

MESTRADO INTEGRADO EM MEDICINA

2022/2023

João Pedro Leal Moreira

The prevalence of gastric neoplasia is increased in chronic liver
disease compared to a healthy screening population

março, 2023

FMUP

U. PORTO



**FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO**

João Pedro Leal Moreira

The prevalence of gastric neoplasia is increased in chronic
liver disease compared to a healthy screening population

Mestrado Integrado em Medicina

Área: Ciências médicas e da saúde > Medicina clínica

Tipologia: Dissertação

Trabalho efetuado sob a Orientação de:

Doutor Rui Jorge Guedes Morais

E sob a Coorientação de:

Prof. Dr. Manuel Guilherme Gonçalves Macedo

Trabalho organizado de acordo com as normas da revista:

GE - Portuguese Journal of Gastroenterology

março, 2023

FMUP

Eu, ___João Pedro Leal Moreira___, abaixo assinado, nº mecanográfico ___201705546___, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter atuado com absoluta integridade na elaboração deste projeto de opção.

Neste sentido, confirmo que **NÃO** incorri em plágio (ato pelo qual um indivíduo, mesmo por omissão, assume a autoria de um determinado trabalho intelectual, ou partes dele). Mais declaro que todas as frases que retirei de trabalhos anteriores pertencentes a outros autores, foram referenciadas, ou redigidas com novas palavras, tendo colocado, neste caso, a citação da fonte bibliográfica.

Faculdade de Medicina da Universidade do Porto, _23/_03/_2023_

Assinatura conforme cartão de identificação:

João Pedro Leal Moreira

NOME

João Pedro Leal Moreira

NÚMERO DE ESTUDANTE

201705546

E-MAIL

joaopl20@gmail.com

DESIGNAÇÃO DA ÁREA DO PROJECTO

Ciências médicas e da saúde > Medicina clínica

TÍTULO DISSERTAÇÃO/~~MONOGRAFIA~~ (riscar o que não interessa)

The prevalence of gastric neoplasia is increased in patients with chronic liver disease compared to a healthy screening population

ORIENTADOR

Rui Jorge Guedes Morais

COORDINADOR (se aplicável)

Manuel Guilherme Gonçalves Macedo

ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTA TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTA TRABALHO (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTA TRABALHO.	☒

Faculdade de Medicina da Universidade do Porto, _23_/_03/_2023_

Assinatura conforme cartão de identificação:

João Pedro Leal Moreira

À minha família, sem vocês nada disto seria possível.

Ao João, por toda a paciência e suporte durante estes anos.

À Maria, pela amizade e companheirismo singulares.

Ao meu orientador, professor Rui, pelo empenho, trabalho e ajuda.

Aos que fizeram questão de estarem presentes.

E, por último, particularizando esta conquista, a ti pai, eu consegui!

“Curar algumas vezes, aliviar muitas vezes e consolar sempre”.

Hipócrates

The prevalence of gastric neoplasia is increased in patients with chronic liver disease compared to a healthy screening population

A prevalência de neoplasia gástrica está aumentada em pacientes com doença hepática crónica comparado a uma população saudável de rastreio

João Moreira^a, Rui Morais^{a,b}, Rui Gaspar^{a,b}, João Antunes-Santos^{a,b}, Margarida Marques^{a,b}, Rosa Alves^c, Joel Silva^{a,b}, Emanuel Dias^{a,b}, Pedro Pereira^{a,b}, Susana Lopes^{a,b}, Hélder Cardoso^{a,b}, Irene Gullo^{a,d,e}, Fátima Carneiro^{a,d,e}, Rodrigo Liberal^{a,b}, Guilherme Macedo^{a,b}

^a Faculty of Medicine of the University of Porto (FMUP)

^b Gastroenterology Department, Centro Hospitalar Universitário São João, Porto, Portugal

^c Internal Medicine Department, Hospital Garcia da Orta

^d Department of Pathology, Centro Hospitalar Universitário de São João

^e i3S - Instituto de Investigação e Inovação em Saúde and Institute of Molecular Pathology and Immunology, University of Porto (Ipatimup)

Short Title: The prevalence of gastric neoplasia is increased in patients with chronic liver disease compared to a healthy screening population

Corresponding author:

Rui Jorge Guedes Morais

Gastroenterology Department

Centro Hospitalar Universitário São João

Porto, Portugal

Tel: 919460418

E-mail: ruimorais20@gmail.com

Number of Tables: 7 (2 supplementary tables)

Number of Figures: 1

Word count: 3320 (manuscript 3979; abstract 341)

Keywords: Gastric neoplasia; advanced chronic liver disease ; gastric cancer screening

Neoplasia gástrica; doença hepática crónica avançada; rastreio cancro gástrico

Abstract

Introduction: Gastric cancer (GC) is a major worldwide health concern. For several years now, numerous studies reported a higher prevalence of GC in patients with advanced chronic liver disease (ACLD). The Baveno VII criteria were proposed to identify patients could safely avoid screening esophagogastroduodenoscopy (EGD). Therefore, our main objective was to evaluate the prevalence of gastric neoplasia in cACLD patients that underwent EGD for screening of gastro-esophageal varices compared to a healthy screening population. We also sought to assess the clinical outcomes after the diagnosis gastric neoplasia in the cACLD population.

Material and Methods: Retrospective case-control study that enrolled all asymptomatic cACLD patients who underwent EGD for gastro-esophageal varices screening from January 2008 to June 2018 in a tertiary reference center. Cases were matched with asymptomatic healthy individuals who underwent EGD for GC screening at the same time as colonoscopy performed for colorectal cancer (CRC) screening in a private-hospital setting between April 2017 and March 2018. All data was arranged, processed and analyzed with SPSS ® v.27.0 data.

Results: A significantly higher prevalence of gastric neoplasia in patients with cACLD compared to controls was observed (4.2% vs. 1.1%; $p < 0.001$). The overall prevalence of gastric carcinoma and dysplasia were 1.4% and 0.7%, respectively, and was significantly higher in cases than in controls. Age ≥ 60 years, absence of *H. pylori* infection, and OLGIM stage $\geq$ III were identified as independent risk factors for gastric neoplasia. Seven cases of gastric neoplasia were diagnosed in patients who, according to the Baveno VII criteria, could avoid EGD for diagnosis of gastro-esophageal varices.

Discussion/conclusion: We found a higher prevalence of gastric neoplasia in patients with cACLD than in healthy controls who were undergoing an already scheduled screening colonoscopy. The Baveno VII criteria suggest that EGD screening for gastro-esophageal varices may be preventable in certain patient groups. Based on our results, we suggest that in countries with intermediate-high risk for GC, continuing to perform EGD could be beneficial, as patients with cACLD are at higher risk for GC, and its early detection may be associated with better outcomes.

Resumo

Introdução: O cancro gástrico é um importante problema de saúde mundial. Há vários anos que numerosos estudos relatam uma maior prevalência de cancro gástrico em doentes com doença hepática crónica avançada. Os critérios Baveno VII foram propostos para identificar doentes que podem evitar com segurança a realização de endoscopia esofagogástrica. Assim, o nosso principal objetivo foi avaliar a prevalência de neoplasia gástrica em pacientes com doença hepática crónica avançada que realizaram endoscopia esofagogástrica para rastreio de varizes gastroesofágicas em comparação com uma população de rastreio saudável. Procuramos também avaliar os resultados clínicos após o diagnóstico de neoplasia gástrica na população com doença hepática crónica avançada.

Material e Métodos: Estudo caso-controlo retrospectivo que inclui todos os participantes assintomáticos com doença hepática crónica avançada que realizaram endoscopia esofagogástrica para rastreio de varizes gastroesofágicas entre janeiro de 2008 e junho de 2018 num centro de referência terciário. Os casos foram comparados com indivíduos saudáveis assintomáticos que realizaram endoscopia esofagogástrica para rastreio de cancro gástrico ao mesmo tempo que a colonoscopia realizada para rastreio de cancro colorrectal num hospital privado entre abril de 2017 e março de 2018. Todos os dados foram organizados, processados e analisados com o software SPSS® v.27.0.

Resultados: Foi observada uma prevalência significativamente maior de neoplasia gástrica em pacientes com doença hepática crónica avançada em comparação com os controlos (4.2% vs. 1.1%; $p < 0.001$). A prevalência global de carcinoma gástrico e displasia foi de 1.4% e 0.7%, respetivamente, e foi significativamente maior nos casos do que nos controlos. Idade ≥ 60 anos, ausência de infeção por *H. pylori* e estadio OLGIM $\geq$ III foram identificados como fatores de risco independentes para neoplasia gástrica. Sete casos de neoplasia gástrica foram diagnosticados em pacientes que, de acordo com os critérios Baveno VII, poderiam evitar a realização de endoscopia esofagogástrica para diagnóstico de varizes gastroesofágicas.

Discussão/conclusão: Encontramos uma maior prevalência de neoplasia gástrica em pacientes com doença hepática crónica avançada do que em controlos saudáveis que realizaram uma colonoscopia de rastreio previamente já agendada. Os critérios Baveno VII sugerem que a realização de endoscopia esofagogástrica para rastreio de varizes gastroesofágicas pode ser evitável em certos grupos de doentes. Com base nos nossos resultados, sugerimos que em países com risco intermédio-alto de cancro gástrico, a continuação da realização de endoscopia esofagogástrica pode ser benéfica, já que os pacientes com doença hepática crónica avançada apresentam um risco mais elevado de cancro gástrico e a sua deteção precoce pode estar associada a melhores outcomes.

Introduction

Gastric cancer (GC) is a major worldwide health concern, as it is the fifth most frequently diagnosed cancer in the world, and the fourth-leading cause of cancer-related deaths [1].

There is a considerable worldwide variation, both in terms of incidence and mortality [1, 2]. In 2020, in Europe, the most affected regions were Central and Eastern Europe (11.3 per 100.000 people). GC incidence and mortality are 2 to 3 times more prevalent in males than in females [2]. GC is most frequently diagnosed in advanced stages, having a five-year survival rate of around 20% [3].

Despite worldwide incidence and mortality rates variation, there isn't a clear geographical pattern [4, 5]. There are countries that don't follow the trend of the region in which they are found, as it is the case of Portugal. Portugal, although being part of Southern Europe, is considered an intermediate to high incidence country, and it has one of the highest GC mortality rates in the world [6-8].

Considering the difficulty in recognition and the poor prognosis of GC, some strategies have been proposed for early detection and prevention: eradication of *Helicobacter Pylori* (Hp) infection, gastric cancer biomarkers and endoscopic screening [9]. Endoscopic screening has been used in GC screening in countries such as Japan [10]. In this country, and in other high-incidence regions, screening by esophagogastroduodenoscopy (EGD) improves survival and it is cost-effective [11]. For countries with intermediate risk of GC, more evidence is needed to understand if the screening by EGD is also cost-effective.

Several risk factors for GC have been described. Hp infection is the most important established risk factor for non-cardia GC [12]. There are also risk factors that are still controversial, such as HBV infection [13]. For several years now, numerous studies have also reported a higher prevalence of GC in patients with advanced chronic liver disease (ACLD) [14-18].

All patients with compensated ACLD (cACLD) should be screened for gastro-esophageal varices [19]. The standard paradigm of screening varices has, for the greater part, involved EGD. However, the Baveno VI criteria and more recently the Baveno VII criteria were proposed to identify patients could safely avoid screening EGD [20, 21]. This current recommendation states that patients with liver stiffness measurement (LSM) by transient elastography (TE) $\geq 20\text{kPa}$ and platelet count (PC) $\leq 150 \times 10^9/\text{L}$ should undergo EGD [20]. Even though several studies have validated Baveno VI criteria, regarding the prediction of presence of gastro-esophageal varices, they have all failed to acknowledge the possible role impact of the non-performed EGD in cACLD patients in screening for a possible concurrent upper gastrointestinal neoplasia [21-24].

In the particular case of early gastric cancer, endoscopic submucosal dissection (ESD) has emerged as the first-line therapy in the therapeutic management of this condition, being a minimally invasive and effective technique, with a low risk of complications, even in ACLD patients [25-27].

Therefore, our main objective was to evaluate the prevalence of gastric neoplasia in cACLD patients that underwent EGD for screening of gastro-esophageal varices (including the missed-lesion rate if the Baveno criteria had been strictly followed), compared to a healthy screening population. We also

sought to assess the clinical outcomes, efficacy and safety after surgery and/or endoscopic resection of gastric neoplasia in the cACLD population.

Materials and Methods

Study Design

Retrospective case-control study at Centro Hospitalar Universitário São João (CHUSJ), Porto, Portugal, that enrolled all asymptomatic cACLD patients who underwent EGD for gastro-esophageal varices screening from January 2008 to June 2018. Cases were matched with asymptomatic healthy individuals who underwent EGD for GC screening at the same time as colonoscopy performed for colorectal cancer (CRC) screening in a private-hospital setting in the region of Porto, Portugal, between April 2017 and March 2018.

cACLD population

During the evaluated period, a total of 4045 patients attended the Hepatology consultation. The Baveno VII criteria were used to identify cACLD patients. As such, patients were included in the study if any of the following criteria were fulfilled: (a) LSM by TE > 15 kPa; (b) LSM by TE of more than 10 kPa with a suggestive clinical history; (c) patients with a liver biopsy result of F3 or F4; (d) patients with clinical data suggestive of advanced disease, such as thrombocytopenia ($PC \leq 150 \times 10^9/L$), ascites or imaging studies suggestive of liver cirrhosis (LC) (e.g. dysmorphic liver).

We only included cases with at least one clinical evaluation after EGD and with at least one EGD performed for gastro-esophageal varices screening.

Patients were excluded if any of the following were present: (a) no evidence of cACLD; (b) prior history of organ transplantation; (c) ECG was performed for a reason other than screening for esophageal varices, (d) surveillance of previous GC or lymphoma, gastrointestinal bleeding, iron deficiency anaemia or other upper gastrointestinal symptoms, (e) age <18 years.

Controls

Patients in whom screening EGD was proposed by the general practitioner at the same time of colonoscopy were identified. Patients were excluded if any of the following were present: (a) surveillance of previous GC or lymphoma, (b) gastrointestinal bleeding, iron deficiency anaemia or other upper gastrointestinal symptoms, (c) age <18 years.

Endoscopic procedures

Regarding cases, all EGD were performed by experienced endoscopists or fellows in training under supervision. Regarding controls, all EGDs were performed by 2 experienced endoscopists.

In both cases and controls, Olympus® gastroscopes (GIF-Q165, GIF-Q180, GIF-H190) were used. The exams were performed under pharyngeal anesthesia and/or conscious sedation or general anesthesia with intravenous propofol in the presence of an anesthesiologist and 2 nurses. Conventional white light and virtual chromoendoscopy with narrow band imaging were used, depending on the endoscopist preference and experience. In the presence of suspicious lesions, biopsies were performed in a separate vial. If no suspicion lesion were identified, when possible, random biopsies from the antrum and gastric

body using separate vials were taken using the updated Sydney system protocol and were sent for histopathologic evaluation [28].

Histopathological examination

All the specimens collected were reviewed by board-certified pathologists. Histopathological findings of GC were classified according to the Lauren classification [29, 30].

In both cases and controls, Hp infection was evaluated using modified Giemsa staining. Regarding evaluation and staging of gastritis, the final histologic diagnosis was reported according to the updated Sydney system. In patients in which at least two biopsies from both the antrum and gastric body were performed in separate vials, the Operative Link on Gastritis Assessment (OLGA) and the Operative Link on Gastritis/Intestinal-Metaplasia Assessment (OLGIM) were retrospectively calculated, for the purpose of gastritis staging [31, 32]. As previously reported, OLGA/ OLGIM 0 was defined as an 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.

