ORIGINAL CONTRIBUTIONS





Closure of Mesenteric Defects in Laparoscopic Gastric Bypass: a Meta-Analysis

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Abstract

Introduction The purpose of the current study was to review the available literature on morbidly obese patients treated with laparoscopic Roux-en-Y gastric bypass (LRYGB) in order to assess the clinical outcomes of the routine closure of the mesenteric defects.

Methods A literature search was performed in PubMed, Cochrane library, and Scopus, in accordance with the PRISMA guidelines.

Results Nine studies met the inclusion criteria. A total of 16,520 patients were incorporated with a mean follow-up ranging from 34 to 120 months. The closure of the mesenteric defects was associated with a lower incidence of internal hernias (odds ratio, 0.25 [95% confidence interval 0.20, 0.31]; p < 0.01), small bowel obstruction (SBO) (0.30 [0.17, 0.52]; p < 0.0001) and reoperations (0.28 [0.15, 0.52]; p < 0.001). Both approaches presented similar complication rates and % excess weight loss (%EWL).

Conclusion The present meta-analysis is the best currently available evidence on the topic and supports the routine closure of the mesenteric defects.

Keywords Roux-en-Y gastric bypass · RYGB · Mesenteric defects · Closure · Internal hernia

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Introduction

Morbid obesity is a global epidemic, and bariatric surgery remains the main therapeutic option providing significant and sustainable weight loss [1], along with diabetes remission and enhancement of the patients' metabolic profile [2]. Currently, laparoscopic Roux-en-Y gastric bypass (LRYGB) is the main operation of choice in many bariatric centers [3] regarding patients with morbid obesity and metabolic disorders or as salvage operation after a failed bariatric procedure [4].

Over the past years, the increased incidence of post-LRYGB small bowel obstruction (SBO) due to internal hernia (IH) after LRYGB has become a major concern. According to recent data, the incidence of post-LRYGB SBO has been estimated at 10–16%, with the IH being the main cause [5, 6]. Nonetheless, the evidence provided by consecutive series of patients undergoing LRYGB suggests that the routine closure of mesenteric defects, both at the Petersen and jejunal sites, might reduce the rate of postoperative IH [7].

Meanwhile, there is a concern that the closure itself might increase the risk for perioperative complications, including the impaired alimentary limb emptying (kinking of the jejunojejunostomy). Despite the absence of conclusive data regarding the effect of routine mesenteric defect closure on the reduction of the incidence of SBO or the extent of the morbidity caused by the closure of the mesenteric defects, the routine closure has been widely adopted [8, 9], even when an antecolic, antegastric LRGYB is performed.

As the number of studies assessing the feasibility of routine mesenteric defects closure during LRYGB increases and new randomized controlled trials (RCTs) have been published, it is necessary to reassess whether the perioperative outcomes of closure and non-closure are at least equivalent. The purpose of this study was to summarize the currently available evidence evaluating the routine closure of mesenteric defects during LRYGB, thus providing the best currently available level of evidence.

Materials and Methods

Search Strategy and Articles Selection

The present study was conducted under the protocol agreed by all authors and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [10]. A thorough literature search was performed in PubMed (Medline), Cochrane Central Register of Controlled Studies (CENTRAL), and Scopus (Elsevier) databases (last search, August 30, 2019) using the following terms in every possible combination: "roux-en-y gastric bypass," "rygb," "internal hernia," "hernia," "small bowel obstruction," "bowel obstruction," "mesenteric defects," "mesenteric defects closure," "petersen defects," "jejunostomy," and "obesity." Inclusion criteria were (1) original comparative reports with ≥ 10 patients, (2) written in the English language, (3) published from 1990 to 2019, (4) conducted on human subjects, and (5) reporting comparative outcomes of closure and non-closure of mesenteric defects during LRYGB on patients with morbid obesity. Two independent reviewers (DEM and VST) extracted the data from the included studies. Any discrepancies between the investigators regarding the inclusion or exclusion of studies were discussed with the senior author (DZ) to include articles that best matched the criteria until consensus was reached. Furthermore, the reference lists of all included articles were assessed for any additional eligible studies. Besides, the kappa coefficient test was applied to assess the level of agreement between the reviewers.

