INPLASY

The role of prophylactic gastrectomy in gastric adenocarcinoma and proximal polyposis of the stomach(GAPPS). A protocol for a systematic review

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 October 2024 and was last updated on 26 February 2025.

INTRODUCTION

Review question / Objective The objective of this systematic review is to investigate the existing literature in order to determine the significance of prophylactic gastrectomy in patients who have been diagnosed with gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS). This study focuses on patients diagnosed with GAPPS who can benefit from either prophylactic gastrectomy or endoscopic follow-up with periodic biopsies to lower the risk of advanced gastric cancer. The primary aims of the study are to examine the circumstances in which prophylactic gastrectomy is recommended, determine the optimal surgical method, assess its benefits and downsides, and explore non-surgical alternatives for managing this condition. Additionally, a crucial goal is to determine the primary steps required for the early detection of this condition as well as identifying the most effective therapeutic approach to avoid the development of advanced gastric cancer in these individuals.

Rationale Gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS) is an autosomal dominant disorder with incomplete penetrance characterized by the presence of a mutation in the promoter 1B region of the adenomatous polyposis coli (APC) gene. Without damaging the stomach antrum, patients with this syndrome acquire a large number of polyps in the fornix and gastric body.

Although the exact risk of gastric malignancy in patients with GAPPS remains unknown, reports have documented cases of gastric cancer as early as 24 years of age. Furthermore, there are currently no established guidelines for determining the appropriate age for prophylactic gastrectomy, the recommended surgical technique, or the extent of lymphadenectomy. Periodic endoscopic examination can be an at least provisional therapeutic alternative to prophylactic

gastrectomy. There are still many questions regarding the age at which endoscopic surveillance should be started and the number and frequency of gastric biopsies. Other important aspects that raise questions are related to the diagnostic stages of the disease. The necessity for colonoscopic evaluation, alongside assessing the state of Helicobacter pylori infection or the history of proton pump inhibitor treatment, as well as abdominal imaging, are critical components in the therapeutic management of these individuals.

Condition being studied GAPPS is a condition characterized by the presence of numerous gastric polyps located in the fornix and gastric body, but not in the gastric antrum. In 2016, researchers identified several mutations of the APC gene promoter 1B responsible for the disease's onset. In the stomach mucosa, the 1A promoter of the APC gene is characteristically hypermethylated, hence rendering the 1B promoter crucial for the proper operation of the APC gene. Unlike patients with familial polyposis, those with GAPPS do not have polyposis in the colon, where isoenzyme 1A can ensure the function of isoenzyme 1B.

Advances in diagnostic techniques may lead to an increase in future cases, despite the limited number of GAPPS instances documented globally to date.

The age of onset for gastric polyposis in these patients, along with the associated risk of stomach cancer, remains undetermined. There have also been reports of pediatric GAPPS cases with high-grade dysplasia that required a prophylactic gastrectomy.

Patients with GAPPS who develop gastric cancer exhibit a reduced survival duration compared to those with spontaneous gastric cancer at the same stage.

Considering all these factors, we assert the necessity of developing diagnostic and therapy guidelines for individuals with GAPPS.

Periodic endoscopic surveillance presents certain drawbacks, including the challenge of determining an appropriate age for commencement and creating an acceptable gap between examinations. Moreover, determining an adequate number of samples is challenging due to the presence of numerous polyps. Prophylactic gastrectomy is the one procedure that completely eliminates the danger of stomach cancer. This surgical surgery carries significant implications, particularly for the pediatric population and women desiring further pregnancies.

In this literature review, we aim to analyze which therapeutic method is most appropriate for patients diagnosed with GAPPS. Therefore, to make a suitable therapy decision, it is essential to undergo specific diagnostic steps. It is crucial to ascertain the Helicobacter pylori infection status in these patients, given the occasional emergence of stomach polyps after the infection's clearance. Conducting a colonoscopy, together with abdominal imaging and recognizing prior proton pump inhibitor medication, can be important considerations in therapeutic decision-making.

METHODS

Search strategy To conduct this systematic review, we intend to examine the specialized literature accessible in Medline through PubMed and Google Scholar.
We will be using the subsequent keywords: "gastric adenocarcinoma and proximal polyposis of the stomach-GAPPS", "hereditary gastric cancer", "prophylactic gastrectomy", "endoscopy", ”gastrectomy”, “gastric tumor” . We will utilize these keywords in diverse combinations to identify eligible studies.
The search strategy will be based on the following combinations of words and the following combinations of free-style keywords and Medical Subjects Headings (MeSH) and Google Scholar:
(gastric adenocarcinoma and proximal polyposis of the stomach) “[MeSH Terms] OR “GAPPS” [All fields] AND (“prophylactic gastrectomy”[MeSH Terms]) OR “gastrectomy”[All Fields]
(gastric adenocarcinoma and proximal polyposis of the stomach) “[MeSH Terms] OR “GAPPS” [All fields] AND (“gastric cancer”)[MeSH Terms]) OR “gastric tumor”[All Fields] OR “hereditary gastric cancer” [All Fields]
(gastric adenocarcinoma and proximal polyposis of the stomach) “[MeSH Terms] OR “GAPPS” [All fields] AND (“gastroscopy”[MeSH Terms]) OR “endoscopy”[All Fields]

(gastric adenocarcinoma and proximal polyposis of the stomach OR GAPPS) AND (prophylactic gastrectomy OR gastrectomy) AND (gastroscopy OR endoscopy) AND (gastric cancer OR gastric tumor OR hereditary gastric cancer).

Participant or population This study will include all individuals diagnosed with gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS), regardless of age, gender, or ethnicity.