Management after EGD

For the purpose of evaluation of clinical outcomes after the diagnosis of gastric neoplasia, only cases were considered. After EGD, patients with a diagnosis of gastric neoplasia were guided according to the MAPS I and II guidelines, in the presence of pre-malignant lesions, and according to the ESMO guidelines, if diagnosed with GC [33–35]. In the latter, after complete staging, cases were discussed by the Esophago-Gastric Multidisciplinary Team of CHUSJ, treatment was decided and pursued [36]. Immediate and post-procedure adverse events (AEs), disease recurrence, mortality and survival (defined as the time from the date of treatment to either death or the last follow-up contact) were evaluated. Surgery AEs were classified according to the Clavien-Dindo classification [37].

Statistical analysis

All data was arranged, processed and analyzed with SPSS ® v.27.0 data. Categorical variables were described through absolute and relative frequencies and continuous variables as mean and standard deviation, median, minimum and maximum. Hypotheses were tested about the distribution of continuous variables by using the independent sample t-test/one-way Anova or nonparametric Mann-Whitney and Kruskal-Wallis test, depending on if normal or non-normal distribution, respectively. Fisher's exact test or Pearson chi-square test, as appropriate, were used to assess the statistical differences between cases and controls regarding demographic data, prevalence of Hp infection, gastritis staging and prevalence of gastric neoplasia.

Binary logistic regression was used to identify factors associated with gastric neoplasia. 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 $p < 0.05$.

Ethical considerations

This study was conducted according to the Declaration of Helsinki. Informed consent to perform EGD was obtained before the procedure. The study was approved by the Ethics Department of CHUSJ.

Results

Of the 4045 patients who attended the Hepatology outpatient clinic between 2008-2018, we identified 481 cACLD patients that met the inclusion and exclusion criteria. Cases were matched with asymptomatic healthy individuals that underwent EGD at the same time as colonoscopy performed for CRC screening (shown in Fig. 1).

Demographic data

We evaluated 1845 patients (481 cases and 1364 controls), 51.7% males, with a median age of 58 years old [interquartile range (IQR) 49-66 years] (Table 1). There was a positive GC family history in 1.5% of the patients. Besides a male predominance in cases, no other demographic characteristic differed between groups.

Characterization of the cACLD population

Of the 481 patients, 148 (30.8%) had active alcohol consumption and 142 (29.6%) had history of smoking. Alcohol was the most common cause of LC (213 cases, 44.3%), followed by hepatitis C virus (HCV) infection (59 cases, 12.3%) and nonalcoholic steatohepatitis (NASH) (40 cases, 8.3%) (Table 2).

One hundred and fifteen patients (23.9% of cases) had simultaneously LSM by TE ≤ 20 kPa and PC $\geq 150000/\text{mm}^3$.

The patients underwent a median number of 3 EGDs (IQR 2-5) for screening of gastro-esophageal varices. The median follow-up time after EGD was 63 months (IQR 33-97).

H. Pylori infection and gastritis staging

The overall Hp infection prevalence was 44.3%, being significantly higher in controls compared to cases (47.2% vs. 30.3%; $p < 0.001$) (Table 3). Regarding evaluation and staging of gastritis, in the cACLD population there was a significantly higher prevalence of both OLGA and OLGIM stages $\geq \text{III}$, compared to controls (10.2% vs. 1.6%; $p < 0.001$; 12.7% vs. 1.9% $p < 0.001$, respectively).

Prevalence of gastric neoplasia

In our study, the overall prevalence of gastric neoplasia was 1.9% (gastric carcinoma 1.4%; gastric dysplasia 0.7%) (Table 4). The prevalence of gastric neoplasia in cACLD population was significantly higher than that observed in healthy population [$n=20$ (4.2%) vs. $n=15$ (1.1%); $p < 0.001$]. In 3 cases from the cACLD population concomitant gastric carcinoma and gastric dysplasia lesions were identified.

Of the 35 patients with gastric neoplasia, 74.3% ($n=26$) had the diagnosis of gastric carcinoma, with statistically significant differences being observed between cases [$n=14$ (2.9%)] and controls [$n=12$ (0.9%)] ($p = 0.003$). As for the location of the lesions, the most commonly affected site was the gastric body [$n=10$ (38.5%)]. Gastric carcinomas were classified according to Lauren's classification, with the vast majority [$n=20$ (80.0%)] being of the intestinal subtype, with no significant differences between cases and controls regarding the histological subtype ($p = 0.560$). In the population of patients with cACLD, there was one case of neuroendocrine carcinoma [$n=1$ (7.1%)].

In our study, the prevalence of gastric dysplasia was 0.7% ($n=12$), which was statistically significantly different between cases and controls [$n=9$ (1.9%) vs. $n=3$ (0.2%); $p < 0.001$]. Similarly to what was

observed in cases of gastric carcinoma, there were no significant differences in terms of location and histological subtype between cases and controls. As for the histological subtype, most cases were low-grade dysplasia [n=7 (58.2%)], with the controls exclusively presenting low-grade dysplasia lesions [n=3 (100.0%)].

Subanalysis according to the Baveno VII criteria

We evaluated patients that according to the Baveno VII criteria could avoid EGD for the diagnosis of gastro-esophageal varices (n=115, 23.9% of cases). In this subgroup, 7 cases of gastric neoplasia (35% of the total number of cases identified in the cACLD population) were diagnosed (including 4 cases of gastric carcinoma).

Risk factors for gastric neoplasia

A multivariable regression model was developed to identify risk factors associated with a higher risk of gastric neoplasia (Table 5). Age ≥ 60 years [odds ratio (OR) 4.732, 95% confidence interval (CI) 1.573–14.233; p=0.006], absence of Hp infection (OR 4.113, 95% CI 1.168-14.486; p=0.028) and OLGIM stage $\geq$ III (OR 7.277, 95% CI 1.647-32.153; p=0.009) were independently associated with a higher risk of gastric neoplasia. Although the presence of cACLD was associated with an increased risk in the univariate analysis, it did not reach statistical significance in the multivariate analysis.

Clinical outcome and management after diagnosis of gastric neoplasia in cACLD population

The clinical outcome and management of cACLD patients after the diagnosis of gastric neoplasia were evaluated (Table 6).

Gastric carcinoma

Regarding cases of gastric carcinoma (n=14), according to the American Joint Committee on Cancer (AJCC) staging system, most cases corresponded to stage IA [n=8 (57.3%)]. Eleven patients (78.6%) underwent surgical treatment, 2 (14.3%) endoscopic treatment and 1 patient (7.1%) was referred for palliative care, after multidisciplinary discussion.

All patients undergoing endoscopic treatment underwent ESD. The resection was curative in one case (corresponding to an adenocarcinoma pT1a) but in the remainder the endoscopic resection was non-curative (adenocarcinoma pT1b SM2 with lymphatic permeation). In this case, after multidisciplinary discussion, endoscopic surveillance was decided. The patient died 3 months after the procedure due to a decompensation of the liver disease. There were no record of adverse events in the two patients that underwent ESD. The median number of days of hospitalization was 2. During the follow-up period, there was no record of tumor recurrence in any of the cases.

Of the 11 patients who underwent surgical treatment, 72.7% underwent total gastrectomy (n=8) and the remaining 27.3% (n=3) underwent subtotal gastrectomy. R0 resection was achieved in all cases. The median number of days of hospitalization was 10 (IQR 9-21). In 54.5% (n=6) of patients who underwent surgery complications were reported. Two patients died due to surgical complications. The complications and management after its occurrence are described in more detail on Table 7.

In 60.0% of the cases submitted to surgical treatment (n=3), there was a need for additional treatment with neoadjuvant chemotherapy in 1 case (33.3%), and adjuvant chemotherapy in 2 cases (66.7%). As in patients undergoing endoscopic treatment, during the follow-up period there was no record of tumor recurrence.

One patient was referred for palliative care after diagnosis of gastric carcinoma (12 mm ulcerated lesion in the antrum corresponding to a intestinal type adenocarcinoma) due to ACLD with a previous history of multiple decompensations. The patient remains alive and asymptomatic 25 months after the diagnosis of gastric carcinoma.

Over the study period, 50.0% (n=7) of patients diagnosed with gastric carcinoma died. Most of the causes of death were not related to the carcinoma [n=4 (57.1%)]. Of the cases in which the cause was related to this diagnosis [n=3 (42.9%)], 2 died due to surgery-related complications (66.7%) and 1 patient died as a result of tumor progression (33.3%). The overall survival after the diagnosis of gastric carcinoma was 38 months (IQR 6-69), with a 3-years mortality-rate of 42.9%.

Gastric dysplasia

Regarding cases of gastric dysplasia (n=9), 3 were diagnosed and treated concomitantly with the diagnosis of gastric cancer. Among the remaining 6 cases, in 1 (indefinite for dysplasia) endoscopic surveillance was decided. Another case (lesion in the antrum with high-grade dysplasia) underwent subtotal gastrectomy and the remaining cases were treated endoscopically (endoscopic mucosal resection=1; ESD=3). No complications were observed in all patients and in all cases the resections were curative. There was no evidence of recurrence or metachronous lesions in the follow-up.

Discussion

In our study, we found a 4-times higher prevalence of gastric neoplasia in patients with cACLD compared to a healthy screening population. The prevalence of gastric dysplasia and carcinoma was 9-times and 3-times higher in cases than in controls, respectively. Previous studies have reported a higher prevalence of gastric lesions in patients with cACLD. Nevertheless, most of these were based on very old databases. In 1995, Sonnenberg et al, retrospectively analyzed data from a national database on US Veterans and reported a significant association between GC and LC (odds ratio 1.47) [14]. Similar results were obtained by an epidemiological study in Denmark that concluded that there was an increased risk of GC in patients with LC (standardized incidence ratio of 1.9) [15]. Later, in 2003, Zullo et al found a significantly higher prevalence of GC in patients with LC compared to the prevalence expected for the general population (2.6-fold increase) [16]. A higher prevalence of AG and IM precursor lesions for GC, was also demonstrated in patients with portal hypertension [17]. More recently, Tae Hoon Ha et al have found a significantly higher prevalence of GC in patients with alcoholic liver disease (ALD) compared to healthy individuals. They additionally suggested that part of this increased risk is due to mechanisms related to, and dependent on liver disease [18].

Hp infection corresponds to one of the most important risk factors for the development of gastric cancer [12]. In our study, the prevalence of Hp infection was significantly higher in controls than in cases. Although these data were not collected in our study, the significant exposure by cACLD patients to antibiotics and proton-pump inhibitors can explain our findings. However, it is also known that the prevalence of Hp infection is typically higher in patients with post-inflammatory LC related to HCV and HBV infections than in patients with LC associated with ALD, and its incidence is also positively correlated with the presence of esophageal varices [38]. In our study, almost half of the patients had an etiology of LC associated with ALD [n=213 (44.3%)] and more than half did not have gastroesophageal varices in at least one EGD [n=283 (58.8%)], which can also, to some extent, explain our results. Contrary to what one might expect, a positive Hp infection represented a protective factor for the development of gastric neoplasia. The status of Hp infection may have been influenced by the

degree of neoplastic involvement with destruction of the infected normal gastric mucosa. Interestingly, despite a lower incidence of Hp infection, the incidence of advanced gastritis stages was significantly higher in cases compared to controls.

Areia et al. studied the option of adding a screening EGD at the same time of screening colonoscopy for CRC, in Portugal. Using a Markov cost-utility analysis they compared three screening strategies and concluded that endoscopic GC screening was cost-effective if combined with a screening colonoscopy [11]. More recently, a review article sought to understand the applicability of screening methods usually adopted in countries with high-risk of GC if used in countries of intermediate and low risk [39]. One of the recommended strategies for countries with intermediate risk, such as Portugal, is to perform EGD after a positive fecal occult blood test [39]. Recognizing the high prevalence and incidence of GC, the Portuguese government recently issued a statement that in 2023 it will carry out pilot programs for GC screening. There is still no defined plan, but it is thought that one of the strategies may be the performance of EGD during colonoscopy performed for CRC screening. Thus, if screening for GC is advised for the general population, in patients with cACLD, who in our study had an overall higher prevalence of gastric neoplasia compared to healthy individuals, its performance seems to be even more relevant.

Most of the patients included in the study had an LSM by TE > 20 kPa [n=289 (60.1%)] and a PC < 150,000/mm³ [n=291 (60.5%)]. According to the proposed Baveno VII criteria [20], a significant proportion of the patients included in the study (23.9%) could safely avoid EGD for the diagnosis of high-risk varices. Nevertheless, we found that 35% of the gastric neoplasia cases in the cACLD population would have been missed if these criteria were strictly followed. These data highlights the possible role of EGD an opportunistic screening method for an early diagnosis of gastric neoplasia in this population.

In our study, ESD was performed in 2 patients with carcinoma and 3 patients with dysplastic lesions, with R0 resections in all procedures and without adverse events in the follow-up. ESD has been accepted as the primary treatment option for EGC, even in patients with LC, with several studies confirming its safety and efficacy [25, 40-42], with postprocedural bleeding being the most common adverse event. Young Kwon Choi et al., performed a study that showed that the group of patients with compensated LC, compared with non-cirrhotic patients, presented ratios of en bloc resection, curative resection and adverse events without statistically significant differences [41]. In previous studies the risk of adverse events seemed to be little affected by the abnormal hemostatic capacity of LC patients [43, 44]. Another possible approach, more represented in our study, is the surgical approach. Abdominal surgery is associated with multiple adverse events, longer hospital stay, higher risk of requiring ICU admission, post-operative acute renal failure, and higher morbidity and mortality in cirrhotic patients [45]. In our study, all treatment-related complications occurred in the surgery group (included 2 cases of severe complications with associated mortality), with a greater number of hospitalization days compared to patients who underwent endoscopic resection. Although the number of patients that underwent endoscopic resection was very limited, our results show that ESD is a safe and effective approach in a theoretically riskier population. Considering the risk of complications with a surgical approach, ESD should be considered the first-line approach for the treatment of early-gastric cancer in this population, similary to what has been defined for the general population.

Our study has some limitations that should be addressed and that are inherent to the study design. Regarding cases, this was a retrospective study based on observational data from a single tertiary hospital in Portugal. In a significant number of patients, it was not possible to collect data regarding

the status of Hp infection and gastritis staging. In controls, all procedures were performed under general anesthesia while in cases many procedures were performed without sedation. In controls, all the procedures were performed by only 2 endoscopists which may be a potential bias, since in cases the procedures were performed by multiple endoscopists, including fellows in training. Second, it is well-known that GC is more common in males, and in our study, there was a significantly male predominance in cases compared to controls. This could have led to an overestimation of GC prevalence in the cACLD group. On the other hand, alcohol consumption and smoking status were not evaluated in controls. Since all of these are significant risk factors for GC this is a potentially important bias that limits our conclusions and does not let us suggest LC as an independently risk factor for gastric neoplasia.

If, on the one hand, some limitations are recognized, there are many positive points to be highlighted in our study. This corresponds to the largest study conducted so far that evaluated and demonstrated an increased prevalence of gastric neoplasia in cACLD patients. The study incorporated a large number of patients, carefully selected according to strict inclusion and exclusion criteria, and had a long follow-up. This was also the first study to suggest that, EGD for varices screening can lead to an early detection of gastric neoplasia. Considering the previously discussed efficacy and safety of endoscopic resection in this population, early detection may lead to better outcomes in a very difficult to treat population. We believe that these data is an additional important information to clinicians to take into account in the approach of cACLD patients in specific countries, especially the ones with an intermediate GC risk where there are not as clear indications about screening for GC.

