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ORIGINAL ARTICLE

The natural history of perforated foregut ulcers after repair by omental patching or primary closure

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Abstract
Background The treatment of perforated foregut ulcers by omental patching (OP) or primary closure has mostly replaced vagotomy and pyloroplasty/antrectomy (VPA). We sought to determine the natural history and recurrence rate of ulceration in patients treated by omental patching or primary closure.
Study design An 11-year retrospective study.
Results From 2004 through 2015, 94 patients had perforated foregut ulcers, 53 gastric, and 41 duodenal. 77 (82%) were treated by OP alone (study group) and 17 (18%) were treated with VPA (comparison group). All OP patients were discharged on PPIs, but only 86% took the drugs for a median of 22 months (1–192, SD 40). Endoscopy in the OP group showed recurrent ulcers in nine (12% recurrence rate) and gastritis in three (4%) This group also had three later recurrent perforations. Another recurrent ulcer hemorrhaged causing death (3% late mortality). Two other patients required non-emergent re-do ulcer operations for recurrent disease/symptoms (surgical re-intervention rate 4%). Total length of follow-up was median 44 months (1–192, SD 40) and was complete in 82 (87%). 18 (23%) patients in the OP group developed recurrent abdominal pain attributed to ulcer disease during follow-up, compared to 2 (12%) in the VPA group ($p = 0.15$). No patient in the VPA group had an endoscopic recurrence or re-intervention.
Conclusion Omental patching does not correct the underlying disease process which causes foregut perforation, and has a 12% endoscopically proven recurrent ulceration rate and a 23% incidence of recurrent symptoms within 44 months. Patients tend to stop taking PPIs after 22 months at which time their risk increases.

Keywords Gastric ulcer · Duodenal ulcer · Perforation · Omental patch · Graham patch · Recurrence

Introduction

For almost three decades now, the standard of care to treat perforated foregut ulcers has been by simple closure with or without an omental patch (OP) and long-term proton pump inhibitor (PPI) therapy, with antibiotic treatment for *Helicobacter pylori* eradication if present [1–3]. This surgical procedure grew in favor over vagotomy with pyloroplasty/antrectomy (VPA) due to being technically easier, and the belief that *H. pylori* eradication and long-term proton pump inhibitor therapy would prevent disease recurrence [4–6]. In some older literature, the incidence of *H. pylori* infection occurring concomitantly with perforation ranged from 81 to 92% and therefore this approach made good sense [4, 7]. We now know that this is not always true because not all patients with perforated foregut ulcers are *H. pylori* positive (21–74%), and the incidence of *H. pylori* colonization in the general population is only 13–24% [8–11]. Furthermore, the addition of a PPI to an *H. pylori* treatment regimen does not improve eradication rates, which consistently remains 69–85% [12–14].

The other assumption is that patients are financially capable and appropriately motivated to continue to take PPIs indefinitely. Even in a socialized country where

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medication cost is covered by the government, patients who were prescribed PPIs only continued to take them for more than 5 years in 4% [15]. Even the concept and appropriateness of indefinite use of PPIs has been called into question due to recent reports that their long-term use may result in bone loss and affect clopidogrel metabolism [16–18].

Although this has been the predominant treatment for perforated ulcers for a long time now, there is very little research that has examined the long-term outcome after surgery and the recurrence rate. With these things in mind, the authors chose to determine the natural history of patients who were treated by primary closure with or without omental patching after having a perforated foregut ulcer. The authors' purpose was not to show superiority or inferiority of any surgical or medical therapy for ulcer disease, but rather, to document the natural history after simple closure with or without omental patching to educate the surgical community on the eventual outcome of this procedure and determine what occurs if and when patients stop taking PPIs.

Methods

An exhaustive 11-year retrospective review was performed for all patients treated at our facility with perforated foregut ulcers of the stomach or duodenum. All patients were included. Chart review and data extraction were performed, and all data were placed into an excel file for analysis. Information from every follow-up visit and every follow-up endoscopy was documented. The operations were all performed by five surgeons in the local community.

