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Frequency and risk factors for malignant evolution of gastric hyperplastic polyps in a country with intermediate-high risk for gastric cancer

Maria Luísa Faro Fernandes

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2024

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Frequência e fatores de risco para a transformação maligna de pólipos gástricos hiperplásicos num país com risco de cancro gástrico intermédio-alto

Mestrado Integrado em Medicina

Área: Gastrenterologia

Tipologia: Dissertação

Trabalho efetuado sob a Orientação de:

Professor Doutor Rui Jorge Guedes Morais

E sob a Coorientação de:

Professor Doutor João Cláudio Faria dos Santos Antunes

Trabalho organizado de acordo com as normas da revista:
Gastrointestinal Endoscopy

Março, 2025

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Gastrenterologia

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GENERATIVO BASEADAS EM LARGE LANGUAGE MODELS

Eu, Maria Luísa Faro Fernandes, abaixo assinado, nº mecanográfico 201907503, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro que:

☒ Não procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* para nenhuma das tarefas no contexto do meu trabalho de Dissertação ou Monografia

☐ Procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia, encontrando-se todas as interacções (*prompts* e respostas) transcritas em anexo bem como a indicação das aplicações utilizadas.

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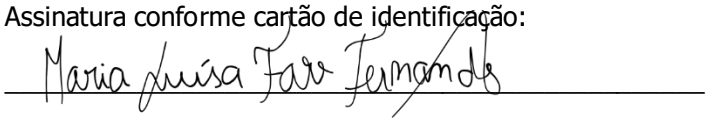

Frequency and risk factors for malignant evolution of gastric hyperplastic polyps in a country with an intermediate-high risk for gastric cancer

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Keywords: Gastric Hyperplastic Polyps, Neoplastic Transformation, Gastric Cancer, Retrospective Cohort.

ABSTRACT

Background and Aims: Gastric hyperplastic polyps (GHPs) carry a neoplastic transformation risk of up to 5%, with previous studies indicating an increased risk with larger polyp size. We aimed to evaluate the frequency and risk factors of its malignant transformation in a Portuguese cohort.

Methods: A multicentric retrospective cohort study was conducted including all patients undergoing endoscopic resection of GHPs ≥10mm from January 2013 to December 2024 in Portuguese tertiary reference centers. Patients with hereditary polyposis syndromes were excluded. Demographic, clinical, endoscopic, and histopathological data were collected.

Results: A total of 782 GHPs from eight centers were evaluated. Evidence of advanced gastritis stage (OLGIM≥3) and synchronous gastric neoplasia was present in 57 (10.2%) and 37 (4.7%) cases, respectively. Most GHPs were removed by endoscopic mucosal resection (86.6%); Neoplastic transformation was observed in 33 polyps (4.2%) – 25 (3.2%) low/high-grade dysplasia and 8 (1.0%) adenocarcinomas; the resection was non-curative in 30.3% of cases. In the multivariate analysis, OLGIM≥3 (OR 4.994, 95%CI 1.036-24.065), lesion size ≥25 mm (OR 7.973, 95%CI 7.973 (1.242-51.180), flat/depressed morphology (OR 9.57, 95%CI 1.096-83.712) and synchronous gastric neoplasia (OR 16.956, 95%CI 2.737-105.045) were independently associated with a higher risk of neoplastic transformation.

Conclusions: The risk of malignant transformation of GHPs is non-negligible, with lesion size, morphology and concomitant precancerous gastric conditions/lesions being associated with a higher risk. Nevertheless, the rate of non-curative endoscopic resection is high. The identification of these features may contribute to optimizing endoscopic resection techniques and surveillance strategies in high-risk patients.

INTRODUCTION AND BACKGROUND

Gastric hyperplastic polyps (GHPs) represent one of the most common types of gastric polyps globally and are particularly common among populations with a high prevalence of *Helicobacter pylori* (HP) infection (1, 2).

GHPs are thought to result from excessive proliferation and increased exfoliation of foveolar cells. Contrary to fundic gland polyps which can arise in healthy mucosa, GHPs are usually found in patients with pre-existent inflammatory gastric conditions (3). Although the exact pathophysiology of GHPs remains incompletely understood, recent studies have shed light on several possible mechanisms. Hypergastrinemia has emerged as a key factor, with studies linking conditions such as HP infection gastritis and autoimmune gastritis to aberrant mucosal proliferation and GHP formation (4-7).

While the majority of GHPs are benign, the risk of neoplastic transformation is non-negligible - 0.8%-9.7% are estimated to progress to dysplasia and 0.6%-3.7% may develop adenocarcinoma (8-14). Previous studies identified lesion size, history of anemia, pedunculated morphology and concomitant epithelial precancerous conditions and lesions in the surrounding mucosa as possible risk factors for the neoplastic progression of GHPs (9, 11, 13, 15). Moreover, a previous study has suggested a higher malignancy risk in the surrounding gastric mucosa than in the polyp itself (10).

Current guidelines offer differing recommendations for the management of GHPs. The *American Society of Gastrointestinal Endoscopy* advocates for the removal of GHPs ≥0.5 cm (16), while the *British Society of Gastroenterology* proposes endoscopic resection of all symptomatic GHPs, as well as those larger than 1 cm or exhibiting a pedunculated morphology (17). Nevertheless, many questions remain regarding the identification of high-risk patients for neoplastic transformation and the endoscopic management of these lesions.

Therefore, our multicentric study aimed to evaluate the frequency and risk factors for neoplastic transformation of GHPs, as well as clinical and oncological outcomes after endoscopic resection, in a country with intermediate-high risk for gastric cancer.

MATERIALS AND METHODS

Study Design, patient selection and data extraction

We conducted a retrospective analysis from 8 centers in Portugal. Patients consecutively undergoing endoscopic resection of GHPs during a 12-year period (January 2013-December 2024) were screened for eligibility.

Patients were enrolled in the study if they met the inclusion criteria: (1) age ≥ 18 years, and (2) GHPs ≥ 10 mm. Patients with hereditary cancer syndromes were excluded from the participant selection.

Retrospectively collected data was obtained from electronic medical records.

Written informed consent was obtained before endoscopic resection of GHPs. The study was approved by the Ethics Committee from the coordinating center (Unidade Local de

Saúde de São João, Porto, Portugal; reference 350/2024). This study followed Strengthening the Reporting of Observational Studies in Epidemiology guidelines. (18)

Endoscopic procedure

All procedures were performed by senior endoscopists/advanced trainees.

Peri-procedure adverse effects (AEs) included major bleeding (hematemesis, melena or anemia), perforation and anesthetic adverse events in the first 7 days after the procedure. Delayed AEs were eligible if they occurred within 30 days after the index endoscopic resection. Intraprocedural bleeding (IPB) was defined as persistent bleeding requiring endoscopic hemostasis. Post-procedural bleeding (PPB) was defined as clinically significant bleeding (hematemesis, melena, or hemoglobin decrease >2 g/dL) resulting in an emergency department visit, admission, or intervention (endoscopy, angioembolization, surgery). Overall AEs included peri-procedure plus delayed AEs.

Technical success was defined as the complete removal of all macroscopically visible tissue during the index endoscopic resection procedure.

En-bloc resection was considered if the lesion was retrieved in a single specimen or *piecemeal* if it was removed in more than one fragment.

In GHPs with neoplastic components, R0 resection was considered whenever pathological evaluation showed free horizontal and vertical margins in an *en-bloc* resected specimen. The probability of curative resection was reported according to the 2022 European Society of Gastrointestinal Endoscopy (ESGE) ESD guidelines criteria (19).

We assumed recurrence of the GHP if it reappeared on the previous area of resection.

Synchronous gastric neoplasia was considered if detected within 6 months of the index endoscopic resection procedure of GHP. If detected >6 months, it was considered metachronous neoplasia.

Histopathological examination

All the specimens collected were analyzed by board-certified pathologists. GHPs with evidence of neoplasia were then reviewed by two expert pathologists with experience in gastrointestinal pathology (IG, FC).

Modified Giemsa staining was performed in tissue sections obtained from formalin-fixed paraffin-embedded blocks of the gastric biopsies for evaluation of H. Pylori infection.

For evaluation and staging of gastritis, in patients in which at least two biopsies from both the gastric antrum and body were obtained in separate vials, the Operative Link for Gastritis Assessment (OLGA) and Operative Link for Gastric Intestinal Metaplasia (OLGIM) scores were retrospectively calculated (20-23). OLGA/OLGIM = 0 was defined as the absence of atrophic gastritis (AG)/intestinal metaplasia (IM). Extensive AG/GIM was defined as OLGA/OLGIM III–IV and non-extensive/focal AG/IM as OLGA/OLGIM I–II.

Evaluated Outcomes

The main evaluated outcome was the frequency and risk factors for neoplastic transformation of GHPs.

Additional outcomes were: a) the frequency of polyp recurrence, b) frequency of synchronous and metachronous neoplastic lesions and c) the efficacy and safety of endoscopic resection techniques in the management of these lesions.

Statistical Analysis

Qualitative variables were described as relative and absolute frequencies. Missing data was excluded from percentages. Quantitative variables were described with mean, median and interquartile range (IQR). Continuous variables were compared using the student t or Mann–Whitney tests, whereas chi-square or Fisher exact tests were used for categoric variables. For variables with missing data, no imputation methods were applied.

Binary logistic regression was used to identify factors associated with neoplastic transformation. Variables having $p<0.05$ on univariate analysis were incorporated into a stepwise multivariate regression model to confirm its independent association with the expected outcome. All significance levels were set at $p<0.05$.

All data was arranged, processed, and analyzed with SPSS ® v.29.0 data (Statistical Package for Social Sciences), Chicago, USA.

RESULTS

Patient characteristics and risk factors for malignancy

Between January 2013 and December 2024, 782 GHPs from 656 patients were included in the study and further analyzed.

In Table 1 we describe patient and GHP characteristics, comparing GHPs with and without neoplastic transformation. In our sample, 58.8% of cases were female and the median age was 68 years (IQR 60-75 years), with no statistically significant differences between groups. Symptoms at diagnosis were evident in almost half of the cases, being iron-deficiency anemia (25.4%) and dyspeptic symptoms (26.5%) the most frequent. There was a history of current/past smoking in 16.6% of cases, being significantly more frequent in the group with neoplasia (OR 2.660, 95%CI 1.039-6.811, p=0.041). No statistically significant differences were observed between groups regarding the history of alcohol consumption or chronic liver disease. A family history of gastric neoplasia was reported in 17.5% of cases (GHP with neoplasia group 13.0% vs. 17.7% GHP without neoplasia).

There was a frequency of H. pylori infection in 42.9% of patients with GHP neoplasia versus 27.3% in the group without neoplasia (OR 2.001, 95%CI 0.930-4.309, p=0.076). The frequency of advanced gastritis stages (OLGA and OLGIM ≥3) was significantly higher in GHPs neoplasia - OLGA≥3 (OR 3.519, 95%CI 1.320-9.385, p=0.012); OLGIM ≥3 (OR 5.705, 95%CI 2.149-15.148, p<0.001).