To conclude, we found a higher prevalence of gastric neoplasia in patients with cACLD than in healthy controls who were undergoing an already scheduled screening colonoscopy. The Baveno VII criteria suggest that EGD screening for gastro-esophageal varices may be preventable in certain patient groups. Based on our results, we suggest that in countries with intermediate-high risk for GC, continuing to perform EGD could be beneficial, as patients with cACLD are at higher risk for GC, and its early detection may be associated with better outcomes.

Statements

Acknowledgement

None to report.

Statement of Ethics

This study was approved by the Ethics Committee of the Centro Hospitalar e Universitário São João/Faculdade de Medicina da Universidade do Porto.

Protection of human and animal subjects: The authors affirm that no experiments involving humans or animals were conducted for this study.

Confidentiality of data: The authors assert that this article does not contain any patient data.

Right to privacy and informed consent: The authors confirm that no patient data is presented in this article.

Conflict of Interest Statement

There were no reported conflicts of interest that could be considered relevant to this article.

Funding Sources

There has been no receipt of any financial support or grant.

Author Contributions

All authors made equal contributions to the research of the literature, design of the study, collection and analysis of the data, interpretation of the results, and writing of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

References

- 1 Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209-49.
- 2 Ferlay J, Colombet M, Soerjomataram I, Parkin DM, Piñeros M, Znaor A, et al. Cancer statistics for the year 2020: An overview. *Int J Cancer*. 2021.
- 3 Ilic M, Ilic I. Epidemiology of stomach cancer. *World J Gastroenterol*. 2022;28(12):1187-203.
- 4 Shah SC, McKinley M, Gupta S, Peek RM, Jr., Martinez ME, Gomez SL. Population-Based Analysis of Differences in Gastric Cancer Incidence Among Races and Ethnicities in Individuals Age 50 Years and Older. *Gastroenterology*. 2020;159(5):1705-14.e2.
- 5 Jin H, Pinheiro PS, Xu J, Amei A. Cancer incidence among Asian American populations in the United States, 2009-2011. *Int J Cancer*. 2016;138(9):2136-45.
- 6 Bastos J, Peleteiro B, Barros R, Alves L, Severo M, de Fátima Pina M, et al. Sociodemographic determinants of prevalence and incidence of *Helicobacter pylori* infection in Portuguese adults. *Helicobacter*. 2013;18(6):413-22.
- 7 Morais S, Ferro A, Bastos A, Castro C, Lunet N, Peleteiro B. Trends in gastric cancer mortality and in the prevalence of *Helicobacter pylori* infection in Portugal. *Eur J Cancer Prev*. 2016;25(4):275-81.
- 8 Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359-86.
- 9 Areia M, Carvalho R, Cadime AT, Rocha Gonçalves F, Dinis-Ribeiro M. Screening for gastric cancer and surveillance of premalignant lesions: a systematic review of cost-effectiveness studies. *Helicobacter*. 2013;18(5):325-37.
- 10 Hamashima C, Group SR, Guidelines GDGfGCS. Update version of the Japanese Guidelines for Gastric Cancer Screening. *Japanese Journal of Clinical Oncology*. 2018;48(7):673-83.
- 11 Areia M, Spaander MC, Kuipers EJ, Dinis-Ribeiro M. Endoscopic screening for gastric cancer: A cost-utility analysis for countries with an intermediate gastric cancer risk. *United European Gastroenterol J*. 2018;6(2):192-202.
- 12 Eslick GD. *Helicobacter pylori* infection causes gastric cancer? A review of the epidemiological, meta-analytic, and experimental evidence. *World J Gastroenterol*. 2006;12(19):2991-9.
- 13 Wei XL, Qiu MZ, Jin Y, Huang YX, Wang RY, Chen WW, et al. Hepatitis B virus infection is associated with gastric cancer in China: an endemic area of both diseases. *Br J Cancer*. 2015;112(7):1283-90.

- 14 Sonnenberg A, Wasserman IH. Associations of peptic ulcer and gastric cancer with other diseases in US veterans. *Am J Public Health*. 1995;85(9):1252-5.
- 15 Sorensen HT, Friis S, Olsen JH, Thulstrup AM, Møller M, et al. Risk of liver and other types of cancer in patients with cirrhosis: a nationwide cohort study in Denmark. *Hepatology*. 1998;28(4):921-5.
- 16 Zullo A, Romiti A, Tomao S, Hassan C, Rinaldi V, Giustini M, et al. Gastric cancer prevalence in patients with liver cirrhosis. *Eur J Cancer Prev*. 2003;12(3):179-82.
- 17 İbrişim D, Cevikbaş U, Akyüz F, Poturoğlu S, Ahishali E, Güllüoğlu M, et al. Intestinal metaplasia in portal hypertensive gastropathy: a frequent pathology. *Eur J Gastroenterol Hepatol*. 2008;20(9):874-80.
- 18 Ha TH, Kim BG, Jeong D, Oh S, Kim W, Jung YJ, et al. Alcoholic Liver Disease Is Associated with an Increased Risk of Gastric Cancer. *Dig Dis Sci*. 2017;62(1):273-9.
- 19 de Franchis R. Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol*. 2010;53(4):762-8.
- 20 de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C. Baveno VII - Renewing consensus in portal hypertension. *J Hepatol*. 2022;76(4):959-74.
- 21 de Franchis R. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. *J Hepatol*. 2015;63(3):743-52.
- 22 Bae J, Sinn DH, Kang W, Gwak GY, Choi MS, Paik YH, et al. Validation of the Baveno VI and the expanded Baveno VI criteria to identify patients who could avoid screening endoscopy. *Liver Int*. 2018;38(8):1442-8.
- 23 Sousa M, Fernandes S, Proença L, Silva AP, Leite S, Silva J, et al. The Baveno VI criteria for predicting esophageal varices: validation in real life practice. *Rev Esp Enferm Dig*. 2017;109(10):704-7.
- 24 Colecchia A, Ravaioli F, Marasco G, Colli A, Dajti E, Di Biase AR, et al. A combined model based on spleen stiffness measurement and Baveno VI criteria to rule out high-risk varices in advanced chronic liver disease. *J Hepatol*. 2018;69(2):308-17.
- 25 Repici A, Pagano N, Hassan C, Cavenati S, Rando G, Spaggiari P, et al. Endoscopic submucosal dissection of gastric neoplastic lesions in patients with liver cirrhosis: a systematic review. *J Gastrointest Liver Dis*. 2012;21(3):303-7.
- 26 Miaglia C, Guillaud O, Rivory J, Lépilliez V, Chambon-Augoyard C, Hervieu V, et al. Safe and effective digestive endoscopic resection in patients with cirrhosis: a single-center experience. *Endoscopy*. 2020;52(4):276-84.
- 27 Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, Repici A, Vieth M, De Ceglie A, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2015;47(9):829-54.
- 28 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.
- 29 Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, et al. The 2019 WHO classification of tumours of the digestive system. *Histopathology*. 2020;76(2):182-8.
- 30 Lauren P. THE TWO HISTOLOGICAL MAIN TYPES OF GASTRIC CARCINOMA: DIFFUSE AND SO-CALLED INTESTINAL-TYPE CARCINOMA. AN ATTEMPT AT A HISTO-CLINICAL CLASSIFICATION. *Acta Pathol Microbiol Scand*. 1965;64:31-49.
- 31 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.

- 32 Capelle LG, de Vries AC, Haringsma J, Ter Borg F, de Vries RA, Bruno MJ, et al. The staging of gastritis with the OLGA system by using intestinal metaplasia as an accurate alternative for atrophic gastritis. *Gastrointest Endosc.* 2010;71(7):1150-8.
- 33 Dinis-Ribeiro M, Areia M, de Vries AC, Marcos-Pinto R, Monteiro-Soares M, O'Connor A, et al. Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHSg), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED). *Endoscopy.* 2012;44(1):74-94.
- 34 Lordick F, Carneiro F, Cascinu S, Fleitas T, Haustermans K, Piessen G, et al. Gastric cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2022;33(10):1005-20.
- 35 Pimentel-Nunes P, Libânio D, Marcos-Pinto R, Areia M, Leja M, Esposito G, et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. *Endoscopy.* 2019;51(4):365-88.
- 36 Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. *CA Cancer J Clin.* 2017;67(2):93-9.
- 37 Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240(2):205-13.
- 38 Pogorzelska J, Łapińska M, Kalinowska A, Łapiński TW, Flisiak R. Helicobacter pylori infection among patients with liver cirrhosis. *Eur J Gastroenterol Hepatol.* 2017;29(10):1161-5.
- 39 Januszewicz W, Turkot MH, Malfertheiner P, Regula J. A Global Perspective on Gastric Cancer Screening: Which Concepts Are Feasible, and When? *Cancers (Basel).* 2023;15(3).
- 40 Kato M, Nishida T, Hamasaki T, Kawai N, Yoshio T, Egawa S, et al. Outcomes of ESD for patients with early gastric cancer and comorbid liver cirrhosis: a propensity score analysis. *Surg Endosc.* 2015;29(6):1560-6.
- 41 Choi YK, Ahn JY, Kim DH, Jung KW, Na HK, Choi KD, et al. Efficacy and safety of endoscopic submucosal dissection for gastric neoplasms in patients with compensated liver cirrhosis: a propensity score-matched case-control study. *Gastrointest Endosc.* 2018;87(6):1423-31.e3.
- 42 Choe WH, Kim JH, Park JH, Kim HU, Cho DH, Lee SP, et al. Endoscopic Submucosal Dissection of Early Gastric Cancer in Patients with Liver Cirrhosis. *Dig Dis Sci.* 2018;63(2):466-73.
- 43 Ryu KW, Lee JH, Kim YW, Park JW, Bae JM. Management of ascites after radical surgery in gastric cancer patients with liver cirrhosis and minimal hepatic dysfunction. *World J Surg.* 2005;29(5):653-6.
- 44 Ikeda Y, Kanda T, Kosugi S, Yajima K, Matsuki A, Suzuki T, et al. Gastric cancer surgery for patients with liver cirrhosis. *World J Gastrointest Surg.* 2009;1(1):49-55.
- 45 Jang HJ, Kim JH, Song HH, Woo KH, Kim M, Kae SH, et al. Clinical outcomes of patients with liver cirrhosis who underwent curative surgery for gastric cancer: a retrospective multi-center study. *Dig Dis Sci.* 2008;53(2):399-404.

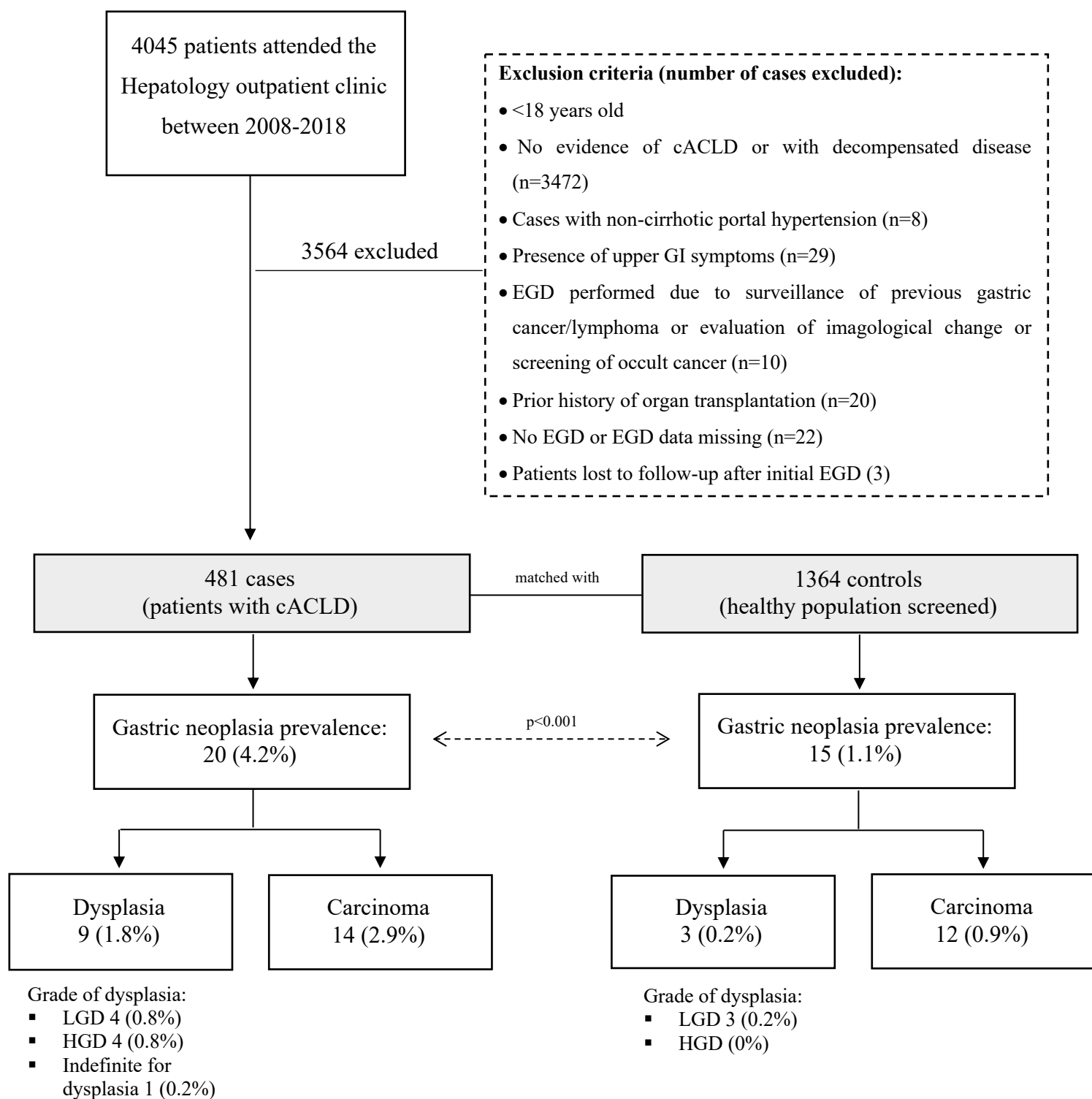


Fig. 1. Study flowchart

cACLD, compensated advanced chronic liver disease; EGD, esophagogastroduodenoscopy; HGD, high grade dysplasia; LGD, Low-Grade Dysplasia.

