

A Prospective Evaluation of Vagotomy-Pyloroplasty and Vagotomy-Antrectomy for Treatment of Duodenal Ulcer

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THERE is no general agreement which considers any specific operative procedure to be optimal for treatment of duodenal ulcer. Selection of a particular operation is based often on intuition, emotional attachment or personal bias. Comparative results of different procedures have been significantly limited because they were performed in non-randomized patients. Frequently the patients were drawn from different populations and the procedures were performed by surgeons who differ in training, indications for operation and methods of evaluation. There are few reports of controlled, prospective studies to evaluate the merits of various operative procedures for the treatment of duodenal ulcer. Our study was designed to compare vagotomy and pyloroplasty with vagotomy, antrectomy and gastroduodenostomy in patients with duodenal ulcers who were candidates for elective operation.

Although proponents of vagotomy-pyloroplasty concede that it is associated with a higher rate of recurrence than is vagotomy-antrectomy, they conclude that it is the optimal choice because of its lower rates of mortality and morbidity.^{3, 4} Others are equally convinced of the superiority of vagotomy-antrectomy because of its asso-

ciation with acceptable mortality and morbidity rates without increased risk of recurrence.^{17, 19} Because of little controlled experience with these two widely used operations which permitted an objective comparative evaluation, our study was considered both ethical and essential.

Plan of Study

Two hundred consecutive male, veteran patients requiring elective operation for duodenal ulcer were studied. Cases accrued to the study between November, 1964 and October, 1967. All clinical data, operative information, postoperative and follow-up data were collected by the authors. Each patient was assigned preoperatively to either truncal vagotomy and Heineke Mikulicz pyloroplasty (V-P) made with one layer of interrupted silk sutures or vagotomy, antrectomy and gastroduodenostomy (V-BI) by selection of operative instructions from a randomized series held in the custody of the study secretary. Surgeons were given the option of substituting gastroenterostomy (V-GE) for pyloroplasty or Billroth II for a Billroth I anastomosis if the pathology involving the duodenum was considered too hazardous to permit the operation indicated by protocol.

In the original randomization, 98 patients were assigned V-P and 102 V-BI. In ten patients, the protocol was violated and a drainage operation performed instead of a resection because resection was considered too hazardous. The operations actually performed were V-P in 94, V-GE in

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TABLE 1. *The Number of Patients Expected and Those Actually Studied at Yearly Intervals After Operation*

		1	2	3	4	5
V-D	Patients expected	106	102	95	53	21
	Patients studied	102	95	84	39	21
V-R	Patients expected	92	90	81	52	21
	Patients studied	90	81	77	45	19

14, V-BI in 73 and V-BII in 19 patients. For discussion, these patients will be divided into two groups, vagotomy-drainage (V-D) 108 and vagotomy-resection (V-R) 92.

Patients were examined in the clinic 1 and 3 months after operation and in the hospital every 6 months up to 3 years and then every year thereafter. Patients were given a standard interview by one of the authors at each follow-up visit. To obtain an impartial evaluation, patients were also interviewed at 3 years by an independent observer not involved in the study.

Upper gastrointestinal roentgenograms were performed prior to operation, 6 months after operation and at other such times as indicated. A two hour basal gastric analysis and a two hour augmented Histalog (Betazole) secretory response (1.7 mg./Kg.)²¹ were performed before operation. The Histalog test was waived if contraindicated by a history of asthma. At each follow-up visit beginning at 6 months,

a 1 hour basal test was followed by a 2-hour Histalog secretory test. On the following day, a 2-hour basal test was followed by a 2-hour insulin test (0.2 u./Kg.). A provocative "dumping" test was performed at 6 months using 150 ml. of 50% glucose administered by stomach tube. The patients were observed for 1 hour for symptoms and physical signs suggestive of "dumping." Six months later a second provocative test was performed using a test meal of 240 ml. of half and half cream and 100 ml. of 50% glucose. All tests were made in a quiet, secretory laboratory by the same, compulsive personnel to insure that the patients were taking no medication, had been properly fasted and their stomachs were empty prior to testing. All tests were begun at 7:00 a.m. to avoid stimulation by the sight or smell of breakfast. Gastric tubes with multiple holes and an air vent were positioned fluoroscopically and connected to Stedman pumps exerting 4 cm. water suction pressure. Throughout each test, patients were under constant surveillance to adjust position and insure patency of the tubes. Gastric juice was collected at 15-minute intervals and aliquots titrated to pH 7.3 with 0.1 N NaOH using an automatic titrator. Total acid, total volume and pH were recorded.

Clinical Material

The number of patients who should have been available for study and those actually studied at each yearly interval are recorded in Table 1. Of the patients lost to follow-up, there were two operative deaths in the V-D group. There were eleven unrelated subsequent deaths, six in the first year, four in the third year, and one in the fifth year. Seven of the eleven patients were in the V-D category and four were in the V-R group. Thirteen patients temporarily lost to follow-up were seen within the past 2 years and have been studied an average of 32 months. Six patients considered perma-

TABLE 2. *Age Distribution of Patients Undergoing Operation*

Age (Yrs.)	V-D		V-R	
	No. of Patients	%	No. of Patients	%
<40	17	16	27	29
40-49	40	37	35	38
50-59	27	25	16	18
>60	24	22	14	15
Totals	108	100	92	100

TABLE 3. *Primary and Secondary Indications for Operation*

		Number and Per Cent of Patients							
		Intractability		Bleeding		Obstruction		Perforation*	
Operation		No.	%	No.	%	No.	%	No.	%
Primary Indication	V-D	70	66	24	22	12	11	1	1
	V-R	71	78	12	13	6	7	2	2
Secondary Indication	V-D	76	72	24	22	6	6	0	0
	V-R	61	68	21	24	5	6	2	2

* Recent reperforation and continued intractability.

nently lost were studied an average of 5 months.