Synchronous gastric neoplasia was diagnosed in 4.7% of cases, being significantly more frequent in GHPs with neoplastic transformation (OR 5.147; 95% CI 1.981-13.374;

p<0.001). A detailed characterization of synchronous neoplasia and its management in the follow-up is reported in Supplementary Table 1.

Lesion Characteristics

The median lesion size was 15 mm (IQR 12-20). GHPs >25 mm were associated with an increased risk of neoplastic progression of the polyp (OR 4.152; CI 1.900-9.072, p<0.001).

The average number of polyps per patient was 2, ranging from 1 to 100 polyps. Nearly all polyps were located in the antrum (63.4%) or body (32.1%). Most had a predominant polypoid morphology (96.8%) with the remaining being flat (2.2%) or depressed (1.1%) lesions. In univariate analysis, non-polypoid morphology was associated with a significantly higher risk of neoplastic progression (OR 6.473; CI 2.265-18.501, p<0.001).

Endoscopic resection techniques and adverse events

In Table 2, we describe the endoscopic resection techniques performed as well as the reported adverse events. The majority of GHPs were removed by endoscopic mucosal resection (EMR) (86.6%), followed by cold snare polypectomy (8.1%), endoscopic submucosal dissection (ESD) (3.6%) and cold snare EMR (1.7%). 72.7% of the GHPs with neoplastic transformation were removed by EMR and 21.2% by ESD. The technical success rate was 99.9%. Endoscopic resection was not possible in a large (50 mm) sessile lesion of the gastric body – the patient was submitted to a total gastrectomy, with the surgical specimen revealing a GHP with concomitant adenocarcinoma (pT1a, without lymphovascular invasion).

En-bloc removal was achieved for 86.6% of cases (81.8% of malignant GHPs). The overall AE rate was 13.8%, in most cases due to major periprocedural bleeding. No patient experienced gastric perforation and only one had anesthetic adverse events. The rate of PPB was 1.2%.

Histopathological characteristics of the neoplastic lesions

Analysis of the histopathological reports revealed that 33 GHPs (4.2%) had evidence of neoplastic transformation. The histopathological characteristics of these lesions are detailed in Table 3. Among these, 13 GHPs had low-grade dysplasia (39.4%), 12 polyps had high-grade dysplasia (36.4%) and 8 had adenocarcinoma (24.2%). A complete R0 resection was achieved in 85.2% of cases, while 14.8% had a R1 resection status. Regarding the staging of GHPs with adenocarcinoma, 87.5% were classified as T1a and 12.5% were T1b>SM1. Positive vertical margins were identified in 25% of cases of adenocarcinoma (n=2). According to the ESGE Guidelines criteria, the resection was non-curative in 28.1% - 21.9% had a local risk resection and 6.1% had a high-risk resection. Of these, one was submitted to surgery with evidence of residual adenocarcinoma in the surgical specimen.

In the multivariate analysis, OLGIM≥3 (OR 4.994, 95%CI 1.036-24.065), lesion size ≥ 25 mm (OR 7.973; 95%CI 1.242-51.180), flat/depressed morphology (OR 9.57, 95%CI 1.096-83.712) and synchronous gastric neoplasia (OR 16.956, 95% CI 2.737-105.045) were independently associated with a higher risk of neoplastic transformation of the GHP.

Long-term outcomes

The median follow-up time was 19 months (IQR 5-50). 42.3% of GHPs recurred during follow-up (43.7% in the group without neoplasia vs. 22.6% in the group with neoplasia, p=0.024). In the group with GHP neoplasia, the recurrence rate was 13.0% in those with very low-risk resection while it was 57.1% in those with local-risk resection (p=0.043).

Metachronous neoplasia was evident in 6.2% of cases (6.1% in the group without neoplasia vs. 7.1% in the group with neoplasia; p=0.688), after a median follow-up of 23 months (IQR 10-40). Characterization and median follow-up time until metachronous neoplasia is reported in Supplementary Table 1.

DISCUSSION

This multicentric study aimed to evaluate the frequency and predictors of neoplastic progression of GHPs in a population with a moderate to high risk for gastric cancer. We found an overall frequency of neoplastic transformation of GHPs of 4.2%. Besides, we found that lesion size and morphology, as well as concomitant advanced gastritis stages and synchronous neoplasia are significant predictors for neoplastic transformation.

Previous Asian studies reported a frequency of neoplastic transformation of GHPs ranging from 0.53%-16.4% of dysplasia and 0.07%-4.5% of adenocarcinoma (9, 12, 13, 15, 24-33). Notably, in the Western setting, these frequencies range between 0.8%-19.3% for dysplasia and between 0.5%-9.7% for adenocarcinoma within the polyp (8, 10, 11, 14, 34, 35). Our study showed a 3.2% frequency of dysplasia and a 1.0% frequency of adenocarcinoma of the GHP, which is in line with recent single-center Portuguese retrospective cohort by João M. et al., which demonstrated a 3.6% and 0.5% rate of dysplasia and adenocarcinoma, respectively (14). On the other hand, a retrospective multinational study from French, Spanish and Croatian hospitals conducted by Forté et al. showed a 10.4% rate of neoplastic progression in a sample of 144 GHPs, where 9.7% showed dysplasia and 0.7% adenocarcinoma (11). It is important to note that Portugal has a higher incidence of gastric cancer compared to most European countries, largely due to the higher prevalence of HP estimated at approximately 49.7% (42.8-56.7%) (36). A previous study from our group found higher than expected rates of gastric neoplasia not only in asymptomatic healthy individuals but also among patients with compensated advanced chronic liver disease (37). Considering that Portugal has a higher gastric cancer incidence than these countries, it was unexpected to find a considerably lower frequency of dysplastic transformation in our study (36, 38). Differences in lesion characteristics, namely lesion size [the median size of GHPs containing neoplasia in Forté et al. was 40.0 mm (17.0-55.0), whereas in our study was 20.0 mm (13.5-30.0)] could explain, to some extent, these findings. This could serve as a possible explanation, as our study and Forté et al. demonstrated, polyp size ≥ 25 mm substantially increases the risk of neoplastic progression (11).

Several polyp and non-polyp-related factors were analyzed. The prevalence of GHPs was higher in females (58.8%), according to previous evidence (1, 14). Interestingly, neoplastic progression was more common in males (54.5%), although no statistically significant differences were found between sexes. Contrary to previous studies, we found that flat or depressed morphology predisposed to a higher risk of GHP neoplasia than a pedunculated shape (9, 39). Cigarette smoking has been described as an independent

risk factor for the development of intestinal metaplasia, dysplasia and gastric adenocarcinoma (40, 41). Additionally, patients who have a smoking habit and atrophic body gastritis have a higher risk of developing benign gastric epithelial polyps compared to the general population (42, 43). We were able to identify that a current or previous history of smoking increases significantly the risk of neoplastic progression of GHPs in the univariate analysis, although it did not remain statistically significant in the multivariate analysis. HP infection is the most important etiological factor for gastric adenocarcinoma and has been associated with the development of GHPs (2, 44). Yasunaga et al hypothesized that interleukin-1 beta and hepatocyte growth factor production by HP could promote epithelial cell proliferation, contributing to GHP formation in patients with enlarged fold gastritis (45). This statement is supported by studies demonstrating an 80% rate of GHP regression and disappearance following HP eradication (46, 47). In our study, HP infection was present in 42.9% of patients with GHP neoplasia compared to 27.3% in the group without neoplasia, although no statistical difference was found between groups. Regarding gastritis staging, a recent systematic review and meta-analysis suggested that patients with OLGA/OLGIM stage III-IV had a significantly higher risk of developing neoplasia of the gastric mucosa (48). Conversely, there is a lack of studies associating an OLGA or OLGIM stage with the neoplastic progression of GHPs. Nevertheless, in the study by Forté et al., the presence of intestinal metaplasia was identified as a risk factor for neoplastic transformation, albeit the staging was not reported (11). Through multivariate analysis, we observed that an OLGIM≥3 was an independent risk factor for the development of neoplasia of the GHP. Nevertheless, the risk is still higher in the surrounding mucosa. In fact, our study revealed that the presence of synchronous neoplasia was an independent risk factor for neoplastic transformation of the GHP, supporting previous research by Abraham et al. (8). In theory, these findings could favor ESD instead of EMR in patients with GHPs and synchronous neoplasia, particularly taking into account the significant high rate of non-curative resections (specially local-risk resections) in the current study and the previously reported high risk of GHP recurrence in the follow-up (11). Patients with neoplastic GHPs had a higher rate of metachronous neoplasia (18.2%) than patients without polyp neoplasia (6.1%), although no statistical differences were found. There is no consensus on which endoscopic modality is best for GHP removal. Recent guidelines from the British Society of Gastroenterology favor ESD over EMR for removing early gastric neoplasia due to higher *en-bloc* resection and R0 resection rates for lesions above 10 mm (17). Notably, we found a lower R0 resection rate than expected. Possibly, ESD could be preferable in high-risk patients to promote a higher R0 resection rate.

Our study has some limitations that are inherent to the study design. First, a selection bias cannot be excluded since all patients were from tertiary referral centers. On the other hand, the previously highlighted gastric carcinogenesis in the Portuguese population may limit the generalization of the results to other Western countries. The missing data on some relevant variables (such as family history of gastric neoplasia, HP infection status and gastritis staging) may have led to residual confounding. Finally, indication bias regarding endoscopic resection technique should be noted, since the choice was dependent on the preference of the endoscopist and that may have influenced the reported outcomes, namely on the rate of non-curative resections and recurrence in the follow-up. Nevertheless, our study has several strengths that should

be mentioned. This is one of the largest studies on this topic, with carefully selected inclusion and exclusion criteria, and a relatively long follow-up time.

This multicenter retrospective cohort study confirms that the risk of neoplastic changes in GHPs should not be undermined, especially if the patient has certain risk factors that could predispose to neoplastic transformation. Nevertheless, the risk of non-curative endoscopic resection and recurrence in the follow-up are significant, as well as metachronous neoplastic lesions. Altogether, our findings suggest that, particularly in patients with larger lesions, advanced gastritis stages and/or synchronous neoplasia, besides careful choice of endoscopic resection technique, tailored and close follow-up after resection may be recommended.

DISCLOSURE

All authors disclosed no conflicts of interest.