Table 1. Demographic data

	Total [n (%)] n=1845	Cases [n (%)] n=481	Controls [n (%)] n=1364	p value
Gender				
Female	892 (48.3%)	150 (31.2%)	742 (54.4%)	0.001
Male	953 (51.7%)	331 (68.8%)	622 (45.6%)	
Age, median (IQR), years	58 (49-66)	58 (49-66)	57 (49-66)	0.492
Family history of gastric cancer	27 (1.5%)	4 (0.8%)	23 (1.7%)	0.268

IQR, interquartile range

Table 2. Characterization of the cACLD population

	Total [n (%)] n=481
Active alcohol consumption	148 (30.8%)
Smoking	
Active smoker	70 (14.6%)
Ex-smoker	72 (15%)
Etiology	
Alcohol	213 (44.3%)
HCV	59 (12.3%)
Alcohol and HCV	29 (6%)
HBV	26 (5.4%)
Alcohol and HBV	7 (1.5%)
NASH	40 (8.3%)
Alcohol and NASH	39 (8.1%)
AIH	18 (3.7%)
PBC	14 (2.9%)
AIH and PBC	10 (2.1%)
PSC	1 (0.2%)
Hemochromatosis	11 (2.3%)
Wilson disease	2 (0.4%)
Alfa-1 antitrypsin deficiency	1 (0.2%)
Cryptogenic	11 (2.3%)
Hepatocellular carcinoma	53 (11%)
Fibrosis staging in liver biopsy (METAVIR)	
F1	1 (0.2%)
F2	2 (0.4%)
F3	18 (3.7%)
F4	141 (29.3%)
No data	319 (66.3%)
Transient elastography liver stiffness measurement, median (IQR), kPa	19.0 (10.2-35.3)
LSM by TE$\leq$20 kPa	192 (39.9%)
Platelets, median (IQR), /mm³	136000 (86000-194000)
Platelets$\geq$150000/mm³	190 (39.5%)
Number of EGDs, median (IQR)	3 (2-5)
Gastro-esophageal varices on at least one EGD	198 (41.2%)
Time of follow-up after initial EGD, median (IQR), months	63 (33-97)

ASH, Alcoholic Steatohepatitis; AIH, Autoimmune hepatitis; HBV, Hepatitis B Virus; HCV, Hepatitis C Virus; LC, Liver Cirrhosis; NASH, Nonalcoholic Steatohepatitis; PBC, Primary Biliary Cirrhosis; PSC, Primary Sclerosing Cholangitis.; EGD, esophagogastroduodenoscopy; LSM, liver stiffness measurement; TE, transient elastography; IQR, interquartile range

Table 3. H. Pylori infection and gastritis staging

	Total [n (%)] n=1845	Cases [n (%)] n=481	Controls [n (%)] n=1364	p value
Hp infection				<0.001
Yes	732 (44.3%)	88 (30.3%)	644 (47.2%)	
No	922 (55.7%)	202 (69.7%)	720 (78.1%)	
No data	191 (10.4%)	191 (39.7%)	-	
Gastric atrophy*				
Antrum				<0.001
No	1177 (71.5%)	190 (67.1%)	987 (72.4%)	
Mild	304 (18.5%)	55 (19.4%)	249 (18.3%)	
Moderate	141 (8.5%)	24 (8.5%)	117 (8.6%)	
Severe	25 (1.5%)	14 (5.0%)	11 (0.8%)	
No data	198 (10.7%)	198 (41.2%)		
Body				<0.001
No	1367 (87.0%)	164 (79.2%)	1203 (76.6%)	
Mild	97 (6.2%)	19 (9.2%)	78 (5.0%)	
Moderate	95 (6.0%)	15 (7.2%)	80 (5.9%)	
Severe	12 (0.8%)	9 (4.4%)	3 (0.2%)	
No data	274 (14.9%)	274 (57.0%)	-	
OLGA				<0.001
0	1024 (65.3%)	130 (63.4%)	894 (65.6%)	
I	309 (19.7%)	37 (18.0%)	272 (20.0%)	
II	192 (12.2%)	17 (8.3%)	175 (12.8%)	
III	31 (2.0%)	12 (5.9%)	19 (1.4%)	
IV	12 (0.8%)	9 (4.4%)	3 (0.2%)	
No data	276 (15.0%)	276 (53.1%)	-	
OLGA≥III	43 (2.7%)	21 (10.2%)	22 (1.6%)	<0.001
No data	276 (15.0%)	276 (53.1%)	-	
Intestinal metaplasia*				
Antrum				<0.001
No	1283 (77.9%)	183 (64.7%)	1100 (80.7%)	
Mild	224 (13.6%)	42 (14.8%)	182 (13.3%)	
Moderate	102 (6.2%)	41 (14.5%)	61 (4.5%)	
Severe	38 (2.3%)	17 (6.0%)	21 (1.5%)	
No data	198 (10.7%)	198 (41.2%)		
Body				<0.001

No	1457 (92.8%)	167 (80.7%)	1290 (92.7%)	
Mild	65 (4.1%)	16 (7.7%)	65 (4.1%)	
Moderate	32 (2.0%)	13 (6.3%)	32 (2.0%)	
Severe	17 (1.1%)	11 (5.3%)	17 (1.1%)	
No data	274 (14.9%)	274 (57.0%)		
OLGIM				<0.001
0	1187 (75.6%)	125 (61.0%)	1062 (77.9%)	
I	239 (15.2%)	33 (16.1%)	206 (15.1%)	
II	91 (5.8%)	21 (10.2%)	70 (5.1%)	
III	37 (2.4%)	18 (8.8%)	19 (1.4%)	
IV	15 (1.0%)	8 (3.9%)	7 (0.5%)	
No data	276 (15.0%)	276 (53.1%)		
OLGIM$\geq$III	52 (3.3%)	26 (12.7%)	26 (1.9%)	<0.001
No data	276 (15.0%)	276 (53.1%)	-	

Hp, Helicobacter Pylori; OLGA, Operative Link on Gastritis Assessment; OLGIM, Operative Link on Gastritis/Intestinal-Metaplasia Assessment

*** Updated Sydney System**

Table 4. Prevalence and characterization of gastric neoplasia

	Total [n (%)] n=1845	Cases [n (%)] n=481	Controls [n (%)] n=1364	p value
Gastric neoplasia	35 (1.9%)	20 (4.2%)	15 (1.1%)	<0.001
Gastric carcinoma	26 (1.4%)	14 (2.9%)	12 (0.9%)	0.003
Location				0.483
Cardia	1 (3.9%)	1 (7.1%)	-	
Fundus	2 (7.7%)	1 (7.1%)	1 (8.3%)	
Body	10 (38.5%)	7 (50.0%)	3 (25.0%)	
Incisura	4 (15.3%)	2 (14.3%)	2 (16.7%)	
Antrum	9 (34.6%)	3 (21.5%)	6 (50.0%)	
Histological subtype*				0.560
Gastric adenocarcinoma	25 (96.2%)	13 (92.9%)	12 (100%)	
Intestinal	20 (80.0%)	11 (84.6%)	9 (75.0%)	
Diffuse	5 (20.0%)	2 (15.4%)	3 (25.0%)	
Neuroendocrine carcinoma	1 (3.8%)	1 (7.1%)	-	
Gastric dysplasia	12 (0.7%)	9 (1.9%)	3 (0.2%)	<0.001
Location				0.177
Body	1 (8.3%)	1 (11.1%)	2 (66.7%)	
Antrum	10 (83.2%)	8 (88.9%)		
Antrum+body ⁺	1 (8.3%)	-	1 (33.3%)	
Histological subtype				0.240
LGD	7 (58.2%)	4 (44.4%)	3 (100.0%)	
HGD	4 (33.3%)	4 (44.4%)		
Indefinite for dysplasia	1 (8.3%)	1 (11.2%)		

* Lauren classification

⁺ Patient with two synchronous lesions

LGD, low-grade dysplasia; HGD, high-grade dysplasia

Table 5. Risks factors for gastric neoplasia

	Unadjusted OR (95% CI)	p value	Covariate adjusted OR (95% CI)	p value
Gender		0.513	-	-
Female	Ref.			
Male	1.253 (0.638- 2.463)			
Age	1.082 (1.045- 1.119)	0.001	-	-
Age ≥60 years	3.176 (1.517- 6.652)	0.002	4.732 (1.573- 14.233)	0.006
Family history of gastric cancer	-	-	-	-
No Hp infection	3.886 (1.475- 10.235)	0.006	4.113 (1.168- 14.486)	0.028
OLGA≥III	25.387 (10.889- 59.188)	<0.001	1.644 (0.304- 8.897)	0.564
OLGIM≥III	23.673 (10.432- 53.718)	<0.001	7.277 (1.647- 32.153)	0.009
cACLD	3.902 (1.981- 7.684)	<0.001	1.606 (0.562- 4.595)	0.377

Hp, Helicobacter Pylori; OLGA, Operative Link on Gastritis Assessment; OLGIM, Operative Link on Gastritis/Intestinal-Metaplasia Assessment; cACLD, compensated advanced chronic liver disease

SUPPLEMENTARY TABLES (Table 6 and Table 7)

Table 6. Outcomes and management after diagnosis of gastric carcinoma in cACLD population

	Total [n (%)] n=14
TNM staging	
T	
T1a	4 (28.6%)
T1b	5 (35.7%)
T2	1 (7.1%)
T3	0 (0%)
T4a	3 (21.5%)
No data	1 (7.1%)
N	
N0	10 (71.5%)
N1	2 (14.3%)
N3a	1 (7.1%)
No data	1 (7.1%)
M	
M0	12 (85.8%)
M1	1 (7.1%)
No data	1 (7.1%)
AJCC Stage	
IA	8 (57.3%)
IB	1 (7.1%)
IIB	1 (7.1%)
IIIA	2 (14.3%)
IV	1 (7.1%)
No data	1 (7.1%)
Type of treatment	
Endoscopic	2 (14.3%)
- ESD	2 (100%)
Resection/ margins (R0)	2 (100%)
Curative resection	1 (50%)
Adverse events	0 (0%)
Re-intervention	0 (0%)
Number of days of hospitalization, median (IQR)	2
Tumor recurrence	0 (0%)

Surgical	11 (78.6%)
- Total gastrectomy	8 (72.7%)
- Subtotal gastrectomy	3 (27.3%)
Resection/ margins (R0)	11 (100%)
Adverse events	5 (54.5%)
Surgical re-intervention	2 (18.2%)
Number of days of hospitalization, median (IQR)	10 (9-21)
Additional treatment	3 (27.3%)
Neoadjuvant chemotherapy	1 (9.1%)
Adjuvant chemotherapy	2 (18.2%)
Tumor recurrence	0 (0%)
Palliative care	1 (7.1%)
Mortality rate in the follow-up	7 (50.0%)
Cause of death	
Related	3 (42.9%)
- Tumor	1 (33.3%)
- Complication	2 (66.7%)
Unrelated	4 (57.1%)
30-days mortality	1 (7.1%)
6-months mortality	3 (21.4%)
3-years mortality	6 (42.9%)
Overall survival, median (IQR), months	38 (6-69)

AJCC, American Joint Committee on Cancer; ESD, Endoscopic Submucosal Dissection; HGD, high grade dysplasia; LGD, Low-Grade Dysplasia; IQR, interquartile range

Table 7. Surgery adverse events classified according to the Clavien-Dindo classification.

	Number of events	Clavien-Dindo	Management
Local complications			
Wound infection	1	II	Antibiotherapy
Anastomotic dehiscence	1	V	Surgery
Bleeding	1	V	Surgery; Blood transfusion
Systemic complications			
Heart failure decompensation	1	I	Conservative
Paroxysmal atrial fibrillation	1	II	Rhythm control therapy
Acute on chronic kidney disease	1	I	Fluid therapy
Nosocomial pneumonia	1	II	Antibiotherapy
Hemoptysis	1	I	Conservative

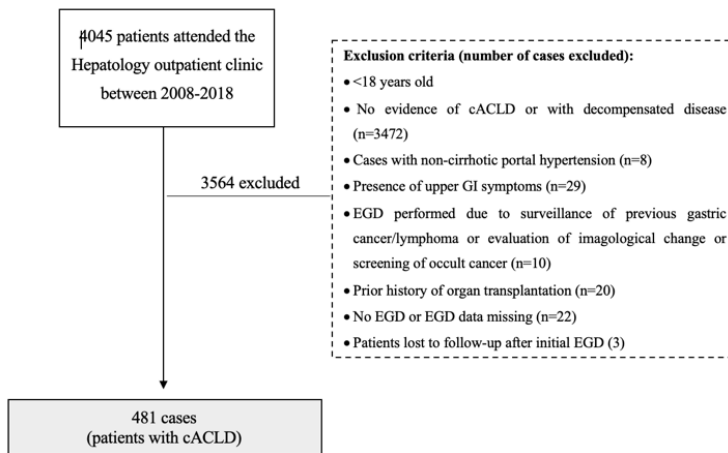
The prevalence of gastric neoplasia is increased in patients with chronic liver disease compared to a healthy screening population

	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 Retrospective case-control study that enrolled all asymptomatic cACLD patients who underwent EGD for gastro-esophageal varices screening from January 2008 to June 2018 in a tertiary reference center.	2,3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found Introduction: Gastric cancer (GC) is a major worldwide health concern. For several years now, numerous studies reported a higher prevalence of GC in patients with advanced chronic liver disease (ACLD). The Baveno VII criteria were proposed to identify patients could safely avoid screening esophagogastroduodenoscopy (EGD). Therefore, our main objective was to evaluate the prevalence of gastric neoplasia in cACLD patients that underwent EGD for screening of gastro-esophageal varices compared to a healthy screening population. We also sought to assess the clinical outcomes after the diagnosis gastric neoplasia in the cACLD population. Material and Methods: Retrospective case-control study that enrolled all asymptomatic cACLD patients who underwent EGD for gastro-esophageal varices screening from January 2008 to June 2018 in a tertiary reference center. Cases were matched with asymptomatic healthy individuals who underwent EGD for GC screening at the same time as colonoscopy performed for colorectal cancer (CRC) screening in a private-hospital setting between April 2017 and March 2018. All data was arranged, processed and analyzed with SPSS ® v.27.0 data. Results: A significantly higher prevalence of gastric neoplasia in patients with cACLD compared to controls was observed (4.2% vs. 1.1%; p<0.001). The overall prevalence of gastric carcinoma and dysplasia were 1.4% and 0.7%, respectively, and was significantly higher in cases than in controls. Age $\geq$ 60 years, absence of <i>H. pylori</i> infection, and OLGIM stage $\geq$ III were identified as independent risk factors for gastric neoplasia. Seven cases of gastric neoplasia were diagnosed in patients who,	2,3

		according to the Baveno VII criteria, could avoid EGD for diagnosis of gastro-esophageal varices. Discussion/conclusion: We found a higher prevalence of gastric neoplasia in patients with cACLD than in healthy controls who were undergoing an already scheduled screening colonoscopy. The Baveno VII criteria suggest that EGD screening for gastro-esophageal varices may be preventable in certain patient groups. Based on our results, we suggest that in countries with intermediate-high risk for GC, continuing to perform EGD could be beneficial, as patients with cACLD are at higher risk for GC, and its early detection may be associated with better outcomes.	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Gastric cancer (GC) is a major worldwide health concern. There is a considerable worldwide variation, both in terms of incidence and mortality. Considering the difficulty in recognition and the poor prognosis of GC, some strategies have been proposed for early detection and prevention. All patients with compensated ACLD (cACLD) should be screened for gastro-esophageal varices. The standard paradigm of screening varices has, for the greater part, involved EGD. However, the Baveno VI criteria and more recently the Baveno VII criteria were proposed to identify patients could safely avoid screening EGD. This current recommendation states that patients with liver stiffness measurement (LSM) by transient elastography (TE) > 20kPa and platelet count (PC) $\leq 150 \times 10^9/L$ should undergo EGD. Even though several studies have validated Baveno VI criteria, regarding the prediction of presence of gastro-esophageal varices, they have all failed to acknowledge the possible role impact of the non-performed EGD in cACLD patients in screening for a possible concurrent upper gastrointestinal neoplasia.	4
Objectives	3	State specific objectives, including any prespecified hypotheses Our main objective was to evaluate the prevalence of gastric neoplasia in cACLD patients that underwent EGD for screening of gastro-esophageal varices (including the missed-lesion rate if the Baveno criteria had been strictly followed), compared to a healthy screening population. We also sought to assess the clinical outcomes, efficacy and safety after surgery and/or endoscopic resection of gastric neoplasia in the cACLD population.	5
Methods			
Study design	4	Present key elements of study design early in the paper Retrospective case-control study that enrolled all asymptomatic	5