Data Extraction

For each eligible study, data was extracted relative to demographics (gastric bypass approach, study sample, female ratio, mean age, preoperative body mass index (BMI), follow-up), along with the intraoperative parameters and postoperative outcomes (mean operative time (MOT), length of hospital stay (LOS), the incidence of postoperative internal hernia, along with the time interval to internal hernia presentation, the incidence of leaks, bleeding, and ulcer). Two authors (DEM and VST) performed the data extraction independently and compared the validity of their data. Any discrepancies were discussed with the senior author (DZ) until consensus was reached.

Statistical Analysis

Regarding the categorical outcomes, the odds ratio (ORs) and 95% confidence interval (CI) were calculated, based on the extracted data, employing the random-effects model (Mantel-Haenszel statistical method). OR < 1 denoted outcome was more frequent in the non-closure group. Continuous outcomes were evaluated utilizing the weighted mean difference (WMD) with its 95% CI, using random-effects (inverse variance statistical method) models, to calculate pooled effect estimates. In cases where WMD < 0, the values in the non-closure group were higher. We selected the random-effects model since we did not expect that all the included studies would share a common effect size. The between-study heterogeneity was assessed through the Cochran Q statistic and by estimating I^2 [11].

In cases that multiple studies incorporated the same population, only the largest study or the one with the longest follow-up was included in the present metaanalysis.

Quality and Publication Bias Assessment

The Newcastle-Ottawa Quality Assessment Scale (NOS) [12] was used as an assessment tool to evaluate the non-RCTs. The scale's range varies from zero to nine stars, and studies with a score equal to or higher than five were considered to have an adequate methodological quality to be included. The RCTs were assessed for their methodological quality with the tools that are used to evaluate the risk of bias according to the Cochrane Handbook for Systematic Reviews of Interventions [11]. Two reviewers (DEM, VST) rated the studies independently and the final decision was reached by consensus.

Our initial aim was to assess the existence of publication bias using the Egger's formal statistical test [13]. However, the statistical evaluation could not be performed because the number of studies included in the analysis was not adequate (less than 10), thus compromising substantially the power of the test.

Results

Article Selection and Patient Baseline Characteristics

The flow diagram of the search of the literature is shown in Fig. 1. Among the 183 articles in PubMed, CENTRAL, and Scopus that were retrieved, nine comparative studies were included in the qualitative and quantitative analysis [14-22]. The level of agreement between the two reviewers regarding the inclusion of the studies was "good" (kappa = 0.768; 95%) CI 0.572, 0.964). The study design was retrospective in six studies [15-20], prospective in one study [14], and RCT in two studies [21, 22]. The included studies were conducted in Norway [14], France [15], Belgium [16], India [17], USA [18, 21], Colombia [19], Mexico [20], and Sweden [22], and they were published between 2010 and 2019. The total study population was 16,520 patients, with a mean follow-up ranging from 34 to 120 months. All patients underwent laparoscopic antecolic, antegastric LRYGB. No comparative studies with retrocolic LRYGB were identified. The closure of the mesenteric defects was performed using a stapler in one study [14], non-absorbable continuous sutures in other studies [15-20,22] and non-absorbable interrupted sutures in one study [21]. The baseline characteristics, along with the NewcastleOttawa rating scale (NOS) assessment of the included studies are demonstrated in Table 1. Both groups were similar regarding age and female ratio. However, the non-closure group was associated with a higher baseline BMI (Table 2). Moreover, the quality assessment of RCTs is presented in Table S1. Pooled ORs, WMDs, I^2 , and p values regarding the baseline characteristics, along with the primary and secondary endpoints are summarized in Table 2.

Primary Endpoints—Efficacy Endpoints

According to our analysis, the incidence of IH was significantly greater in the non-closure group (OR 0.25 [95% CI: 0.20, 0.31]; p < 0.01) (Fig. 2). In the subgroup analysis, an increased incidence of IH was reported at both the Petersen (OR 0.26 [95% CI 0.18, 0.37]; p < 0.01), ranging from 0 to 5%, and the jejunal site (OR 0.25 [95% CI 0.18, 0.35]; p < 0.01), ranging from 0 to 4.8%, regarding the non-closure group. These outcomes were further certified by sensitivity analysis. In fact, we re-assessed the incidence of IH by including only the RCTs and found a higher IH rate in patients allocated at the non-closure group (Fig. S1). The time interval to IH presentation was greater to the non-closure group (WMD – 10.73 [–12.85, –8.60]; p < 0.01) (Fig. S1).