REFERENCES

1. Sonnenberg A, Genta RM. Prevalence of benign gastric polyps in a large pathology database. Digestive and Liver Disease. 2015;47(2):164-9.
2. Elhanafi S, Saadi M, Lou W, Mallawaarachchi I, Dwivedi A, Zuckerman M, et al. Gastric polyps: Association with Helicobacter pylori status and the pathology of the surrounding mucosa, a cross sectional study. World journal of gastrointestinal endoscopy. 2015;7(10):995-1002.
3. Markowski AR, Markowska A, Guzinska-Ustymowicz K. Pathophysiological and clinical aspects of gastric hyperplastic polyps. World journal of gastroenterology. 2016;22(40):8883-91.
4. Waldum H, Fossmark R. Gastritis, Gastric Polyps and Gastric Cancer. International journal of molecular sciences. 2021;22(12).
5. Jeong CY, Kim N, Lee HS, Yoon H, Shin CM, Park YS, et al. Risk Factors of Multiple Gastric Polyps according to the Histologic Classification: Prospective Observational Cohort Study. The Korean journal of gastroenterology = Taehan Sohwagi Hakhoe chi. 2019;74(1):17-29.
6. Zouridis S, Michael M, Arker SH, Sangha M, Batool AJDMR. Gastric hyperplastic polyps: a narrative review. 2022. 2022;6.
7. Massironi S, Elvevi A, Gallo C, Laffusa A, Tortorella A, Invernizzi P. Exploring the spectrum of incidental gastric polyps in autoimmune gastritis. Digestive and Liver Disease. 2023;55(9):1201-7.
8. Abraham SC, Singh VK, Yardley JH, Wu TT. Hyperplastic polyps of the stomach: associations with histologic patterns of gastritis and gastric atrophy. The American journal of surgical pathology. 2001;25(4):500-7.
9. Kang HM, Oh TH, Seo JY, Joen TJ, Seo DD, Shin WC, et al. [Clinical factors predicting for neoplastic transformation of gastric hyperplastic polyps]. The Korean journal of gastroenterology = Taehan Sohwagi Hakhoe chi. 2011;58(4):184-9.
10. Orlowska J, Jarosz D, Pachlewski J, Butruk E. Malignant transformation of benign epithelial gastric polyps. The American journal of gastroenterology. 1995;90(12):2152-9.
11. Forté E, Petit B, Walter T, Lépilliez V, Vanbiervliet G, Rostain F, et al. Risk of neoplastic change in large gastric hyperplastic polyps and recurrence after endoscopic resection. Endoscopy. 2020;52(6):444-53.
12. Terada T. Malignant transformation of foveolar hyperplastic polyp of the stomach: a histopathological study. Medical Oncology. 2011;28(4):941-4.
13. Han AR, Sung CO, Kim KM, Park CK, Min BH, Lee JH, et al. The clinicopathological features of gastric hyperplastic polyps with neoplastic transformations: a suggestion of indication for endoscopic polypectomy. Gut and liver. 2009;3(4):271-5.
14. João M, Areia M, Alves S, Elvas L, Taveira F, Brito D, et al. Gastric Hyperplastic Polyps: A Benign Entity? Analysis of Recurrence and Neoplastic Transformation in a Cohort Study. GE Portuguese journal of gastroenterology. 2021;28(5):328-35.
15. Hu H, Zhang Q, Chen G, Pritchard DM, Zhang S. Risk factors and clinical correlates of neoplastic transformation in gastric hyperplastic polyps in Chinese patients. Scientific reports. 2020;10(1):2582.

16. Evans JA, Chandrasekhara V, Chathadi KV, Decker GA, Early DS, Fisher DA, et al. The role of endoscopy in the management of premalignant and malignant conditions of the stomach. Gastrointestinal Endoscopy. 2015;82(1):1-8.
17. Banks M, Graham D, Jansen M, Gotoda T, Coda S, di Pietro M, et al. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. 2019;68(9):1545-75.
18. Cuschieri S. The STROBE guidelines. Saudi journal of anaesthesia. 2019;13(Suppl 1):S31-s4.
19. Pimentel-Nunes P, Libânio D, Bastiaansen BAJ, Bhandari P, Bisschops R, Bourke MJ, et al. Endoscopic submucosal dissection for superficial gastrointestinal lesions: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022. Endoscopy. 2022;54(6):591-622.
20. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. Am J Surg Pathol. 1996;20(10):1161-81.
21. Rugge M, Meggio A, Pennelli G, Piscioli F, Giacomelli L, De Pretis G, et al. Gastritis staging in clinical practice: the OLGA staging system. Gut. 2007;56(5):631-6.
22. Rugge M, Fassan M, Pizzi M, Farinati F, Sturniolo GC, Plebani M, et al. Operative link for gastritis assessment vs operative link on intestinal metaplasia assessment. World J Gastroenterol. 2011;17(41):4596-601.
23. Rugge M, Genta RM. Staging and grading of chronic gastritis. Human Pathology. 2005;36(3):228-33.
24. Ahn JY, Son DH, Choi KD, Roh J, Lim H, Choi K-S, et al. Neoplasms arising in large gastric hyperplastic polyps: endoscopic and pathologic features. Gastrointestinal Endoscopy. 2014;80(6):1005-13.e2.
25. Daibo M, Itabashi M, Hirota T. Malignant transformation of gastric hyperplastic polyps. The American journal of gastroenterology. 1987;82(10):1016-25.
26. Hizawa K, Fuchigami T, Iida M, Aoyagi K, Iwashita A, Daimaru Y, et al. Possible neoplastic transformation within gastric hyperplastic polyp. Surgical Endoscopy. 1995;9(6):714-8.
27. Horiuchi H, Kaise M, Inomata H, Yoshida Y, Kato M, Toyoizumi H, et al. Magnifying endoscopy combined with narrow band imaging may help to predict neoplasia coexisting with gastric hyperplastic polyps. Scandinavian journal of gastroenterology. 2013;48(5):626-32.
28. Meng L, Zhou L, Li Y, Zhang H, Jin Z, Cui R. [Analysis of clinical, endoscopic and pathological characteristics of gastric hyperplastic polyps]. Zhonghua yi xue za zhi. 2015;95(28):2285-7.
29. Murakami K, Mitomi H, Yamashita K, Tanabe S, Saigenji K, Okayasu I. p53, But Not c-Ki-ras, Mutation and Down-Regulation of p21WAF1/CIP1 and Cyclin D1 Are Associated With Malignant Transformation in Gastric Hyperplastic Polyps. American journal of clinical pathology. 2001;115(2):224-34.
30. Qin S, Xu Y. Progress in clinical diagnosis and treatment for gastric polyps. Zhong nan da xue xue bao Yi xue ban = Journal of Central South University Medical sciences. 2020;45(1):74-8.

31. Zea-Iriarte W-L, Sekine I, Itsuno M, Makiyama K, Naito S, Nakayama T, et al. Carcinoma in gastric hyperplastic polyps. Digestive Diseases and Sciences. 1996;41(2):377-86.
32. Hattori T. Morphological range of hyperplastic polyps and carcinomas arising in hyperplastic polyps of the stomach. Journal of clinical pathology. 1985;38(6):622-30.
33. Bar N, Kinaani F, Sperber AD, Amir-Barak H, Dekel R. Low Risk of Neoplasia and Intraprocedural Adverse Events in Gastric Hyperplastic Polypectomy. 2021;55(10):851-5.
34. Muehldorfer SM, Stolte M, Martus P, Hahn EG, Ell C. Diagnostic accuracy of forceps biopsy versus polypectomy for gastric polyps: a prospective multicentre study. Gut. 2002;50(4):465-70.
35. Ginsberg GG, Al-Kawas FH, Fleischer DE, Reilly HF, Benjamin SB. Gastric polyps: relationship of size and histology to cancer risk. The American journal of gastroenterology. 1996;91(4):714-7.
36. Chen Y-C, Malfertheiner P, Yu H-T, Kuo C-L, Chang Y-Y, Meng F-T, et al. Global Prevalence of Helicobacter pylori Infection and Incidence of Gastric Cancer Between 1980 and 2022. Gastroenterology. 2024;166(4):605-19.
37. Morais R, Moreira J, Gaspar R, Santos-Antunes J, Marques M, Coelho R, et al. Higher frequency of gastric neoplasia in advanced chronic liver disease patients: Impact of screening endoscopy in an intermediate-high risk country. Dig Liver Dis. 2024.
38. Ferlay J. LM, Ervik M. Global Cancer Observatory: Cancer Today. International Agency for Research on Cancer; Lyon, France2020 [cited 2025 march]. Available from: https://gco.iarc.fr/today/home.
39. Zhang DX, Niu ZY, Wang Y, Zu M, Wu YH, Shi YY, et al. Endoscopic and pathological features of neoplastic transformation of gastric hyperplastic polyps: Retrospective study of 4010 cases. World journal of gastrointestinal oncology. 2024;16(11):4424-35.
40. Hatta W, Koike T, Asano N, Hatayama Y, Ogata Y, Saito M, et al. The Impact of Tobacco Smoking and Alcohol Consumption on the Development of Gastric Cancers. 2024;25(14):7854.
41. Inoue M. Epidemiology of Gastric Cancer—Changing Trends and Global Disparities. 2024;16(17):2948.
42. Di Giulio E, Lahner E, Micheletti A, Milione M, D'Ambra G, Bordi C, et al. Occurrence and risk factors for benign epithelial gastric polyps in atrophic body gastritis on diagnosis and follow-up. Alimentary pharmacology & therapeutics. 2005;21(5):567-74.
43. Wang FW, Young SC, Chen RY, Lin KH, Chen YH, Hsu PI, et al. The Prevalence and Risk Factors of Gastric Polyp in Asymptomatic Patients Receiving Health Examination. Gastroenterology research and practice. 2018;2018:9451905.
44. Mbulaiteye SM, Hisada M, El-Omar EM. Helicobacter Pylori associated global gastric cancer burden. Frontiers in bioscience (Landmark edition). 2009;14(4):1490-504.
45. Yasunaga Y, Shinomura Y, Kanayama S, Higashimoto Y, Yabu M, Miyazaki Y, et al. Increased production of interleukin 1 beta and hepatocyte growth factor may contribute to foveolar hyperplasia in enlarged fold gastritis. Gut. 1996;39(6):787-94.

46. Ji F, Wang ZW, Ning JW, Wang QY, Chen JY, Li YM. Effect of drug treatment on hyperplastic gastric polyps infected with Helicobacter pylori: a randomized, controlled trial. World journal of gastroenterology. 2006;12(11):1770-3.
47. Ohkusa T, Takashimizu I, Fujiki K, Suzuki S, Shimoi K, Horiuchi T, et al. Disappearance of hyperplastic polyps in the stomach after eradication of Helicobacter pylori. A randomized, clinical trial. Annals of internal medicine. 1998;129(9):712-5.
48. Yue H, Shan L, Bin L. The significance of OLGA and OLGIM staging systems in the risk assessment of gastric cancer: a systematic review and meta-analysis. Gastric Cancer. 2018;21(4):579-87.

