Immediate Definitive Surgery for Perforated Duodenal Ulcers

A Prospective Controlled Trial

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A prospective, randomized, double-blind trial was conducted in 101 patients to evaluate the safety and benefits of immediate definitive surgery for perforated duodenal ulcers. These patients, who were judged by predefined criteria to be medically fit and to have perforations in chronic ulcers, were randomized to undergo simple closure (35 patients), truncal vagotomy and drainage (VD) (32 patients), or proximal gastric vagotomy with closure (PGV) (34 patients). Patients were followed with endoscopic assessment for up to 39 months. There was no mortality and only a few minor postoperative complications. At 39 months follow-up, the cumulative rates of recurrence were 63.3%, 11.8% and 3.8% after closure, VD, and PGV, respectively (p < 0.001). With the exception of the one recurrence after PGV, all relapses were symptomatic, and eight of these 18 required reoperation. Relapse rates and Visick scores between VD and PGV were not significantly different. Both safe as well as effective, immediate, nonresective, definitive operation is indicated for good-risk patients who have perforations in chronic duodenal ulcers.

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W ITH THE DECLINE in the mortality of perforated duodenal ulcers, there arose considerable controversy over their optimal treatment. Nowadays, the nonoperative approach espoused by Herman Taylor[1] is limited chiefly to cases in which there is spontaneous sealing of the perforation.[2-4] Simple and safe, oversewing or patching the perforation with omentum[5] remains the standard operation in many hospitals.[6-10] However, struck by the high frequency of relapse after simple closure, Yudine, G. L. Jordan, and many others[11-25] adopted the more aggressive surgical policy of immediate definitive operation. Over the past several decades, many retrospective studies have expounded the relative merits of these opposing views. Amidst the debate there lies two fundamental issues. The first consideration is whether emergency curative surgery can be performed as safely as simple closure. The other point is whether the reduction in recurrence achieved by acid-reducing operations warrants the risk of side effects in those pa-

tients who would have remained well after closure alone. In order to critically assess both of these questions, we conducted a prospective, randomized, double-blind trial of immediate definitive operation for perforated duodenal ulcers. In this study, the authors also attempted to evaluate clinical criteria for selecting patients who are likely to benefit from curative surgery.

Patients and Methods

Between November 1978 and August 1981, 216 consecutive patients underwent operation for acutely perforated duodenal ulcers. Patients were eligible for entry into the trial if they had chronic ulcer disease as evidenced by scarring of the duodenum along with an ulcer history of more than three months duration preceding the perforation. Patients who had acute ulcers (no scarring or an ulcer history of less than three months), acute drug ingestion or stress ulceration, pyloric stenosis, or previous ulcer surgery were not included. In addition, individuals with any of the following features were deemed medically unfit or unsuitable, and were also excluded from the study: age above 70 years; preoperative shock (blood pressure below 100 mmHg); poorly controlled concurrent illness (cardiorespiratory, renal or hepatic failure, severe diabetes, steroid usage); laparotomy more than 24 hours from the time of acute onset; gross peritoneal contamination (abscess formation, or the inability to cleanse the peritoneal cavity of fibrin and other debris despite copious saline lavage); and technical inability to perform any of the trial operations satisfactorily. One hundred and fifteen patients were not suitable candidates and reasons for their exclusion are listed in Table 1. One hundred and six of them underwent simple closure, and another nine had vagotomy and pyloroplasty performed because of py-

loric stenosis or reperforation after previous closure. The overall mortality rate for the entire series was 4.6%, and the deaths are described in detail elsewhere.[26] At 36 months follow-up, a cumulative 33.2% of these excluded patients had documented ulcer relapses.

One hundred and one patients consented to participate in the trial. The 94 men and seven women had a mean age of 42.2 (SD 14.5) years. Pre-existing ulcer symptoms were present for a mean average of 70.1 months. The median duration of perforation was 9.4 hours. Cephalothin was administered intravenously to every patient, and this was given before operation in all except five cases. By the numbered, sealed-envelope method, patients were randomly assigned to undergo either closure alone, truncal vagotomy with gastric drainage (pyloroplasty in all except one patient who had a gastrojejunostomy), or proximal gastric vagotomy with closure of the perforation. Operations were performed under general endotracheal anesthesia, and absorbable sutures were utilized for plication. Peritoneal lavage with saline (minimum three liters) was performed in every case, and no drains were used. All patients had primary skin closure.

The comparability of the three study groups is shown in Table 2. The average operating time was 43 (SD 12), 82 (SD 22), and 127 (SD 33) minutes for closure, vagotomy and drainage, and proximal gastric vagotomy with closure, respectively (p < 0.001).

