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Review Article

Perforated giant duodenal ulcer: A review

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Abstract

Giant duodenal ulcer is a rare cause for perforated peptic ulcers but is associated with higher morbidity and mortality compared to a smaller ulcer. Despite that, no single surgical approach has yet been shown to be superior to others. This review will discuss options available based on current evidence. The Google Scholar and PubMed databases were searched. The surgical option is divided into resection and non-resection approaches. The latter was further subdivided into omental based, jejunal based, and tube-based repair. Based on a review of literature and analysis, an omental based plug repair with or without triple tube ostomies was associated with much lower morbidity and mortality than others. The resection approach must be reserved for salvage procedure and preferably done in stages.

Keywords: duodenal ulcer; peptic ulcer; perforation

1. Introduction

Perforated peptic ulcer (PPU) is a common life-threatening surgical emergency with mortality ranges between 10-40% [1,2]. Duodenum is the commonest site (60%) followed by the antrum of the stomach (20%) and its lesser curvature (20%) and most perforations were less than 1 cm in diameter [3,4]. Surgeons rarely encounter an ulcer with a diameter of more than 2 cm which is often considered a giant ulcer. It comprises of only 1-2 % of all duodenal ulcers [5-8]. Its definition and ideal surgical management are not well established. The objective of this review is to establish the prior issues based on the most recent evidence.

2. Methods

2.1. Review strategy

This review employed the PubMed and Google Scholar databases between 1980 and 2019 and applied the search words "perforated duodenal ulcer" and "perforated giant duodenal ulcer". Any type of human study on the operative management of perforated duodenal ulcer in adult (age > 18 years old) which stated the size of perforation and specifically analyzed outcome of the repair for ulcers more than 2 cm in diameter were included.

A commentary paper, case report with only one case, non-English abstract or research paper, and duodenal repair of non-peptic related

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perforation were excluded. Studies on the operative repair of giant non-perforated (bleeding) duodenal ulcers were also rejected. In addition, researches with a combined analysis of both perforated gastric and duodenal ulcer were also excluded. Relevant abstracts and original papers were retrieved and reviewed. Relevant articles identified by cross-referencing were also retrieved and reviewed. The two authors independently appraised the data from each series.

2.2. Statistical analysis

Statistical analysis was done for comparative studies. The denominator for any outcome measure was the total number of patients in each series in relation to the outcome. The results are presented as the mean or an actual number of cases documented. Comparisons between the groups were performed by using the independent samples t-test (numerical variables) and the Chi-square tests for categorical variables. A $p < 0.05$ value is considered to be statistically significant.

3. Results

The initial search from the PubMed database yielded 427 abstracts. Figure 1 demonstrates a flow chart of the search history that yielded only 2 studies on operative management of perforated giant duodenal ulcer between 1980 until 2019. More relevant articles were identified with a Google Scholar database search. Among the first 200 abstracts reviewed, 13 articles fulfilled the criteria established [Figure 2].

3.1. Quality of the studies for this review

The total number of cases is small with most studies were from India. There was only one randomized study conducted by Jani et al [8]. The majority were retrospective comparative studies with many shortcomings in the design and reporting of results. Vashist et al. included bleeding cases also in their analysis thus affecting outcome analysis [23]. In addition to that Agarwal et al. included all sizes of duodenal perforations and focusing on other indications for triple tube ostomies such as very late presentation (> 3 days) and high APACHE score (> 10) [28]. The majority had no clear definition of each morbidity with no statistical analysis done. Gupta et al. had a good number of patients but unfortunately didn't highlight the actual percentage of the patients with ulcers of more than 2 cm [14].