The age distribution of patients is listed in Table 2. Random assignment of patients to operation resulted in a greater percentage of patients below age 40 undergoing resection and a greater percentage of patients over 60 undergoing drainage procedures. The indications for operation are listed in Table 3. Intractability was the most common indication. The significance and reliability of a careful clinical history was the most important evidence upon which the diagnosis of ulcer and the decision whether or not to recommend operation for intractability were made. In their past histories, 193 patients had had pain, 29 had required blood transfusions, 28 had perforated and 19 had evidence of obstruction. Twenty-one patients had significant pulmonary disease and 56 per cent of all patients had type O blood. The symptoms at the time of operation were similar to those the patients had had in the past with the exception that 43 of 44 patients who required blood preoperatively had never required a previous transfusion. Only one of the 28 patients with obstruction as the primary indication for operation required transfusion. The indications for operation in the 28 patients that had previously perforated was intractability in 22 (three had perforated twice) bleeding in three and obstruction in three.

The roentgenograms were interpreted as demonstrating an ulcer in 99 patients, de-

formity suggesting the existence of ulcer in 190 and no evidence of ulcer in ten. At the time of operation on these ten patients, there was an active ulcer in seven and evidence of a healed ulcer in three.

Although gastric analyses were performed preoperatively, they were of limited value in establishing a diagnosis or in making the decision whether or not to operate. Failure of a patient to secrete acid under basal conditions suggested that either the study was improperly performed or that no ulcer was present. Extremely high acids suggested the possible co-existence of a Zollinger-Ellison tumor although none was found in this study. Table 4 shows the range of acid recovered during the 2-hour preoperative basal secretory tests. For comparison, the range of acid secretion in 102 control patients without gastrointestinal complaints is provided. There was a greater number of low secretors in the V-R group than in the V-D group but the number of patients secreting in excess of 10 mEq. per hour was greater in the V-R than in the V-D group.

Operation and Operative Findings

Nine operations were performed by attending staff. Fourth year residents performed 89 and second and third year residents performed 102. A staff member was available should the need arise during operations and served as the first assistant in 66 cases, primarily when second or third year residents were operating.

TABLE 4. *Basal Secretory Rates for Preoperative Patients and Controls*

No. of Patients	Per Cent of Patients		
	V-D 80	V-R 73	Controls 102
MEq.HCl/2 hrs.			
0-2	7	18	46
2.1-4	11	14	15
4.1-6	19	14	13
6.1-8	21	7	13
8.1-10	13	8	2
10.1-20	20	24	10
>20	9	15	1

At operation, the primary active ulcer or the residual scar was located in the duodenum in 184 and in the pre-pyloric area, at the pylorus or just proximal to the pylorus, in 16 patients. A second ulcer was present in the duodenum in 39, in the pre-pyloric area in two and in the gastric fundus in two patients. The primary ulcer was resected in 77 of 92 patients treated by resection.

Secondary operative procedures included appendectomy in 41 patients, hiatal hernia repair in 11, cholecystectomy in nine, ventral hernia repair in six, splenectomy in four, liver biopsy in two, pancreatic biopsy in two, an aorta-bilateral femoral bypass graft in two, resection of a leiomyoma of the jejunum in one and a variety of other intra- and extra-abdominal minor procedures.

The average operating time required by the Chief Residents was 36 minutes less for V-P than that required for V-BI. Blood transfusions were administered during operation or in the immediate postoperative period to 19 patients, 11 undergoing V-D and 8 V-R. Thirteen of the 19 patients received only one unit. Six of 13 patients given a single transfusion had received multiple transfusions preoperatively.

All tissue suspected of being vagus nerve was submitted for pathologic confirmation. There were 43 patients from whom more than two specimens were reported as nervous tissue and three patients from whom

only one specimen was identified as nerve. This was recognized at operation in one of the three patients by frozen section. Further search failed to identify the second nerve in that instance. Nevertheless, each of these three patients was believed to have a complete vagotomy for they have been studied for more than 4 years, have had multiple negative Hollander tests and have shown no evidence of recurrence. On the other hand, identification of two specimens of nervous tissue does not guarantee complete vagotomy, for two specimens of nerve tissue were removed at operation in all patients subsequently shown to have incomplete vagotomies.

Immediate Postoperative Results

In the series of 200 patients, there were two operative deaths; both occurred in the V-P group. One patient, 73 years old, died of pulmonary embolus while ambulating, 36 hours postoperatively. The other patient, 33 years old, developed hepatitis and a fistula from the pyloroplasty closure. He died of hepatic failure 20 days after operation.

The average time that nasogastric suction was required postoperatively and the average time of starting liquid and solid feedings were essentially the same for patients undergoing V-D as they were for those having V-R. The 6 days of postoperative gastric suction required for patients operated on with obstruction was only two more than the average required by the remaining patients. That the time was not longer, was attributed to the practice of instituting gastric decompression for 3 to 5 days prior to operation.