Follow-up data were obtained by phone, chart review, and office visits for all patients. Patients were specifically questioned about recurrence, abdominal pain, follow-up tests, medication history, and endoscopies. Phone follow-up was performed by talking to the patient directly on the phone and discussing their symptoms, or lack thereof, and current health status. They were asked about pain, nausea, antacid, PPI, and histamine blocker use and current medications they were taking. A thorough discussion took place with every patient. If patients were taking PPIs, they were asked how long they had been taking them and why it was started or continued. For the few patients who could not be reached by phone or office follow-up, the medical record was searched for current medications.

Patients were tested for *H. pylori* by tissue biopsy at the time of surgery, by Clo test or by serological testing after the procedure. Only 74% of the patients were tested because some surgeons chose to treat every patient with empirical therapy using antibiotics against *H. pylori*, and therefore testing was not performed in those patients.

If patients were started on any anti-ulcer medication by their physician for recurrent symptoms during follow-up, this was considered a symptomatic recurrence. But only patients who had repeat endoscopy documenting a recurrent ulcer or bleeding/gastritis were grouped as a proven recurrence. Statistical analysis of the data was performed by an independent professional statistician (JN). The SAS System (Chicago, IL) was used to determine the Mantel–Haenszel Chi-square and Fisher's exact test with two-sided probability as indicated. The Lifetest procedure was used to determine survival estimates which were used to make Kaplan–Meier disease-free survival curves. Wilcoxon and log-rank statistics were used to compare the VPA and OP groups. Data are listed as median with standard deviation as appropriate.

Results

From 2004 to 2015, 94 patients had perforated foregut ulcers treated at our institution, 53 gastric and 41 duodenal, 49 patients were male and 45 were female. Of the gastric perforations, 35 were type III, 7 type I, 4 type IV, 3 type II, and 4 occurred at the gastrojejunal anastomosis from prior gastric bypass surgery. Ten (11%) were *H. pylori* positive and 13 (14%) were taking high dose non-steroidal medications, leaving 71 (75%) of the patients with a hypersecretory or idiopathic etiology for their ulcer.

77 (82%) were treated by OP alone (study group) and 17 (18%) were treated with VPA (comparison group). There is not a local protocol as to which operation should be done, and it is left to the discretion of the surgeon. For those patients who did have antrectomy or pyloroplasty, the operative reports indicated that the decision was based upon a very large size of the perforation occurring near the pylorus, such that closure would have likely created a gastric outlet obstruction. All patients treated with OP were discharged on PPIs, but only 86% of the patients took the drugs, for a median of 22 months (1–192, SD 40) after surgery. Eleven (14%) patients never took the PPIs at all. The ten patients found to be *H. pylori* positive were all treated with triple antibiotic therapy, but follow-up testing for eradication was only performed in three patients who were all later negative.

Six (35%) of the VPA patients and 22 (29%) who had OP had at least one follow-up endoscopy at a median of 24 months (1–144, SD 37) after surgery. Follow-up endoscopy was not routinely performed in all patients. The reasons for follow-up endoscopy were for the symptoms of abdominal pain in 20 (71%), surveillance in 7 (25%), and a hiatal hernia in 1 (4%) (Table 1). Endoscopy in the OP group showed recurrent ulcers in 9 (12% recurrence rate) and gastritis in 3 (4%) This group also had 3 later recurrent

Table 1 Patient data

	Omental patch	Vagotomy/antrectomy/pyloroplasty
Total number	77 (82%)	17 (18%)
Gastric ulcer	47 (50%)	6 (6%)
Duodenal ulcer	30 (32%)	11 (12%)
Later endoscopy	22 (29%)	6 (35%)
Reason for endoscopy		
Pain	18	2
Surveillance	3	4
Hiatal hernia	1	0
Recurrent ulcer	9 (12%)	0
Recurrent gastritis	3 (4%)	0
Recurrent perforation	3 (4%)	0
Recurrent hemorrhage	1 (1%)	0
Later second operation	2 (3%)	0
Recurrent symptoms	18 (23%)	2 (12%)