TABLES

	Total (n=782)	**Polyp neoplasia (n = 33)**	**Absence of neoplasia (n = 749)**	**Unadjusted OR (95% CI)**	***P* value**	**Covariate adjusted**	
Sex, n (%) Male	322 (41.2)	18 (54.5)	304 (40.6)	Ref			
Female	460 (58.8)	15 (45.5)	445 (59.4)	0.569 (0.283-1.147)	0.115		
Age, years ≤65	310 (40)	10 (31.3)	300 (40.4)	Ref			
>65	465 (60)	22 (68.8)	443 (59.6)	1.490 (0.696-3.191)	0.305		
Missing	7	1	6				
Symptoms at diagnosis, n (%) Yes	367 (49.9)	11 (37.9)	356 (50.4)	0.601 (0.280-1.290)	0.191		
No	368 (50.1)	18 (62.1)	350 (49.6)	Ref			
Missing	47	4	43				
Smoking, n (%) No	413 (83.4)	14 (66.7)	399 (84.2)	Ref			
Yes	82 (16.6)	7 (33.3)	75 (15.8)	2.600 (1.039-6.811)	**0.041**		
Missing	287	12	275				
Alcohol consumption, n (%) No	305 (64.1)	15 (71.4)	290 (63.7)	Ref			
Yes	171 (35.9)	6 (28.6)	165 (36.3)	0.703 (0.268-1.847)	0.475		
Missing	306	12	294				
Chronic liver disease, n (%) Yes	49 (6.3)	1 (3.0)	48 (6.5)	0.451 (0.06-3.368)	0.437		
No	724 (93.7)	32 (97.0)	692 (93.5)	Ref			
Missing	9	0	9				
Cirrhosis etiology, n (%) Alcoholic	28 (9.4)	0	28 (10.0)	2.265 (0.258-19-905)	0.461		
HCV	5 (1.7)	0	5 (1.8)				
HBV	1 (0.3)	0	1 (0.4)				
NASH	7 (2.4)	1 (5.6)	6 (2.2)				
NASH+Alcoholic	5 (1.7)	0	5 (1.8)				

Alcohol + HCV	2 (0.7)	0	2 (0.7)				
other	1 (0.3)	0	1 (0.4)				
No	248 (83.5)	17 (94.4)	231 (82.8)	Ref			
Missing	485	15	470				
Family history of gastric neoplasia, n (%) Yes	84 (17.5)	3 (13.0)	81 (17.7)	0.696 (0.202-2.399)	0.566		
No	396 (82.5)	20 (87.0)	376 (82.3)	Ref			
Missing	302	10	292				
H. pylori status, n (%) Positive	202 (27.9)	12 (42.9)	190 (27.3)	2.001 (0.930-4.309)	0.076		
Negative	523 (72.1)	16 (57.1)	507 (72.7)	Ref			
Missing	57	5	52				
OLGA, n (%) ≥ Stage 3	58 (10.3)	6 (27.3)	52 (9.6)	3.519 (1.320-9.385)	**0.012**		
< Stage 3	504 (89.7)	16 (72.7)	488 (90.4)	Ref			
Missing	220	11	209				
OLGIM, n (%) ≥ Stage 3	57 (10.2)	7 (36.8)	50 (9.3)	5.705 (2.149-15.148)	**<0.001**	**4.994 (1.036-24.065)**	**0.045**
< Stage 3	501 (89.8)	12 (63.2)	489 (90.7)	Ref		Ref	
Missing	223	14	210				
Synchronous neoplasia, n (%) Yes	37 (4.7)	6 (18.2)	31 (4.1)	5.147 (1.981-13.374)	**<0.001**	**16.956, 95% CI 2.737-105.045**	**0.002**
No	745 (95.3)	27 (81.8)	718 (95.9)	Ref		Ref	
Missing	0	0	0				
Metachronous neoplasia, n (%) Yes	31 (6.2)	2 (7.1)	29 (6.1)	1.180 (0.267-5.219)	0.827		
No	471 (93.8)	26 (92.9)	445 (93.9)	Ref			
Missing	280	28	275				
Polyp size, median (IQR), mm	15 (12-20)	20 (14-30)	15 (12-20)	1.065 (1.035-1.097)	**<0.001**		
≤ 25 mm, n (%)	701 (89.6)	23 (69.7)	678 (90.5)	Ref		**Ref**	

> 25 mm, n (%)	81 (10.4)	10 (30.3)	71 (9.5)	4.152 (1.900-9.072)	**<0.001**	**7.973; 95%CI 1.242-51.180**	**0.029**
Polyp location, n (%) Antrum	495 (63.4)	18 (54.5)	477 (63.8)	Ref	0.220		
Body	251 (32.1)	14 (42.4)	237 (31.7)	1.565 (0.765-3.202)			
Fundus	20 (2.6)	0 (0.0)	20 (2.7)				
Incisura	15 (1.9)	1 (3.0)	14 (1.9)	1.893 (0.236-15.191)	0.548		
Missing	1	0	1				
Lesion morphology, n (%) Polypoid	753 (96.8)	28 (84.8)	725 (97.3)	Ref			
Flat	17 (2.2)	4 (12.1)	13 (1.7)				
Depressed	8 (1.1)	1 (3.0)	7 (0.9)				
Non-polypoid morphology, n (%)	25 (3.3)	5 (15.1)	20 (2.6)	6.473 (2.265-18.501)	**<0.001**	OR 9.57, 95%CI 1.096-83.712	**0.041**
Follow-up time (IQR), months	19 (5-51)						
Recurrence polyp, n (%) Yes	210 (42.3)	7 (25.9)	203 (43.3)	0.459 (0.190-1.106)	0.082		
No	286 (57.7)	20 (74.1)	266 (56.7)	Ref			
Missing	286	6	280				

Table 1: Demographics and lesion-related data. (CI - confidence interval; HCV - Hepatitis C Virus; HBV - Hepatitis B Virus; NASH - Non-alcoholic Steatohepatitis; OLGA - Operative Link for Gastritis Assessment; OLGIM - Operative Link for Gastric Intestinal Metaplasia; IQR - Interquartile Range; OR – Odds ratio)

	Total (n=782)	**Polyp neoplasia (n = 33)**	**Absence of neoplasia (n = 749)**	***P* value**
Endoscopic technique, n (%) Cold snare polypectomy	63 (8.1)	1 (3.0)	62 (8.3)	**<0.001**
Cold snare EMR	13 (1.7)	1 (3.0)	12 (1.6)	
EMR	677 (86.6)	24 (72.7)	653 (87.2)	
ESD	28 (3.6)	7 (21.2)	21 (2.8)	
EFTRD	1 (0.1)	0	1 (0.1)	
Missing	0	0	0	
Technical success, n (%)				
Yes	781 (99.9)	32 (97.0)	749 (100.0)	**0.042**
No	1 (0.1)	1 (3.0)	0 (0)	
Removal, n (%) En bloc	677 (86.6)	27 (81.8)	650 (86.8)	**<0.001**
Piecemeal	104 (13.3)	5 (15.2)	99 (13.2)	
Non feasible	1 (0.1)	1 (3.0)	0 (0.0)	
Missing	0	0	0	
Overall adverse events, n (%) Yes	108 (13.8)	5 (15.2)	103 (13.8)	0.820
No	674 (86.2)	28 (84.8)	646 (86.2)	
Missing	0	0	0	
Adverse events periprocedure, n (%) Yes	103 (13.2)	4 (12.2)	99 (13.2)	0.855
No	679 (86.8)	29 (87.9)	650 (86.8)	
Missing	0	0	0	
Major bleeding periprocedure, n (%) Yes	103 (13.2)	4 (12.2)	99 (13.2)	0.855
No	679 (86.8)	29 (87.9)	650 (86.8)	
Missing	0	0	0	
Late adverse events, n (%) Yes	10 (1.3)	1 (3.0)	9 (1.2)	0.360

No	772 (98.7)	32 (97.0)	740 (98.8)	
Missing	0	0	0	
Late major bleeding, n (%)				
Yes	9 (1.2)	1 (3.0)	8 (1.1)	0.490
No	769 (98.8)	32 (97.0)	737 (98.9)	
Missing	4	0	4	

Table 2: Endoscopic resection techniques and adverse events. (EMR – Endoscopic Mucosal Resection; ESD – Endoscopic Submucosal Dissection; EFTRD – Endoscopic full-thickness resection device)

Neoplasia (n=33)	
Stage of neoplasia, n (%)	
Low-grade dysplasia	13 (39.4)
High-grade dysplasia	12 (36.4)
Adenocarcinoma	8 (24.2)
Resection status, n (%)	
R0	23 (85.2)
R1	4 (14.8)
NA	6
Horizontal margins, n (%)	
H0	23 (85.2)
H1	4 (14.8)
NA	5
Vertical margins, n (%)	
V0	6 (75.0)
V1	2 (25.0)
NA	25
Curative resection criteria (ESGE Guidelines), n (%)	
Very low risk	23 (71.9)
Low risk	0 (0.0)
Local risk	7 (21.9)
High-risk	2 (6.3)
Non-applicable	1
Adenocarcinoma (n=8)	
Lymphatic invasion, n (%)	
Yes	0 (0.0)
No	8 (100.0)
NA	25
Venous invasion, n (%)	
Yes	0 (0.0)
No	8 (100.0)
NA	25
Perineural invasion, n (%)	

Yes	0 (0.0)
No	8 (100.0)
NA	25
Stage adenocarcinoma, n (%)	
T1a	7 (87.5)
T1b>SM1	1 (12.5)

Table 3: Histopathological characteristics of the neoplastic lesions. (ESGE – European Society of Gastrointestinal Endoscopy; NA – non-applicable)

SUPLEMMENTARY TABLES

Synchronous neoplasia (n=37)	
Stage of synchronous neoplasia, n (%)	
Low-grade dysplasia	23 (2.9)
High-grade dysplasia	4 (0.5)
Adenocarcinoma	10 (1.3)
Management of synchronous neoplasia, n (%)	
Surveillance	1 (2.7)
ESD	26 (70.3)
Surgery	5 (13.5)
Loss of follow-up	2 (5.4)
Surgery of GHP with neoplasia	1 (2.7)
Chemotherapy	2 (5.4)
Metachronous neoplasia (n=31)	
Median follow-up time until neoplasia, months (IQR)	23 (10-40)
Stage of metachronous neoplasia, n (%)	
Low-grade dysplasia	24 (4.8)
High-grade dysplasia	2 (0.4)
Adenocarcinoma	5 (1.0)

Suplemmentary table 1: Characterization and management of synchronous and metachronous neoplasia in follow-up. (ESD – Endoscopic Submucosal Dissection; IQR - Interquartile Range)