Early postoperative complications related to operative technic are summarized in Table 5. There were 16 wound infections, 11 staphylococcal, four enteric and one streptococcal, equally divided between the V-D and V-R groups. Six (15%) of 41 patients who had incidental appendectomies developed wound infections, one of which

TABLE 5. Major Complications Associated with Operative Technic

Complications	V-P	V-GE	V-A-BI	V-A-BII
Total No. of Patients	94	14	73	19
Wound infection	7	1	5	3
Wound disruption	2	0	0	0
Stomal dysfunction	7	3	1	1
Reoperation for stomal dysfunction	2	2	0	1
Duodenal fistula	2	0	1	1
Reoperation for intestinal obstruction	1	0	0	0
Patients hospitalized postoperatively in excess of 10 days	29	7	18	12
Average postoperative hospitalization (days)	12	16	11	18

was a subphrenic abscess. There were four duodenal fistulae, two occurred after V-P and two after V-R. Wound dehiscence followed premature removal of retention sutures in one patient with severe emphysema. He developed a fistula from the pyloroplasty that healed spontaneously. A second patient, one of the two operative fatalities, was reoperated on the 12th day for an abscess in juxtaposition to the pyloroplasty that resulted from a leak at the suture line. Both patients had had incidental appendectomies. A third patient with arrested bilateral tuberculosis developed an enteric wound infection after V-BI for a giant ulcer that was densely adherent to the colon. Subsequently, a gastroduodenal colic fistula developed which was resected 3.5 months later. This complication was

best explained by a leak at the anastomosis or of the colon rather than a complication of a marginal ulcer. The fourth fistula was manifested by a wound abscess after V-BII and incidental appendectomy. The wound was drained and the fistula healed without reoperation. Stomal dysfunction occurred in 12 patients, ten after V-D and two after V-R. Reoperation was required after V-P in two patients, V-GE in two and V-BII in one. One patient required lysis of adhesions for intestinal obstruction within the first month after V-D. The mean postoperative hospital stay was essentially the same after V-D as after V-R.

Follow-up Studies

The gastrointestinal post-operative complaints elicited from the patients are tabu-

TABLE 6. Frequency of Postoperative Gastrointestinal Symptoms

Years	V-D					V-R				
	1	2	3	4	5	1	2	3	4	5
Patients studied	102	95	84	39	21	90	81	77	45	19
No. of patients with symptoms										
Pain	10	11	8	3	0	5	8	10	2	0
Dysphagia	23	8	10	4	0	14	8	8	5	2
Early fullness	35	14	12	5	0	44	24	18	10	4
Nausea	28	14	12	5	2	16	11	15	10	4
Vomiting	17	12	9	3	2	21	18	17	10	5
Abdominal cramps	12	9	10	6	2	12	14	8	2	0
Sweating	14	15	18	10	3	15	21	26	8	4
Palpitation	12	13	18	8	3	10	14	15	5	4
Weakness	26	21	18	10	2	24	26	26	11	6
Need to lie down after eating	15	13	18	6	1	10	18	18	6	4

TABLE 7. *Change in Weight* One Year After Operation*

V-D			V-R		
Weight of Patients Preop.		Weight of Patients Postop.	Weight of Patients Preop.		Weight of Patients Postop.
under	— 8	under — 1 normal — 6 over — 1	under	— 8	under — 4 normal — 4 over — 0
normal	— 48	under — 4 normal — 35 over — 9	normal	— 47	under — 1 normal — 37 over — 9
over	— 40	under — 0 normal — 11 over — 29	over	— 23	under — 0 normal — 8 over — 15

* Pre- and postoperative weights are based on Metropolitan Life Insurance Table of Ideal Weights.

lated in Table 6. "Pain" refers to all abdominal discomfort identified as pain and was not limited to the type of pain experienced by the patient before operation. More patients acknowledged some type of discomfort associated with swallowing than was anticipated. Usually, these symptoms were minor and consisted only of the sensation of food sticking at the lower end of the sternum with the first few bites of a meal. While this complaint disappeared spontaneously early in the postoperative course in some and was improved by dilation shortly after operation in others, significant dysphagia persisted in a few. In some patients persistent dysphagia was due to esophageal motor disorders that either followed vagotomy or that were present but asymptomatic preoperatively and became manifest postoperatively. Evidence of a hiatal hernia and/or gastroesophageal reflux was demonstrated in 18 patients after V-R and 14 patients after V-D. These patients complained of dysphagia and/or the symptoms of gastroesophageal reflux that were more severe after V-R than after V-D. Although it was difficult to accurately assess the number of complaints referable to hiatus hernia because of the variability in symptomatology, the incidence was sufficiently impressive to suggest that the hiatus

should be reconstituted after transabdominal, periesophageal trunkal vagotomy.

Many patients complained of early fullness after V-D as well as V-R. This sensation caused patients to limit the size of their meals. Nausea and vomiting were more frequent after V-R than after V-D. Cramps, nausea and vomiting generally resulted only when patients knowingly overate.