Early assessment during hospitalization included mortality, septic and other complications, interval until an oral diet was tolerated, and length of hospital stay. After discharge from the hospital, the patients were not given any antacids or other antiulcer medications beyond the first month after operation. Each patient was evaluated independently by two surgeons who were unaware of the type of operation performed. A questionnaire form incorporating a modified Visick score[27] was completed at each visit. Endoscopy was performed in patients who developed any symptom suggestive of ulcer disease. In addition, 56 of the 71 patients who remained asymptomatic for more than a year after operation consented to elective endoscopy. A diagnosis of

TABLE 1. *Reasons for Excluding 115 Patients from the Controlled Trial of Perforated Duodenal Ulcers*

Reason for Exclusion	No. Patients*
Preoperative shock	10
Concurrent illnesses	17
Duration of perforation >24 hours	35
Gross peritonitis	22
Age above 70 years	32
Ulcer history < 3 months	61
Minimal duodenal scarring	46
Previous ulcer operation	6
Technically difficult/pyloric stenosis	8

* Seventy-two patients had more than one reason for exclusion.

relapse, symptomatic or asymptomatic, was confirmed either by endoscopy or by reoperation. Endoscopic evidence of recurrence consisted of an active ulcer crater or marked mucosal inflammation along with pyloric stenosis. Late follow-up assessment comprised ulcer relapse (including complications), secondary reoperations, and Visick scores.

Statistical analysis was by one-way analysis of variance, Kruskal–Wallis comparison of nonparametric data, and the generalized Wilcoxon comparison of recurrence-free rates determined by Kaplan–Meier actuarial analysis.[28] Statistical significance was accepted at the 1% level.

Results

Hospital Results

There was no hospital death, wound, or intraperitoneal infection among the 101 trial patients. Pneumonia was the only postoperative complication, and this occurred in one patient after vagotomy and pyloroplasty, and in three others following proximal gastric vagotomy with closure. An oral diet was taken after a median average of three days after operation, and the average hospital stay was five days in each of the three groups. There was no statistical difference in any of these parameters among the three groups.

TABLE 2. *Clinical Profile of the Three Trial Groups of Patients*

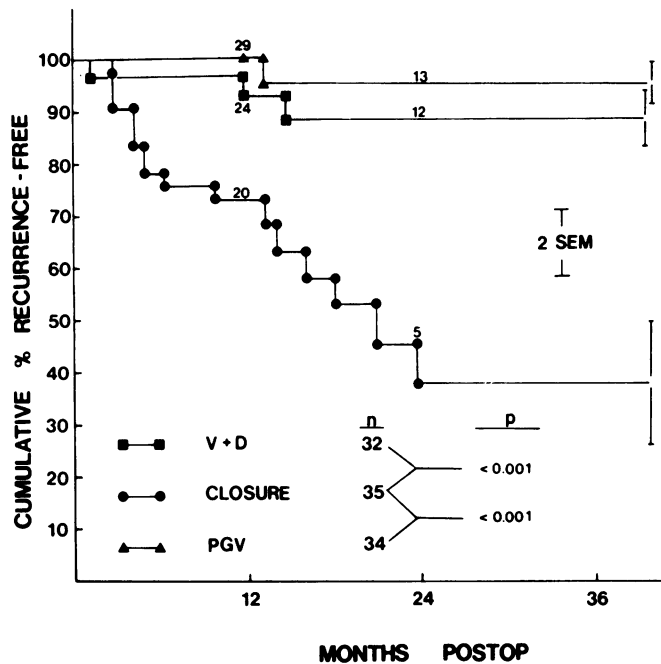|	Operation			Significance p
	Closure Alone	Vagotomy and Drainage	Proximal Gastric Vagotomy and Closure	
No.	35	32	34	—
Men, No.	31	31	32	NS
Age, mean ± SD years	41.5 ± 15.2	42.6 ± 14.4	42.7 ± 14.3	NS
Previous ulcer symptoms, mean ± SD mos	59.5 ± 100.8	72.0 ± 55.0	79.2 ± 82.7	NS
Duration of perforation, median hrs	9.0	8.5	12.0	NS
Follow-up period, mean mos	20.5	20.8	20.5	NS

FIG. 1. Actuarial rates of recurrence after surgical treatment of perforated duodenal ulcer. V + D = vagotomy and drainage; PGV = proximal gastric vagotomy with closure.