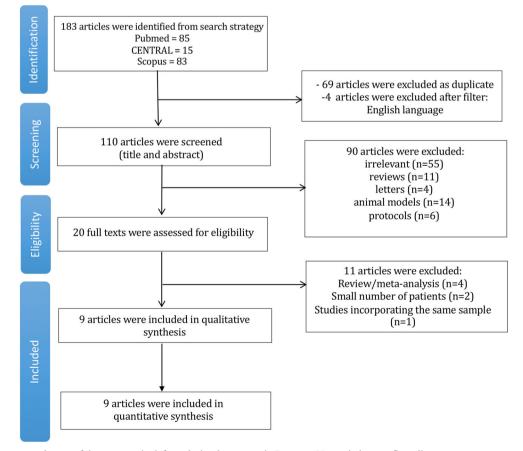


Fig. 1 Closure vs. non-closure of the mesenteric defects during laparoscopic Roux-en-Y gastric bypass flow diagram

Study ID, Year	Journal	Country	Time Stu period des	Study Approach Mesenteric closure design technique	Patients, n	, <i>n</i> Mean BMI, kg/m ²	, kg/m ²	Internal hernia 30-day rate, n (%) compli rate, n	t 30-day complication rate, n (%)	Follow-up, months	Nos
					Closed Open	Open Closed	Open	Closed Open	Closed Open		
Aghajani et al., 2017 [14]	Surg Endosc	Norway	2005–2015 P	Antecolic Stapling	2443	1570 40 (30–81) 42 (, 42 (31–6-	47 152 (1 (9 0) 7)	42 29 (1.7) (1 8)	60	∞
Amor et al., 2019 [15]	Obes Surg	France	1998–2013 R	Antecolic Non-absorbable continuous sutures	1672	421 41.8 (35–55)	43.5 (21–6-	(0 (1 (0 (1 (7))	(o 	120	Г
Blockhuys et al., 2018 [16]	Obes Surg	Belgium	2011–2013 R	Antecolic Non-absorbable continuous sutures	1538	1586 –	Ê I	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1	42	9
Chowbey et al., 2016 [17]	Obes Surg	India	2005–2014 R	Antecolic Non-absorbable continuous sutures	976	$600\ 45.9\pm7.08\ 46.4\pm6.7$	46.4 ± 6.7	10	4 (0.4) 6 (1)	60	9
de la Cruz-Muñoz et al., Surg Obes 2011 [18] Relat Di	l., Surg Obes Relat Dis	USA	2001–2009 R	Antecolic Non-absorbable continuous sutures	2079	- 6	I			60	5
Lopera et al., 2018 [19]	H	Colombia	a – R	Antecolic Non-absorbable continuous sutures	346	321 –	I	1 (0.3) 4 (1	1	36	S
Rodriguez et al., 2010 [20]	Obes Surg	Mexico	2004-2008 R	Antecolic Non-absorbable continuous sutures	172	187 43.1±7.7	$43.5 \pm 6.3 \ 2 \ (1.2)$	27	I I	36	9
Rosas et al., 2015 [21]	Surg Endosc	NSA	- RCT	T Antecolic Interrupted braided polyester sutures	48	$54 \ 46.2 \pm 0.9$	$48.1 \pm 0.9 \ 0 \ (0)$	$\begin{array}{c} 4 \\ 0 (0) & 1 \\ (1- \\ 9) \end{array}$	$ \begin{array}{cccc} 6 & 10 \\ (12 & (1- \\ 5) & 8 \\ \end{array} $	34	Ι
Stenberg et al., 2016 [22]	The Lancet	Sweden	2010–2011 RCT	T Antecolic Non-absorbable continuous sutures	1259	1248 42.3±4.9 42.4±5.2	42.4 ± 5.2	27 84 (2 (6 1) 7)	136 12 (10 8)	36	I

closure, the number of participants, and the number of female patients, along with the mean age, the