Vasomotor symptoms of sweating, palpitation and weakness were often difficult to evaluate. Patients sometimes recognized that these symptoms occurred in mid-morning or mid-afternoon and were relieved by eating a small snack. Some patients thought these symptoms were due to overwork, particularly in hot weather. In some patients, vasomotor symptoms clearly occurred after eating and were attributed to "dumping." They could usually be avoided by dietary adjustments and in no instance were they disabling. The vasomotor symptoms of "dumping" appeared evenly distributed between V-D and V-R. There was no difference in the frequency of any of the gastrointestinal symptoms recorded for drinkers compared with non-drinkers or for smokers compared with non-smokers.

Based on ideal weights published by the

TABLE 8. Frequency of Diarrhea after Operation

Years	V-D					V-R				
	1	2	3	4	5	1	2	3	4	5
No. of patients studied	102	95	84	39	21	90	81	77	45	19
% With any diarrhea	31	29	26	18	5	21	17	13	18	11
% With significant diarrhea	19	15	13	13	5	16	14	12	16	5

Metropolitan Life Insurance Company, patients were divided into three categories; underweight, if preoperative weight was more than 10 per cent below ideal weight; normal if within plus or minus 10 per cent of ideal weight; and overweight if preoperative weight was more than 10 per cent of ideal weight. There was essentially no difference in the frequency and magnitude of weight changes observed after V-D and V-R (Table 7).

A third of the patients in each operative group had soft bowel movements postoperatively and nearly all patients constipated preoperatively were improved. Diarrhea occurred commonly and was observed with greater frequency after V-D than after V-R. Diarrhea that occurred early after operation tended to improve with time but

that which developed later was more persistent and usually more bothersome to the patient. Arbitrarily, diarrhea was considered significant if the patient had one or more attacks of diarrhea per week, lasting 2 or more days and consisting of three or more stools per day or if he had explosive diarrhea which resulted in soiling. Using these criteria, significant diarrhea occurred with nearly equal frequency after V-D and V-R (Table 8).

Nearly all patients were able to eat an ordinary diet postoperatively. Not infrequently an individual learned to exclude certain items of food because he found that they produced cramps, "gas" or diarrhea. Milk, sweets and leafy green vegetables were common offenders. Rather than what the patient ate, how much and how

TABLE 9a. Patients Reoperated for Suspected Recurrence

Patients	Preop. Basal mEq./hr.	Orig. Operation	Time of Recurrence (months)	Insulin Test	Indication of Recurrence	Reoperation Performed	Operative Abdominal Findings	Nerve Tissue Re-ected at 2nd Op	Postop Insulin Test	Postop. Results
1. C. G.	4.1	V-P	12	+	Pain	TTV*	—	+	+	Asymp.— (3½ yrs)
2. T. S.	1.3	V-P	19	+	Pain	TTV	—	+	—	Asymp.— (4 yrs)
3. H. V.	3.9	V-P	12	+	Bleeding	TTV	—	+	+	Asymp.— (3 yrs)
4. G. D.	3.3	V-P	24	+	Pain and Bleeding	TTV	—	+	—	Asymp.— (2 yrs)
5. A. B.	2.1	V-P	12	+	Pain	Gastrotomy TAV**	No Ulcer	+	+	Intestinal obstructions (2 yrs)
6. D. W.	13.5	V-P	9	+	Pain and Obst.	Gastrotomy TAV	Pre-Pyloric Ulcer	+	+	Pain (21 mo.) (?Recurrence)
7. A. G.	2.7	V-P	11	+	Pain	Antrectomy and BI	Duodenal Ulcer		+	Asymp.— (1½ yrs)
8. M. M.	6.3	V-P	32	+	Bleeding	TAV	Gastric Ulcer	0	Equiv-ocal	Asymp.— (1½ yrs)

* Transthoracic vagotomy.

** Transabdominal vagotomy.

TABLE 9b. *Patients Regarded as Suspicious for Recurrence but not Reoperated*

Patients	Preop Basal mEq./hr.	Orig. Op.	Time of Recurrence of Symptoms	Insulin Test	Indication of Recurrence
1. W. P.	3.5	V-P	13 mo.	+	Pain
2. H. G.	4.2	V-GE	33 mo.	+	Pain
3. R. M.	1.7	V-P	48 mo.	+	Pain

fast he ate, were more important in terms of producing postprandial complaints. Although patients in both groups acknowledged with equal frequency the feeling of early fullness during a meal, those undergoing V-R admitted to eating smaller meals more often than those having V-D. After the first and second years, 11 and 8 per cent of the patients having V-D ate smaller meals while at the same time periods, 28 and 34 per cent of the patients undergoing V-R ate smaller meals than before operation.

The work record after operation was essentially the same for patients in both groups. The type of operation performed had little effect on the rehabilitation of patients who had worked part time or had not worked at all preoperatively. Many of these patients failed to work postoperatively because they were elderly and already retired rather than because of any adverse effect of the operation performed. Of the patients working full-time before operation, 85 per cent of those who had V-R returned to full and part-time work at the end of one year compared with 86 per cent of patients who had V-D.

Eight patients have undergone reoperation for recurrent ulcer (Table 9a). All of these patients were in the V-D group. Four were treated by trans-thoracic vagotomy, three by transabdominal vagotomy, and one by antrectomy. An ulcer was present in three of the latter four patients. One and a half to 3½ years after operation, the Hollander insulin test remains positive in five, is suspected of being positive in one and is negative in two of the patients who underwent reoperation. All are asymptomatic ex-

cept for one patient. Currently, this patient and three others (Table 9b) who also had V-D are suspected of having recurrent ulcer.