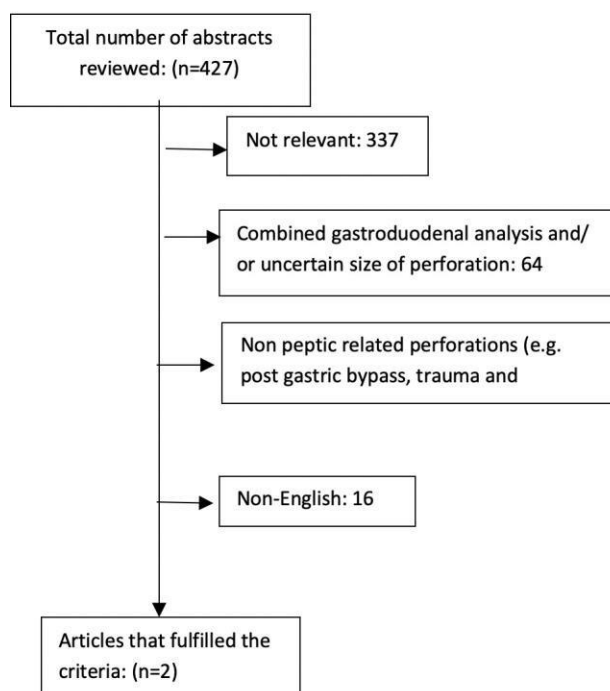


Figure 1. Flow chart outlining the search history for published reports on operative management of perforated giant duodenal ulcer from the PubMed database.

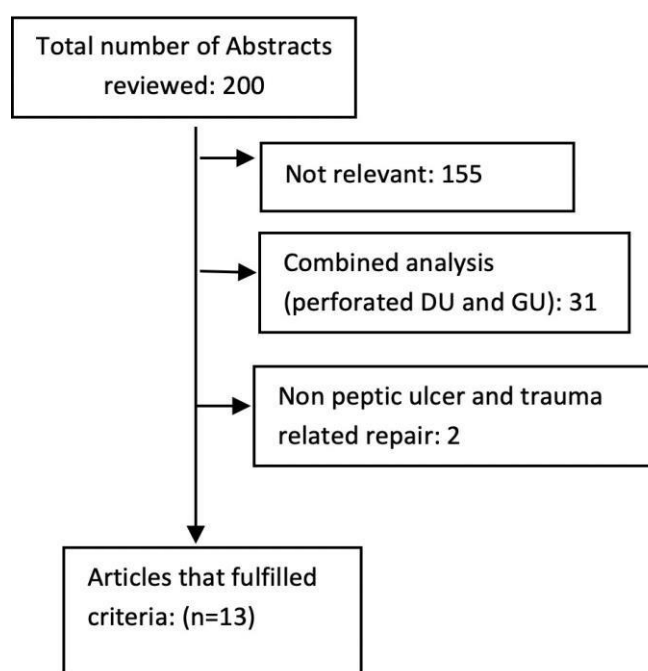


Figure 2. Flow chart outlining the search history for published reports on operative management of perforated giant duodenal ulcer from Google Scholar database.

4. Discussion

4.1. Definition of perforated giant duodenal ulcer

There is no standard definition of either small, large, or giant duodenal ulcer (DU) perforation even though the size correlates well with an operative outcome [10,14]. In general, the mortality rate was only 6% for perforation size less than 5 mm but rose to 24% for those more than 10 mm [9]. Some authors even had demonstrated a much higher mortality rate for giant peptic ulcer perforation (17–40%) [13]. Such a high mortality rate is expected as a giant duodenal ulcer (GDU) typically associates with major duodenal tissue loss, friable edges, and severe surrounding inflammation [9]. A standard definition is warranted as it affects management, prognosis, and facilitates future research. Studies have shown, the majority of perforated GDU (PGDU) was between 2 – 3 cm. Gujar et al. have demonstrated 33 patients from their series (92%) were in that range with only three ulcers sized more than 3 cm [10]. Most authors excluding Yogesh et al. defined PGDU when the size more than 2 or 2.5 cm in diameter [6,8-10,12,13,15,25-27]. However, Gupta et al. proposed size of more than 3 cm to be considered as giant as they noted, those between 2 – 3 cm in diameter behaved similarly to those size 1 – 2 cm [14]. Until a definitive definition is made, any ulcer with a diameter of more or equal to 2 cm should be considered as a giant. This is to avoid confusion, facilitate future study, and to respect the majority of authors.