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 Table 1
 Characteristics of the studies that were finally included in the meta-analysis. The first

Table 2 Summary of the analysis of the baseline characteristics and outcomes

Categorical outcomes	п	OR [95% CI]*	р	Heterogeneity	
				I^2	р
Female ratio	4	1.02 [0.90, 1.16]	0.74	0%	0.65
Total incidence of IH	16	0.25 [0.20, 0.31]	< 0.01	1%	0.44
Incidence of IH at Petersen site	8	0.26 [0.18, 0.37]	< 0.01	7%	0.38
Incidence of IH at jejunal mesenteric site	8	0.25 [0.18, 0.35]	< 0.01	10%	0.35
Incidence of IH—RCTs only	4	0.31 [0.20, 0.48]	< 0.01	0%	0.98
Incidence of IH at Petersen site-RCTs only	2	0.33 [0.15, 0.73]	< 0.01	N/A	-
Incidence of IH at jejunal mesenteric site-RCTs only	2	0.30 [0.18, 0.50]	< 0.01	0%	0.91
Early SBO	5	2.83 [1.29, 6.22]	0.01	0%	0.51
Late SBO	5	0.27 [0.17, 0.43]	< 0.01	68%	< 0.01
Leak	4	1.15 [0.68, 1.95]	0.59	0%	0.51
Marginal ulcer	3	1.69 [0.46, 6.24]	0.43	0%	0.95
Bleeding	3	0.82 [0.54, 1.26]	0.37	0%	0.53
Reoperations	8	0.28 [0.15, 0.52]	< 0.01	87%	< 0.01
Continuous outcomes	n	WMD [95% CI]	р	Heteroger	neity
				I^2	р
Age	6	0.32 [-1.23, 1.87]	0.68	93%	< 0.01
Preoperative BMI	6	-1.10 [-1.96, -0.25]	0.01	91%	< 0.01
Time-interval to IH	4	-10.73 [-12.85, -8.60]	< 0.01	39%	0.18
%EWL	3	2.74 [-5.51, 10.99]	0.52	55%	0.11

IH, internal hernia; *RCT*, randomized control trial; *SBO*, small bowel obstruction; *BMI*, body mass index; %EWL, % excess weight loss; *OR*, odds ratio; *WMD*, weighted mean difference; *CI*, confidence intervals

Primary Endpoints—Safety Endpoints

Both groups were associated with similar outcomes regarding the incidence of bleeding (OR 0.82 [95% CI 0.54, 1.26]; p =0.37), leakage (OR 1.15 [0.68, 1.95]; p = 0.59), and marginal ulcer (1.69 [0.46, 6.24]; p = 0.43) (Fig. S1). Nonetheless, the non-closure group presented a higher incidence of late SBO (OR 0.27 [95% CI 0.17, 0.43]; p < 0.0001) (Fig. 3a), which is mainly attributed to internal hernia, or in more rare cases to adhesions. This finding is in accordance with the higher incidence of IH in the non-closure group. In contrast, the incidence of early SBO, mainly attributed to kinking of the jejunostomy due to the stiffening of the anastomosis by the mesenteric closure, was higher in the closure group (OR 2.83 [95% CI 1.29, 6.22]; p = 0.010), but the number of cases was limited. In fact, only two studies [14, 22] reported cases of SBO due to the kinking of the jejunostomy. According to the first study [14], there was no significant difference between the two groups regarding the kinking of the jejunojejunostomy. On the other hand, the second study [22] reported a significantly higher incidence of kinking in the closure group. Due to the limited provided data, no further analysis could be performed regarding the kinking of the jejunojejunostomy. In addition, the risk of reoperation due to SBO was significantly greater in the non-closure group (0.28 [0.15, 0.52]; p < 0.001) (Fig. 3b). The mortality rate was zero in the non-closure group. Only one case of postoperative death has been reported in the closure group, attributed to port-site hernia with incarcerated bowel.

Secondary Endpoint—Weight Loss

In the present meta-analysis, we evaluated the % excess weight loss (%EWL) reported in both groups since it has been identified as a risk factor for reoperation because of SBO caused by IH [22]. No significant difference was reported between the two groups regarding the % excess weight loss (%EWL) (WMD 2.74 [95% CI – 5.51, 10.99]; p = 0.52), as shown in Fig. S1.