Ten patients with positive postoperative insulin tests have undergone re-vagotomy, seven for treatment of recurrent ulcers and three performed incidental to other intra-abdominal procedures. In these patients, the insulin test remains positive in six, negative in two and equivocal in two. These results indicate the unreliability of re-vagotomy to convert a patient with a positive Hollander test to a negative one. This supports a similar observation made by Woodward.²⁰

In addition to reoperation for recurrent ulcer, early stomal obstruction and fistulae, there have been a variety of other operations performed that were directly related to the gastric operations. Late stomal obstruction requiring reoperation occurred in two patients 2 months and 6 months after Billroth I anastomosis. These were both due to adhesions between the liver and the anastomosis. One patient had splenectomy at the time of vagotomy and pyloroplasty and 2 years later required internal drainage of a pancreatic pseudocyst. Hiatal hernia necessitating repair developed in this patient and in five others. Three occurred after V-D and three after V-R. Lysis of adhesions for intestinal obstruction in three patients, repair of an incisional hernia in one patient and caudal pancreatectomy for pancreatitis 3 years after operation in one patient were performed.

Results of Postoperative Gastric Studies

To test completeness of vagotomy, gastric analysis was performed utilizing the

TABLE 10. Results of Hollander Insulin Tests Performed Six Months to Five Years after Operation

	V-D			V-R		
	No. of Patients	No. Valid Tests	% Reduction in Max. Hist.	No. of Patients	No. Valid Tests	% Reduction in Max. Hist.
All Patients	92	300		85	259	
All tests negative	46	130	89	74	229	97
All tests positive	17	53	66	3	3	77
Both pos. and neg. tests*	29	117	67	8	27	82

* Any single positive test results in patient being classified as "positive Hollander."

insulin hypoglycemic stimulation test described by Hollander.¹² This test was performed 559 times on 177 patients from 6 months to 5 years after operation. A summary of the data is recorded in Table 10. An additional 45 tests were performed but the results were invalid since glucose levels after insulin failed to drop at least 50 per cent below the control levels and to below 40 mg./100 ml. An average of three valid tests were performed in each patient. All tests were negative in 50 per cent of patients after V-D and 87 per cent of patients after V-R. If the results of any single test was positive, that patient was classified as having a positive Hollander test even if other tests were negative. In 14 of the 29 drainage patients and five of the eight resection patients who had both positive and negative tests, the first tests were negative. Had these been the only tests performed, we would have erroneously concluded that 62 per cent of the V-D patients and 94 per cent of the V-R patients had a negative insulin test.

The basal and the augmented Histalog gastric secretory tests were significantly reduced by both V-D and V-R but the reductions were greatest after V-R (Table 11). The postoperative reduction in basal secretion and the augmented Histalog stimulation test may be equally if not more informative than the Hollander test in postoperative evaluation of operative procedures to reduce acid secretion in the stomach.

Following administration of the meal for the provocative "dumping" test, a number of observations including the urge to defecate, the occurrence of a loose stool, weakness, dizziness, flushing, headache, cramps, sweating and nausea were made. Pulse and blood pressure were measured at 5-minute intervals. Many of the patients had some of the signs and symptoms of "dumping" but none demonstrated the severe vasomotor disturbances that occur with disabling dumping. Arbitrarily, response to the provocative test was considered significant if a patient's systolic pressure fell 10 or more mm. Hg, the pulse rate increased

TABLE 11. Mean of the Basal and Maximal Histalog Gastric Secretory Responses Six Months after Operation

		V-D	V-R
		Mean ± S.D.	Mean ± S.D.
Basal (mEq.HCl/2 hrs.)	PreOp.	9.16 ± 7.51	10.54 ± 11.60
	PostOp.	1.20 ± 2.34	0.05 ± 0.13
Histalog (mEq.HCl/2 hrs.)	PreOp.	64.75 ± 22.07	68.53 ± 23.75
	PostOp.	15.68 ± 12.60	3.30 ± 5.07

TABLE 12. *Patient's Evaluation One to Five Years after Operation*

Operation	Years Postop	No. of Pts. Studied	Much Better (%)	Some Better (%)	No Change (%)	% Worse
V-D	1	102	90	6	0	4
	2	95	86	12	1	1
	3	84	89	9	1	1
	4	39	87	10	0	3
	5	21	90	5	5	0
V-R	1	90	86	8	0	6
	2	81	85	13	1	1
	3	77	83	13	3	1
	4	45	89	11	0	0
	5	19	84	11	5	0

more than 20 beats per minute and the patient had a loose bowel movement within 30 minutes after completion of the test. Using these criteria, there were positive responses in seven of 85 patients having V-D and 19 of 92 patients having V-R. The test was of little value in recognition of patients who had clinical "dumping" for the test was as often positive in those who had no symptoms of "dumping" as in those who did.