APPENDIX

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract *"A multicenter retrospective cohort study was conducted"* (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found *"We aimed to evaluate the frequency and risk factors of its malignant transformation in a Portuguese cohort. (...) Demographic, clinical, endoscopic, and histopathological data were collected. (...) A total of 782 GHPs from eight centers were evaluated. Evidence of advanced gastritis stage (OLGIM≥3) and synchronous gastric neoplasia were present in 57 (10.2%) and 37 (4.7%) cases, respectively. Most GHPs were removed by endoscopic mucosal resection (86.6%); Neoplastic transformation was observed in 33 polyps (4.2%) – 25 (3.2%) low/high-grade dysplasia and 8 (1.0%) adenocarcinomas; the resection was non-curative in 30.3% of cases. In the multivariate analysis, OLGIM≥3 (OR 4.994, 95%CI 1.036-24.065), lesion size ≥25 mm (OR 7.973, 95%CI 7.973 (1.242-51.180), flat/depressed morphology (OR 9.57, 95%CI 1.096-83.712) and synchronous gastric neoplasia (OR 16.956, 95%CI 2.737-105.045) were independently associated with a higher risk of neoplastic transformation."*	7
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported *"GHPs are thought to result from excessive proliferation and increased exfoliation of foveolar cells. Contrary to fundic gland polyps which can arise in healthy mucosa, GHPs are usually found in patients with pre-existent inflammatory gastric conditions (3). "Current guidelines offer differing recommendations for management of GHPs. The American Society of Gastrointestinal Endoscopy advocates for the*	8

		removal of GHPs ≥0.5 cm (16), while the British Society of Gastroenterology proposes endoscopic resection of all symptomatic GHPs, as well as those larger than 1 cm or exhibiting a pedunculated morphology (17). Nevertheless, many questions remain regarding the identification of high-risk patients for neoplastic transformation and the endoscopic management of these lesions. "	
Objectives	3	State specific objectives, including any prespecified hypotheses *"Therefore, our multicenter study aimed to evaluate the frequency and risk factors for neoplastic transformation of GHPs, as well as clinical and oncological outcomes after endoscopic resection, in a country with intermediate-high risk for gastric cancer. "*	8
Methods			
Study design	4	Present key elements of study design early in the paper *"We conducted retrospective analysis from 8 centers in Portugal. Patients consecutively undergoing endoscopic resection of GHPs during a 12-year period (January 2013-December 2024) were screened for eligibility."*	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection *"We conducted retrospective analysis from 8 centers in Portugal. Patients consecutively undergoing endoscopic resection of GHPs during a 12-year period (January 2013-December 2024) were screened for eligibility. (...) Retrospectively collected data was obtained from electronic medical records. (...) The median follow-up time was 19 months (IQR 5-50)."*	8,12
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *"Patients were enrolled in the study if they met the inclusion criteria: (1) age ≥ 18 years, and (2) GHPs ≥ 10 mm. Patients with hereditary cancer syndromes were excluded from the participant selection.*	8

		Retrospectively collected data was obtained from electronic medical records. " (*b*) For matched studies, give matching criteria and number of exposed and unexposed N/A	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable *"Peri-procedure adverse effects (AEs) included major bleeding (hematemesis, melena or anemia), perforation and anesthetic adverse events in the first 7 days after the procedure. Delayed AEs were eligible if they occurred within 30 days after the index endoscopic resection. Intraprocedural bleeding (IPB) was defined as persistent bleeding requiring endoscopic hemostasis. Post-procedural bleeding (PPB) was defined as clinically significant bleeding (hematemesis, melena, or hemoglobin decrease >2 g/dL) resulting in an emergency department visit, admission, or intervention (endoscopy, angioembolization, surgery). Overall AEs included peri-procedure plus delayed AEs. Technical success was defined as the complete removal of all macroscopically visible tissue during the index endoscopic resection procedure. En-bloc resection was considered if the lesion was retrieved in a single specimen or piecemeal if it was removed in more than one fragment. In GHPs with neoplastic components, R0 resection was considered whenever pathological evaluation showed free horizontal and vertical margins in an en-bloc resected specimen. The probability of curative resection was reported according to the 2022 European Society of Gastrointestinal Endoscopy (ESGE) ESD guidelines criteria (20). We assumed recurrence of the GHP if it reappeared on the previous area of resection. Synchronous gastric neoplasia was considered if detected within 6 months of the index endoscopic resection procedure of GHP. If detected >6 months, it was considered metachronous neoplasia. (...) The main evaluated outcome was the frequency and risk factors for neoplastic transformation of GHPs. Additional outcomes were: a) the frequency of polyp recurrence, b) frequency synchronous and metachronous neoplastic lesions and c) efficacy and*	8-10

		safety of endoscopic resection techniques in the management of these lesions. (...) Between January 2013 and December 2024, 782 GHPs from 656 patients were included in the study and further analyzed"	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group *"Retrospectively collected data was obtained from electronic medical records."*	8
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at *"Patients were enrolled in the study if they met the inclusion criteria: (1) age ≥ 18 years, and (2) GHPs ≥ 10 mm. Patients with hereditary cancer syndromes were excluded from the participant selection. Retrospectively collected data was obtained from electronic medical records. (...) Between January 2013 and December 2024, 782 GHPs from 656 patients were included in the study and further analyzed"*	8,10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why *"Quantitative variables were described with mean, median and interquartile range (IQR)."*	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding *"Qualitative variables were described as relative and absolute frequencies. Missing data was excluded from percentages. Quantitative variables were described with mean, median and interquartile range (IQR). Continuous variables were compared using the student t or Mann–Whitney tests, whereas chi-square or Fisher exact tests were used for categoric variables. Binary logistic regression was used to identify factors associated with neoplastic transformation. For variables with missing data, no imputation methods were applied. Variables having $p < 0.05$ on univariate analysis were incorporated*	10

		into a stepwise multivariate regression model to confirm its independent association with the expected outcome. All significance levels were set at p < 0.05. All data was arranged, processed, and analyzed with SPSS ® v.29.0 data (Statistical Package for Social Sciences), Chicago, USA." (*b*) Describe any methods used to examine subgroups and interactions *"Variables having p< 0.05 on univariate analysis were incorporated into a stepwise multivariate regression model to confirm its independent association with the expected outcome. All significance levels were set at p < 0.05."* (*c*) Explain how missing data were addressed *"For variables with missing data, no imputation methods were applied."* (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage *"Between January 2013 and December 2024, 782 GHPs from 656 patients were included in the study and further analyzed."* (c) Consider use of a flow diagram	10
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders *"In Table 1 we describe patient and GHPs characteristics, comparing GHPs with and without neoplastic transformation. In our sample, 58.8% of cases were female and the median age was 68 years (IQR 60-75 years), with no statistically significant differences between groups. Symptoms at diagnosis were evident in almost half of the cases, being iron-deficiency anemia (25.4%) and dyspeptic symptoms*	10-11

		(26.5%) the most frequent. There was a history of current/past smoking in 16.6% of cases, being significantly more frequent in the group with neoplasia (OR 2.660, 95%CI 1.039-6.811, p=0.041). No statistically significant differences between groups were observed regarding history of alcohol consumption or history of chronic liver disease. A family history of gastric neoplasia was reported in 17.5% of cases (GHP with neoplasia group 13.0% vs. 17.7% GHP without neoplasia). There was a frequency of H. pylori infection in 42.9% of patients with GHP neoplasia versus 27.3% in the group without neoplasia (OR 2.001, 95%CI 0.930-4.309, p=0.076). The frequency of advanced gastritis stages (OLGA and OLGIM ≥3) was significantly higher in GHPs neoplasia - OLGA≥3 (OR 3.519, 95%CI 1.320-9.385, p=0.012); OLGIM ≥3 (OR 5.705, 95%CI 2.149-15.148, p<0.001). Synchronous gastric neoplasia was diagnosed in 4.7% of cases, being significantly more frequent in GHPs with neoplastic transformation (OR 5.147; 95% CI 1.981-13.374; p<0.001). A detailed characterization of synchronous neoplasia and its management in the follow-up is reported in Supplementary Table 1." (b) Indicate number of participants with missing data for each variable of interest *"In Table 1 we describe patient and GHPs characteristics, comparing GHPs with and without neoplastic transformation.* (c) Summarise follow-up time (eg, average and total amount) *"The median follow-up time was 19 months (IQR 5-50)."*	12
Outcome data	15*	Report numbers of outcome events or summary measures over time *"The median lesion size was 15 mm (IQR 12-20). GHPs >25 mm were associated with an increased risk of neoplastic progression of the polyp (OR 4.152; CI 1.900-9.072, p<0.001). The average number of polyps per patient was 2, ranging from 1 to 100 polyps. Most polyps were located in the antrum (63.4%) or body (32.1%). Most had a predominant polypoid morphology (96.8%) with the remaining being flat (2.2%) or depressed (1.1%)*	10-11

		lesions. (...) In Table 2, we describe the endoscopic resection techniques performed as well as the reported adverse events. The majority of GHPs were removed by endoscopic mucosal resection (EMR) (86.6%), followed by cold snare polypectomy (8.1%), endoscopic submucosal dissection (ESD) (3.6%) and cold snare EMR (1.7%). 72.7% of the GHPs with neoplastic transformation were removed by EMR and 21.2% by ESD. Technical success rate was 99.9%. Endoscopic resection was not possible in a large (50 mm) sessile lesion of the gastric body – the patient was submitted to a total gastrectomy, with the surgical specimen revealing a GHP with concomitant adenocarcinoma (pT1a, without lymphovascular invasion). En bloc removal was achieved for 86.6% of cases (81.8% of malignant GHPs). The overall AE rate was 13.8%, in most cases in relation to major periprocedural bleeding. No patients experienced gastric perforation and only one had anesthetic adverse events. The rate of PPB was 1.2%. Analysis of the histopathological reports revealed that 33 GHPs (4.2%) had evidence of neoplastic transformation. The histopathological characteristics of these lesions are detailed in Table 3. Among these, 13 GHPs had low-grade dysplasia (39.4%), 12 polyps had high-grade dysplasia (36.4%) and 8 had adenocarcinoma (24.2%). A complete R0 resection was achieved in 85.2% of cases, while 14.8% had a R1 resection status. Regarding the staging of GHPs with adenocarcinoma, 87.5% were classified as T1a and 12.5% were T1b>SM1. Positive vertical margins were identified in 25% of cases of adenocarcinoma (n=2). According to the ESGE Guidelines criteria, the resection was non-curative in 28.1% - 21.9% had a local risk resection and 6.1% had a high-risk resection. Of these, one was submitted to surgery with evidence of residual adenocarcinoma in the surgical specimen. "	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized	11

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period *"In the multivariate analysis, OLGIM≥3 (OR 4.994, 95%CI 1.036-24.065), lesion size ≥ 25 mm (OR 7.973; 95%CI 1.242-51.180), flat/depressed morphology (OR 9.57, 95%CI 1.096-83.712) and synchronous gastric neoplasia (OR 16.956, 95% CI 2.737-105.045) were independently associated with a higher risk of neoplastic transformation of the GHP."*	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses *"In the multivariate analysis, OLGIM≥3 (OR 4.994, 95%CI 1.036-24.065), lesion size ≥ 25 mm (OR 7.973; 95%CI 1.242-51.180), flat/depressed morphology (OR 9.57, 95%CI 1.096-83.712) and synchronous gastric neoplasia (OR 16.956, 95% CI 2.737-105.045) were independently associated with a higher risk of neoplastic transformation of the GHP."*	11
Discussion Key Results	18	Summarise key results with reference to study objectives *"This multicentric study aimed to evaluate the frequency and predictors of neoplastic progression of GHPs in a population with a moderate to high risk for gastric cancer. We found an overall frequency of neoplastic transformation of GHPs of 4.2%. Besides, we found that lesion size and morphology, as well as concomitant advanced gastritis stages and synchronous neoplasia are significant predictors for neoplastic transformation. "*	12