Intervention In this systematic review, we aim to investigate the role of prophylactic gastrectomy in patients diagnosed with GAPPS. Prophylactic gastrectomy is a surgical procedure that removes the stomach to eliminate the chance of developing gastric cancer. Although it is the only treatment that completely prevents the development of stomach cancer, it has significant repercussions for the entire body. There are still no standards specifying the age at which this intervention should be conducted in the case of patients diagnosed with GAPPS or what the ideal surgical strategy is. Extension of lymphadenectomy is another issue that needs to be investigated. Given the significant number of polyps and the risk of detecting gastric cancer on the prophylactic gastrectomy piece, some authors propose D2 lymphadenectomy; however, this correlates with increased operating and postoperative risks.
Monitoring and addressing postoperative dietary deficits is another critical concern.

Comparator Periodic endoscopic follow-up is the main alternative to prophylactic gastrectomy in patients diagnosed with GAPPS. In this systematic review, we want to look at the benefits and drawbacks of this approach over prophylactic gastrectomy.
What age should this investigation begin, and how should it be carried out? How many biopsies should be taken during endoscopy to detect dysplastic or cancer tumors early? Is endoscopic excision of dysplastic lesions effective in the prevention of stomach cancer in GAPPS patients? These are few inquiries for which we seek answers.

Study designs to be included Given the relatively recent discovery of this syndrome and the modest number of cases available in the literature, we propose to include in this systematic review any studies that involve patients diagnosed with GAPPS, independent of research type.

Eligibility criteria This systematic review will include research involving patients diagnosed with GAPPS who benefited from prophylactic gastrectomy, endoscopic monitoring, therapeutic gastrectomy, or the patients with advanced gastric cancer and GAPPS who benefited only from chemotherapy, regardless of patient age or study type. Similarly, the language of the study's publication will not serve as an exclusion factor.
We will exclude from the study articles in which the diagnosis of GAPPS is not specified, such as patients who underwent prophylactic gastrectomy due to an increased risk of hereditary diffuse gastric cancer (HDGC) or familial gastric cancer of the intestinal type (FIGC).
We will also exclude studies that included patients who had prophylactic gastrectomy for an increased risk of gastric cancer within other familial cancer syndromes such as hereditary nonpolyposis colorectal cancer (HNPCC) - Lynch syndrome; Li-Fraumeni syndrome (LFS); Familial adenomatous polyposis (FAP); and Peutz-Jeghers syndrome.

Information sources To conduct this systematic review, we will meticulously examine the specialized literature accessible in the following databases: Medline via PubMed and Google Scholar.

Main outcome(s) This systematic review aims to identify the most effective therapy option for people diagnosed with GAPPS.
What are the benefits and drawbacks of preventive gastrectomy in comparison to endoscopic surveillance in patients with GAPPS?
What is the appropriate age for prophylactic gastrectomy, the optimal surgical technique, and the extent of lymphadenectomy required?

Additional outcome(s) To make a proper therapy selection, it is important to undergo specific diagnostic phases.
Determining the status of Helicobacter pylori infection is crucial in these patients, as stomach polyps have been noted to occasionally arise following the clearance of this infection.
Conducting a colonoscopy, along with abdominal imaging and recognizing prior proton pump inhibitor medication, can be important factors in therapeutic decision-making.

Data management Two independent authors will perform data extraction using a Microsoft Excel form. We will extract the relevant information from each study, including the first author's name, the study type, the publication year, the authors' country of origin, the patients' nationality, the definitive diagnosis of GAPPS according to diagnostic criteria, the type of mutation in the 1B promoter of the APC gene, the presence of a familial history of GAPPS or other malignancies, the total number of cases included in the study, the patients' age and gender, the number of cases undergoing prophylactic gastrectomy, the number of cases receiving only follow-up, and the number of cases diagnosed with both GAPPS and gastric cancer. Also, the result of upper digestive endoscopy, colonoscopy, and abdominal imaging examinations will be noted for each case. We will record the presence of Helicobacter pylori infection and the history of proton pump inhibitor treatment. In the case of patients who have benefited from

prophylactic gastrectomy, the duration between diagnosis and the performance of prophylactic gastrectomy, the type of gastrectomy performed, and the method of surgical approach will be determined. In addition to these parameters, we also want to obtain data on the extent of lymphadenectomy, the way to restore digestive continuity, the way, the time of postoperative follow-up, and the postoperative treatment. We will also examine the histopathological findings detailed in each paper.
Disagreements between researchers will be resolved by discussion and consultation with the other authors of the present study.

Quality assessment / Risk of bias analysis To assess the risk of bias, we will use the Newcastle-Ottawa Scale (NOS). It has 3 domains and 8 items, with a maximum score of 9. The 3 domains are selection, comparability, and exposure. Studies that achieve a score between 0-3 will be considered low-quality studies, those with a score of 4-6 will be classified as medium-quality studies, and those with a score of 7-9 will be considered high-quality studies.

Strategy of data synthesis We anticipate identifying a small number of papers with substantial heterogeneity, given the recent discovery of the examined condition. Thus, we suggest a narrative presentation of the components of interest identified in the included papers rather than a meta-analysis. We will present the findings in the form of tables and graphs, and discuss the most significant features.

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Language restriction There will be no language restrictions in the search strategy.

Country(ies) involved The systematic review will be conducted in Romania.

Contributorship Cosmina Fugăreţu, Catalin Misarca, Stefan Patrascu, Marin Valeriu Surlin, - These authors contributed equally to this work.

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Keywords gastric adenocarcinoma and proximal polyposis of the stomach; GAPPS; hereditary gastric cancer; prophylactic gastrectomy; endoscopy; gastrectomy; gastric tumor.

Dissemination plans We intend to share the findings of this study by publishing them in a high-impact journal.

Contributions of each author
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