Evaluation of Patients

The patient's last evaluation of his condition for each postoperative year is recorded in Table 12. There was no difference in the evaluations made by patients in the two groups, for 86-90 per cent of patients after V-D and 83-89 per cent of patients after V-R considered themselves much better as a result of operation. The

author's evaluation was considered more reliable even though it was based on subjective and often leading questions. Based on our interviews, patients were classified as: 1) asymptomatic; 2) improved, not asymptomatic but the symptoms were not troublesome and were easily controlled; or 3) symptomatic, symptoms suggestive of recurrence, altered dietary habit, "dumping syndrome," post-cibal hypoglycemia and diarrhea were bothersome and difficult to control. Our appraisals, tabulated in Table 13, were more critical than those made by the patient for we classified some patients as having symptoms although they personally rated their condition as "much better."

The results of evaluations made by independent observers as patients return to the hospital after 3 years are tabulated in Table 14. The total percentage of patients asymp-

TABLE 13. *Author's Evaluation One to Five Years after Operation*

Operation	Years Postop.	No. of Patients Studied	% Asymptomatic	% Improved (Minor Sympt.)	% With Significant Symptoms
V-D	1	102	70	16	14
	2	95	76	17	7
	3	84	76	18	6
	4	39	69	21	10
	5	21	81	14	5
V-R	1	90	57	22	21
	2	81	67	27	6
	3	77	65	31	4
	4	45	69	31	0
	5	19	53	47	0

TABLE 14. *Independent Physician Evaluation Three Years after Operation*

Operation	No. of Patients Studied	% Asymptomatic	% Improved	% With Significant Symptoms*	
V-D	46	65	26	Dumping (2)	9
				Susp. Recur. (2)	
V-R	42	60	33	Small Pouch (2)	7
				Dumping (1)	

* Symptoms for which patients may have been reoperated earlier are not included in this table.

tomatic and improved was virtually the same for patients with V-D as it was for patients with V-R. These results were comparable to those recorded by the authors.

Discussion

The purpose of this study was to institute a controlled, prospective clinical trial of two operative technics with the expectation that it would provide substantive data which might be helpful in objective deliberations concerning the best operative procedure to use for treatment of duodenal ulcer. It is one of the few prospective, randomized studies designed to evaluate two operative procedures for duodenal ulcer in which the patients were restricted to those requiring elective operation.

It is known that the incidence of recurrent ulcer is greater after V-P than after V-BI. This increased recurrence rate has been justified on the basis that V-P is a safer operation, particularly in less skilled hands, requires less time and is associated with fewer postoperative complications. The most cogent argument by those who favor V-P is that its higher recurrence rate is a small price to pay for a lower mortality rate. One might reasonably expect that the complications of V-R in patients with chronic ulcer disease and severe inflammation will be greater than those following V-D. On the other hand, our results suggest that it is unnecessary to subject all patients to the increased risk of recurrence to achieve the best operative results, for the problem of recognizing the difficult case and avoiding the untoward consequences

of resection can be mastered as is indicated by the decisions of the house staff to substitute a drainage operation for a resection in ten instances. The fact that both operative deaths in our study occurred after V-D does not lead us to conclude that V-R can be performed exclusively with lower mortality and morbidity than can V-D. Our results do show that if resection is avoided when transection of the duodenum may be expected to create technical difficulties, surgeons may confer on 90 per cent of patients the protection against ulcer recurrence provided by V-R with the same mortality rate reported for V-D.

It has been stated that pyloroplasty is a safer operation than antrectomy because it is technically easier. We agree with Harrington⁹ that it seems unwarranted to recommend vagotomy and pyloroplasty as the operation of choice for duodenal ulcer because of the presumption that most operations for duodenal ulcer are performed by the occasional operator. We would like to suggest that pyloroplasty is not an operation of such simplicity but is subject to the same technical problems as occurs with resection. Completion of an adequate pyloroplasty that avoids leakage without producing a degree of obstruction is an operation requiring the skill and finesse of as competent a surgeon as is necessary to perform a gastric resection, particularly if the inflammatory response to the ulcer is extensive. In Hoerr's¹¹ opinion, the mortality for gastric resection is higher than generally appreciated because those reporting mortality results usually do so from centers

where there has been extensive experience by a few highly qualified surgeons. This is undoubtedly correct but the same reasoning can be used to explain the low mortality reported for pyloroplasty which actually may be associated with a great many more complications than we generally realize.

The incidence of incomplete vagotomy (i.e., a positive Hollander response) after V-D was four times that observed after V-R. Observations made at the time of testing indicated that this difference was not the result of greater neutralization by reflux of duodenal contents into the stomach of patients with V-R than in those with V-D. Since patients were selected randomly and the study extended over 3 years, involving approximately 50 resident surgeons, explanation for this difference in incidence of incomplete vagotomy cannot be due to performance of more technically correct vagotomies after V-R than after V-D. It is more likely that the degree of incompleteness of vagotomy was similar in the two groups and resulted from extra vagal, parasympathetic secretory fibers to the stomach as well as from retained vagal fibers. The existence of such extra-vagal innervation was supported by the high failure rate of patients with positive insulin tests to revert to a negative test after re-vagotomy.

It was demonstrated by Üvnas¹⁸ and confirmed by others that gastrin is released from the antrum by vagal stimulation. Later, it was shown that parietal cell response to vagal stimulation is potentiated by gastrin.^{13, 15} The availability of gastrin when the antrum is preserved may potentiate the effect of any remaining parasympathetic fibers going to the stomach. It is likely that the completeness of vagotomy was equal in both groups of patients and that loss of gastrin potentiation was responsible for a greater number of negative Hollander tests observed after V-D than after V-R. It is our conclusion that one of the advantages of antrectomy over a drain-

age procedure is its ability to compensate for an incomplete vagotomy.