4.2. Clinical features

Perforated peptic ulcer was a disease of a middle-aged man. A similar demographic pattern was also seen in perforated giant duodenal ulcer (GDU). The mean age at presentation was 48 years old with 79% were male [3]. Few prior studies have also demonstrated a similar pattern, 87.4% were men with the majority (75%) between 30 – 50 years old [8-10,26] [Table 1]. The majority of GDU (80%) present either with life-threatening hemorrhage, perforation or gastric outlet obstruction, thus early diagnosis is the pillar of treatment as failure to do so leads to high mortality [8]. Fortunately, the majority of GDU bled rather than perforated as demonstrated by Nussbaum et al. and Mathumita et al. Only 9% of their 32 GDU patients in the former authors had perforation with the majority (75%) bled. Similarly, the latter group demonstrated that only 3.2% of their series of 718 cases of perforated peptic ulcers were due to GDU [9,19]. It is compelling to note that, majority of patients presented late with extensive soiling. Sixty percent to 80% of them presented more than 48 hours after the onset of peritonitis with more than 1000 ml of purulent fluid intra-peritoneally in 70% of them [10,12,13,26,28] [Table 2]. In contrast, the majority (89%) of typical (non-giant) perforated peptic ulcer (PPU) cases presented within 24 hours of the onset of peritonitis [3].

4.3. Operative management of perforated giant duodenal ulcer

There is a well-accepted single operative technique for such ulcers despite the high leak and mortality rate. Lack of good clinical evidence further complicates the matter [6,12,14]. Repair of GDU perforations is risky due to extensive duodenal tissue loss with surrounding

inflammation and edema [12,28]. Inflammatory necrosis occurs which can affect both anterior and posterior walls of the duodenum [6]. Likewise, adhesion to the surrounding organs is a rule [19]. A simple omental patch is dangerous as it is associated with a high leak rate (12%) [2,12,27,28]. The size of perforation has been shown by multivariate analysis to be one of the independent risk factors for leaking other than low albumin and hemoglobin level (< 25 g/dl and Hb < 10 g/dl respectively) [16].

Table 1. Patients demography and type of studies done

	Authors / year of publication	Age / year old (mean)	Gender (M:F)	No of patient	Type of study
1	Wasif Mohammad Ali / 2018	51.5	24:10	34	Retrospective descriptive study
2	Nitin Agarwal / 2017	44.6	17:3	20	Prospective observational study
3	Suman Parihar / 2016	NA	28:2	30	Prospective comparative (non-randomized)
4	Gujar et al / 2014	59.9	29:7	36	Retrospective comparative
5	Nishikant Gujar / 2013	NA	30:6	36	Retrospective comparative (omental plug vs tube duodenostomy)
6	Yogesh et al / 2012	57 (median)	63%:37%	88 perforated (36 bleeding cases)	Retrospective case-control
7	Mathumita et al / 2011	52.2	23:0	23	Prospective non-randomized
8	Pawanidra et al / 2009	NA 75% (30 – 50 years old)	31:9	40	Retrospective comparative
9	Jia et al / 2006	78.2	9:1	10	Case series
10	Kalpesh et al / 2006	39.2	89:11	100	Prospective randomized
11	Sanjay et al / 2005	47.1	37:1	38	Retrospective comparative series (compare with different sizes of ulcer)
12	Sharma et al / 2000	NA	NA	7	Case series
13	Clifford et al / 1988	55.1	3:3	6	Comparative case series

NA: Not available.

On the other hand, doing a complex surgical procedure in an ill patient with generalized peritonitis increases the risk of suture line leak significantly [6]. Moreover, closure of the duodenal stump is a challenge, and resection of such ulcers is risky [23]. Occasionally, the antrum of the stomach was also involved thus precludes antrectomy [13]. There are a few important points to be considered before deciding which operative technique is to be selected. The most crucial is the hemodynamic stability of the patient intra-operatively. In an emergency setting with a seriously ill patient, it is not appropriate to do a major resection procedure [2,14,17]. Therefore, damage control surgery (DCS) must be considered [2]. The location of the defect must be objectively verified. The majority of the studies did not document it. It is equally important to establish whether the defect can be primarily closed or not. Unfortunately, the majority of ulcer edges are too delicate for simple closure with a high risk of suture line failure [9]. The surgeons must also establish the resection status of the antrum and the involved duodenum. In diffuse peritonitis, resection and anastomosis are not advisable [2]. Based on the above parameters, the operative technique can be divided into two major approaches; resection or non-resection technique [Figure 3].