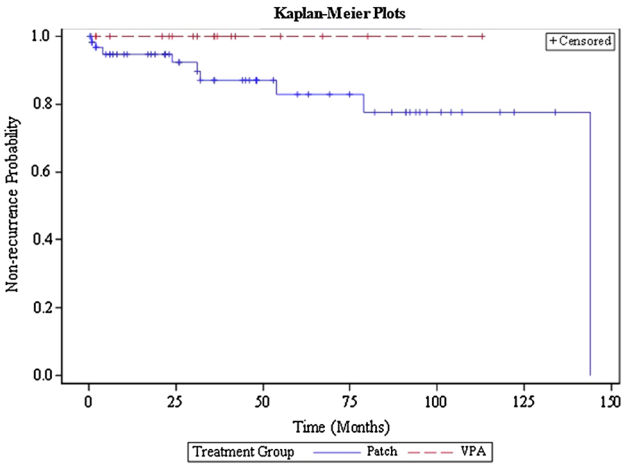

Fig. 1 Kaplan–Meier ulcer-free survival curve showing omental patch (OP) and vagotomy/pyloroplasty/antrectomy (VPA) groups

perforations: one microperforation was managed non-operatively, one was made comfort-care and died, and one had emergency surgery. Another recurrent ulcer led to hemorrhage causing death (3% late mortality rate). Two other patients required non-emergent repeat ulcer operations for recurrent disease/symptoms (total surgical re-intervention rate 4%). Thus, out of the 77 patients treated by OP, 18 (23%) eventually had an ulcer recurrence, bleeding, perforation, or repeat surgical intervention. Of note, the median time the patients stopped taking PPIs was 22 months, and the median time of recurrence, bleeding, or perforation was 41 months. No patient in the VPA group had an endoscopic recurrence or required any re-intervention, but the number of patients in this group was relatively small.

Total length of follow-up was a median of 44 months (2–192, SD 40) and was complete in 82 (87%) patients. Only 12 patients were lost to follow-up. 17 (18%) patients died during the follow-up period and were censored at their date of death. An additional 18 (23%) patients in the OP group developed recurrent abdominal pain attributed to ulcer disease during follow-up and were treated medically (symptomatic recurrence) but did not have endoscopy to confirm the diagnosis, compared to two (12%) in the VPA group ($p = 0.15$).

Discussion

There are only five causes of stomach ulceration: malignancy, non-steroidal anti-inflammatory drug (NSAID) abuse, *H. pylori* infection, splanchnic vascular insufficiency or gastric mucosal vasoconstriction mostly mediated by gastric mucosal endothelin-1 ("stress" ulcer from sepsis, burns, cocaine, etc.), and hypersecretory states causing excessive acid production [12, 13, 19–24]. For patients who have abused NSAIDs or those who are *H. pylori* positive, discontinuation of the medication and antibiotic treatment, respectively, will cure the problem and so simple closure of the perforation with or without omental patch should be sufficient treatment. However, NSAID abusers are a minority of the patients, and *H. pylori* eradication is only successful in 69–85% [12–14]. Those patients with perforations due to gastric hypoperfusion or hypersecretory states rely on excellent acid suppression therapy to heal their ulcer and the surgical repair site [23]. While this is readily accomplished in the ICU setting, after discharge, the uninsured, the noncompliant, the acid overproducer, and the *H. pylori* recidivist will all be prone to recurrence. As our study shows, over-time patients became more noncompliant with taking acid suppression medication, and when asked why they stopped, most responded that they felt they no longer needed it. The median time the patients stopped taking their PPIs was after 22 months, and this corresponded to an increase in complications after that point (Fig. 1).

