

PREVALENCE, SURGICAL MANAGEMENT, AND OUTCOME OF PERFORATION OF THE GASTER ASSOCIATED WITH LONG TERM CORTICOSTEROID USE: A COMPREHENSIVE SYSTEMATIC REVIEW

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ABSTRACT

Background: In the general population, gastroduodenal perforation can occur as a complication of pre-existing peptic ulcer disease (PUD). In this scenario, the morbidity and mortality are already well documented. The lifetime risk of perforation is approximately 2–10% in cases of untreated PUD, and despite an improvement in resuscitation, and intensive and surgical care, the mortality rate remains around 25%.

The aim: The aim of this study to show about prevalence, surgical management, and outcome of perforation of the gaster associated with long term corticosteroid use.

Methods: By the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. This search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed, SagePub, and Google Scholar were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

Result: In the PubMed database, , the results of our search get 28 articles, whereas the results of our search on SagePub get 9 articles, on Google Scholar 1680 articles. Records remove before screening are 759, so we get 958 articles fos screening. After we screened based on record exclude, we compiled a total of 10 papers. We included five research that met the criteria.

Conclusion: The location of ulcers within the stomach affects the surgical procedure. They may appear with a smaller sac abscess, commonly linked with peritonitis or retroperitoneal abscess. Gastric perforation is a serious and fatal disorder, especially in those who are underweight. Early diagnosis, basic care, primary management, stabilization, nutrient diet, and surgical exploration are all part of initial management.

Keyword: Gaster, perforation, corticosteroid, surgical, outcome.

INTRODUCTION

Steroids, since their introduction in 1935, have been used for a wide range of indications. Initially, its indication was restricted to Addison's disease, but their anti-inflammatory and immuno-modulating property form the basis of their numerous indications and widespread use. Fraser *et al.* (1952), for the first time, reported the adrenal insufficiency which presented as intractable intraoperative hypotension during a major orthopedic surgery in a patient on chronic steroid therapy. The sudden preoperative withdrawal or inadequate preoperative dose of corticosteroid was hypothesized to be the culprit and therefore, the concept of perioperative suprathysiologic "stress dose" corticosteroid (up to four times of baseline) arose to avoid the precipitation of adrenal crisis. Various controversies have been linked to this concept over the last few decades. Therefore, the objective of the present review is to evaluate the changing concept of perioperative "stress dose" of corticosteroids, its pharmacokinetics, clinical relevance, and the related controversies such as the need and the appropriate dose.^{1,2}

The association between corticosteroid use and gastrointestinal (GI) adverse effects, including bleeding or perforation, has been a source of debate since the 1950s. Since GI bleeding and perforation are rare events, no single randomised controlled trial has been large enough to show any increased risk for GI bleeding with the use of corticosteroids. Adverse effects and studies of rare events can often be effectively investigated in observational studies. Thus controlled, observational studies may be the method of choice to detect rare adverse effects. For corticosteroid use, several observational studies have been performed to clarify whether corticosteroids do induce GI bleeding or not, but there is still uncertainty whether this adverse effect is a result of corticosteroid use, use of other medications, underlying disease or other causes.³

In a double-blind placebo-controlled trial by Venekamp *et al.* 174 adult patients clinically diagnosed with ARS received either 30 mg/day prednisolone or placebo for 7 days. The incidence of gastrointestinal complaints did not differ between treatment groups. In a large nested case-control analysis based on the UK General Practice Research Database, 2105 cases of upper gastro-intestinal complications were compared to 11,500 controls and then evaluated for exposure to certain drugs e.g. corticosteroid use. The adjusted OR for current use of oral GCS was 1.8 (95% CI 1.3–2.4) for upper gastrointestinal complications overall. No statistically significant difference could be objectified for lower versus higher dosage of GCS. To our knowledge no studies in upper airway disease patients report on systemic steroid treatment and peptic ulceration.⁴

METHODS PROTOCOL

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

CRITERIA FOR ELIGIBILITY

For the purpose of this literature review, we compare and contrast prevalence, surgical management, and outcome of perforation of the gaster associated with long term corticosteroid use. It is possible to accomplish this by researching or investigating prevalence, surgical management, and outcome of perforation of the gaster associated with long term corticosteroid use. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about prevalence, surgical management, and outcome of perforation of the gaster associated with long term corticosteroid use. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2014, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

SEARCH STRATEGY

We used "prevalence, surgical management, and outcome of perforation of the gaster associated with long term corticosteroid use." as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: ("Corticosteroids"[MeSH Subheading] OR "long term corticosteroids"[All Fields] OR "Perforation of gaster" [All Fields]) AND ("Risk of long term corticosteroid use"[All Fields] OR "Prevalence of gaster perforation"[All Fields]) AND ("Surgical management") [All Fields]) AND ("Long-term impact of corticosteroids"[All Fields] OR ("Complications of long-term corticosteroid" [All Fields])) used in searching the literature.