		cACLD patients who underwent EGD for gastro-esophageal varices screening and cases were matched with asymptomatic healthy individuals who underwent EGD for GC screening at the same time as colonoscopy performed for colorectal cancer (CRC) screening.	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection This study were developed at Centro Hospitalar Universitário São João (CHUSJ), Porto, Portugal, and enrolled all asymptomatic cACLD patients who underwent EGD for gastro-esophageal varices screening from January 2008 to June 2018. Cases were matched with asymptomatic healthy individuals who underwent EGD for GC screening at the same time as colonoscopy performed for colorectal cancer (CRC) screening in a private-hospital setting in the region of Porto, Portugal, between April 2017 and March 2018. The period analyzed was from the moment they were recruited in the consultation, until the date of data collection: December 2022.	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cases: cACLD population The Baveno VII criteria were used to identify cACLD patients. As such, patients were included in the study if any of the following criteria were fulfilled: (a) LSM by TE > 15 kPa; (b) LSM by TE of more than 10 kPa with a suggestive clinical history; (c) patients with a liver biopsy result of F3 or F4; (d) patients with clinical data suggestive of advanced disease, such as thrombocytopenia ($PC \leq 150 \times 10^9/L$), ascites or imaging studies suggestive of liver cirrhosis (LC) (e.g. dysmorphic liver). We only included cases with at least one clinical evaluation after EGD and with at least one EGD performed for gastro-esophageal varices screening. Patients were excluded if any of the following were present: (a) no evidence of cACLD; (b) prior history of organ transplantation; (c) ECG was performed for a reason other than screening for esophageal varices, (d) surveillance of previous GC or lymphoma, gastrointestinal bleeding, iron deficiency anaemia or other upper gastrointestinal symptoms, (e) age <18 years. Controls Patients in whom screening EGD was proposed by the general practitioner at the same time of colonoscopy were identified. Patients were excluded if any of the following were present: (a) surveillance of previous GC or lymphoma, (b) gastrointestinal	5

		bleeding, iron deficiency anaemia or other upper gastrointestinal symptoms, (c) age <18 years.	
		(b) For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable To evaluation of clinical outcomes after the diagnosis of gastric neoplasia, only cases were considered. After EGD, patients with a diagnosis of gastric neoplasia were guided according to the MAPS I and II guidelines, in the presence of pre-malignant lesions, and according to the ESMO guidelines, if diagnosed with GC. In the latter, after complete staging, cases were discussed by the Esophago-Gastric Multidisciplinary Team of CHUSJ, treatment was decided and pursued. Immediate and post-procedure adverse events (AEs), disease recurrence, mortality and survival (defined as the time from the date of treatment to either death or the last follow-up contact) were evaluated. Surgery AEs were classified according to the Clavien-Dindo classification.	6
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 The Baveno VII criteria were used to identify cACLD patients. Sources of data to know if these criteria were fulfilled: medical records for cases and controls.	5
Bias	9	Describe any efforts to address potential sources of bias To overcome the absence of some data and the poor representation, we performed a multivariate analysis.	5
Study size	10	Explain how the study size was arrived at We selected all asymptomatic cACLD patients who underwent EGD for gastro-esophageal varices screening from January 2008 to June 2018.	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Categorical variables were described through absolute and relative frequencies and continuous variables as mean and standard deviation, median, minimum and maximum.	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding Hypotheses were tested about the distribution of continuous variables by using the independent sample t-test/one-way Anova or nonparametric Mann-Whitney and Kruskal-Wallis test,	6

		depending on if normal or non-normal distribution, respectively. Fisher's exact test or Pearson chi-square test, as appropriate, were used to assess the statistical differences between cases and controls regarding demographic data, prevalence of Hp infection, gastritis staging and prevalence of gastric neoplasia. Binary logistic regression was used to identify factors associated with gastric neoplasia. 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.	
		(b) Describe any methods used to examine subgroups and interactions	8
		A multivariable regression model was developed to identify risk factors associated with a higher risk of gastric neoplasia (Table 5).	
		(c) Explain how missing data were addressed	6
		They were excluded from analysis. To overcome that, we performed a multivariate analysis, additionally to the univariate analysis.	
		(d) If applicable, explain how matching of cases and controls was addressed	NA
		(e) Describe any sensitivity analyses	NA
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 Cases (data only available for cases): Of the 4045 patients who attended the Hepatology outpatient clinic between 2008-2018, we identified 481 cACLD patients that met the inclusion and exclusion criteria.  <pre> graph TD A["4045 patients attended the Hepatology outpatient clinic between 2008-2018"] --> B["481 cases (patients with cACLD)"] A -- "3564 excluded" --> C["Exclusion criteria (number of cases excluded): • <18 years old • No evidence of cACLD or with decompensated disease (n=3472) • Cases with non-cirrhotic portal hypertension (n=8) • Presence of upper GI symptoms (n=29) • EGD performed due to surveillance of previous gastric cancer/lymphoma or evaluation of imagological change or screening of occult cancer (n=10) • Prior history of organ transplantation (n=20) • No EGD or EGD data missing (n=22) • Patients lost to follow-up after initial EGD (3)"] </pre>	7, Fig.1
		(b) Give reasons for non-participation at each stage	7, Fig.1

- Exclusion criteria (number of cases excluded):**
- <18 years old
 - No evidence of cACLD or with decompensated disease (n=3472)
 - Cases with non-cirrhotic portal hypertension (n=8)
 - Presence of upper GI symptoms (n=29)
 - EGD performed due to surveillance of previous gastric cancer/lymphoma or evaluation of imagological change or screening of occult cancer (n=10)
 - Prior history of organ transplantation (n=20)
 - No EGD or EGD data missing (n=22)
 - Patients lost to follow-up after initial EGD (3)

(c) Consider use of a flow diagram

7,
Fig.1

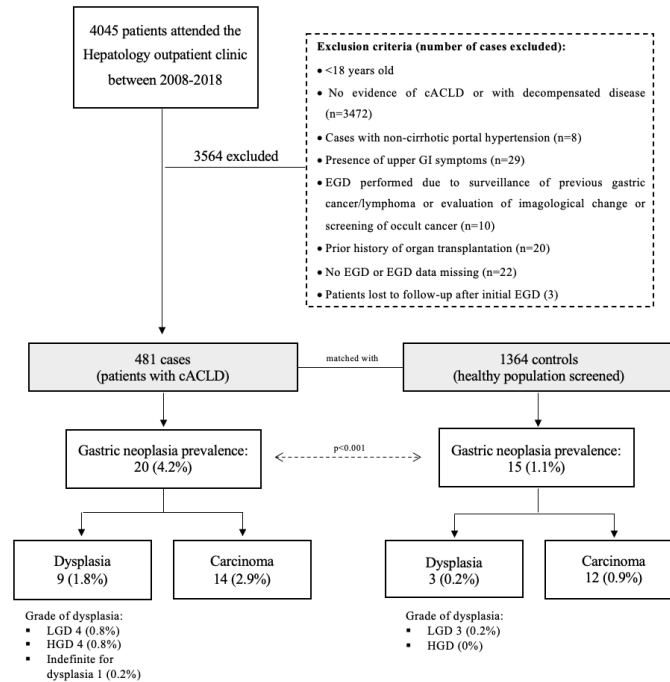


Fig. 1. Study flowchart

cACLD, compensated advanced chronic liver disease; EGD, esophagogastroduodenoscopy; HGD, high grade dysplasia; LGD, Low-Grade Dysplasia.

Descriptive data

14*

(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders

7

Cases:

Demographic data

We evaluated 1845 patients (481 cases and 1364 controls), 51.7% males, with a median age of 58 years old [interquartile range (IQR) 49-66 years] (Table 1). There was a positive GC family history in 1.5% of the patients. Besides a male predominance in cases, no other demographic characteristic differed between groups.

Characterization of the cACLD population

Of the 481 patients, 148 (30.8%) had active alcohol consumption and 142 (29.6%) had history of smoking. Alcohol was the most common cause of LC (213 cases, 44.3%), followed by hepatitis C virus (HCV) infection (59 cases, 12.3%) and nonalcoholic steatohepatitis (NASH) (40 cases, 8.3%) (Table 2).

		One hundred and fifteen patients (23.9% of cases) had simultaneously LSM by TE ≤ 20 kPa and PC ≥150000/mm³. The patients underwent a median number of 3 EGDs (IQR2-5) for screening of gastro-esophageal varices. The median follow-up time after EGD was 63 months (IQR 33-97). Controls: No data available																															
		(b) Indicate number of participants with missing data for each variable of interest Cases Smoking = 339 Hepatocellular carcinoma= 428 Fibrosis staging in liver biopsy (METAVIR)= 319 Fibrosis staging= 6 Hp infection=191 Gastric atrophy= 198 (antrum), 274 (body) OLGA= 276 Intestinal metaplasia= 198 (antrum), 274 (body) OLGIM= 276 TNM stage= 1 Controls: No data available	7,8,9																														
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure Demographic data <table><tr><th></th><th>Total [n (%)] n=1845</th><th>Cases [n (%)] n=481</th><th>Controls [n (%)] n=1364</th><th>p value</th></tr><tr><td>Gender</td><td></td><td></td><td></td><td></td></tr><tr><td>Female</td><td>892 (48.3%)</td><td>150 (31.2%)</td><td>742 (54.4%)</td><td>0.001</td></tr><tr><td>Male</td><td>953 (51.7%)</td><td>331 (68.8%)</td><td>622 (45.6%)</td><td></td></tr><tr><td>Age, median (IQR), years</td><td>58 (49-66)</td><td>58 (49-66)</td><td>57 (49-66)</td><td>0.492</td></tr><tr><td>Family history of gastric cancer</td><td>27 (1.5%)</td><td>4 (0.8%)</td><td>23 (1.7%)</td><td>0.268</td></tr></table> IQR, interquartile range Characterization of the cACLD population		Total [n (%)] n=1845	Cases [n (%)] n=481	Controls [n (%)] n=1364	p value	Gender					Female	892 (48.3%)	150 (31.2%)	742 (54.4%)	0.001	Male	953 (51.7%)	331 (68.8%)	622 (45.6%)		Age, median (IQR), years	58 (49-66)	58 (49-66)	57 (49-66)	0.492	Family history of gastric cancer	27 (1.5%)	4 (0.8%)	23 (1.7%)	0.268	7,8,9
	Total [n (%)] n=1845	Cases [n (%)] n=481	Controls [n (%)] n=1364	p value																													
Gender																																	
Female	892 (48.3%)	150 (31.2%)	742 (54.4%)	0.001																													
Male	953 (51.7%)	331 (68.8%)	622 (45.6%)																														
Age, median (IQR), years	58 (49-66)	58 (49-66)	57 (49-66)	0.492																													
Family history of gastric cancer	27 (1.5%)	4 (0.8%)	23 (1.7%)	0.268																													

	Total [n (%)] n=481
Active alcohol consumption	148 (30.8%)
Smoking	
Active smoker	70 (14.6%)
Ex-smoker	72 (15%)
Etiology	
Alcohol	213 (44.3%)
HCV	59 (12.3%)
Alcohol and HCV	29 (6%)
HBV	26 (5.4%)
Alcohol and HBV	7 (1.5%)
NASH	40 (8.3%)
Alcohol and NASH	39 (8.1%)
AIH	18 (3.7%)
PBC	14 (2.9%)
AIH and PBC	10 (2.1%)
PSC	1 (0.2%)
Hemochromatosis	11 (2.3%)
Wilson disease	2 (0.4%)
Alfa-1 antitrypsin deficiency	1 (0.2%)
Cryptogenic	11 (2.3%)
Hepatocellular carcinoma	53 (11%)
Fibrosis staging in liver biopsy (METAVIR)	
F1	1 (0.2%)
F2	2 (0.4%)
F3	18 (3.7%)
F4	141 (29.3%)
No data	319 (66.3%)
Transient elastography liver stiffness measurement, median (IQR), kPa	19.0 (10.2-35.3)
LSM by TE$\leq$20 kPa	192 (39.9%)
Platelets, median (IQR), /mm³	136000 (86000-194000)
Platelets$\geq$150000/mm³	190 (39.5%)
Number of EGDs, median (IQR)	3 (2-5)
Gastro-esophageal varices on at least one EGD	198 (41.2%)
Time of follow-up after initial EGD, median (IQR), months	63 (33-97)

H. Pylori infection and gastritis staging

	Total [n (%)] n=1845	Cases [n (%)] n=481	Controls [n (%)] n=1364	p value
Hp infection				<0.001
Yes	732 (44.3%)	88 (30.3%)	644 (47.2%)	
No	922 (55.7%)	202 (69.7%)	720 (78.1%)	
No data	191 (10.4%)	191 (39.7%)	-	
Gastric atrophy*				<0.001
Antrum				
No	1177 (71.5%)	190 (67.1%)	987 (72.4%)	
Mild	304 (18.5%)	55 (19.4%)	249 (18.3%)	
Moderate	141 (8.5%)	24 (8.5%)	117 (8.6%)	
Severe	25 (1.5%)	14 (5.0%)	11 (0.8%)	
No data	198 (10.7%)	198 (41.2%)	-	
Body				<0.001
No	1367 (87.0%)	164 (79.2%)	1203 (76.6%)	
Mild	97 (6.2%)	19 (9.2%)	78 (5.0%)	
Moderate	95 (6.0%)	15 (7.2%)	80 (5.9%)	
Severe	12 (0.8%)	9 (4.4%)	3 (0.2%)	
No data	274 (14.9%)	274 (57.0%)	-	
OLGA				<0.001
0	1024 (65.3%)	130 (63.4%)	894 (65.6%)	
I	309 (19.7%)	37 (18.0%)	272 (20.0%)	
II	192 (12.2%)	17 (8.3%)	175 (12.8%)	
III	31 (2.0%)	12 (5.9%)	19 (1.4%)	
IV	12 (0.8%)	9 (4.4%)	3 (0.2%)	
No data	276 (15.0%)	276 (53.1%)	-	
OLGA$\geq$III	43 (2.7%)	21 (10.2%)	22 (1.6%)	<0.001
No data	276 (15.0%)	276 (53.1%)	-	
Intestinal metaplasia*				<0.001
Antrum				
No	1283 (77.9%)	183 (64.7%)	1100 (80.7%)	
Mild	224 (13.6%)	42 (14.8%)	182 (13.3%)	
Moderate	102 (6.2%)	41 (14.5%)	61 (4.5%)	
Severe	38 (2.3%)	17 (6.0%)	21 (1.5%)	
No data	198 (10.7%)	198 (41.2%)	-	
Body				<0.001

No	1457 (92.8%)	167 (80.7%)	1290 (92.7%)	
Mild	65 (4.1%)	16 (7.7%)	65 (4.1%)	
Moderate	32 (2.0%)	13 (6.3%)	32 (2.0%)	
Severe	17 (1.1%)	11 (5.3%)	17 (1.1%)	
No data	274 (14.9%)	274 (57.0%)		
OLGIM				<0.001
0	1187 (75.6%)	125 (61.0%)	1062 (77.9%)	
I	239 (15.2%)	33 (16.1%)	206 (15.1%)	
II	91 (5.8%)	21 (10.2%)	70 (5.1%)	
III	37 (2.4%)	18 (8.8%)	19 (1.4%)	
IV	15 (1.0%)	8 (3.9%)	7 (0.5%)	
No data	276 (15.0%)	276 (53.1%)		
OLGIM≥III	52 (3.3%)	26 (12.7%)	26 (1.9%)	<0.001
No data	276 (15.0%)	276 (53.1%)	-	