With the widespread use of PPIs and the effective treatment of *H. pylori*, the number of overall ulcer-related complications requiring surgery has greatly diminished [25]. However, several recent publications have documented that those patients who now present with the complications related to peptic ulcer disease, especially perforation, tend to not be *H. pylori* positive (only 26–48% of the patients) and tend to be from lower socioeconomic status, uninsured, and have poor access to medical care [9, 26–28]. For these reasons, some authors are now recommending a return to vagotomy for definitive acid suppression in these high-risk patient populations

[26, 27]. Our study found similar results. Only 11% of the patients with perforations were found to be *H. pylori* positive, although 24 patients (26%) were never tested because some surgeons chose to treat with antibiotics empirically for presumptive infection. If these 24 patients were all found to be *H. pylori* positive, the total infectious incidence would still be only 36% which is similar to other recent studies documenting rates of 26–48% for patients who present with perforation [26–28].

Further, even with triple or quadruple antibiotic therapy to treat *H. pylori*, the eradication rate remains well below 90%, mostly due to colonization of the gastrointestinal tract and antibiotic resistance [30]. For those treated patients, the incidence of recurrent infection ranges from 13 to 30% [31, 32]. This culminates in a large number of patients at high risk for recurrent disease and therefore at high risk for recurrent complications. In all, 12% of the patients in this study did have recurrent ulceration found during follow-up endoscopy, and this number may have been higher if all patients had been evaluated by endoscopy. Although a larger percentage of the VPA patients had a follow-up endoscopy (35%) compared to the OP patients (29%), none of them had an endoscopic recurrence.

This study is not the first to describe a large patient experience with *Helicobacter*-negative, complicated or perforated ulcers that followed an aggressive clinical course [9, 26–29, 33]. In the majority of these studies, the etiology remained unknown. However, this study does present unique data that describe the recurrence and relapse trends over 10 years for patients who were treated by simple closure or OP. And that data are very hard to find. The first author to document the long-term outcome of simple closure for perforated duodenal ulcers in 1990 followed the patients for a median period of 43 months and found an overall ulcer recurrence rate of 42%, and 5/113 patients (4%) required emergency repeat surgery for bleeding or re-perforation, which was the exact same percentage found in this study (4%) [34]. Only two other studies have documented the endoscopically proven ulcer recurrence rate after the initial perforation was treated by simple closure, but both studies only followed the patients for 1 year. Those studies found that the endoscopically proven ulcer recurrence rate was 30 and 38% if *H. pylori* was not eradicated from the patients, but only 5 and 6% if *H. pylori* was effectively eradicated [4, 35]. This is similar to our data which showed that those patients with simple closure or OP had a 23% incidence of recurrent ulcer, bleeding, perforation, or repeat surgical intervention. Another interesting study that looked at gastric perforations due to cocaine use that were repaired by OP found a 56% recurrent ulceration rate after a median of 20 months, while those patients who had undergone VPA had zero recurrences [36].

Conclusions

Omental patching does not correct the underlying disease process which causes foregut perforation, and has a 12% endoscopically proven recurrent ulceration rate and a 23% incidence of recurrent symptoms within 44 months. Patients tend to stop taking PPIs after 22 months at which time their risk increases. Patients treated with omental patching or simple closure need to be followed to ensure *H. pylori* eradication or they are at high risk for recurrence. The bottom line is that omental patching for foregut perforations is not an ideal therapy and our manuscript documents all of the problems that can and do occur at later time points. These late complications are what the global surgical literature is missing. There are many recurrences of ulcers and gastritis, and even recurrent perforations. Omental patching is a temporary solution, not a definitive cure.

Author contributions Carr—conception and design, acquisition, analysis, drafting, revising, approval, accountable. Smith—conception and design, acquisition, analysis, drafting, approval, accountable. Roeser—conception and design, acquisition, drafting, approval, accountable. Naranjo—conception and design, analysis, revising, approval, and accountable.

Compliance with ethical standards

Conflict of interest The authors, John Carr, Daniel Smith, Mark Roeser, and Joshua Naranjo, have no conflicts of interest, no financial relationships to disclose, and have received no funding or any support to perform this research.

Ethical standards Institutional Review Board and ethical approval was obtained from the Allegiance Health Institutional Review Board prior to starting this study, and this study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Since the study was retrospective in nature, the need to obtain individual patient consent was waived by the review board.

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