GL/PL cytology	1 (4.76%)	9 (21.95%)	< 0.000
Mean operative time (min)	191 (41 <sup>a</sup> )	203 (40a)	0.197
Mean estimated blood loss (ml)	186 (148 <sup>a</sup> )	157 (116 <sup>a</sup> )	0.284
Surgeons acting only one technique	1 (6.25%)	11 (68.75%)	0.0006
Postoperative and oncological features			
Overall morbidity	17 (50%)	31 (32%)	0.061
Clavien score ≥3	10 (28.57%)	17 (17.52%)	0.166
Intestinal leak	8 (22.85%)	13 (13.68%)	0.210
Reflux gastritis*	3 (8.3%)	4 (4%)	0.284
Mean LOS (days)	22.8 (23a)	15.7 (12a)	0.022
Mean postoperative LOS (days)	16.6 (23a)	13.6 (11a)	0.108
Readmission	10 (28.57%)	3 (3.1%)	<0.000
90-day mortality	0	0	NC
Mean time to metastasis/recurrence/GSC (mo)	14.8 (14a)	29.2 (30a)	0.141
GSC	4 (11.76%)	7 (7.3%)	0.434
Adjuvant therapy	17 (54.83%)	54 (56.84%)	0.845

Yo: Years, aStandard deviation; mo: months; min: minutes; LN: lymph node; LNR: lymph node ratio; LVI: lymphovascular invasion; PnI: perineural invasion; vs..: versus; R0: curative resection; R1: infiltrated margins; GL: gastric lavage with positive cytology; PL: peritoneal washing with positive cytology; ml: milliliters; LOS: length of stay; GSC: gastric stump carcinoma; NC: not classifiable, \*shown on postoperative endoscopy plus biopsy. Significant p-values (<0.05) are written in bold type.

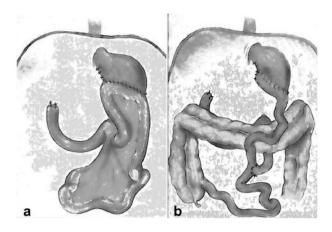


Figure 1. Types of reconstruction after distal gastrectomy: (a) Billroth 2 gastrojejunostomy (Finsterer's variant); (b) Roux-en-Y reconstructive method

morbidity, major complication (Clavien grade  $\geq$ 3), anastomotic or intestinal leak, mean postoperative days, reflux gastritis, mean time to metastasis or recurrence (including gastric stump carcinoma), adjuvant chemoradiotheraphy. No death occurred at 30 and 90 days in any group (0%, p-value: not classifiable).

Prognostic analysis. The one-way ANOVA revealed that readmission rate showed significant differences between the two surgical techniques (p<0.001, Table II, upper half). Such a result was upheld by multivariate analysis: in fact, reconstruction method was a significantly independent predictive factor for readmission (p<0.0001, Table II, lower half). Furthermore, to eliminate possible confounding factors, we verified if readmission rate was higher (or lower) with some surgeons or for advanced (versus initial) stages of disease. Multiple regression analysis showed no association of readmissions with these 2 variables (p=0.0006 and p=0.0037 respectively, Table II, lower half). In this manner, the higher readmission rate for B2 in comparison with RY can be ultimately substantiated with certainty.

## Discussion

Christian Albert Theodore Billroth reported the first successful partial gastrectomy for GC in 1881 (30). Since then, B1, B2 and RY became the three methods of gastrointestinal continuity restoration most studied and commonly practiced after DG for GC; currently, B1 and RY are the preponderant practice in East Asia, whereas RY and B2 techniques are more frequently undertaken in Western countries (16). As of 2017, however, the surgical community has not reached a full consensus concerning the preferable

Table II. Univariate (upper) and multivariate (lower) analysis of main outcomes in B2 vs. RY group.

		Techniques			
	B2*	SD	RY*	SD	<i>p</i> -Value
Outcome					
Readmission	0.28	0.45	0.03	0.17	< 0.001
Morbidity	0.50	0.50	0.31	0.46	NS (0.061)
GL/PL	0.04	0.21	0.21	0.41	NS (0.084)
Others					NS (>0.1)

	Ite	em: Readmissi	on
Variables	MRC	SD	<i>p</i> -Value
Type of reconstruction	0.53	0.38	< 0.0001
Histological grade	0.25	0.44	0.0037
Surgeons°	0.29	0.42	0.0006

\*Mean values according to Scheffé test for comparisons, vs.: versus; SD: standard deviation; MRC: multiple correlation coefficient; GL: gastric lavage with positive cytology; PL: peritoneal lavage with positive cytology; NS: not significant (p>0.05). \*To be intended as surgical parentage of each reconstructive act. Multiple regression analysis was performed only if the p-value of the outcome in the univariate analysis was <0.05. Significant p-values and corresponding outcomes/items are written in boldface.