Prevalence of gastric neoplasia

	Total [n (%)] n=1845	Cases [n (%)] n=481	Controls [n (%)] n=1364	p value
Gastric neoplasia	35 (1.9%)	20 (4.2%)	15 (1.1%)	<0.001
Gastric carcinoma	26 (1.4%)	14 (2.9%)	12 (0.9%)	0.003
Location				0.483
Cardia	1 (3.9%)	1 (7.1%)	-	
Fundus	2 (7.7%)	1 (7.1%)	1 (8.3%)	
Body	10 (38.5%)	7 (50.0%)	3 (25.0%)	
Incisura	4 (15.3%)	2 (14.3%)	2 (16.7%)	
Antrum	9 (34.6%)	3 (21.5%)	6 (50.0%)	
Histological subtype*				0.560
Gastric adenocarcinoma	25 (96.2%)	13 (92.9%)	12 (100%)	
Intestinal	20 (80.0%)	11 (84.6%)	9 (75.0%)	
Diffuse	5 (20.0%)	2 (15.4%)	3 (25.0%)	
Neuroendocrine carcinoma	1 (3.8%)	1 (7.1%)	-	
Gastric dysplasia	12 (0.7%)	9 (1.9%)	3 (0.2%)	<0.001
Location				0.177
Body	1 (8.3%)	1 (11.1%)	2 (66.7%)	
Antrum	10 (83.2%)	8 (88.9%)	1 (33.3%)	
Antrum+body ⁺	1 (8.3%)	-		
Histological subtype				0.240
LGD	7 (58.2%)	4 (44.4%)	3 (100.0%)	
HGD	4 (33.3%)	4 (44.4%)		
Indefinite for dysplasia	1 (8.3%)	1 (11.2%)		

Risk factors for gastric neoplasia

	Unadjusted OR (95% CI)	p value	Covariate adjusted OR (95% CI)	p value
Gender		0.513	-	-
Female	Ref.			
Male	1.253 (0.638-2.463)			
Age	1.082 (1.045-1.119)	0.001	-	-
Age ≥60 years	3.176 (1.517-6.652)	0.002	4.732 (1.573-14.233)	0.006
Family history of gastric cancer	-	-	-	-
No Hp infection	3.886 (1.475-10.235)	0.006	4.113 (1.168-14.486)	0.028
OLGA≥III	25.387 (10.889-59.188)	<0.001	1.644 (0.304-8.897)	0.564
OLGIM≥III	23.673 (10.432-53.718)	<0.001	7.277 (1.647-32.153)	0.009
cACLD	3.902 (1.981-7.684)	<0.001	1.606 (0.562-4.595)	0.377

Clinical outcome and management after diagnosis of gastric neoplasia in cACLD population

	Total [n (%)] n=14
TNM staging	
T	
T1a	4 (28.6%)
T1b	5 (35.7%)
T2	1 (7.1%)
T3	0 (0%)
T4a	3 (21.5%)
No data	1 (7.1%)
N	
N0	10 (71.5%)
N1	2 (14.3%)
N3a	1 (7.1%)
No data	1 (7.1%)
M	
M0	12 (85.8%)
M1	1 (7.1%)
No data	1 (7.1%)
AJCC Stage	
IA	8 (57.3%)
IB	1 (7.1%)
IIB	1 (7.1%)
IIIA	2 (14.3%)
IV	1 (7.1%)
No data	1 (7.1%)
Type of treatment	
Endoscopic	2 (14.3%)
- ESD	2 (100%)
Resection/ margins (R0)	2 (100%)
Curative resection	1 (50%)
Adverse events	0 (0%)
Re-intervention	0 (0%)
Number of days of hospitalization, median (IQR)	2
Tumor recurrence	0 (0%)
Surgical	11 (78.6%)
- Total gastrectomy	8 (72.7%)
- Subtotal gastrectomy	3 (27.3%)
Resection/ margins (R0)	11 (100%)
Adverse events	5 (54.5%)
Surgical re-intervention	2 (18.2%)
Number of days of hospitalization, median (IQR)	10 (9-21)
Additional treatment	3 (27.3%)
Neoadjuvant chemotherapy	1 (9.1%)
Adjuvant chemotherapy	2 (18.2%)
Tumor recurrence	0 (0%)
Palliative care	1 (7.1%)
Mortality rate in the follow-up	7 (50.0%)
Cause of death	
Related	3 (42.9%)
- Tumor	1 (33.3%)
- Complication	2 (66.7%)
Unrelated	4 (57.1%)
30-days mortality	1 (7.1%)
6-months mortality	3 (21.4%)
3-years mortality	6 (42.9%)
Overall survival, median (IQR), months	38 (6-69)

	Number of events	Clavien-Dindo	Management
Local complications			
Wound infection	1	II	Antibiotherapy
Anastomotic dehiscence	1	V	Surgery
Bleeding	1	V	Surgery; Blood transfusion
Systemic complications			
Heart failure decompensation	1	I	Conservative
Paroxysmal atrial fibrillation	1	II	Rhythm control therapy
Acute on chronic kidney disease	1	I	Fluid therapy
Nosocomial pneumonia	1	II	Antibiotherapy
Hemoptysis	1	I	Conservative

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	NA
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives In our study, we found a 4-times higher prevalence of gastric neoplasia in patients with cACLD compared to a healthy screening population. The prevalence of gastric dysplasia and carcinoma was 9-times and 3-times higher in cases than in controls, respectively. We found that 35% of the gastric neoplasia cases in the cACLD population would have been missed if these criteria were strictly followed.	9,10
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 should be addressed and that are inherent to the study design. Regarding cases, this was a retrospective study based on observational data from a single tertiary hospital in Portugal. In a significant number of patients, it was not possible to collect data regarding the status of Hp infection and gastritis staging. In controls, all procedures were performed under general anesthesia while in cases many procedures were performed without sedation. In controls, all the procedures were performed by only 2 endoscopists which may be a potential bias, since in cases the procedures were performed by multiple endoscopists, including fellows in training. Second, it is well-known that GC is more common in males, and in our study, there was a significantly male predominance in cases compared to controls. This could have led to an overestimation of GC prevalence in the cACLD group. On the other hand, alcohol consumption and smoking status were not evaluated in controls. Since all of these are significant risk factors for GC this is a potentially important bias that limits our conclusions and does not let us suggest LC as an independently risk factor for gastric neoplasia.	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Our data highlights the possible role of EGD an opportunistic screening method for an early diagnosis of gastric neoplasia in this population.	10,11

		We found a higher prevalence of gastric neoplasia in patients with cACLD than in healthy controls who were undergoing an already scheduled screening colonoscopy. The Baveno VII criteria suggest that EGD screening for gastro-esophageal varices may be preventable in certain patient groups. Based on our results, we suggest that in countries with intermediate-high risk for GC, continuing to perform EGD could be beneficial, as patients with cACLD are at higher risk for GC, and its early detection may be associated with better outcomes.	
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
		Recognizing the limitations of our study, what we propose is that the results obtained be taken into account, for future studies, but also in the daily clinical approach to patients who find themselves in these situations, as it may make sense not to strictly follow what is recommended by the guidelines.	
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	NA

*Give information separately for cases and controls.

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>.

GE - Portuguese Journal of Gastroenterology

Author Guidelines

About the Journal

Aims and Scope

The GE – Portuguese Journal of Gastroenterology (formerly Jornal Português de Gastreenterologia), founded in 1994, is the official publication of the Sociedade Portuguesa de Gastreenterologia (Portuguese Society of Gastroenterology), Sociedade Portuguesa de Endoscopia Digestiva (Portuguese Society of Digestive Endoscopy), and Associação Portuguesa para o Estudo do Fígado (Portuguese Association for the Study of the Liver). The journal publishes clinical and basic research articles on gastroenterology, digestive endoscopy, hepatology, and related topics. Review articles, clinical case studies, images, letters to the editor, and other articles such as recommendations or papers on gastroenterology clinical practice are also considered. Only articles written in English are accepted.

Journal Sections

Images in Gastroenterology and Hepatology

This section is intended for the publication of clinical, radiological, histological, and surgical images related to gastroenterological or hepatological cases. The text should include a short clinical history and relevant data from the physical examination, laboratory tests, and clinical progression as appropriate. Submissions to this section should be submitted under the article type "Case Reports" and should have no more than 6 authors.

Endoscopic Snapshots

This section is intended for the publication of rare or educational cases or novel techniques in digestive endoscopy. Submissions to this section should be submitted under the article type "Case Reports" and should have no more than 6 authors.

Clinical Case Study

Clinical Case Studies are Case Reports which present a case study, case report, or other description of a case. Case Reports present significant new insights or cases with an unusual and noteworthy course. Submissions can be based on a case or a number of similar cases. The most important aspect of the presentation is that it should provide a new perspective on a recognized clinical scenario or may represent an entirely new clinical condition. The novelty of the case(s) may lie in the phenotype, the presentation, the investigation, and/or the management. Submissions to this section should be submitted under the article type "Case Reports" and should have no more than 6 authors.

Article Types

Research Article

Research Articles report on primary research. They must describe significant and original observations. Consideration for publication is based on the article's originality, novelty, and scientific soundness, and the appropriateness of its analysis.

Research Articles are reports of original work. Authors are asked to follow the [EQUATOR Network](#) for Research Articles.

Prior approval from an Institutional Review Board (IRB) or an Ethics Review Committee is required for all investigations involving human subjects.

A downloadable template is available below.

Documents

[Research Article](#) (DOCX, 29.19 KB)

Research Articles should contain up to 4'000 words, 60 references, 6 tables and/or figures.

Review Article

Review Articles are considered reviews of research or summary articles. They are state-of-the-art papers covering a current topic by experts in the field. They should give evidence on and provide answers to a well-defined aspect or question in a particular area. Review Articles must include a critical discussion of the reported data and give a clear conclusion with potential impacts on the standard of care.

A downloadable template is available below.

Documents

[Review Article](#) (DOCX, 23.82 KB)

Review Articles are usually published by invitation only. They should contain up to 4'000 words, 100 references, 6 tables and/or figures.

Systematic Review

Systematic Reviews are literature reviews focused on a research question that synthesizes all high-quality research evidence relevant to that question. Systematic Reviews should be presented in the Introduction, Methods, Results, Discussion format. The subject must be clearly defined. The objective of a Systematic Review should be to arrive at an evidence-based conclusion. The Methods section should give a clear indication of the literature search strategy, data extraction procedure, grading of evidence, and kind of analysis used. We strongly encourage authors to comply with the [Preferred Reporting Items for Systematic Reviews and Meta-Analyses \(PRISMA\) guidelines](#).

A downloadable template is available below.

Documents

[Systematic Review](#) (DOCX, 27.75 KB)

Systematic Reviews should contain up to 4'000 words, 100 references, 6 tables and/or figures.

Case Report

Case Reports can present a case study, case report, or other description of a case. Case Reports present significant new insights or cases with an unusual and noteworthy course. Submissions can be based on a case or a number of similar cases. The most important aspect of the presentation is that it should provide a new perspective on a recognized clinical scenario or may represent an entirely new clinical condition. The novelty of the case(s) may lie in the phenotype, the presentation, the investigation, and/or the management. We strongly encourage authors to comply with the [CARE guidelines](#). The manuscript must include a statement detailing that written informed consent for publication was obtained and from whom (e.g. "Written informed consent was obtained from the patient for publication of this case report and any accompanying images."). If the patient has died, consent for publication must be obtained from their next of kin. If the patient described in the case report is a minor or vulnerable, then consent for publication must be obtained from the parent/legal guardian. The completed consent form must be made available to the Editor if requested, and will be treated confidentially.

A downloadable template is available below.

Documents

[Images in Gastroenterology and Hepatology](#) (DOCX, 26.39 KB)

[Endoscopic Snapshots](#) (DOCX, 26.32 KB)

[Clinical Case Study](#) (DOCX, 27.27 KB)

Authors may wish to submit one of the following Case Reports:

Images in Gastroenterology and Hepatology: Intended for the publication of clinical, radiological, histological, and surgical images related to gastroenterological or hepatological cases. The text should not exceed 500 words, up to 5 references, and up to 4 figures but without tables or plots. The title should have no more than 8 words. Figures should be of high quality and educational value and may be in color or black and white. An abstract is not required, but the manuscript should have a title and keywords in Portuguese. The text should have no more than 6 authors.

Endoscopic Snapshots: Intended for the publication of rare or educational cases or novel techniques in digestive endoscopy. The text should not exceed 500 words and up to 5 references. Up to 3 figures with brief captions may be included. An abstract is not required, but the manuscript should have a title and keywords in Portuguese. The text should have no more than 6 authors.

Clinical Case Study: Intended for the publication of Case Reports which present significant new insights or cases with an unusual and noteworthy course. The abstract should be structured, and a title, abstract and keywords should also be provided in Portuguese. The text should contain up to 2'000 words, 25 references and should have no more than 6 authors.

Brief Report

Brief Reports are short and/or rapid announcements of research results. They must contain data derived from cutting-edge research and be of potential interest to a large proportion of the readership. They are independent, concise reports representing a significant contribution to the field. Such communications should represent complete, original studies and should be arranged in the same way as full-length manuscripts with subheadings.

A downloadable template is available below.

Documents

[Brief Report](#) (DOCX, 27.04 KB)

Editorial

Editorials provide a viewpoint on specific articles or on general subjects directly relevant to the journal. Editorials are written by an editor or other member of the journal.

A downloadable template is available below.

Documents

[Editorial](#) (DOCX, 25.11 KB)

Editorials should contain up to 1'500 words, 20 references, 1 table & 1 figure. An abstract is not required, but should have a title and keywords in Portuguese.

Letter

Letters may explore subjects related to matters discussed in the journal, providing the author's perspective on a subject. Letters may discuss a recently published article and may lend support or constructively critique the article in line with the author's experience. The editors reserve the right to share such letters to the authors of the article concerned prior to publication in order to permit response, ideally in the same issue of the journal. Letters should not include original data.

A downloadable template is available below.

Documents

[Letter](#) (DOCX, 24.36 KB)

Letters should contain up to 600 words, 10 references, 1 table or 1 figure.

Methods Article

Methods Articles describe methods or protocols used to perform an experiment or carry out a research plan. They should not report research results. Authors may submit a Study Protocol outlining a research and/or statistical analysis plan for proposed, or ongoing, but incomplete, research studies, including but not limited to, clinical trials, population-based studies, clinical outcome studies, and service evaluations. Only study protocols that have received ethical approval will be considered and, where expected by community convention, study protocols must be pre-registered and the trial/study registration number should be provided in the manuscript. Manuscripts reporting study protocols must adhere to the relevant reporting guidelines for their study design, such as the [>SPIRIT](#), [>PRISMA-P](#) or other relevant reporting guidelines as detailed on the [>Equator Network website](#).

A downloadable template is available below.

Documents

[Method Article](#) (DOCX, 32.86 KB)

[Method Article for Study Protocol](#) (DOCX, 34.02 KB)

Guidelines

Guidelines are statements intended to guide clinical care. They should describe the clinical problem to be addressed, the mechanism by which the statement was generated, a review of the evidence for the statement and the statement on practice itself.

A downloadable template is available below.

Documents

[Guidelines](#) (DOCX, 24.83 KB)

Contact Information

Should you have any problems with your submission, please contact the editorial office:

Mrs. Andreia Neto

Tel. +351 93 799 55 32

andreia.neto@spg.pt

Editorial and Journal Policies

General Conditions

Only papers written in English are considered. The articles should be comprehensible to a reader who is fluent in English and should be edited prior to submission to ensure that standard English grammar and usage are observed. Use of a professional [language editing service](#) prior to submission can help avoid delays with the review process.

All manuscripts are subject to editorial review.

The presentation of manuscripts should follow the [Uniform Requirements for Manuscripts Submitted to Biomedical Journals from the International Committee of Medical Journal Editors \(ICMJE\)](#).