Follow-up Results

On follow-up extending up to 40 months after operation, 21 patients complained of ulcer-like symptoms, and 18 of them had relapses confirmed. Of these, 12 had recurrent pain only, three had bleeding ulcers as well as pain, two obstruction (one with concomitant bleeding), and one reperforation. Eight patients underwent reoperation of which five were nonelective procedures for major complications. Recurrent symptoms have subsided in ten patients, nine of whom are still receiving H2-antagonist drugs. Only one patient was found to have an incidental asymptomatic ulcer on routine endoscopy. This patient had undergone proximal gastric vagotomy with closure and is currently well without any medication.

Although relapses were not confined to the closure alone group, they occurred significantly less often in

TABLE 3. *Visick Scores After Operation for Perforated Duodenal Ulcers*

	Visick Scores			
Operation	1	2	3	4
Closure only	18	2	0	15
Vagotomy and drainage	25	4	0	3
Proximal gastric vagotomy and closure	30	3	0	1*

* Asymptomatic recurrence.

those who underwent definitive operation (Fig. 1). Ulcer recurrence occurred at a steady rate after closure alone and was especially notable during the first two years after operation. At 39 months follow-up, the actuarial recurrence-free rates after closure alone was 36.7%, which was significantly lower than the 88.2% and the 96.2% seen after vagotomy with drainage and proximal gastric vagotomy with closure, respectively ($p < 0.001$). Three symptomatic recurrences developed after vagotomy and drainage at 1, 12, and 15 months after operation. The endoscopic recurrence at one month after surgery was in a patient who had both transected vagi confirmed histologically, and a negative Hollander test after operation. This case probably represents an unhealed ulcer rather than a recurrence because repeat endoscopy ten months later showed no ulcer, and the patient has remained asymptomatic ever since. The other two recurrences after vagotomy and drainage lacked histological confirmation of the vagi and had positive Hollander tests suggesting incomplete vagotomies; both of these patients are well after reoperation. Although there was only one recurrence after proximal gastric vagotomy with closure, this result was not statistically superior to that achieved by vagotomy and drainage.

Excluding the patients who had recurrences, there was no appreciable difference in Visick scores among the three groups (Table 3). Nearly all patients in the proximal gastric vagotomy with closure group had Visick I scores. No instance of symptomatic dumping or gastroesophageal reflux was encountered in any patient despite careful and repeated inquiries. One patient initially noted episodic diarrhea which subsequently abated. The most common symptom elicited on questioning was vague postprandial epigastric fullness which usually resolved spontaneously several weeks after operation.

Discussion

Judicious patient selection enables immediate definitive operation to be performed as safely as simple closure for perforated duodenal ulcers. In this prospective study, curative surgery neither incurred any mortality or serious morbidity, nor did it produce any delay in tolerating an oral diet after operation or prolongation of the hospital stay. The readily determined clinical features employed in this study have been shown here and elsewhere[12,16,18] to reliably identify patients who might safely undergo curative operation. In a detailed analysis of operative risk factors in perforated ulcers,[26] concurrent illness, preoperative shock, and perforation exceeding 48-hours duration were found to be the major determinant features that characterized the high-risk patient who should undergo closure alone. These risk

factors being present in only 14.8% of our 216 patients would indicate that definitive operation is feasible in most patients with perforated ulcers.

Compared with simple closure, both vagotomy and drainage as well as proximal gastric vagotomy with closure significantly reduce the rate of recurrence after perforation. Because it is not uniformly accepted that all patients have an appreciable tendency to relapse after simple closure, the study was confined to patients who had chronic ulcer disease as manifested by duodenal scarring and pre-existing ulcer symptoms. Among these patients with comparable ulcer disease, the cumulative recurrence-free rates at 39 months follow-up were 36.7%, 88.2%, and 96.2% for closure alone, vagotomy and drainage, and proximal gastric vagotomy with closure, respectively. After simple closure, there is an inexorable rise in both the number of patients who develop recurrent symptoms as well as the proportion who require reoperation.[14,29,30] In view of the young average age of patients who have perforated ulcers,[3,9,10,23,25] and also our relatively short length of follow-up, the already large differences between the closure alone and definitive operation groups may become even more pronounced on subsequent evaluation. These observations underscore again the imperative of close postoperative surveillance, ideally with routine endoscopic monitoring, in patients after simple closure. It also strengthens the impression that perforation is uncommonly an isolated, self-limiting complication of chronic ulcer disease; indeed, it seems to designate an ulcer diathesis that is unlikely to resolve without additional treatment.