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias *"Our study has some limitations that are inherent to the study design. First a selection bias cannot be excluded since all patients were from tertiary referral centers. On the other hand, the previously highlighted gastric carcinogenesis in the Portuguese population may limit the generalization of the results to other Western countries. The missing data on some relevant variables (such as family history of gastric neoplasia, HP infection status and gastritis staging) may have led to residual confounding. Finally, indication bias regarding endoscopic resection technique should be noted, since the choice was dependent on the preference of the endoscopist and that may have influenced the reported outcomes, namely on the rate of non-curative resections and recurrence in the follow-up. "*	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence *"Previous Asian studies reported a frequency of neoplastic transformation of GHPs ranging from 0.53%-16.4% of dysplasia and 0.07%-4.5% of adenocarcinoma (9, 12, 13, 15, 25-34). Notably, in the Western setting, these frequencies range between 0.8%-19.3% for dysplasia and between 0.5%-9.7% for adenocarcinoma within the polyp (8, 10, 11, 14, 35, 36). Our study showed a 3.2% frequency of dysplasia and a 1.0% frequency of adenocarcinoma of the GHP, which is in line with recent single-center Portuguese retrospective cohort by João M. et al., which demonstrated a 3.6% and 0.5% rate of dysplasia and adenocarcinoma, respectively (14). On the other hand, a retrospective multinational study from French, Spanish and Croatian hospitals conducted by Forté et al. showed a 10.4% rate of neoplastic progression in a sample of 144 GHPs, where 9.7% showed dysplasia and 0.7% adenocarcinoma (11). It is important to note that Portugal has a higher incidence of gastric cancer compared to most of other European countries, largely due to the higher prevalence of HP estimated at approximately 49.7% (42.8-56.7%) (37). A previous study from our group found higher than expected rates of gastric neoplasia not only in asymptomatic healthy individuals but also among patients with compensated advanced chronic liver disease (38). Considering that Portugal has a higher gastric cancer incidence than these countries, it was unexpected to find a considerably lower frequency of dysplastic transformation in our study (37, 39). Differences in lesion characteristics, namely lesion size [the median size of GHPs containing*	12-14

neoplasia in Forté et al. was 40.0 mm (17.0-55.0), whereas in our study was 20.0 mm (13.5-30.0)] could explain, to some extent, these findings. This could serve as a possible explanation, as our study and Forté et al. demonstrated, polyp size ≥ 25 mm substantially increases the risk of neoplastic progression (11). Several polyp and non-polyp-related factors were analyzed. The prevalence of GHPs was higher in females (58.8%), according to previous evidence (1, 14). Interestingly, neoplastic progression was more common in males (54.5%), although no statistically significant differences were found between sexes. Contrary to previous studies, we found that flat or depressed morphology predisposed for a higher risk of GHP neoplasia than a pedunculated shape (9, 40). Cigarette smoking has been described as an independent risk factor for the development of intestinal metaplasia, dysplasia and gastric adenocarcinoma (41, 42). Additionally, patients who have a smoking habit and atrophic body gastritis have a higher risk of developing benign gastric epithelial polyps compared to the general population (43, 44). We were able to identify that a current or previous history of smoking increases significantly the risk of neoplastic progression of GHPs in the univariate analysis, although it did not remain statistically significant in the multivariate analysis. HP infection is the most important etiological factor for gastric adenocarcinoma and has been associated with the development of GHPs (2, 45). Yasunaga et al hypothesized that interleukin-1 beta and hepatocyte growth factor production by HP could promote epithelial cell proliferation, contributing to GHP formation in patients with enlarged fold gastritis (46). This statement is supported by studies demonstrating an 80% rate of GHP regression and disappearance following HP eradication (47, 48). In our study, HP infection was present in 42.9% of patients with GHP neoplasia compared to 27.3% in the group without neoplasia, although no statistical difference was found between groups. Regarding gastritis staging, a recent systematic review and meta-analysis suggested that patients with OLGA/OLGIM stage III-IV had a significantly higher risk of developing neoplasia of the gastric mucosa (49). Conversely, there is a lack of studies associating an OLGA or OLGIM stage with the neoplastic progression of GHPs. Nevertheless, in the study by Forté et al the presence of intestinal metaplasia was identified as a risk factor for neoplastic transformation, albeit the staging was not reported (11). Through multivariate analysis, we observed that an OLGIM≥3 was an independent risk factor

		for the development of neoplasia of the GHP. Nevertheless, the risk is still higher in the surrounding mucosa. In fact, our study revealed that the presence of synchronous neoplasia was an independent risk factor for neoplastic transformation of the GHP, supporting previous research by Abraham et al. (8). In theory, these findings could favor ESD instead of EMR in patients with GHPs and synchronous neoplasia, particularly taking into account the significant high rate of non-curative resections (specially local-risk resections) in the current study and the previously reported high risk of GHP recurrence in the follow-up (11). Patients with neoplastic GHPs had a higher rate of metachronous neoplasia (18.2%) than patients without polyp neoplasia (6.1%), although no statistical differences were found. There is no consensus on which endoscopic modality is best for GHP removal. Recent guidelines from the British Society of Gastroenterology favor ESD over EMR for removing early gastric neoplasia due to higher en-bloc resection and R0 resection rates for lesions above 10 mm (17). Notably, we found a lower R0 resection rate than expected. Possibly, ESD could be preferable in high-risk patients in order to promote a higher R0 resection rate."	
Generalisability	21	Discuss the generalisability (external validity) of the study results *"Nevertheless, our study has several strengths that should be mentioned. This is one of the largest studies on this topic, with carefully selected inclusion and exclusion criteria, and a relatively long follow-up time."*	13-14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based *"All authors disclosed no financial interests."*	14

*Give information separately for exposed and unexposed groups.**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Guide for Authors

Guide for authors

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- At the discretion of the Editor, images and tables may appear in the print version of the Journal, the electronic version, or both.

  Random figures will be checked for image manipulation.

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- All videos or graphics submitted must be of the highest quality possible.
- Submissions of videos that were originally recorded through the S-video or RGB outputs of the endoscope processor are desired.
- *Gastrointestinal Endoscopy* may edit any video or computer graphics. Reviewers, following the usual policy with illustrations, may suggest changes in the video or computer graphic.
- A sound track is highly recommended, but not required.
- Each video file must be less than 300 MB in size. If the file is larger than 300 MB, you will need to break it up into two or more smaller files.
- Maximum cumulative length of videos or computer graphics is 8 minutes, and materials may be divided into several smaller clips not to exceed 8 minutes in total. If the video or animation is divided into several clips, each clip should be identified at the beginning of the section (eg, Video Clip 1, Graphic 1) and on the disk. Several videos/graphics may be on the same disk, but if they are separate clips, they must be saved as separate files. When needed, use of simple transitions, eg, fade in/out dissolve, dip to color dissolve, are suggested.

- Concise legends (typed on a separate page) must accompany each video clip or computer graphic presentation.
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References

References must be cited in the text in consecutive order and identified by superscript numbers.

- It is the author's responsibility to check the accuracy of all references by verifying them against the original documents. Citations can be verified by using PubMed's Citation Matcher (http://www.ncbi.nlm.nih.gov/entrez/query/static/citmatch.html).
- Examples of correct forms of reference, in accordance with Uniform Requirements for Manuscripts Submitted to Biomedical Journals,1 are given in the online submission instructions.
- Follow Index Medicus for journal title abbreviations (http://www.ncbi.nlm.nih.gov/nlmcatalog/journals).
- References should follow "Vancouver style." See the examples at http://www.nlm.nih.gov/bsd/uniform_requirements.html.
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PCs. Cmd-A for Macs), highlight the entire text of the file, including the references. (2) Use the keystroke command Ctrl-6 for PCs or Cmd-6 for Macs. (3) Save. This will remove the links (permanently) without disturbing the reference numbers or the citations. It is recommended that you save one copy of your manuscript with the EndNote links in place (for your reference) and one copy of your manuscript without the EndNote links (for submission purposes).

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1. International Committee of Medical Journal Editors. Uniform requirements formanuscripts submitted to biomedical journals. Available at: http://www.icmje.org . Accessed June 11, 2004.

2. Office of Research Integrity. Managing allegations of scientific misconduct: a guidancedocument for editors.

3. World Medical Association Declaration of Helsinki. Recommendations guidingphysicians in biomedical research involving human subjects. JAMA 1997;277:925-6.

4. Institute of Laboratory Animal Resources, National Research Council. Guide for the careand use of laboratory animals. Washington, DC: National Academy Press, 1996.

5. Moher D, Schulz KF, Altman D; CONSORT Group (Consolidated Standards of ReportingTrials). The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. JAMA 2001;285:1987-1991.

6. Iverson CL, Flanagin A, Fontanarosa PB, Glass RM, Giltman P, Lantz JC, et al. AmericanMedical Association manual of style: a guide for authors and editors. 9th ed. Baltimore, MD: Williams Wilkins; 1998. p. 319-28.

Updated May 2021

The content on this site is intended for healthcare professionals.

Centro de Epidemiologia Hospitalar

Tomei conhecimento. Nada a opor. À DC CSH.

07 de Fevereiro de 2025

A Diretora do Centro de Epidemiologia Hospitalar

(Prof.ª Doutora Ana Azevedo)

DIRECÇÃO CLÍNICA

2025 -02- 10

n.º 350 / 2024

SÃO JOÃO

PEDIDO DE AUTORIZAÇÃO

Realização de Investigação

Deliberado concordar, nos termos legais em vigor.

CONSELHO DE ADMINISTRAÇÃO DA ULS SÃO JOÃO, EPE - REUNIÃO DE
Presidente do Conselho de Administração

(Prof.ª Doutora Maria João Baptista) 13 FEV. 2025

Diretora Clínica para a área dos cuidados de saúde hospitalares	Diretora Clínica para a área dos cuidados de saúde primários	Enfermeiro Diretor	Vogal Executiva	Vogal Executivo
Elisabete Barbosa	Dra. Ligia Silva	Enf. Pablo Emilio		

Exmo(a). Senhor(a) Presidente do Conselho de Administração do Centro Hospitalar Universitário de São João

Nome do Investigador Principal:
Rui Jorge Guedes Morais

Título da Investigação:
Frequency and risk factors for malignant evolution of gastric hyperplastic polyps in a country with an intermediate-high risk for gastric cancer

Pretendendo realizar no(s) Serviço(s) de:
Gastrenterologia

a investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efetivação.