Karger Publishers is a member of the Committee on Publication Ethics (COPE). Karger journals aim to adhere to the [COPE Code of Conduct and Best Practice Guidelines](#).

All articles in this journal are Open Access and meet the requirements of funding bodies and academic institutions. By default, articles are published under a Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) license. Other licenses are available on request if required by funding bodies. More information about Creative Commons licensing options is available on the [Karger website](#).

Please contact Karger's Open Access team at openaccess@karger.com with questions regarding your funding body.

The copyright of the article is retained by the authors. The authors grant S. Karger AG, Basel, an exclusive unlimited license to publish the article under a Creative Commons license and identify S. Karger AG as the original publisher. Submission of a manuscript for publication implies the authors' consent to publication under the applicable Creative Commons license and the terms and conditions of the Publisher's Licensing Agreement.

Karger recommends the use of original images and materials whenever possible. If a submitted manuscript contains third-party copyright material(s), it is the authors' sole responsibility to obtain permission from the relevant copyright holder for reusing the material(s), including any associated licensing fee. The copyright and usage information needs to be checked carefully to avoid copyright infringement.

Most publishers offer a quick and easy way to clear permissions for their content via the built-in website application RightsLink or via > <https://www.copyright.com/get-permissions/>. Another widely used licensing tool is > [PLSClear](#). Please check the publishers' websites for the available options and user instructions.

Statements

All submitted manuscripts must contain a statements section after the main body of the text, but before the reference list.

Statement of Ethics

Published research must comply with internationally-accepted standards for research practice and reporting. Manuscripts may be rejected if the editors believe that the research has not been carried out within an appropriate ethical framework, and concerns raised after publication may lead to a correction, retraction, or expression of concern in line with > [COPE guidelines](#).

Studies involving human subjects (including research on identifiable human material and data) must have been performed with the approval of an appropriate ethics committee and with appropriate participants' informed consent in compliance with the > [Helsinki Declaration](#).

In the manuscript, authors should specify the name of the ethics committee or other relevant authority who approved the study protocol and provide the reference number where appropriate. If ethics approval was not required, or if the study has been granted an exemption from requiring ethics approval, this should also be detailed in the manuscript (including the name of the ethics committee who made that decision).

For all research involving human subjects, written informed consent to participate in the study should be obtained from participants (or their parent/legal guardian where appropriate) and a statement detailing this should appear in the manuscript. For studies involving vulnerable participants or participants at risk of potential coercion, detailed information regarding the steps taken to ensure informed consent must be provided. If consent was not obtained, please specify why and whether this was approved by the ethics committee.

In line with the > [ICMJE recommendations](#) on the protection of research participants, authors must avoid providing identifying information unless strictly necessary for the submission and participants' identifiable attributes must be anonymized in the manuscript and its supplementary files, if any. If identifying information is necessary, authors must confirm that the individual has provided written consent for the use of that information in a publication.

Research involving human embryonic stem cells, embryonic germ cells or induced pluripotent stem cells should comply with the ISSCR '> [Guidelines for the Conduct of Human Embryonic Stem Cell Research](#)' or an equivalent set of guidelines or applicable regulations.

Case Reports: Manuscripts reporting a case report must include a statement detailing that written informed consent for publication was obtained and from whom (e.g. "Written informed consent was obtained from the patient for publication of this case report and any accompanying images."). If the patient has died, consent for publication must be obtained from their next of kin. If the patient described in the case report is a minor or vulnerable, then consent for publication must be obtained from the parent/legal guardian. The completed consent form must be made available to the Editor if requested, and will be treated confidentially.

Clinical Trials: In accordance with the > [ICMJE recommendations](#), all clinical trials should be registered in a publicly available registry approved by the WHO or ICMJE (see the list > [here](#)) and the clinical trial number must be clearly stated in the manuscript. Manuscripts reporting clinical trials must adhere to the relevant reporting guidelines for their study design, such as > [CONSORT](#) for randomized controlled trials, > [TREND](#) for non-randomized trials, or other relevant reporting guidelines as detailed on the > [Equator network website](#).

Karger follows the > [WHO definition](#) of clinical trials *"A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes [...] Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc. This definition includes Phase I to Phase IV trials."*

Studies involving animals: Experimental research on vertebrates or any regulated invertebrates must have been approved by the authors' Institutional Animal Care and Use Committee (IACUC) or equivalent ethics committee and must follow internationally recognized guidelines such as the > [ARRIVE](#) guidelines. In the manuscript, authors should specify the name

of the ethics committee or other relevant authority who approved the study protocol and provide the reference number where appropriate.

If ethics approval was not required, or if the study has been granted an exemption from requiring ethics approval, this should also be detailed in the manuscript (including the name of the ethics committee who made that decision). Additional information is expected for studies reporting death of a regulated animal as a likely outcome or planned endpoint. Other types of studies including field studies and non-experimental research on animals must comply with local or international guidelines, and where appropriate must have been approved by an appropriate ethics committee.

Please note if authors are submitting to a journal with a double blind peer review policy, the Ethics Statement should be anonymized where appropriate.

Conflict of Interest Statement

Karger endorses the [ICMJE recommendations](#) on the 'Disclosure of Financial and Non-Financial Relationships and Activities, and Conflicts of Interest'. Authors are required to disclose any relationship that could reasonably be perceived by a reader as a potential conflict of interest at the time of submission. All forms of support and financial involvement (e.g. employment, consultancies, honoraria, stock ownership and options, expert testimony, grants or patents received or pending, royalties) which took place in the previous three years should be listed, regardless of their potential relevance to the paper. Also the nonfinancial relationships (personal, political, or professional) that may potentially influence the writing of the manuscript should be declared. The role of the funder in study design; collection, analysis, and interpretation of data; writing of the report; any restrictions regarding the submission of the report for publication should be declared. If the funder had no role in any of the above, this should be clearly stated in the manuscript's funding section.

Please note if authors are submitting to a journal with a double blind peer review policy, the Conflict of Interest statement should be anonymized where appropriate.

Author Contributions Statement

In the Author Contributions section, a short statement detailing the contributions of each person named as an author should be included. Contributors to the paper who do not fulfill the [ICMJE Criteria for Authorship](#) should be credited in the Acknowledgement section. If an author is removed from or added to the listed authors after submission, an explanation and a signed statement of agreement confirming the requested change are required from all the initially listed authors and from the author to be removed or added.

Please note if authors are submitting to a journal with a double blind peer review policy, the Author Contributions statement should be anonymized where appropriate.

Group Authorship

For group authorship, the > ICMJE recommends that:

"When a large multi-author group has conducted the work, the group ideally should decide who will be an author before the work is started and confirm who is an author before submitting the manuscript for publication. All members of the group named as authors should meet all four criteria for authorship, including approval of the final manuscript, and they should be able to take public responsibility for the work and should have full confidence in the accuracy and integrity of the work of other group authors."

When submitting a manuscript authored by a group, the submitting author should specify the group name in the manuscript file and enter the information of the group members who can take credit and responsibility for the work as authors in the submission system. The non-author group members should be listed elsewhere in the manuscript, typically in the Acknowledgements.

Data Availability Statement

The journal's data sharing policy strongly encourages authors to make all datasets on which the conclusions of the paper rely available to editors, reviewers and readers without unnecessary restriction wherever possible. Authors are required to provide a Data Availability Statement in their article that details whether data are available and where they can be found. In cases where research data are not publicly available on legal or ethical grounds, this should be clearly stated in the Data Availability Statement along with any conditions for accessing the data. The decision to publish will not be affected by whether or not authors share their research data.

Examples of Data Availability statements:

- The data that support the findings of this study are openly available in [repository name e.g "figshare"] at [http://doi.org/\[doi\]](http://doi.org/[doi]), reference number [reference number]
- Publicly available datasets were used in this study. These can be found in [repository name e.g "figshare"] at [http://doi.org/\[doi\]](http://doi.org/[doi]), reference number [reference number]
- All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.
- All data generated or analyzed during this study are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.
- The data that support the findings of this study are not publicly available due to [REASON WHY DATA ARE NOT PUBLIC e.g. their containing information that could compromise the privacy of research participants] but are available from [e.g. the corresponding author [author initials] OR Data sharing committee [PROVIDE CONTACT DETAILS including email address] upon reasonable request]
- The data in this study was obtained from [third party source] where [RESTRICTIONS/LICENCE] may apply. Such dataset may be requested from [source contact information].

Please note if authors are submitting to a journal with a double blind peer review policy, the data availability statement should be anonymized where appropriate.

Definition of research data: This policy applies to the research data that would be required to verify the results of research reported in articles published in the journal. Research data include data produced by the authors ("primary data") and data from other sources that are analysed by authors in their study ("secondary data"). Research data includes any recorded factual material that are used to produce the results in digital and non-digital form. This includes, but is not limited to, tabular data, code, images, audio, documents, video, maps, raw and/or processed data.

For images, Karger requests that individual/unique features within an image are not modified, and image-processing methods do not alter the original image information (the use of software and/or enhancement technique must be disclosed in the methods section). Any concerns raised over inappropriate image modification will be investigated in accordance with COPE guidelines.

Policy exceptions: This policy does not require public sharing of quantitative or qualitative data that could identify a research participant unless participants have consented to data release. The policy also does not require public sharing of other sensitive data, such as the locations of endangered species. Alternatives to public sharing of sensitive or personal data include:

- Depositing research data in controlled access repositories
- Anonymizing or deidentifying data before public sharing
- Only sharing metadata about the research data
- Stating the procedures for accessing your research data in the article and managing data access requests from other researchers

Embargoes: Embargoes on data sharing are permitted but should be clearly stated in the data availability statement, including the reason for embargo, date of the end of the embargo period and how and where the data can be accessed following the end of the embargo period. Please note that all datasets on which the conclusions of the paper rely must be made available to editors and reviewers if requested to facilitate the review process.

Data repositories: The preferred mechanism for sharing research data is via public data repositories. We encourage authors to select a data repository that issues a persistent identifier, preferably a Digital Object Identifier (DOI), and has established a robust preservation plan to ensure the data is preserved in perpetuity. Additionally, we highly encourage researchers to consider the > [FAIR Data Principles](#) when depositing data. Authors are encouraged to deposit their research data in a repository that has been widely adopted within their research community, suitable repositories per each area and data type can be searched using the FAIRsharing database tool (> <https://fairsharing.org/databases/>) or via > <https://repositoryfinder.datacite.org>.

If no such database is available authors may use a general data repository. Examples of general data repositories include:

- Figshare (> www.figshare.com)
- Dryad (> www.datadryad.org)
- Zenodo (> www.zenodo.org)

- Open Science Framework (><https://osf.io/>)

If authors are submitting an article to a journal with a double blind peer review policy, they should deposit their data in a repository that allows them to temporarily preserve anonymity such as Figshare (“private sharing link”) or Dryad (“private for peer review”).

Data citation: The journal encourages authors to cite any publicly available research data in their reference list. References to datasets (data citations) must include a persistent identifier (such as a DOI). Citations of datasets, when they appear in the reference list, should include the > minimum information recommended by DataCite (e.g. author(s), title, publisher (repository name), DOI) and follow journal style.

Data licensing: The journal encourages research data to be made available under open licences that permit reuse freely. The journal does not enforce particular licenses for research data, where research data are deposited in third party repositories. The publisher of the journal does not claim copyright for research data.

Reference: Hrynaszkiewicz, I, Simons, N, Hussain, A, Grant, R and Goudie, S. 2020. Developing a Research Data Policy Framework for All Journals and Publishers. Data Science Journal, DOI: > <http://doi.org/10.5334/dsj-2020-005>.

Plagiarism

Plagiarism, whether intentional or not, is not tolerated in Karger’s journals. Plagiarism includes, but is not limited to, copying or reusing text, ideas, images or data from other sources without clear attribution, and goes against the principle of academic publishing. Karger may subject any manuscripts to a plagiarism-detection software (Crossref Similarity Check, powered by iThenticate) and if the software raises any concerns, there will be a follow-up investigation in line with > COPE guidelines. At any stage of peer-review, publication, or post-publication, if plagiarism is detected the manuscript may be rejected, corrected or retracted, as appropriate, and we reserve the right to inform the authors' institutions about any plagiarism detected. We expect that our editors and reviewers will inform the journal about any concerns related to plagiarism.

Further Conditions

Editorial Freedom

The GE – Portuguese Journal of Gastroenterology adopts the World Association of Medical Editors’ definition of editorial freedom, which holds that Editors-in-Chief have full authority over the entire editorial content of their journal and the timing of publication of that content. Journal owners should not interfere in the evaluation, selection, scheduling, or editing of individual articles either directly or by creating an environment that strongly influences decisions. The Editor-in-Chief bases editorial decisions on the validity of the work and its importance to the journal’s readers, not on the commercial implications for the journal, and is free to express

critical but responsible views about all aspects of medicine without fear of retribution, even if these views conflict with the commercial goals of the publisher. The Editor-in-Chief of the GE – Portuguese Journal of Gastroenterology has the final say in decisions about which advertisements or sponsored content, including supplements, the journal will or will not carry, and he should have the final say in the use of the journal brand and in the overall policy regarding commercial use of journal content.

Peer Review

Peer Review Policy

All Karger journals employ a rigorous peer-review process to confirm the validity and ensure scientific accuracy of published articles. Independent researchers with relevant expertise assess submitted manuscripts to help journal editors determine whether a manuscript should be published in their journal.

Peer Review Type

GE - Portuguese Journal of Gastroenterology uses a single-blind peer review system where reviewers know the names of the authors, but the authors do not know who reviewed their manuscript.

Peer Review Process

The Editor-in-Chief and the international Editorial Board ensure a thorough and fair peer-review process with the highest scientific publishing standards. The editorial office performs preliminary checks on submitted manuscripts to ensure compliance with submission guidelines, editorial policies and ethical standards. After completion of internal checks, each submission is assessed by the Editor-in-Chief (and/or Managing Editor) who decides whether to proceed with peer review and may assign a suitable handling Editor (Associate Editor, Editorial Board Member or Guest Editor). Handling Editors guide the peer-review process for manuscripts within their areas of expertise with the help of reviewers who are well qualified and up-to-date on the subject matter and/or methodology. All articles, except for Editorials and some Correspondence articles, are externally peer reviewed, typically by at least two individuals with expertise in the manuscript content area and/or research methods, before a final decision is made about acceptance for publication. If an Editor, Editorial Board Member, or employee submits a manuscript, it is assigned to an independent Editor who will handle the peer review, and details of the review process, beyond the anonymized review and decision, are not accessible to the Editor, Editorial Board Member, or employee. All Editors, reviewers and authors shall adhere to Karger's editorial policies and best practices in line with > [COPE Core Practices](#) to maintain high standards of peer-review.

Peer Reviewers

Authors may suggest reviewers, who must have a recent publication record in the area of the submission, must not have published with the authors in recent years, and must not be from the same institution as the authors. Whether or not to consider these reviewers is at the Editor's discretion, and in line with Karger's Editorial policy. Where possible, institutional email addresses or information which will facilitate verifying the identity of the reviewer should be provided.

Appeals and Complaints

Any appeal on a decision or complaint during peer-review, or post-publication, must be submitted in writing to the corresponding Karger's editorial office (see "Journal Contact"). All cases will be handled in line with [COPE guidelines](#).

Reproducibility

Availability of materials

The Methods section of the article must contain sufficient information to allow a reader to replicate the study. Karger encourages authors to use protocols.io as an open access repository for their detailed methodology. For protocols registered in [protocols.io](#), please cite this record in your methods section and include the record DOI in the references. Karger supports the inclusion of Research Resource Identifiers in the methods section, for further information please see the [Resource Identification Portal](#). Supplier and catalogue numbers should be included for any chemical and reagents.