DATA RETRIEVAL

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources

for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and cannot have been seen anywhere else.

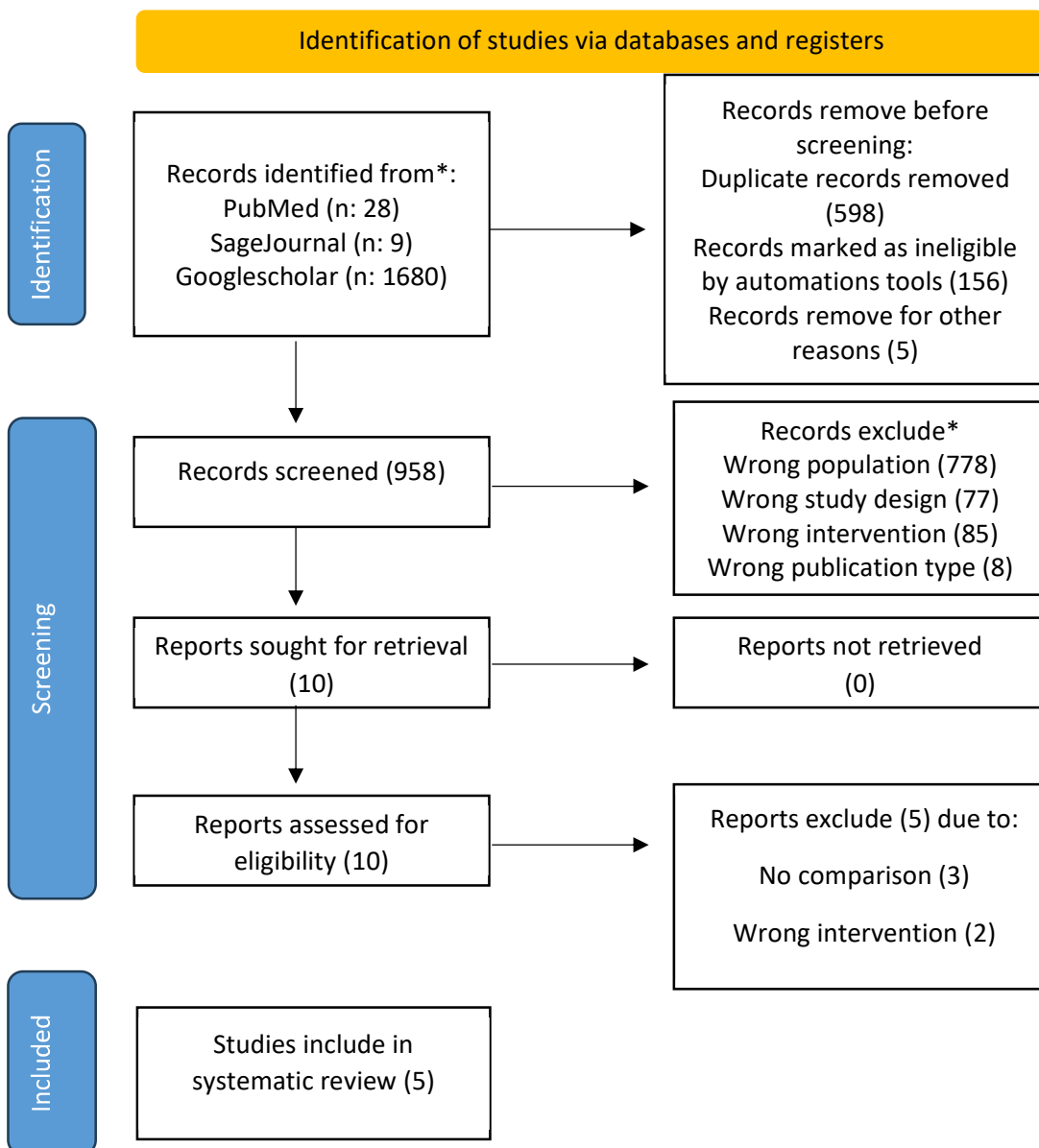


Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

QUALITY ASSESSMENT AND DATA SYNTHESIS

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. In order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

From the PubMed database, the results of our search get 28 articles, whereas the results of our search on SagePub get 9 articles, on Google Scholar 1680 articles. Records remove before screening are 759, so we get 958 articles for screening.

After we screened based on record exclude, we compiled a total of 10 papers. We included five research that met the criteria.

Mazepa, MM et al (2023)⁵ showed patients with gastroduodenal perforation and oncologic treatment present high mortality, regardless of receiving recent CMT.