Table 2. Peri-operative outcomes and definitions used

	Authors / year of publication	Definition of GDU used	Duration of peritonitis / hours(H)	Type of intervention / number of patients (n)	Operative time / minutes (mean)	Morbidity / number of cases	Postoperative stay / days (mean)	Mortality
1	Wasif et al / 2018	≥ 2 cm	NA	Triple tube ostomy / 34	NA	Wound infection: 56% Burst abdomen: 38%	16.8 days	5.8%
2	Nitin Agarwal et al / 2017	≥ 1.5 cm	NA	Omentopexy and triple tube ostomy	NA	Wound infection: 45% Chest infection: 20% Burst abdomen: 25% Postoperative leak: 5%	22.0 days	20%
3	Suman et al / 2014	≥ 2 cm	NA	Graham's patch omentopexy (n=15) vs omental plug (n=15)	NA	Omentopexy vs omental plug Wound infection: 20% vs 13% (NS) Intra- abdominal abscess: 6% vs 6% (NS) Lung infection: 20% vs 13% (NS)	NA	Omentopexy vs omental plug 20% vs 6.6%
4	Gujar et al / 2014	> 2 cm (92%: 2- 3 cm)	< 48 H (15 pt: 41.6%) > 48H (21: 58.4%)	Omentopexy / 18 Vs Omental plug / 18	Omentopexy vs omental plug. 63.4 Vs 104.3 (p < 0.001))	Omentopexy vs Omental plug Total morbidity (61% vs 44%: ? sig) Wound infection (22% vs 16%; ? sig)	Omentopexy vs omental plug 17.9 vs 16.2 days (NS)	Omentopexy vs omental plug 11.1% vs 5.5% (? Sig)

						Respiratory infection (17% vs 16%; ? sig)		
5	Nishikant Gujar / 2013	> 2 cm (90%: 2-3 cm)	< 48 H (16 pts; 42%) > 48 H (20 pts; 58%)	Omental plug (n=18) vs triple tube duodenostomy (n=18)	Omental plug (63.4 mins) vs tube duodenostomy (112.38 min)	Omental plug vs tube duodenostomy Total morbidity (61% vs 44%; ? sig) Wound infection (22% vs 22%; ? sig) Respiratory infection (16% vs 11%; ? sig) Pelvic abscess (1.5% vs 1.5%; ? sig)	Omental plug vs tube duodenostomy 17.9 vs 14.1 days; ? sig	Omental plug vs tube duodenostomy 11.1% vs 5.5%; ? sig
6	Mathumita et al / 2011	> 2 cm	NA	Omentopexy / 13 vs Omental plug / 10	Omentopexy vs omental plug 83 vs 108 (NS)	Omentopexy vs omental plug. Duodenal fistula (23% vs 0%: NS) Wound infection (30% vs 20%: NS) Lung complications / sepsis (30% vs 20%: NS)	Omentopexy vs omental plug 14.2 vs 12.6 days (NS)	Omentopexy vs omental plug 5/13 vs 10% (NS)
7	Pawanidra et al/ 2009	> 2 cm (32% >3 cm)	> 48 H (77.5%)	Primary closure and triple ostomies / 20 vs	NA	Triple ostomies vs control	Triple ostomies group: 12 – 20 days (95%). Control group: all > 25 days	Triple ostomies group: 1/20 Control group: 13/20