Ross and Kay¹⁶ reported that 38 per cent of their V-D patients had a positive Hollander test 10 days after operation. Since we performed multiple rather than a single test on each patient beginning 6 months rather than 10 days after operation, our incidence of a positive Hollander test increased to 50 per cent. Had we included among the negative Hollanders those patients with a positive Hollander test in which the test was negative on first testing, our incidence of positive tests would have declined to 35 per cent or the same as that reported by Ross and Kay.¹⁶

We concur with Ross and Kay¹⁶ that a positive Hollander test need not necessarily reflect a clinically inadequate vagotomy, particularly when the positive response occurs late in the second hour after insulin as described by Bell.¹ A patient in whom vagotomy is adequate to prevent recurrence of ulcer may have a positive Hollander test. After all, the criteria for a positive Hollander test are arbitrary and are not immutable. They were derived from animal studies and the validity of their application to human gastric secretion remains open to question. Eventually, there may be better criteria for accurate assessment of completeness of vagotomy. Since we cannot estimate the degree of gastric denervation required or produced at operation, we attempt total gastric vagotomy, not knowing whether total anacidity that develops in those patients who also undergo antrectomy might not result in serious late complications such as gastritis, B₁₂ deficiency and anemia. Our patients have not been followed sufficiently long to be able to comment further on this point. The persistence of negative Hollander tests in 87 per cent of patients with V-R with little evidence that the test becomes positive does not support the concept of recovery of gastric secretion² after incomplete vagotomy by nerve sprouting.¹⁴

Our study suggests that with the exception of a higher recurrence rate after V-D than after V-R, the clinical results were not significantly different in the two groups of patients. In a controlled, prospective study by Goligher *et al.*⁵ sub-total gastrectomy was compared with vagotomy, antrectomy and gastrojejunostomy and vagotomy and gastroenterostomy. With the exception of better protection against recurrent ulcer after the first two operations, he was unable to make a conclusive statement concerning the superiority of any one operation over the others in terms of gastrointestinal symptoms and dysfunction. In a later publication, Goligher *et al.*⁶ showed that the 5- to 8-year follow-up results were essentially the same as those reported earlier. He subsequently reported the results obtained in a group of patients treated by vagotomy and pyloroplasty and compared these results with those obtained with the three operations used in his controlled study.⁷ He concluded that the overall functional results after vagotomy and pyloroplasty were less satisfactory than those obtained after any of the three methods used in his original study. As is true with most published comparisons of this type its value was obscured because of the dissimilarity in the series of cases contrasted, the very problem Goligher attempted to avoid by his earlier, randomized study.

There have been excellent prospective studies performed to evaluate a particular operation^{3, 10} utilized for treatment of duodenal ulcer. It is of interest that studies which have evaluated only one operation or have evaluated more than one operation sequentially or retrospectively usually conclude that one operation is either superior or inferior to some other operation. By contrast, prospective,⁸ randomized^{5, 6} studies, including our own, have shown that with the exception of the number of recurrent ulcers, there is a surprising comparability in the results obtained in surviving patients who have undergone different operations.

Our results with vagotomy and antrectomy are not an accurate reflection of its intrinsic hazards if the operation were applied as the routine, elective operative procedure. Our study does show that if vagotomy and drainage procedures are done in the technically difficult cases, the majority of cases can be treated by vagotomy and antrectomy with an operative mortality and clinical results equivalent to those obtained by vagotomy and drainage but without its inherent risk of recurrent ulcer.

Perhaps the value of prospective studies such as ours is to emphasize the need for more controlled studies if we are to obtain solutions of the problems faced by surgeons with the responsibility of selecting an operation for a particular patient afflicted with the ubiquitous duodenal ulcer.

Summary

Two hundred consecutive patients requiring elective operation for duodenal ulcer were studied. Prior to operation, the choice between vagotomy and pyloroplasty and vagotomy, antrectomy and gastroduodenostomy was made by random selection. The protocol was violated because of potential technical difficulties in ten patients. The operations performed included vagotomy and pyloroplasty in 94, vagotomy and gastroenterostomy in 14, vagotomy, antrectomy and gastroduodenostomy in 73 and vagotomy antrectomy and gastrojejunostomy in 19.

There were two operative deaths in the vagotomy and drainage group and none in the vagotomy and antrectomy group. This represented neither a significant difference in the mortality between the two groups nor the mortality for vagotomy and antrectomy if this procedure was applied as the routine, elective, operative procedure. The results suggested that if one abstained from resection in patients where technically, difficulties with the duodenum could be expected, vagotomy and antrectomy could be performed in the remaining pa-

tients with as low a mortality rate as usually reported for vagotomy and pyloroplasty. The immediate postoperative morbidity and the incidence of alimentary dysfunction for the two groups of patients were similar. There was no patient in either group that was disabled by operation.

There was evidence of an incomplete vagotomy in 50 per cent of patients after vagotomy-drainage and in 13 per cent of patients after vagotomy and antrectomy. In the drainage group, eight patients have been reoperated for suspected recurrent ulcer and three are under observation for possible recurrence. No patient in the vagotomy-antrectomy group has had a diagnosis of recurrent ulcer.