Para o efeito, anexo toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar Universitário de São João respeitante à investigação, à qual enderecei pedido de apreciação e parecer.

Com os melhores cumprimentos.

O Investigador/ Promotor

Porto, 09 *de* setembro *de* 2024 .

assinatura

Centro Hospitalar São João
Centro de Epidemiologia Hospitalar

5/2/2025

SÃO JOÃO

Encarregado de Proteção de Dados
Data Protection Officer

Entrada 5/2/2025

CES-IM005-2

Parecer da Comissão de Ética do
Centro Hospitalar Universitário de São João
Unidade Local de Saúde de São João

Título do Projeto: Frequency and risk factors for malignant evolution of gastric hyperplastic polyps in a country with an intermediate-high risk for gastric cancer

Nome do Investigador Principal: Prof. Doutor Rui Jorge Guedes Morais (assistente hospitalar em Gastrenterologia na ULS São João e docente na FMUP). São co-investigadores o Dr. João Cláudio Faria dos Santos Antunes, a Dra. Maria João Neto Almeida e Maria Luísa Faro Fernandes (estudante da FMUP).

Onde decorre o Estudo: No Serviço de Gastrenterologia da ULS de São João. Apresentou declaração do Prof. Doutor Guilherme Macedo.

Objetivos do Estudo:
Determinar quais os fatores de risco que mais contribuem para a progressão dos pólipos gástricos hiperplásicos para neoplasia gástrica, de modo a otimizar a vigilância e a terapêutica nestes doentes.
Estudo realizado no âmbito do Mestrado Integrado em Medicina da FMUP de Maria Luísa Faro Fernandes, sob orientação do Prof. Doutor Rui Jorge Guedes Morais.

Conceção e Pertinência do estudo:
O estudo é pertinente e adequado, porquanto consta no protocolo submetido à CE: "O objetivo primário será determinar quais os factores de risco que mais contribuem para a progressão dos pólipos gástricos hiperplásicos para neoplasia gástrica, de modo a optimizar a vigilância e terapêutica nestes doentes".
Serão incluídos todos os doentes submetidos a ressecção endoscópica de pólipos acima de 10 mm (de janeiro de 2013 a janeiro de 2024), em hospitais de Portugal, que aceitarem o convite para participar na investigação.
O objetivo é comparar pólipos com e sem neoplasia para identificar os fatores preditivos de malignidade. Adicionalmente, os doentes que foram diagnosticados com neoplasia gástrica após este procedimento também serão incluídos.
Estão definidos os critérios de inclusão e as variáveis a ser recolhidas: data de nascimento, sexo, peso, altura, sintomas associados à presença de pólipos gástricos hiperplásicos, presença e caracterização do consumo alcoólico, tabágico e da doença hepática crónica, história familiar de neoplasia gástrica, história de infeção pela Helicobacter pylori, características macroscópicas e microscópicas do pólipo, tipo de terapêutica endoscópica realizada, efeitos adversos relacionados com o tratamento, presença de neoplasias síncronas e metácronas, datas das endoscopias de follow-up. Sugere-se que a data de nascimento seja substituída pela idade de forma a não fragilizar o processo de anonimização.

Benefício/risco:
Não aplicável, visto que se trata de um estudo observacional retrospetivo sem intervenção, não estão previstos riscos/incómodos para os participantes.

Confidencialidade dos dados:
No âmbito do projeto de investigação, não serão usados dados quer permitam a identificação do doente. Adicionalmente usar-se-á codificação dos dados recolhidos.
Apresentou um pedido de reutilização de registos clínicos para Investigação e Desenvolvimento ao RAI, e uma 'avaliação sobre o impacto da proteção de dados' para o EPD.

Respeito pela liberdade e autonomia do sujeito de ensaio: Não aplicável

***Curriculum* do investigador**: Adequado à investigação.

Data previsível da conclusão do estudo: dezembro de 2024. Ressalva-se que a data de início do estudo só pode ser posterior à data de aprovação (e não junho de 2024 como indicado no Formulário).

Conclusão: Proponho um parecer favorável à realização do estudo. Sugere-se que a data de nascimento seja substituída pela idade de forma a não fragilizar o processo de anonimização.

Porto, 18 de outubro de 2024

O Relator da CE, Prof. Doutor Paulo Chaves

Conclusão: Todas as questões foram esclarecidas. Proponho um parecer favorável à realização do estudo.

Porto, 30 de outubro de 2024

O Relator da CE, Prof. Doutor Paulo Chaves

Questionário eletrónico

n.º 350 / 2024

SÃO JOÃO

SUBMISSÃO DE PROJETO DE INVESTIGAÇÃO PARA PARECER E AUTORIZAÇÃO

Preenchimento em formato digital obrigatório

Caro/a Investigador/a

Este questionário vai ser objeto de apreciação pela Comissão de Ética (CE), que emitirá o competente parecer; pelo Responsável de Acesso à Informação (RAI), que emitirá um despacho de autorização ou indeferimento, relativamente à reutilização da informação a que pretende ter acesso; pelo Encarregado de Proteção de Dados (EPD), que emitirá um parecer, mediante a 'avaliação do impacto sobre a proteção de dados' (que deve anexar a este pedido); pelo Centro de Epidemiologia Hospitalar; sendo enviado, num último momento, para decisão institucional do Conselho de Administração do CHUSJ. Os respetivos despachos de parecer e autorização serão exarados no final deste documento, e enviados posteriormente, de modo a poder iniciar, nesse momento, a investigação a que se propõe.

IDENTIFICAÇÃO DO ESTUDO

Título do projeto:

Frequency and risk factors for malignant evolution of gastric hyperplastic polyps in a country with an intermediate-high risk for gastric cancer

Data prevista para início: 01 / 06 /2024 Data prevista para o término: 31 / 12 /2024

EQUIPA DE INVESTIGAÇÃO

1. Investigador principal

Nome: Rui Jorge Guedes Morais

Afiliação institucional: ☒ CHUSJ ☒ FMUP Outro:

Serviço/ Departamento: Gastrenterologia

Grupo profissional: Assistente Hospitalar Cédula Profissional n.º: 56647

Contacto telefónico: 919460418 Endereço eletrónico institucional: ruimorais20@gmail.com

Formação em Boas Práticas Clínicas (GCP): ☐ Não ☒ Sim

2. Co-investigadores

Nome: João Cláudio Faria dos Santos Antunes

Afiliação institucional: CHUSJ

Grupo profissional: Assistente Hospitalar Cédula Profissional n.º: 50017

Contacto telefónico: 917490406 Endereço eletrónico institucional: joao.claudio.antunes@gmail.com

Nome: Maria Luísa Faro Fernandes

Afiliação institucional: FMUP

Grupo profissional: Estudante Cédula Profissional n.º:

Contacto telefónico: 936198436 Endereço eletrónico institucional: luisafaro21@gmail.com

(acrescentar nº de investigadores, se apropriado ao projeto de investigação)

3. Promotor *(se aplicável)*:

CARACTERIZAÇÃO DA INVESTIGAÇÃO

1. Metodologia da investigação

☐ Qualitativa ☒ Mista (qualitativa+quantitativa) ☐ Outra. Qual? _____

Se quantitativa:

☐ Experimental ☒ Observacional ☐ Sem intervenção ☐ Com intervenção

Se experimental ou observacional com intervenção, qual o tipo de intervenção?

☐ Algoritmo de decisão diagnóstica/terapêutica ☐ Comunicação

☐ Outra. Qual? _____

2. Aleatorização dos braços de intervenção: ☐ Não ☒ Sim

3. Se observacional, qual o desenho?

☐ Coorte prospetivo ☒ Coorte retrospetivo ☐ Caso-controlo

☐ Transversal ☐ Ecológico ☐ Outro. Qual? _____

REALIZAÇÃO DA INVESTIGAÇÃO

Local onde se realiza a investigação: ☒ CHUSJ ☐ FMUP ☐ Outro

Serviço/ Departamento: Serviço de Gastroenterologia

Existem outros Centros onde se realizará a investigação? ☐ Não ☒ Sim. Quais? Convidados todos os centros

ENTIDADE(S) QUE TUTELA(M) A INVESTIGAÇÃO

1. CHUSJ – Serviço: Gastroenterologia

2. FMUP – Departamento: _____

3. Outra instituição. Qual? _____

ORIENTADOR *(se aplicável)*

Nome: Rui Jorge Guedes Morais

Afiliação: Centro Hospitalar e Universitái Endereço eletrónico institucional: ruimorais20@gmail.com

PROFISSIONAL DE LIGAÇÃO *(se aplicável - ver anexo)*

Nome: _____ Serviço: _____

ENQUADRAMENTO DA INVESTIGAÇÃO

Em trabalho académico? ☐ Não ☒ Sim Conferidor de grau? ☐ Não ☒ Sim

Síntese dos objetivos:

O objetivo primário será determinar quais os fatores de risco que mais contribuem para a progressão dos pólipos gástricos hiperplásicos para neoplasia gástrica, de modo a otimizar a vigilância e a terapêutica nestes doentes.

Fundamentação ética *(incluir informação sumária sobre o estado da arte, ganhos em conhecimento/inovação, ponderação geral sobre benefícios/risco)*:

PARTICIPANTES PREVISTOS PARA A INVESTIGAÇÃO

Estão definidos critérios de inclusão / de exclusão de doentes? ☐ Não ☒ Sim

Onde e como serão recrutados os participantes no estudo?

Serão recrutados participantes de todos os hospitais públicos portugueses que aceitaram o convite para participar

Qual é o tamanho amostral? Doentes que cumprirem os critérios de seleção dos centros convidados que aceitaram

Está prevista a recolha de material biológico específico para a investigação?

☐ Não ☒ Sim. Identifique e justifique:

Será recolhido tecido gástrico de pólipos hiperplásicos para avaliação histológica, de modo a determinar quais as características específicas dos pólipos que evoluiram para neoplasia.

BENEFÍCIO/RISCO DECORRENTE DA PARTICIPAÇÃO

Descreva os benefícios previsíveis:

Não aplicável, visto que se trata de um estudo observacional retrospetivo sem intervenção, não estão previstos ris

Descreva os riscos/incómodos previsíveis:

Não aplicável, visto que se trata de um estudo observacional retrospetivo sem intervenção, não estão previstos riscos/incómodos para os participantes.

CONSENTIMENTO INFORMADO, ESCLARECIDO E LIVRE

Prevê a obtenção de consentimento informado? ☐ Sim ☒ Não

Se não, justifique: _____

Prevê informação escrita para os participantes? ☐ Sim. **Enviar modelo preenchido.**

☒ Não. Justifique: _____

O modelo para obtenção de consentimento é o modelo institucional do CHUSJ? ☐ Sim ☐ Não

PROTEÇÃO DE DADOS PESSOAIS

Necessita consultar registos clínicos? ☐ Não ☒ Sim

Está previsto o tratamento de dados pessoais? ☐ Não ☒ Sim

Se sim, de que forma é garantida a pseudonimização dos dados recolhidos? *(codificação, uso de filtros, siglas...)*

No âmbito do projeto de investigação, não derão usados os seguintes dados: nome, número de identificação civil/fiscal, número de utente de saúde, morada que poderiam permitir a identificação do doente. Adicionalmente usar-se-á codificação dos dados.