Image presentation

Where authors include a representative image of an experimental group or outcome it is expected that no image enhancements or adjustments are applied to that image. Where necessary for clarity of interpretation, for example, image cropping or brightness adjustment, this should be applied to the whole image, be detailed in the Methods section of the article and the original images must be uploaded as supplementary material.

Statistics

Karger recommends following The [SAMPL Guidelines](#) when reporting statistical analyses. Sample size must be reported for each study in the methods section tables and Figure legends. Where statistical testing for the significance of an effect is carried out, a dedicated section for statistical methodology must be included in the Methods. This section should provide sufficient information that would allow, with access to the full data set, reproduction of the article's results. The choice of statistical tests and any post-hoc tests must be justified in this section. The threshold for significance, alpha, should be defined here as well as how multiple comparisons are adjusted for, where applicable. When reporting the results of statistical tests it is not sufficient to only report the p-value. For example, for a Student's t-test, it is necessary to report the degrees of freedom, t-statistic as well as the exact p-value.

Materials Design Analysis Reporting Framework

Karger Publishers endorses the Materials Design Analysis Reporting (MDAR) Framework for minimum reporting standards in the life sciences and encourages authors to consider all aspects of the [MDAR Framework](#) relevant to their study when submitting a manuscript. Authors are encouraged to submit a completed [MDAR Checklist](#) with their manuscripts.

Misconduct

Karger takes seriously all allegations of potential misconduct and will follow relevant [COPE Guidelines](#). Concerns regarding a published article should be raised to the Research Integrity and Publication Ethics Manager at [publication.ethics\[at\]karger.com](mailto:publication.ethics[at]karger.com). All efforts will be made to resolve concerns raised about a published article without undue delay and an Erratum or Retraction will be issued, where necessary. An Expression of Concern may be published to inform readers of ongoing matters in line with [COPE guidance](#). In cases of suspected research or publication misconduct, it may be necessary for the Editor or Publisher to contact and share submission details with third parties including authors' institutions and ethics committees in line with [COPE Guidelines](#). Advice may also be sought directly from COPE.

Article Preparation

Formatting

The preferred word processing program for manuscripts is Microsoft Word. Page and line numbering should be activated, and the level of subheadings should be indicated clearly.

Footnotes should be avoided. When essential, they should be numbered consecutively and appear at the foot of the appropriate page.

Abbreviations (with the exception of those clearly well established in the field) should be explained when they are first used both in the abstract and in the main text.

Units of measurement should be expressed in SI units wherever possible.

Generic names of drugs (first letter: lowercase) should be used whenever possible. Registered trade names (first letter: uppercase) should be marked with the superscript registration symbol ® or ™ when they are first mentioned.

The manuscript text, tables and illustrations must be submitted in separate files.

For further technical specifications, including those regarding tables, figures, and illustrations, please refer to the [Karger website](#).

Further Formatting Instructions

Documents

[Graphical Abstract Template](#) (PPTX, 62.99 KB)

Graphical Abstract

A graphical abstract may be submitted together with the manuscript. It will also be peer-reviewed for online publication next to the abstract text. It is the authors' responsibility to ensure its quality, resolution and accuracy. The image file may consist of only one single panel and should fit the white area in the following template. The image must be in jpg format, 1200 pixels square at 300 dpi, and with the font Arial at 9–12 points for any text it may contain within the image.

Manuscript Arrangement

Title Page

The first page should contain a short and concise title plus a running head of no more than 80 characters. Abbreviations should be avoided.

Below the title, list all the authors' names as outlined in the article sample, which can be downloaded under Article Types. Each listed author must have an affiliation, which comprises the department, university, or organization and its location, city, state/province (if applicable), and country.

Place the full postal address of the corresponding author at the bottom of the first page, including at least one telephone number and e-mail address.

Keywords relevant to the article should be listed below the corresponding author information.

Body

Please refer to the Article Types section of the Guidelines for Authors for information on the relevant article structure, including maximum word counts and downloadable samples.

Online Supplementary Material

Online Supplementary Material may be used to enhance a publication and increase its visibility on the Web. Supplementary files (directly relevant but not essential to the conclusions of the paper) will undergo editorial review and should be submitted in a separate file with the original manuscript and with all subsequent submissions. The Editor(s) reserve(s) the right to limit the scope and length of supplementary material. Supplementary material must meet production quality standards for publication without the need for any modification or editing. For ease of reader access, we strongly recommend that files be less than 10 MB. Authors wishing to associate larger amounts of supplementary material with their article should deposit their data in an appropriate public data repository. Figures must have legends and tables require headings. All files must be named clearly. Acceptable files and formats are Word or PDF files, Excel spreadsheets (if the data cannot be converted properly into a PDF file), and multimedia files (MPEG, AVI, or QuickTime formats). All supplementary material should be referred to in the main text. A DOI number will be assigned to supplementary material, and it will be hosted online at > <https://karger.figshare.com> under a > [CC BY license](#).

References

In-Text Citation

References in the text should be identified using Arabic numerals [in square brackets].

The reference list should not be alphabetized, but the references should be numbered consecutively in the order in which they are first mentioned in the text. Material submitted for publication but not yet accepted should be labelled as 'unpublished' and may not be included in the reference list. Other pre-published or related materials with a DOI, e.g. preprint manuscripts, datasets, and code, may be included.

Further information and examples can be found in the downloadable article samples in Article Types. If you are using reference management software, we recommend using the Vancouver Referencing Style.

Reference Management Software

The use of EndNote is recommended to facilitate formatting of citations and reference lists. The journal output style can be downloaded from > <http://endnote.com/downloads/styles>.

Author Services

Karger Publishers offer a range of services to assist authors with the preparation of their manuscript, including discounts for language editing services offered by third parties.

More information is available on the [➤ Author Resources](#) section of the Karger homepage.

When submitting a manuscript, authors can add their [➤ ORCID number](#) to their Karger account to ensure that their paper is accredited to them correctly.

Cost of Publication

Page Charges/Article Processing Charges

Charges are not levied in this journal, meaning **publication is free of charge**.

Online Supplementary Material

We strongly encourage authors to make all the datasets on which the conclusions of the manuscript are based available. Online supplementary material is hosted for free with a published article. For ease of reader access, we strongly recommend that files be less than 10 MB. Authors wishing to associate larger amounts of supplementary material with their article should deposit their data in an appropriate public data repository.

Illustration Charges

Color illustrations are reproduced free of charge.

Journal Policies

Copyediting and Proofs

Manuscripts accepted for publication by Karger Publishers will undergo basic proofreading to check for obvious spelling and grammar mistakes. If you would prefer a more in-depth [➤ language editing service](#) to improve clarity and style, please consult a service provider prior to submission. Please note that the use of a language editing service before submission is not a requirement for publication in the journal and does not guarantee that the manuscript will be considered for peer review or accepted.

Karger Publishers' house style is based on internationally recognized standard manuals, including [➤ The Chicago Manual of Style](#).

An e-mail containing a link to download the PDF proofs will be sent to the corresponding author. The authors should check the PDF document and respond to any questions that have been raised during proofreading within 48 hours.

Alterations made to proofs, other than the correction of errors introduced by the Publisher, are charged to the authors and may require editorial approval.

Please note that the revised proofs are not sent to the authors prior to typesetting and online publication unless there are exceptional circumstances. The article layout will be created according to the Karger standard.

DOI Number

A DOI number will be available as a unique identifier on the title page of each article. DOIs are useful for identifying and citing articles published online without volume or issue information (for more information, see www.doi.org).

Licenses and Copyright

Articles published in GE - Portuguese Journal of Gastroenterology are licensed by default under a Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) license, unless otherwise agreed with Karger Publishers. When sharing or reusing any article, attribution must be given to the original source, using the statement "The final, published version of this article is available at [http://www.karger.com/?doi=\[insert DOI number\]](http://www.karger.com/?doi=[insert DOI number])" (e.g., <http://www.karger.com/?doi=10.1159/000365070>).

More information is available on the [Karger website](#).

The copyright of the article is retained by the authors. The authors grant S. Karger AG, Basel, an exclusive unlimited license to publish the article under a Creative Commons license and identify S. Karger AG as the original publisher. Submission of a manuscript for publication implies the authors' consent to publication under the applicable Creative Commons license and the terms and conditions of the Publisher's Licensing Agreement.

Please note that metadata – essentially, data tags about article information such as authors and keywords that helps make articles discoverable by, for example, search engines – is governed by a separate policy. Refer to the [FAQ on our Open Access web pages](#) for details.

Archiving and Self-Archiving

All articles are archived in Portico. Articles may also be archived in PubMed Central if the journal is indexed there. Karger permits authors of Open Access articles to post the Version of Record (VOR) of their articles in Open Access repositories or on other websites. Preprints may be shared without restriction. Re-posted Open Access articles must follow the terms of the relevant Creative Commons license.

To ensure citations are credited to the Version of Record, Karger encourages authors to link to the published article on www.karger.com and include the following statement: "The Version of Record of this article is available at [http://www.karger.com/?doi=\[insert DOI number\]](http://www.karger.com/?doi=[insert DOI number])(e.g. <http://www.karger.com/?doi=10.1159/000365070>)."

Manuscripts to be archived in PubMed Central due to NIH funding requirements will be submitted by Karger on the authors' behalf, as outlined under Funding Organizations.

Karger policies on Open Access, licensing and self-archiving can also be found at [> Sherpa Romeo](#).

Funding Organizations

If the authors are affiliated with an organization that has an Open Access agreement with Karger, the authors are prompted during submission to select from a list of these organizations. By choosing one of the listed organizations, eligibility can then be assessed.

NIH-Funded Research

The US National Institutes of Health (NIH) Public Access Policy mandates that the Author's Accepted Manuscript must be archived in its digital repository PubMed Central (PMC) within 12 months of the official publication date. As a service to authors, Karger Publishers submits the Version of Record of Open Access NIH-funded papers to PMC upon publication.

Plan S

To facilitate compliance with Coalition S/Plan S Open Access mandates, Karger publishes Plan S-funded Open Access articles with a CC BY license. Some Coalition S funders, such as Wellcome Trust, Bill & Melinda Gates Foundation and FWF, designate PMC as the repository in which to archive articles. Where PMC is the designated repository, Karger will deposit the Version of Record on the author's behalf with a CC BY license. Authors should refer to their funders' policies for details. Authors should check their funders' requirements about how to declare their funding and any associated mandates within their manuscript.

Karger publishes some journals under the Transformative Journals model, compliant with Plan S. Find more information about Transformative Journals on the [> Karger website](#).

Other Funding Sources

Karger Publishers also complies with other funders' requirements for submission to PMC. Authors should inform Karger about their grant providers during submission and include information on their grants in the Funding Sources section of their papers.

More information on funding sources can be found on the [➤ Karger website](#).

Errata and Retractions

Karger is committed to maintaining the accuracy and integrity of the scientific record.

Retractions will be issued where required in accordance with [➤ COPE guidelines](#). Errors in an article that affect the content of the article, such as figures or results, or the article metadata, such as the author list, will be corrected through the publication of an Erratum. Please note that the corrections of other errors introduced by authors and missed during the final manuscript proofing stage may be declined. Authors should [➤ contact us](#) or use the [➤ Error Report form](#) to report errors in their articles. Please state journal name, volume, issue and page numbers, the DOI number if the article has not yet been printed, as well as article title and the nature of the error.

Submission

Manuscript Submission

Manuscripts should be submitted online via the GE - Portuguese Journal of Gastroenterology submission and peer review system by the manuscript's corresponding author. The corresponding (submitting) author will automatically be the contact person for the manuscript throughout the publication process.

The corresponding (submitting) author is solely responsible for managing all communication between the journal and all co-authors and acts on behalf of all listed authors. This ensures that all correspondence reaches a unique contact and thereby secures swift communication in particular throughout the submission, peer review and production process. Articles can be published with more than one corresponding author (usually limited to three), but only one (the submitting author) can be accommodated during the submission, peer review and production process.

The corresponding (submitting) author's specific responsibilities include:

- Ensuring all the listed authors have approved the manuscript submission to the journal and agreed to all of the content including the author list
- Handling the revision(s) and re-submission(s) of the manuscript until acceptance

- Upon acceptance, ensuring that all listed authors agree to the license agreement, including the Submission Declaration
- After acceptance, manuscript proof reading and approving the final proof
- Arranging for payment of Page Charges/Article Processing Charges where required. The affiliation of the corresponding (submitting) author will be used to determine eligibility for discounted or waived charges including discounted or waived APCs under read and publish/offsetting/OA agreements
- Act as the point of contact for queries about the published article. It is their responsibility to inform all co-authors of any matters arising in relation to the published article including questions relating to publication ethics, availability of data, materials, etc.

Please note that the author names entered into the manuscript submission and peer review system should be identical to the information presented on the title page of the manuscript, including the sequence of authorship. The author names submitted should reflect the official publication names. It is the corresponding (submitting) author's responsibility to ensure the accuracy of all content in the proof, including the names of co-authors, addresses and affiliations.

Before submission, please read the Guidelines for Authors for specific requirements for manuscript preparation.

A brief cover letter outlining how your study contributes to the current scientific literature and how it fits the aims and scope of the Journal should be provided. If your submission is part of a special issue of the journal, please refer to the specific name of the special issue in your cover letter and specify who invited the submission where appropriate.

Submission Declaration

The submitting author will submit, on behalf of all authors, their manuscript for potential publication after full peer-review. All co-authors will confirm that the submitting author has authority to act on their behalf via the verification link sent out to all authors upon completion of the submission. Please refer to the Submission Declaration PDF for details.

Documents

[Submission Declaration](#) (PDF, 65.62 KB)

Parecer da Comissão de Ética do
Centro Hospitalar Universitário de São João / Faculdade de Medicina da Universidade do Porto

Título do Projeto: The prevalence of gastric neoplasia is increased in patients with chronic liver disease compared to a healthy screening population

Nome do Investigador Principal: Dr. Rui Jorge Guedes Morais

Onde decorre o Estudo: No Serviço de Gastreenterologia do CHUSJ. Apresentou declaração do Prof. Doutor Guilherme Macedo.

Objetivos do Estudo:

Avaliar de forma retrospectiva a prevalência de neoplasias gástricas em doentes com cirrose submetidos a EGD de rastreio de varizes, num país com risco intermédio a alto de cancro gástrico; avaliar se doentes com doença hepática crónica avançada têm uma prevalência de cancro gástrico superior ao da população em geral, neste caso comparando com indivíduos saudáveis; avaliar se os critérios Baveno VII podem ser adequados para o diagnóstico de varizes, mas também como triagem 'oportunistas' para neoplasia gástrica.

Conceção e Pertinência do estudo:

Estudo caso-controlo retrospectivo com doentes assintomáticos que realizaram EGD para rastreio de cancro gástrico entre janeiro de 2008 e junho de 2018, ao mesmo tempo que foi realizado rastreio de cancro colorretal com colonoscopia.

Os dados serão recolhidos na Consulta de Gastreenterologia.

É pretendido recolher a data de nascimento. Solicita-se a retirada da data de nascimento, por fragilizar a anonimização pretendida, ficando só com idade, sem que, com isso, se altere o alcance dos objetivos do estudo.

Estão definidos critérios de inclusão e as variáveis a recolher.

Benefício/risco: Não aplicável

Confidencialidade dos dados:

A cada participante será atribuído um código aleatório.

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 2022

Conclusão: Proponho um parecer favorável à realização do estudo, após o esclarecimento da questão assinalada.

Porto, 18 de novembro de 2022

O Relator da CE, Doutor Pedro Brito