				Pedicle omentopexy/ 18 and jejuna patch / 2 (control group)		Anastomotic Leak: 0% vs 14/20 Intra-abdominal sepsis: 4/20 vs 12/20 Lung infection: 8/20 vs 12/20 (No statistical analysis)	(No statistical analysis)	(No statistical analysis)
8	Jia et al / 2006	> 2.5 cm (mean size: 3.2 cm)	All > 48 H	Gastric body partition (primary duodenal closure, duodenostomy and gastrojejunostomy) only	122 + 52 mins	Wound infection: 20% Minor leak: 40% (no statistical analysis)	NA	10%
9	Kalpesh et al / 2006	> 2 cm (2–3 cm only)	NA	Omentopexy / 50 vs omental plug / 50	NA	Omentopexy vs omental plug. Leak: 12% vs 0% (p < 0.05) GOO (endoscopic diagnosis at 6 weeks post op): 12% vs 0% (p < 0.05) GOO (Ba diagnosis at 6 months post-op): 24% vs 10% (NS)	Omentopexy vs omental plug 8.8 vs 8.0 days	Omentopexy vs omental plug 8% vs 16% (NS)

10	Sanjay et al / 2005	Giant defined as > 3 cm. Large (1-3 cm)	NA	Large group (38 patients): Cellan Jones omental patch /30 Jej serosal patch / 4 Antrectomy / 4	NA	Overall leak rate: 12.5% (5 patients: 3 patch, 1 jej patch, 1 antrectomy)	13.6 days	15.8%
11	Sharma et al / 2000	> 2.5 cm	NA	Free omental plug series 4 pt – primary 3 pt – salvage procedure, failed Graham patch	NA	Minor wound infection	NA	14.2% (septic shock with MOF)
12	Clifford et al / 1988	>2 cm (all >3 cm)	NA	Gastric disconnection (GD) (antrectomy with triple ostomies: duodenostomy, jejunostomy, and gastrostomy) vs Billroth II	NA	NA	NA	GD vs Billroth II (0% vs 66%)

GDU: Giant duodenal ulcer, NA: Not available, NS: Not significant, GOO: Gastric outlet obstruction.

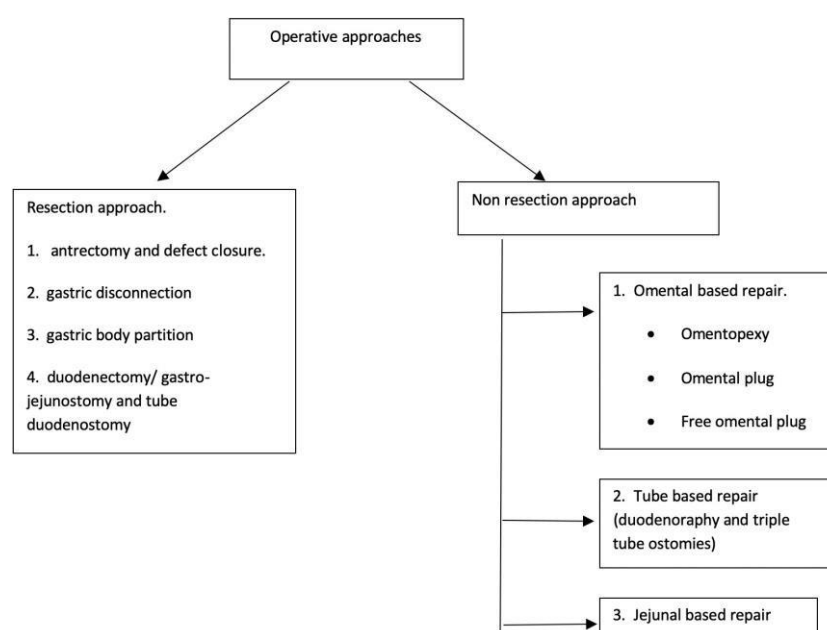


Figure 3. Summary of operative options for perforated giant duodenal ulcer.

4.4. Resection approach

This approach is preferred if the general state of a patient allows and the duodenal defect can be closed.

Unfortunately, the duodenal mass is often inflamed and indurated thus dissection is unsafe [2]. Four resection procedures are available.