Dalal, AA et al (2016)⁶ showed a significant dose-response relationship was found between the long-term use of systemic corticosteroids and the risk of developing systemic corticosteroid-related complications in patients with severe asthma, resulting in increased burden and costs on the health care system that intensified with systemic corticosteroid exposure.

Table 1. The literature include in this study

Author	Origin	Method	Sample Size	Result
Mazepa, MM et al., 2023 ⁵	Brazil	A retrospective analysis of patients who underwent emergency surgery with an intraoperative finding of gastroduodenal perforation.	45	Among 45 patients included, 16 (35.5%) were classified as the CMT group and the remaining 29 (64.5%) patients as the non-CMT group. There was no difference between the groups regarding sex, age, BMI, comorbidity, and laboratory exams. ECOG 2-3 was significantly more frequent in the CMT group (68.8% vs. 34.5% $p = 0.027$). Major postoperative complications were similar between both groups (75% vs. 58.6%, $p = 0.272$). The sepsis of abdominal focus was the main postoperative complication. The 30-day mortality was 55.6%, with no difference between non-CMT and CMT groups (62.5% vs. 51.7%, respectively; $p = 0.486$). A multivariate analysis of risk factors showed that only an age of ≥ 65 years was related to 30-day mortality.
Dalal, AA et al., 2016 ⁶	USA	This is a retrospective study using administrative claims data from a large commercial database between 2003 and 2014.	12697	A total of 12,697 corticosteroid users and as many matched nonusers were identified. The odds of developing associated complications increased significantly in a dose-dependent manner with systemic corticosteroid exposure: odds ratios were 2.50, 2.95, and 3.32 (P values < 0.05) for low (defined as < 5 mg/day), medium (≥ 5 -10 mg/day), and high (> 10 mg/day) exposure, respectively, relative to no exposure. Health care resource utilization increased significantly with levels of systemic corticosteroid exposure. Hence, incidence rate ratios for inpatient visits with low, medium, and high exposure relative to none were estimated to be 1.86, 2.40, and 3.37, respectively ($P < 0.05$).

<p>Zhang, L et al., 2023⁷</p>	<p>China</p>	<p>Patients diagnosed with PG-DLBCL were enrolled in this retrospective study.</p>	<p>52</p>	<p>A total of 52 patients received preventative treatment, while 146 patients did not. Among patients with stage I, II-1, and II-2 disease, the prevention group had a lower rate of hemorrhage and perforation (0/40) than the control group (10/78, $p = 0.044$). At a median follow-up time of 25 months, the 5-year event-free survival (EFS) rates were 97.1% in the prevention group and 66.1% in the control group ($p = 0.025$), and the 5-year overall survival (OS) rates were 100% and 72.0%, respectively ($p = 0.021$). However, the differences in the 5-year EFS and OS of patients with disseminated disease were not statistically significant.</p>
<p>Dadfar, A & Edna, TH., 2020⁸</p>	<p>Norway</p>	<p>This was a single-centre, retrospective, cohort study of all patients admitted to Levanger Hospital, Norway, with PPU from 1978 to 2017.</p>	<p>209</p>	<p>Two hundred and nine patients were evaluated, including 113 (54%) men. Forty-six (22%) patients were older than 80 years. Median age increased from the first to the last decade (from 63 to 72 years). The incidence rate increased with increasing age, but we measured a decline in recent decades for both sexes. A significant increase in the use of acetylsalicylic acid, from 5% (2/38) to 18% (8/45), was observed during the study period. Comorbidity increased significantly over the 40 years of the study, with 22% (10/45) of the patients having an American Society of Anaesthesiologists (ASA) score 4-5 in the last decade, compared to 5% (2/38) in the first decade. Thirty-nine percent (81/209) of the patients had one or more postoperative complications. Both 100-day mortality and long-term survival were associated with ASA score, without significant variations between the decades.</p>
<p>Broersen, LHA et al., 2017⁹</p>	<p>Netherlands</p>	<p>A cohort study based on medical databases including all patients ≥ 18 years in Denmark (source</p>	<p>4640</p>	<p>The study included 4640 patients with perforated diverticular disease. Of these, 3743 (80.7%) had not used corticosteroids in the year before admission and 725 (15.6%) had been exposed to systemic corticosteroid treatment. The remaining 172</p>

		<p>population 5 289 261 inhabitants) admitted to a hospital with incident perforated diverticular disease between 2005 and 2013.</p>	<p>patients had been exposed to either inhaled or intestinal acting corticosteroid therapy. Mortality risk in non-users was 4.4% after 7 days and 15.6% after 1 year. This risk was doubled for corticosteroid users who filled their last prescription during the 90 days before admission, with mortality risks ranging from 14.2% after 7 days to 47.6% after 1 year. 1-year mortality risk was even higher for corticosteroid users with a first filled prescription ≤90 days before admission: 52.5%.</p>
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Zhang, L et al (2023)⁷ showed Preventative treatment can decrease the risk of hemorrhage and perforation in patients with localized PG-DLBCL during immunochemotherapy, leading to better EFS and OS in these patients. However, preventative treatment failed to reduce the risk of gastric hemorrhage and perforation and did not improve survival (EFS and OS) in advanced-stage patients.