Descreva o património informacional a que pretende ter acesso *(v.g.: nome, idade, data nascimento, idade, morada, diagnóstico, história clínica, tratamento…)*:

Data de nascimento, Sexo, Peso, Altura, Sintomas associados à presença de pólipos gástricos hiperplásicos, Presença e caracterização do consumo alcoólico, tabágico e da doença hepática crónica, História familiar de neoplasia gástrica, História de infeção pela Helicobacter pylori, Características macroscópicas e microscópicas do pólipo, Tipo de terapêutica endoscópica realizada, Efeitos adversos relacionados com o tratamento, Presença de neoplasias síncronas e metácronas, Datas das endoscopias de follow-up,

Está prevista a criação de um Banco de Dados? ☐ Não ☒ Sim

Está previsto o registo de som ou de imagem dos participantes? ☒ Não ☐ Sim

O estudo envolve investigação genética? ☒ Não ☐ Sim

PROPRIEDADE INTELECTUAL

De quem será a propriedade intelectual da investigação e seus resultados?

☒ Investigador ☐ Promotor ☐ Serviço/CHUSJ ☐ Todos

DIVULGAÇÃO DOS RESULTADOS

Está prevista a divulgação dos resultados da investigação? ☐ Não ☒ Sim

Se sim, estão definidos critérios de publicação? ☒ Não ☐ Sim. Quais? _____

CONTRAPARTIDAS PARA OS PARTICIPANTES

Estão previstas contrapartidas para os participantes? ☒ Não ☐ Sim

Pela participação? ☒ Não ☐ Sim

Pelas deslocações? ☒ Não ☐ Sim

Pelas perdas salariais? ☒ Não ☐ Sim

Por outras perdas e/ou danos? ☒ Não ☐ Sim

EXAMES COMPLEMENTARES DE DIAGNÓSTICO

Estão previstos exames complementares de diagnóstico, para além dos inerentes à rotina assistencial?

☒ Não ☐ Sim. Quais? _____

Por quem serão suportados estes custos?

PROTOCOLO FINANCEIRO

Existe protocolo financeiro com o CHUSJ? ☒ Não ☐ Sim

SEGURO

Este estudo prevê intervenção clínica que implique a existência de um seguro para os participantes?

☒ Não ☐ Sim *(se sim, junte cópia da respetiva Apólice)*

Data previsível para fim do acesso aos dados: 31 / 12 / 2024

DOCUMENTOS ANEXOS *(em suporte digital)*

- [x] Pedido de autorização ao Presidente do Conselho de Administração do CHUSJ
- [x] Protocolo do estudo
- [ ] Caderno de recolha de dados (CRF)
- [x] Declaração Diretor(es) Serviço(s)
- [x] Informação Orientador
- [ ] Profissional de ligação
- [ ] Informação aos participantes
- [ ] Modelo de consentimento a utilizar
- [ ] Instrumentos de avaliação *(escalas, inquéritos)* _____
- [x] Curriculum/a vitae *(investigador/es)*
- [ ] Questionário para Encarregado de Proteção de Dados (EPD)
- [ ] Termo de Responsabilidade do Centro Académico Clínico *(para investigadores da FMUP que não pertençam ao CHUSJ)*
- [ ] Protocolo financeiro
- [ ] Outros: _____

TERMO DE RESPONSABILIDADE

Aceitação dos termos e condições de reutilização

Cumulativamente com as obrigações decorrentes da *Lei n.º 26/2016, de 22 de agosto*, maxime dos *n.º 2 e 3 do artigo 21 e o n.º 1 e 2 do artigo 12*, ao submeter o presente pedido, concordo e fico ainda juridicamente vinculado aos seguintes termos e condições:

- Comprometo-me a manter confidencial toda a informação à qual vou ter acesso;
- Após explicação do RAI do CHUSJ, embora a Lei 26/2016, de 22 de agosto, imponha como requisito a anonimização sem possibilidades de reversão, tal desiderato, é não só uma impossibilidade matemática já comprovada, como ainda resulta num prejuízo para a investigação, face à quantidade e à qualidade da informação a retirar à fonte, razão pela qual, concordando com o RAI, assumimos como compromisso a pseudonimização, o que impõe uma avaliação e gestão do risco, num quadro ético-jurídico que aceitamos e nos comprometemos a colaborar e respeitar;
- Não vou elaborar registos, suscetíveis de identificar ou tornar identificável a identidade das pessoas a quem os mesmos dizem respeito;
- Comprometo-me a consultar os processos clínicos nos termos e locais que me forem indicados para o efeito;
- Tomei conhecimento, que a violação de qualquer dos compromissos aqui assumidos, poderá resultar no apuramento de responsabilidades disciplinares, civis e penais, e ainda, à impossibilidade futura de aceder a informação de saúde para fins de investigação.
- Independentemente de requerer a Certidão de Reutilização, DAta REuse Certificate for Research (DARE), comprometo-me a citar as fontes, sempre que publicitar, no todo ou em parte, resultados da presente investigação.

COMPROMISSO DE HONRA E DECLARAÇÃO DE INTERESSES

Eu, Rui Jorge Guedes Morais ,

abaixo assinado, na qualidade de Investigador Principal, declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes na Declaração de Helsínquia (1960, e sucessivas emendas), da Organização Mundial de Saúde, da Convenção de Oviedo e das 'Boas Práticas Clínicas' (GCP/ICH) no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CE de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo, nos últimos três meses. Comprometo-me a entregar à CE o relatório final da investigação, assim que concluído.

Data: 09 / 09 / 2024

Rui Morais
assinatura

COMISSÃO DE ÉTICA CHUSJ/FMUP

~~Centro Hospitalar~~ **~~São João~~**

Parecer da CE, emitido na reunião plenária de 18 / 10 / 2024

Aguarda esclarecimentos.

CONSIDERADOS QUE FORAM COMO SATISFATÓRIOS OS ESCLARECIMENTOS PRESTADOS PELO(A) INVESTIGADOR(A), A CES APROVA POR UNANIMIDADE O PARECER DO RELATOR, PELO QUE NADA TEM A OPOR À REALIZAÇÃO DESTE PROJETO DE INVESTIGAÇÃO.

30/10/2024

Centro Hosp. Univ. São João
Comissão de Ética
Manuel Vaz Silva
Presidente

Centro Hosp. Univ. São João
Comissão de Ética
Manuel Vaz Silva
Presidente

RAI 24019528

RAI - Responsável pelo Acesso à Informação no Centro Hospitalar Universitário de São João (Art. 9º, Lei 26/2016 de 22 de Agosto)

Recebido em
05/11/2024
TM

P'G
13/11/2024

CENTRO DE EPIDEMIOLOGIA HOSPITALAR

ENCARREGADO DE PROTEÇÃO DE DADOS (EPD)
UNIDADE LOCAL DE SAÚDE SÃO JOÃO, E.P.E.

Paulo Alexandre Mota da Silva

Encarregado de Proteção de Dados da ULS SÃO JOÃO

epd@ulssjoao.min-saude.pt

Ref.ª CES ULSSJOAO: **350 / 2024**

Ref.ª EPD: **474 / 2024**

Título do Projeto Frequency and risk factors for malignant evolution of gastric hyperplastic polyps in a country with an intermediate-high risk for gastric cancer.

Responsável pelo tratamento	Rui Jorge Guedes Morais
Instituição	Unidade Local de Saúde de São João (ULS SÃO JOÃO)
	Faculdade de Medicina da Universidade do Porto (FMUP)
Investigador	**Interno** Externo
Contacto telefónico	919460418 **Endereço Electrónico** u011791@chsj.min-saude.pt
Profissional de Ligação	Não aplicável
Amostra	100

Análise de Risco Tolerável: **Baixo** Elevado Muito Elevado

Parecer do EPD: 49/2025 **Data:** 04/02/2025

Finalidade: determinar quais os fatores de risco que influenciam a progressão maligna dos pólipos gástricos hiperplásicos.

Licitude: fundamento previsto no artigo **9(2)**(j), com as garantias do **89(1)** do **RGPD**, e artigo **31(1)** da **LERGPD**.

Categorias de dados pessoais: variáveis identificadas com detalhe na AIPD, datada de 15/11/2024, **ponto 13**, tendo presente o **princípio da minimização dos dados.**

Conservação: os dados serão alvo de **pseudonimização**, armazenados em **local seguro**, em área restrita com acesso limitado ao Investigador Principal, com acesso a ficheiros protegido por **palavra-passe**, efetuando-se a conservação até a conclusão da investigação, durante o prazo máximo de **quatro (4) meses**. Os dados recolhidos serão destruídos após a finalização do estudo.

Comunicação de Dados: **não há partilha** de dados pessoais.

Conclusão: Face ao exposto, e observadas as recomendações, entende-se que o presente projeto está em conformidade com o RGPD pelo que sou de parecer **favorável** quanto à sua realização.

Recomendações:

1. Reforçar as medidas de segurança previstas para a conservação dos documentos em formato de papel que impeçam o acesso à informação a pessoas não autorizadas, bem como o seu manuseamento indevido;
2. Garantir medidas de segurança adicionais no transporte dos dados com recurso a dispositivos electrónicos de armazenamento (Laptop, Pen), nomeadamente através de medidas de cifragem e autenticação;
3. Garantir medidas de segurança adicionais (ex. transformar os dados com recursos a técnicas de generalização, perturbação e/ou como último recurso, a supressão de dados) para os dados que, ainda que pseudonimizados, contém elementos informativos que no seu conjunto possibilitam a re-identificação dos participantes, tendo presente a amostra em estudo (doentes com diagnóstico histológico de pólipos gástricos hiperplásicos), em particular na fase de disseminação ou publicação dos resultados (incluindo repositórios científicos).
4. A chave de descodificação que permite a re-identificação dos titulares dos dados (doentes) deve ficar sempre na posse do Investigador Principal ULS SÃO JOÃO e protegida de acessos indevidos / terceiros;
5. Em caso de necessidade de extensão de prazo e/ou de qualquer alteração dos pressupostos atinentes ao presente parecer o Investigador Principal deverá solicitar a reapreciação do projeto de investigação junto do EPD.

Revisão AIPD:

☐ Data da próxima revisão:

☒ Não carece de revisão.

Anexos:

1. Processo CES n.º 350/2024
2. Parecer CES (30/10/2024)
3. AIPD (15/11/2024)
4. Protocolo de investigação

Encarregado de Proteção de Dados
Assinado por: **PAULO ALEXANDRE MOTA DA SILVA**
Data: 2025.02.04 16:29:40+00'00'
Localização: ULS SÃO JOÃO

CARTÃO DE CIDADÃO

FACULDADE DE **MEDICINA**