technique to adopt (7). Such a longstanding indecision derives from the fact that each reconstruction is not exempt from disadvantages and limits and therefore no definite data can be concluded (31). Ours is the third study comparing B2 and RY reconstructions and the second from a Western country dealing with an open approach for this types of gastrojejunostomy (16, 17). Although many outcomes resulted to be similar between the two groups (no differences in mortality, Clavien score≥3, enteral leakage, postoperative reflux gastritis, mean time to recurrence/metastasis, development of GSC), we think that some of our results are clinically interesting and deserve discussion. Compared to RY, B2 reconstruction was significantly associated with a greater mean number of harvested lymph nodes (26.3 vs. 21.6 nodes, p=0.045). Indeed, such a feature can better assess both staging and prognosis for GC patients as suggested by the current AJCC (27). Actually, we do not know the explanation of this specific finding for a certainty. Such a parameter has been rarely investigated by the previous works dealing with these types of reconstructions and, furthermore, results were discordant and rarely significant (16, 17, 19, 20). Individual capabilities of surgeons can undoubtedly impact nodal harvest but more studies are needed in order to determine whether this phenomenon is fortuitous or peculiar to B2. On the other

Table III. Review of the recent PubMed literature (2010-2017) on B1, B2 and RY reconstructions.

References	Reconstructions	Nature of the study	Main statistical significant outcomes
(1)	oB1, oRY	RCT questionnaire	B1: lower weight loss (0.046)
			RY: lower RG (<0.001) and BR (<0.001)
(2)	oB1, oRY	Metanalysis of RCTs	B1: shorter OT (0.003)
		and OCS	RY: lower BR (0.001), RG (10-5), RE (0.02)
(5)	o/l B1, o/l RY	Multi-institutional questionnaire	NS for dumping syndrome
(6)	o/l B1, o/l RY,	Multi-institutional questionnaire	B1: lower weight loss (0.022),
			RY lower RE symptoms (<0.0001)
(7)	oB1, oB2, oRY	Multi-institutional questionnaire institutions	RY stasis reported by 71% of the
(8)	oB1, oRY	Retrospective questionnaire	B1: higher RE (0.0098)
			RY: lower RG (0.0277)
(9)	oB1, oRY	Multi-institutional RCT	RY: lower RE (0.0037) and RG (0.0013)
(10)	1B1, 1RY	Retrospective	B1: lower weight loss (0.0002)
(11)	oB1, oRY	Retrospective	RY: lower RG (<0.05)
(14)	oB1, oRY	Retrospective	RY: greater visceral fat loss (0.0104)
(16)	oB2, oRY	Retrospective	RY: longer OT (0.001), higher BL (0.033)
(17)	1B2, 1RY	Prospective	RY: longer LOS (0.037)
(18)	oB1, oB2, oRY	Retrospective questionnaire	NS
(19)	1B1, 1B2, 1RY	Retrospective	B1: shorter OT (<0.001) and LOS (0.004)
		•	RY: lower RE and RG (<0.001)
(20)	1B1, 1B2, 1RY	Retrospective	NS for RE and RG
(21)	oB1, oB2, oRY	Meta-analysis of RCTs	B1: higher local recurrence (<0.0001)
		•	B2: higher AL (0.02)
			RY: lower RE and RG (<0.0001)
(22)	oB1, oB2, oRY	Retrospective	NS for GSC
(24)	oB1, oB2	Meta-analysis	B2: amelioration of type 2 diabetes
(25)	lB2, lRY	Pro-retro-spective	B2: shorter length of operation (0.001)
(26)	1B2, 1RY	Retrospective	B2: shorter length of operation (<0.010)
(31)	lB1, lRY	Retrospective	B1: shorter OT (0.017), less BL (<0.0001) RY: higher RY stasis (0.017) longer LOS (0.0039)

O: Open surgery; l: laparoscopy; RCT: randomized clinical trial; OCS: observational clinical studies; NS: not statistically significant; RE: reflux esophagitis; RG: remnant gastritis; BR: bile reflux; LOS: length of hospital stay; OT: mean operative time; BL: mean intraoperative blood loss; AL: anastomotic leakage; GSC: gastric stump carcinoma.