Publication Bias

Heterogeneity was high regarding the baseline BMI and age, along with the incidence of SBO. On the other hand, heterogeneity was low regarding all the primary and secondary endpoints. The Egger's test could not be performed due to the inadequate number of the included studies. The funnel plots that were produced to assess the publication bias are shown in Fig. S2. The funnel plot regarding the incidence of IH was symmetrical. The asymmetries that were found in the funnel plots regarding the other endpoints are mainly attributed to the small number of the included studies and the possible bias regarding the selection of the patients, thus proposing that

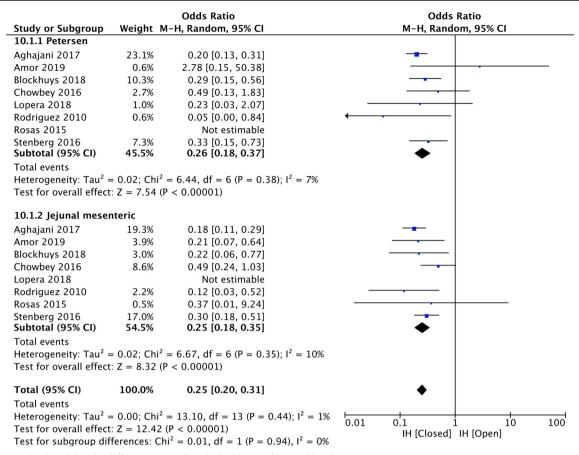


Fig. 2 Forest plot describing the differences regarding the incidence of internal hernia (IH)

additional studies are necessary in order to reduce the potential publication bias.

Discussion

LRYGB is one of the most popular bariatric procedures worldwide and the most frequently performed operation in west Europe and North America mainly due to its advantages in the early and late postoperative courses [23]. Despite the fact that initially, the description of LRYGB did not include the closure of the mesenteric defects, recent evidence has triggered an extensive debate regarding the establishment of the mesenteric closure as the standard of care in LRYGB [24]. The defects of interest include the mesenteric defects at the jejunojejunostomy, subsequent to the creation of the roux limb, along with the space posterior to the roux limb and distal to the mesocolon referred as Petersen defect. In fact, SBO caused by IH following LRYGB remains a significant risk that is associated with postoperative morbidity and mortality [25]. However, there is only limited high-quality evidence available provided by only two RCTs [21, 22] so as to reach a consensus regarding the best practice. To our best knowledge, the present study is the first meta-analysis, assessing the potential superiority of closure of mesenteric defects compared with non-closure that incorporates evidence provided by RCTs, thus providing the best level of evidence currently available. A previous meta-analysis [9] that incorporated studies published until 2013 failed to include any RCTs, thus limiting the level of evidence, while the analyses evaluating the incidence of IH were associated with high heterogeneity.

According to our outcomes, the closure of the mesenteric defects with running, non-absorbable sutures during LRYGB significantly reduces the incidence of IH. Given the increase of internal hernia incidence over time, the non-absorbable materials are considered to be superior compared to absorbable. Nonetheless, the use of sutures compared with other techniques such as glue or clips remains debatable. Clips and interrupted sutures were used for mesenteric closure in each study [14, 21], with similar outcomes. Sutures provide higher tensile strength [26], but clips were also associated with increased efficiency [7]. The most efficient technique for closure of mesenteric defects should be assessed in future comparative studies.

Our outcomes also demonstrate that the routine closure of mesenteric defects is associated with similar rates of postoperative complications. Closure of the mesenteric defects has been associated with an increased rate of a.

b.

