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1. RAPD Objectives and characteristics: The Revista Andaluza de Patología Digestiva is the official publication of the Andalusian Society of Digestive Pathology (SAPD), which since 2007 has been published in electronic format only, under the name RAPD Online. Its purpose is to disseminate all epidemiological, clinical, basic and sociological aspects of digestive diseases, through the contributions sent to the journal from Andalusia and from the entire scientific community. The official language for the publication of this journal is Spanish, but some contributions may be accepted in the author's original language in English, French or Italian. RAPD Online is published bimonthly, with one of the issues being specially dedicated to the Annual Meeting of the SAPD and the Editorial Board deciding to reserve one or more issues per year for the monographic development of a topic related to the speciality.

All submitted contributions must be original and not be simultaneously under review for publication in another journal. The publication of abstracts or posters is not considered duplicate publication. Manuscripts will be evaluated by expert reviewers, appointed by the editorial board, before being accepted for publication, in a process that will take less than 30 days.

2. RAPD Contents: regular numbers of RAPD Online include defined sections such as:

- Original articles on clinical or basic research.
- Thematic reviews on specific aspects of Gastroenterology.
- Consensus documents.
- Clinical cases.
- Clinical cases with videos or Videoforum.
- Images of the month.
- News and updates on gastroenterology and hepatology.
- Letters to the Editor.

Other contributions that are considered of interest by the Editorial Board, relating to different aspects of clinical practice in the recent past, biographical comments, or other contents of a cultural nature, or related to scientific activities in any territorial area, will be inserted in RAPD Online in sections designed specifically for this purpose.

3. Submission of manuscripts: The preferred way to submit manuscripts is through the SAPD website (<https://www.sapd.es>), by accessing the RAPD Online page and clicking on the "Submit an original" button located on the same access page to the journal. This will take you to the Manuscript Centre, from where you will be able to send manuscripts and all the re-

quired documentation. To use this tool you must be previously registered, access requires a username and password. If you are a member of the SAPD, you can use your usual username. If you are not a member, you can request a username for access to the Manuscript Centre using the form on the website. You can write to sulime@sulime.net or RAPDonline@sapd.es, for the solution of any problem in the submission of manuscripts.

4. Writing standard for manuscripts: monographic numbers, thematic reviews, updates and annotated articles will be commissioned by the Editorial Board, but the submission of any of these contributions at the request of an author will be considered by the RAPD Online Management and evaluated with great interest for inclusion in the journal.

All manuscripts will be subject to specific rules, depending on the type of contribution, and to common ethical and legal standards.

A) Specific standard for manuscripts writing

They refer to the recommended length and structure of each type of manuscript. As a basic unit of length for the text, in any of the contributions, a page of 30-31 lines, spaced 1.5 lines apart, with a font size of 12, with 75-80 characters without spaces per line and a total of 400-450 words per page is considered. Texts should be sent spell-checked and in editable format in all their applications (main text, figures, legends or figure captions, tables, graphs, drawings).

Originals: originals can be up to 12 pages long (5,100 words), excluding bibliographical references and captions to figures and tables. It is not advisable to insert more than 10 images, including tables and figures. Colour illustrations and videos will not represent an economic charge for the authors, but the insertion of videos, for technical reasons, will be previously agreed with the editor. However, the editing method of RAPD Online allows, in specific cases, the acceptance of longer manuscripts, or the inclusion of a greater number of images, provided that the characteristics of the material presented so require. It is not advisable to have more than 9 authors, except in the case of collaborative works. In these originals, the first nine participants will be listed at the head of the paper and the rest of the participants will be listed at the end of the first page of the manuscript.

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- Main body of the manuscript, containing:

1° Structured abstract in Spanish (optional also in English) and 3-5 keywords. The abstract will have a maximum length of 250 words and should be structured as follows:

- a) Introduction and objectives
- b) Material and methods
- c) Results
- d) Conclusions

2° List of abbreviations used in the text.

3° Text: it will include the following sections:

- a) Introduction
- b) Material and methods
- c) Results

- d) Discussion
- e) Conclusions; each of them appropriately headed.

4° Bibliography: according to the specifications established in the group of common standards (See common standards and other supporting documents).

5° Acknowledgements.

6° Figure captions.

7° Tables and figures in text.

Thematic Reviews: texts on Thematic Reviews can be up to 15 pages long (6,375 words), excluding bibliographical references and captions to figures and tables, and chapters corresponding to Update series up to 20 pages (8,500 words). In both cases the number of inserted images should not exceed 15, including tables and figures. However, the RAPD Online editing method allows, in specific cases, for manuscripts of greater length, or the inclusion of a greater number of images, provided that the characteristics of the material presented so require. Illustrations in colour will not be charged to the authors. Exceptionally, the inclusion of videos will be accepted. It is not advisable to include more than 4 authors per chapter.