4.4.1. Antrectomy and defect closure

This approach is believed to be the safest method of DCS as suggested by Di Saverio et al. However, the duodenal defect must be closed and upper gastrointestinal division is accomplished by antrectomy. The proximal gastric remnant will be decompressed by a nasogastric tube. An anastomosis should be averted in a hypotensive patient requiring vasopressor post-operatively. Laparostomy must be constructed and re-laparotomy will be done after 48 hours to restore continuity. Biliary decompression is strongly advocated also [2].

4.4.2. Gastric disconnection (antrectomy and 3 tube ostomies)

Cranford et al. had proposed this stages approach nearly 30 years ago but looks promising. During an initial surgery, the duodenal defect is closed and antrectomy is created followed by 3 tube ostomies; duodenostomy, gastrostomy (to decompress the stomach), and jejunostomy for feeding. Gastro-jejunostomy will be established a month later as an elective procedure. They retrospectively reviewed six patients with a mean duodenal defect of 12.25 cm² (2 – 24 cm²) and concluded that the procedure was much safer than Billroth II resection [6] [Figure 4].

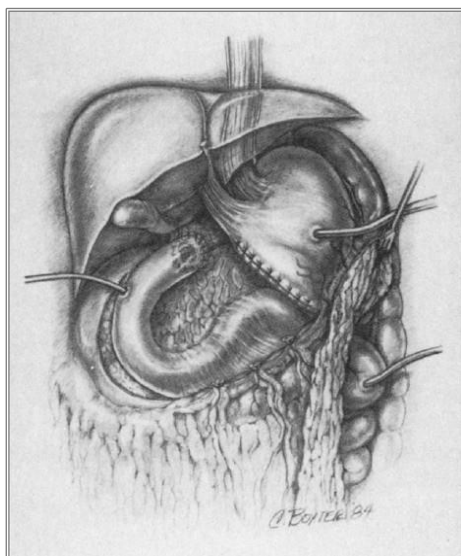


Figure 4. Gastric disconnection technique for perforated giant duodenal ulcer perforation.

4.4.3. Gastric body partition

This approach was advocated by Shyu et al. The duodenal defect is closed primarily followed by gastric body transaction (stapler). Gastro-jejunostomy was then created followed by lateral tube duodenostomy. They concluded that the procedure is quite safe even in septic shock elderly patients (mean age 78.2 years old) with delayed surgery (mean 96.5 hours) as the mortality rate was only 10% with no major complications [13].

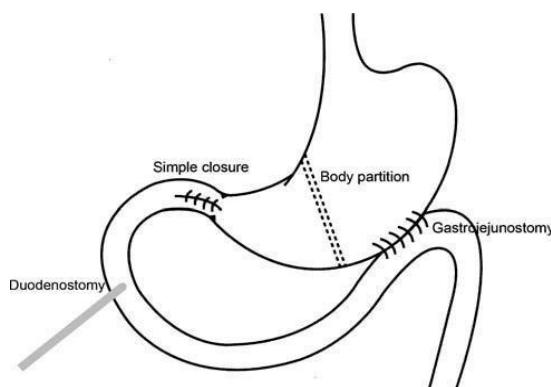


Figure 5. Gastric body partition approach for perforated giant duodenal ulcer.

4.4.4. Duodenectomy, gastro-jejunostomy, and tube duodenostomy

This technique was highlighted by Nussbaum et al. many years ago where an involved duodenum is resected and primarily closed. Subsequently, gastro-jejunostomy and tube duodenostomy were created [19].

4.5. Non-resection approach

The majority of the authors advocate this approach. Most of the techniques can be done quickly even by a young surgeon with a minimum suture line. It can be further sub-divided into 3 types based on organ or material used [Figure 3].