hand, counter to B2, RY procedure entailed a significantly shorter mean hospital stay (15.7 vs. 22.8 days, p=0.022) and a lower readmission rate (3.1% vs. 28.57%, p < 0.0001). Of note, data on readmissions were further validated by univariate and multivariate analyses: in fact, the reconstructive method resulted to be a significantly independent predictive factor for this specific outcome (p<0.001 and p<0.0001 on uni- and multi-variate analysis)respectively, entire Table II). To eliminate confounding factors, the multiple regression analysis was extended to the variables of histological grade and the 16 paternal surgeons acting the techniques (Table II, lower half): similarly to the type of surgical procedure, also these items were found to be significant independent prognostic and predictive factors for readmission (respectively p=0.0037 and p=0.0006). Differently from other works, in our study the mean length of stay described for both procedures was far longer (22 and 15 days respectively for B2 and RY in lieu of 7 to 9 days

generally reported) (16, 17, 19, 20). This outcome is very likely to be related to the elevated mean age, severe comorbidities and high number of advanced stages of our patient population. The remaining clinicopathological features which showed statistical significance (such as ASA score and, in particular, cytological analysis of gastric lavage/peritoneal washing) (p=0.029 and < 0.0006,respectively) in this study, brought no clinical value but description differently from our previous works (32-35). Among the outcomes failing to reach statistical strength, overall morbidity had the lowest p-value (p=0.061) pleading in favor of a better trend for RY over B2 (32% vs. 50%). Our data are in accordance with the world literature on B2 and RY reconstructions after DG for GC: just like that, we could not establish the preferable reconstructive procedure to perform (1-30, 36, 37). In our case, this is probable due to the retrospective nature of our study and limited number of subjects. On the other hand, all the other papers hitherto published on B1, B2 and RY failed this object, although being prospective randomized works, meta-analyses, multiinstitutional observational studies or questionnaires (1, 2, 4-31). We also made a systematic review of the literature on the three reconstructions published in PubMed from 2010 through 2017 and summarized it in Table III. B1 reconstruction is thought to provide three main advantages: technical simplicity with only one anastomosis, physiological route for food passing through the duodenum (that means natural regulation of gastrointestinal hormones with positive effect on digestion and absorption of food) and ease of postoperative endoscopy with access to the papilla of Vater (1, 2, 4). On the other hand, as a consequence of the absence of the pyloric sphincter and a significantly larger angle of His, rapid gastric emptying, duodenogastric gastroesophageal reflux can frequently occur; if chronic, the latter two conditions can lead to severe remnant gastritis up to GSC, lower esophagitis, Barrett's esophagus and cancer (2, 3, 16). Moreover, some authors describe a higher fistula rate for gastroduodenostomy than gastrojejunostomy (B2 and RY) due to excessive devascularization of duodenal stump and tension on the anastomosis (2, 3). Athwart B1, it is said that RY is the reconstruction having opposite advantages and disadvantages (8). Recently, due to some benefits such as prevention of bile reflux, alkaline gastritis and GSC, the frequency of RY reconstruction has been gradually increasing worldwide (8). On the other hand, RY necessitates a more articulate surgery with two anastomoses, meal runs an unphysiological course and postoperative endoscopic survey of the pancreatico-biliary system is improbable (8). Furthermore, three more problems have been associated with this reconstruction: stoma ulcer, Roux stasis syndrome and Petersen's internal hernia (8). The first complication occurs when the alkaline bile reflux into the stomach is reduced to zero and too much acid content impairs the vulnerable anastomosed mucosa of jejunum (36). The second occurs with Roux limb longer than 40 cm or when large section of the upper stomach left by the surgeon gets stuffed with food (1, 3, 8). B2 reconstruction share some pros and cons belonging to B1 (not so demanding technique, feasibility of biliopancreatic investigation by postoperative endoscopy as well as greater incidence of duodenoenteric reflux into the gastric remnant with possible alkaline gastritis and stump cancer 15 to 20 years after surgery) as well as RY method (not physiological food passage, marginal ulcer, small gastric remnant or obese patients as preferable indications) (17, 22, 23, 37). Additionally, some advantages (amelioration of type 2 diabetes mellitus) and complications (such as afferent and efferent loop syndrome) accrue from B2 reconstruction only (3, 24). Compared to RY restoration, B2 entails shorter length of operation as demonstrated by our and other two recent dedicated works (25, 26). In this study, we found no significant differences in outcomes between the B2 and RY

group: in our opinion, such a result could have been conditioned by some limitations lying in the structure of the search itself. First, the numerical discrepancy between the two examined populations (36 B2 *versus* 96 RY patients): a closer proximity could provide not only statistical power, but also a more reliable clinical significance. Second, the retrospective nature of our study could not exclude the fact that surgeons chose the right reconstruction for their individual patients. To obviate this encumbrance, our caveat is that double blind studies should be conducted for this type of comparison in the future. Third, a multi-institutional survey digging into larger amounts of patients could corroborate (or confute) our findings and come to more certain conclusions.

### Conclusion

In light of our results, we propose B2 and RY two extremely cogent methods to adopt for gastrointestinal reconstruction after DG for GC. In particular, we think B2 deserves a more careful investigation of the one made today. Surgical studies dealing with fashions of gastrointestinal reconstruction after DG should not omit including this procedure in order to better assess advantages and encumbrances of each restorative technique and establish the preferable anastomotic practice.

### **Conflicts of Interest**

The Authors declare no conflicts of interest.

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