It is concluded as a result of this prospective, randomized study, that vagotomy and antrectomy is superior to vagotomy and drainage as the operation of choice for elective treatment for duodenal ulcer in the majority of patients because of its lower recurrence rate without the association of increased morbidity or mortality. The choice of operation is best made on the basis of technical problems in each case; the higher recurrence rate after vagotomy and drainage being acceptable in those cases where the risk of resection is great.

References

1. Bell, P. R. F.: The Long Term Effect of Vagotomy on the Maximal Acid Response to Histamine in Man. *Gastroenterology*, **46**:387, 1964.
2. Clark, C. G.: Recovery of Gastric Function after Incomplete Vagotomy. Abstract 8, Presented at the British Surgical Research Society, Belfast, May 22, 1959.
3. Eisenberg, M. M., Woodward, E. R., Carson, T. J. and Dragstedt, L. R.: Vagotomy and Drainage Procedure for Duodenal Ulcer: The Results of Ten Years' Experience. *Ann. Surg.*, **170**:317, 1969.
4. Evans, R. H., Zajtechuk, R. and Menguy, Rene: Role of Vagotomy and Gastric Drainage in the Surgical Treatment of Duodenal Ulcer. Results of a Ten-year Experience at the University of Chicago. *Surg. Clin. N. Amer.*, **47**:141, 1967.
5. Goligher, J. C., Pulvertaft, C. N. and Watkinson, G.: Controlled Trial of Vagotomy and Gastro-enterostomy, Vagotomy and Antrectomy, and Subtotal Gastrectomy in Elective Treatment of Duodenal Ulcer: Interim Report. *Brit. Med. J.*, **1**:455, 1964.
6. Goligher, J. C., De Dombal, F. T., Duthie, H. L., Latchmore, A. J. C., Smiddy, F. G., Pulvertaft, C. N., Conyers, J. H., Feather, D. B., Shoesmith, J. H. and Willson-Pepper, J.: Five to Eight-year Results of Leeds-York Controlled Trial of Elective Surgery for Duodenal Ulcer. *Brit. Med. J.*, **2**:781, 1968.
7. Goligher, J. C., Pulvertaft, C. N., De Dombal, F. T., Clark, C. G., Conyers, J. H., Duthie, H. L., Feather, D. B., Latchmore, A. J. C., Matheson, T. S., Shoesmith, J. H., Smiddy, F. G. and Willson-Pepper, J.: Clinical Comparison of Vagotomy and Pyloroplasty with Other Forms of Elective Surgery for Duodenal Ulcer. *Brit. Med. J.*, **2**:787, 1968.
8. Hamilton, J. E., Harbrecht, P. J., Robbins, R. E. and Kinnaird, D. W.: A Comparative Study of Vagotomy and Emptying Procedure Versus Subtotal Gastrectomy Used Alternately in the Treatment of Duodenal Ulcer. *Ann. Surg.*, **153**:934, 1961.
9. Herrington, J. L.: Competitive Operations for Duodenal Ulcer. *Surg. Gynec. Obstet.*, **123**:1309, 1966.
10. Herrington, J. L.: Vagotomy-Pyloroplasty for Duodenal Ulcer. A Critical Appraisal of Early Results. *Surgery*, **61**:698, 1967.
11. Hoerr, S. O.: Pyloroplasty with Transabdominal Vagus Transection for Chronic Duodenal Ulcer. *Ann. N. Y. Acad. Sci.*, **99**:198, 1962.
12. Hollander, F.: The Insulin Test for the Presence of Intact Nerve Fibers after Vagal Operations for Peptic Ulcer. *Gastroenterology*, **7**:607, 1946.
13. Jordan, Paul H., Jr. and De La Rosa, C.: Magnitude of the Antrum's Role in the Cephalic Phase of Gastric Secretion. *Gastric Secretion, Mechanisms and Control*. Oxford and New York, Pergamon Press, 1967.
14. Murray, G.: Sprouting of Nerves: Some Consequences of Vagotomy and Sympathectomy. *Gastroenterology*, **42**:197, 1962.
15. Olbe, L.: Significance of Vagal Release of Gastrin During the Nervous Phase of Gastric Secretion in Dogs. *Gastroenterology*, **44**:463, 1963.
16. Ross, B. and Kay, A. W.: The Insulin Test after Vagotomy. *Gastroenterology*, **46**:379, 1964.
17. Scott, H. W., Sawyers, J. L., Gobbel, W. G., Harrington, J. L., Edwards, W. H. and Edwards, L. W.: Vagotomy and Antrectomy in Surgical Treatment of Duodenal Ulcer Disease. *Surg. Clin. N. Amer.*, **46**:349, 1966.
18. Övnas, B.: The Part Played by the Pyloric Region in the Cephalic Phase of Gastric Secretion. *Acta Physiol. Scand.*, **13**:1, 1942.
19. Welch, C. E.: Subtotal Gastrectomy for Duodenal Ulcer. *Surg. Clin. N. Amer.*, **46**:339, 1966.
20. Woodward, E. R.: Personal Communication.
21. Zatkera, S. and Neves, D. P.: Maximal Gastric Secretion in Human Subjects after Histalog Stimulation. *Gastroenterology*, **47**:251, 1964.