4.5.1. Omental-based repair; omental-plasty (patch), omental plug, or free omental plug

a) Omental patch (omental-plasty or omento-pexy): An extensive review by Gupta et al. involving 162 duodenal ulcer perforations with 23% of them (34 patients) had perforation sized 1 to 3 cm. They have demonstrated an omental patch remains a good option for that range of ulcers but not beyond that. Unfortunately, the exact number of patients with ulcer size 2 – 3 cm (giant ulcer) was not specified. Interestingly, their leak rate was only 12.5% with a 15% mortality rate. They concluded that the Cellan Jones technique is simple and remains dependable even for the closure of large size perforation up to 3 cm in size [14]. No suggestion can be made for ulcers more than 3 cm as only two of their patients (1.2%) had it. In addition to that, some patients also had tube duodenostomy and pyloric exclusion/draining gastrostomy and feeding jejunostomy [14] [Table 2].

b) Omental plug: Most authors advocate this approach for GDU perforation which was initially proposed by Karanjia et al [20]. The basic principle of physics in the omental plug is as part of the omentum is inside the stomach, even with high intragastric pressure it is still in contact with gastric mucosa compared to the patch. Furthermore, the plug easily turns into granulation and fibrous tissue which is then readily integrated into the gastric or duodenal wall and subsequently replaced with normal intestinal tissue [21]. Few randomized studies have been done comparing plug with omental patch technique [Table 2]. An excellent randomized controlled study conducted by Jani et al. involving 100 patients provides the best evidence [8]. All ulcers ranged from 2 to 3 cm. The plug group was compared to standard Graham's technique. Following surgery, a routine gastrografen test was done on a postoperative day (POD) 7 followed by an OGDS six weeks later. All post-operative leaks were from the patch group (12%) and none survived. In addition, no one in the plug group (0%) but 12% from the patch group developed gastric outlet obstruction 6 weeks after surgery. They concluded that the plug technique is safer as evidenced by a lower mortality rate (8%) compared to the patch technique (16%) and effective. Mukhopadhyay et al. did a similar comparative (non-randomized) study [9]. Among 718 patients with perforated duodenal ulcers, only 23 of them were due to GDU (3.2%). They have demonstrated a few interesting findings in favour of the plug technique such as the absence of intestinal fistula complication compared to the omentopexy group (23%). The incidence of wound infection and lung-related morbidity were much less in the plug group. The mortality rate in the plug group was also much less (10% vs 38%) [Table 2]. In addition to that, Gujar et al. also did a similar comparative study. Ninety-two percent (n=33) of their patients had a perforation of 2 – 3 cm. Overall morbidity and mortality were much less in plug group (44.4% vs 61.1% and 5.5% vs 11.1% respectively) [10]. Combined analysis of all omentopexy versus plug group has demonstrated significantly lower mortality (18.7% vs 7.5%) and anastomotic leak rate (13.2% vs 1.4%) in the plug group [Table 3]. Therefore, the omental plug technique appears to be a very promising approach and able to become a “stand alone” procedure.

Table 3. Summary of the results on comparative studies of omentopexy versus omental plug repair for perforated giant duodenal ulcers

	Omentopexy series		Omental plug series		p-value
	No. of patients available for analysis	Results	No. of patients available for analysis	Results	
Total number of patients	96		93		
Mean operative time (mins)	31	146.4 min	28	212.3 min	P< 0.05
Wound infection	46	11	43	7	0.370 (NS)
Intra-abdominal abscess	46	4	43	4	0.920 (NS)
Chest infection	46	10	43	7	0.512 (NS)
Anastomotic leak	68	9	68	1	0.008
Hospital stay/days (mean)	81	13.6 days	78	12.2 days	P> 0.05 (NS)
Mortality	96	18	93	7	0.026

c) Free omental plug: Sharma et al. have proposed this technique but not strong evidence-based. They retrospectively reviewed seven patients with peptic perforation. The actual size of each ulcer wasn't mentioned and three of them had it for salvage surgery. Interestingly, they had no significant morbidity with a only 14% mortality rate. They believed the FOP technique is indicated in an ill patient with giant perforation and a friable edge [15].