Experience with emergency curative operations for perforated ulcers was initially confined to gastric resection.[11,12,21] To avoid the disabling side effects occasionally seen after gastrectomy, the authors compared nonresective truncal and proximal gastric vagotomy operations. Both of these procedures are technically feasible for perforated ulcers as shown previously by Johnston, by Jordan, and others.[3,4,13,15,17,18,23-25] Emergency proximal gastric vagotomy for perforation was associated with fewer relapses and better Visick scores than vagotomy and drainage, but these differences were not statistically significant with the relatively few patients in this study. Other investigators also reported predominantly Visick I scores (or excellent results) whenever proximal gastric vagotomy has been applied to acute perforations.[15,17,19,20,22,24,25] In an elective setting these two operations have similar relapse rates, but proximal gastric vagotomy produces fewer side effects.[27,31-33] Most recurrent ulcers after proximal gastric vagotomy develop within three years of operation. Thus, a longer period of observation is needed to ascertain whether this operation when carried out under emergency conditions will yield long-term results comparable with that achieved by vagotomy and pyloroplasty or antrectomy, or elective proximal gastric vagotomy.

The definitive operation chosen for perforated ulcers will depend on the degree of stenosis and deformity as well as the experience and preference of the surgeon. Jordan and Korompai[18] in comparing truncal vagotomy and drainage with vagotomy and antrectomy for perforated ulcers in a controlled trial found no important differences in their side effects. Hence, they recommended vagotomy and antrectomy because of a lower recurrence rate. However, the reported deaths caused by anastomotic complications[12,23] may deter some surgeons who believe that gastric resection under these circumstances is an inherently more dangerous procedure.[8] Among more than 350 collected cases of proximal gastric vagotomy performed for perforated ulcers, there have been only two recorded deaths.[15,17,19,20,22,24,25] Possibly, truncal vagotomy and pyloroplasty may receive broader acceptance, while proximal gastric vagotomy may be preferred by those who are already adept at this operation.

Despite the manifold advantages of immediate definitive operation, many surgeons continue to advocate closure alone for perforated duodenal ulcers.[6-10,30] The major reasons supporting their view include the fact that curative surgery is assumed to entail greater mortality and morbidity, that not all plicated perforations eventually recur and necessitate reoperation, that relapses may be amenable to drug treatment after operation, and that medically recalcitrant or relapse-prone cases may undergo elective secondary reoperation. In weighing these arguments, one point overlooked too often in treating perforated ulcers is that just as in persistently bleeding ulcers, the primary issue is not whether to operate on the patient but rather which operation is most optimal for him. Compared with patients who do relapse after closure alone, the authors have shown that definitive operations can be performed as safely, and that they drastically lower the rate of recurrence in chronic ulcers and thereby obviate any subsequent medical or surgical treatment. Measured against those who would not have recurred after closure, nonresective operations do not give rise to undue troublesome side effects in the vast majority of patients. Consequently, the authors believe that the performance of nonresective definitive operation, especially proximal gastric vagotomy, for perforated ulcers reduces the above objections to mostly theoretical concerns.

No doubt, because ulcer disease behaves in a complex and heterogenous manner, the propensity to relapse will vary from one individual to another. Accordingly, some surgeons restrict definitive operation to patients who are at a higher risk for relapse.[3,4,12,14,16] Unfortunately, most features that purportedly identify individuals prone to

relapse yield imperfect results. Just as patients who have perforated chronic ulcers do not invariably develop relapses, neither are those who have an acute ulcer history completely immune to recurrence.[7,10,13,22,34] The authors previously reported on the fate of 60 patients who had an acute ulcer history of less than three months duration before perforation.[34] Even though these patients fared significantly better after simple closure than those who had a chronic history (more than three months), 29.5% of the acute history group developed symptomatic relapses within two years of operation. As noted by Jordan and by Greco and Cahow,[8,18] it may well be possible to predict the likelihood of relapse in general categories of patients, but as yet this may not be accomplished with assurety in individual cases. More dependable clinical parameters that foretell relapse are needed to refine the selection of patients for curative surgery. At present, the authors feel that definitive operations are desirable for perforated ulcers in patients who have chronic scarring of the pyloroduodenal area as well as an antecedent ulcer history.

Perforation, though usually less life-threatening than major hemorrhage, is nonetheless an important surgical complication of duodenal ulcer disease. The authors believe that perforated ulcers should be regarded in a similar fashion as severely bleeding ulcers, and that both of these complications frequently require curative surgery for sustained relief. Although closure alone offers a safe and acceptable solution, nonresective definitive operation should be undertaken more often in the treatment of perforations in chronic duodenal ulcers.

Acknowledgment

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