Dadfar, A & Edna, TH (2020)⁸ showed Declining incidence rates occurred in recent years, but the patients were older and had more comorbidity. The ASA score was associated with both short-term mortality and long-term survival.

Broersen, LHA et al (2017)⁹ showed Corticosteroid use was associated with clearly increased mortality risk after perforated diverticular disease. Thus, use of corticosteroids should be regarded as an important clinical prognostic factor for mortality in patients with this condition.

DISCUSSION

Perforation of the stomach is a full-thickness injury of the wall of the organ. Since the peritoneum completely covers the stomach, perforation of the wall creates a communication between the gastric lumen and the peritoneal cavity. If the perforation occurs acutely, there is no time for an inflammatory reaction to wall off the perforation, and the gastric contents freely enter the general peritoneal cavity, causing chemical peritonitis. Perforations occurring over a prolonged period may be contained locally by the inflammatory reaction. Perforation may be suspected based upon the patient’s clinical presentation, or the diagnosis become obvious through a report of extraluminal ”free air” on diagnostic imaging performed to evaluate for abdominal pain or another symptom. Treatment is a surgical repair. During surgery, most of the perforations are linear and found high in the stomach and along the greater curvature. The perforation is usually closed with a patch made of omentum or the perforated area may undergo a wedge resection.¹⁰

Corticosteroids are hormone mediators produced by the cortex of adrenal glands that are further categorized into glucocorticoids (major glucocorticoid produced by the body is cortisol), mineralocorticoids (major mineralocorticoid produced in the body is aldosterone), and androgenic sex hormones. Endogenous cortisone was first isolated in 1935 and synthesized in 1944. In 1948, Dr. Philip S Hench published administered cortisone (called Compound E at that time) to a 29-year-old woman who was bed-ridden secondary to active rheumatoid arthritis. The patient was able to walk after three days of treatment. This case was published in 1949, and in 1950, Philip S. Hench, Edward C. Kendall, and Tadeusz Reichstein were awarded the Nobel Prize in Physiology or Medicine "for their discoveries relating to the hormones of the adrenal cortex, their structure, and biological effects."¹¹

Gastrointestinal perforations are a complication of 2–10% of duodenal ulcers. There are a variety of etiologies associated with duodenal ulcer formation and its complications. Corticosteroid use is associated with an increased risk of duodenal ulcer perforation, with the first documented case in 1950. Other important medications associated with perforation include NSAIDs and opioids. Beyond medication, one of the most common disease processes, chronic obstructive pulmonary disease (COPD), has been found to be associated with peptic ulcer disease. Up to 30% of COPD patients have been found to have peptic ulcers, and COPD frequency in peptic ulcer disease is 2–3 times the general population. We herein present a case of an acute duodenal ulcer perforation in a patient receiving corticosteroid treatment for an acute COPD exacerbation.^{12,13}

As with PUD, the concomitant use of glucocorticoids and nonsteroidal antiinflammatory drugs increases the risk of GI bleeding. In 1 study, patients who were taking low-dose aspirin plus high-dose corticosteroid therapy had a relative risk of 4.3 (95% CI, 2.10-9.34) for developing upper GI bleeding compared to those taking low-dose aspirin alone. Patients taking low-dose aspirin with low- or medium-dose corticosteroids, however, did not have increased risk.⁶ It is not clear

whether glucocorticoid use alone increases GI bleeding.6-9 A metaanalysis of 71 controlled, randomized trials showed a low but independent risk of bleeding caused by steroids.¹⁴

Globally perforated peptic ulcer is among the most frequent surgical emergencies. Gastric Perforations have an elevated mortality rate (40%) as compared to a duodenal ulcer (10%). The omental patch is an effective and useful surgical treatment for gastric antral perforation. However, it may not be accessible in uncommon situations such as deep perforations, previous omental surgery, and inflammation. High doses of steroids and antibiotics inhibit the biosynthesis of gastric alkaline responses and enzyme activity inside the stomach walls and may lead to biochemical dysfunction, gastric perforation, and lesions.¹⁵

CONCLUSION

The location of ulcers within the stomach affects the surgical procedure. They may appear with a smaller sac abscess, commonly linked with peritonitis or retroperitoneal abscess. Gastric perforation is a serious and fatal disorder, especially in those who are underweight. Early diagnosis, basic care, primary management, stabilization, nutrient diet, and surgical exploration are all part of initial management.

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