4.5.2. Jejunal based repair

Jejunum can also be used to close the duodenal defect either in a form of a serosal patch or the creation of Roux-n-Y duodeno-jejunostomy (jejunal flap). Unfortunately, no series of such cases were ever published and most were part of other techniques. An animal study by Ziaian et al. highlighted a few important clinical points. The jejunal flap leads to better results compare to the serosal patch and the former is more versatile regardless of the size of duodenal defect or perforation. A defect of nearly 10 cm can be closed satisfactorily with this technique [22]. The effectiveness of this approach has been demonstrated by Vashist et al. in their case-control study. Sixty-two patients from each arm had undergone either the classic Nissen Bsteh technique or the duodeno-jejunostomy (DJ) technique for closure of the duodenal defect. The leak and mortality rates were 29% vs 14% and 16% vs 4.8% respectively and were statistically significant [23].

4.5.3. Tube-based repair

Following the primary closure of the duodenal defect, some authors rely strongly on tube drainage as an adjuvant procedure. Pawanindra et al. did a retrospective comparative study between tubes over conventional repair (omental patch) in forty patients. All of their patients had ulcer perforation more than 2 cm with a significant percentage (32%) were > 3 cm. After closing the duodenal defect, two tubes were inserted (retrograde duodenostomy and feeding jejunostomy). The majority from the omental patch group leaked (14 from 18 patients; 78%) with a 65% mortality rate. Interestingly, only one death from a study group (5%) and that was not directly related to surgery (fulminant tuberculosis) [12]. A gastrostomy may also be added if required. They concluded that the triple ostomies technique is simple and suitable in the morbid patient compared to other complex surgery [Table 2]. It is crucial to ensure all drains are functioning well, not blocked, and must be regularly flushed. In addition to that, few other authors also believe tube duodenostomy is crucial to decompress high intra-luminal duodenal pressure which is postulated as a cause for stump leakage [24]. Preferably the tube is inserted through a healthy non-inflamed area (lateral duodenostomy) as placing it through chronically scarred tissue is associated with a high leak rate [24]. Another good option is retrograde duodenostomy where the tube is inserted at proximal jejunum and can be fixed to the anterior abdominal wall which results in a shorter intra-peritoneal portion of fistula. Proponents of this approach consider this as an ideal damage control procedure in patients with significant co-morbidities and/or hemodynamically unstable [17].

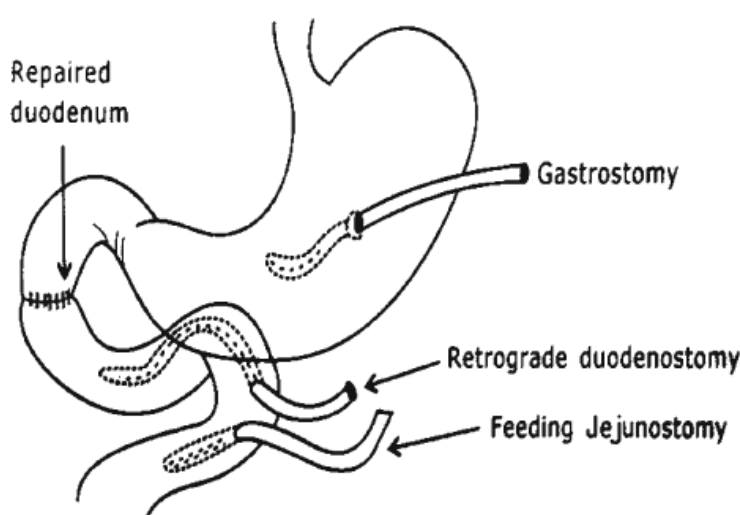


Figure 6. Triple tube ostomies with duodenoraphy for perforated giant duodenal ulcer.

4.6. Conclusion and recommendations

Based on available evidence, any perforated duodenal ulcer of more than 2 cm in diameter is to be defined as a giant ulcer. During an initial surgery, a non-resection omental plug approach with or without triple tube ostomies is advisable. An omental patch or omental-pxy technique can be effectively done for perforation less than 2 cm. The resection approach is preferably reserved for s alvage procedure and must be done in stages in a form of damage control surgery.

Conflict of interest

The authors have no conflict of interest to declare.

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