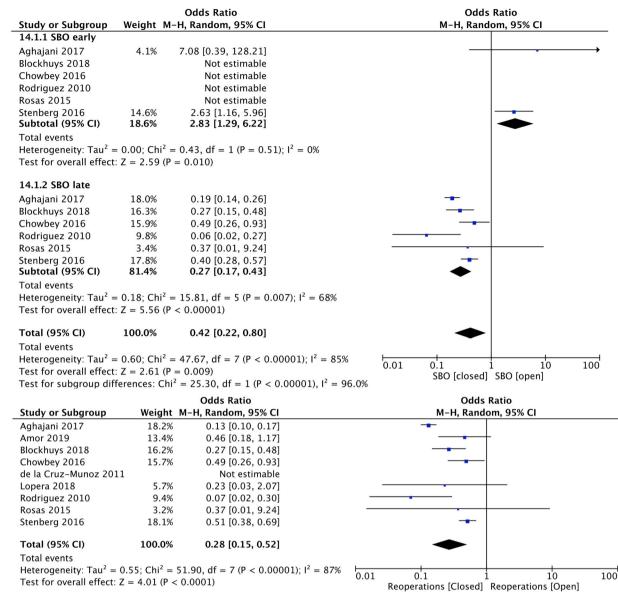


Fig. 3 Forest plot describing the differences in \mathbf{a} small bowel obstruction (SBO), \mathbf{b} incidence of reoperations. \mathbf{a} The incidence of SBO was greater in the non-closure group. \mathbf{b} The incidence of reoperations was greater in the non-closure group

kinking of the jejunojejunostomy. A potential pathophysiological mechanism explaining this phenomenon is the increased rigidity and stiffening of the jejunojejunostomy as a consequence of the antecolic location of the anastomosis, along with the closure of the mesenteric defects [27]. In the present meta-analysis, only two studies [14, 22] reported contradicted outcomes regarding the kinking of the jejunostomy. In fact, different techniques have been proposed in order to reduce the incidence of kinking of the jejunojejunostomy, such as setting an anti-obstructive stitch [28], and the wide division of the mesentery, along with the double stapling of the jejunojejunostomy. Nonetheless, the currently available evidence to support these preventive measures is weak and new studies are needed to further assess this issue. In many studies, the efficacy of the closure of mesenteric defects was assessed in terms of IH rate. Nonetheless, the presence of IH is in many cases challenging to be defined [29]. In the same context, SBO attributed to other causes might be underestimated, thus posing a significant bias regarding the evaluation of the efficacy of the mesenteric defect closure. Nonetheless, in the present meta-analysis, the rate of reoperations due to SBO was also assessed. According to our outcomes, the non-closure group presented a significantly higher risk of reoperations.

The current meta-analysis demonstrates that the routine closure of the mesenteric defects during LRYGB is effective, safe, and is associated with a significantly lower incidence of IH, late SBO, and reoperations. Nonetheless, a higher incidence of early IH caused by kinking of the jejunojejunostomy is reported in the closure group. The present meta-analysis also highlights the need for additional studies assessing the closure of mesenteric defects. Ideally, these would be randomized controlled studies, with prospective design and longer follow-up in order to compare the different techniques and materials proposed for mesenteric closure, along with the techniques suggested in order to reduce the incidence of kinking of the jejunojejunostomy.

The limitations of this meta-analysis reflect the limitations of the studies included. One study [14] was prospective and six [15–20] retrospective, thus posing a certain limitation in the present study. Two studies [21, 22] were RCTs. Moreover, the heterogeneity was high regarding the baseline BMI and age, along with the incidence of SBO. Furthermore, the non-closure group was associated with a higher baseline BMI. Finally, the differences among institutions regarding the data definitions and the lack of standardization of the surgical techniques pose another limitation.

On the other hand, the strengths of the current metaanalysis include (1) the clear protocol, (2) the welldefined inclusion-exclusion criteria, (3) the literature search in three different databases, (4) the quality assessment of the included studies, and (5) the up-to-date demonstration of the outcomes of data extraction and analysis.

Conclusion

The present meta-analysis identified and included 9 studies assessing the routine closure of the mesenteric defects during LRYGB. These studies suggest that the mesenteric closure is associated with a lower incidence of IH, late SBO, and reoperations, along with a similar level of feasibility and safety. The present meta-analysis provides the best currently available level of evidence on the topic and supports the routine closure of the mesenteric defects. Nonetheless, surgeons should be aware of the potential risk of early postoperative SBO due to kinking of the jejunojejunostomy. Future studies with longer follow-up are necessary to further assess the different techniques/materials suggested for closure, along with the proposed measures for the prevention of kinking of the jejunostomy.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Does not apply.

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