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- 3° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).
- 4° Acknowledgements.
- 5° Figure captions
- 6° Tables and Figures in the text.

Consensus documents: texts on Consensus documents are not limited in length in terms of text or images and tables. Exceptionally, the inclusion of videos is allowed. It is not advisable to have more than 10 authors per chapter.

Through the Manuscript Centre, and for the submission of Reviews and Updates, the following information will be required:

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- 5° Declaration on the existence or non-existence of a source of funding for the work, or conflicts of interest.

- Main body of the manuscript, containing:

- 1° Structured abstract in Spanish and English. 3-5 key words. The abstract will have a maximum length of 350 words, emphasising the

most important aspects of the manuscript.

2° Text: Structured according to the criteria of the author(s), for a better understanding of the topic developed.

3° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).

4° Acknowledgements

5° Figure captions.

6° Tables and Figures in the text.

Clinical Cases: the manuscripts included in this section will include 1-5 clinical cases, which due to their infrequent or unusual clinical behaviour, or because they provide some diagnostic or therapeutic novelty, deserve to be reported.

The length of the texts in the Clinical Cases section should not exceed 5 pages (2,125 words), excluding bibliographical references and captions to figures and tables, and the number of inserted images should not exceed 5, including tables and figures. However, the RAPD Online editing method allows, in specific cases, the acceptance of longer manuscripts, or the inclusion of a greater number of images, provided that the characteristics of the material presented so require. Colour illustrations and videos will not represent a financial charge for authors, but the insertion of videos, for technical reasons, will be previously agreed with the editor. No more than 5 authors will be admitted, except in specific and reasoned cases.

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- 1° Structured abstract in Spanish and English. 3-5 key words. The abstract will have a maximum length of 250 words.
- 2° Introduction. To present the clinical problem reported.
- 3° Description of the clinical case.
- 4° Discussion. To highlight the peculiarities of the case and its consequences.
- 5° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).
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- 7° Figure captions.
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Clinical Cases with Videos or Videoforum: the manuscripts included in this section will include 1-5 clinical cases, which due to their infrequent or unusual clinical behaviour, or because they provide some diagnostic or therapeutic novelty, deserve to be communicated.

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Videos should be submitted in AVI, MPEG, MP4 OR MOV format, and at a recommended high quality resolution (720p or 1080p). They must not contain personal data of the patients. It is recommended that they be edited to minimise editing time, which should not exceed 10 minutes. If the video includes sound, it must be processed in MP3 format. If the videos to be included are in other formats, please contact the publisher

to verify their validity. They should not exceed 2GB. Through the Manuscript Centre, and for the submission of Clinical Cases - Videoforum, the following information will be required:

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- Main body of the manuscript, containing:

- 1° Structured abstract in Spanish and English. 3-5 key words. The abstract will have a maximum length of 250 words.
- 2° Introduction. To present the clinical problem reported. 3° Description of the clinical case.
- 4° Discussion. To highlight the peculiarities of the case and its consequences.
- 5° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).
- 6° Acknowledgements. 7° Figure captions.
- 8° Tables and figures in text.
- 9° Videos.

Link tutorial videos: <https://www.sapd.es/videoteca/varios/tutoriales/>

Images of the month: the manuscripts included in this section can take two formats, depending on the authors' preference.

- Format A. Images with educational value: these shall include images of any kind, clinical, radiological, endoscopic, anatomopathological, macro and microscopic, which contribute to postgraduate training and therefore deserve to be shown because of their peculiarity, or because they represent a characteristic example.
- Format B. Key images for a diagnosis: These will include images of any kind, clinical, radiological, endoscopic, anatomopathological, macro and microscopic, together with a summarised clinical history, which will provide the possible final diagnostic resolution. This will be presented in a separate section in the same issue of the journal.

The length of the texts in the Images of the Month section must not exceed 1 page (425 words) in the clinical approach to the image presented and 2 pages (850 words), excluding bibliographical references and captions to figures and tables, in the commentary on the image (Format A) or in the diagnostic resolution of the case (Format B). However, the RAPD Online editing method allows, in specific cases, the acceptance of longer manuscripts, or the inclusion of a greater number of images, provided that the characteristics of the material presented so require. Colour illustrations and videos will not represent a financial charge for authors, but the insertion of videos, for technical reasons, will be previously agreed with the editor. No more than 3 authors will be accepted, except in specific and reasoned cases.

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-Main body of the manuscript, containing:

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- 2° Description of the image.
- 3° Comments on the image.

4° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).

5° Figure captions.

New developments and updates in gastroenterology and hepatology: this section will be devoted to commenting on the scientific and medical developments that have occurred in recent years in the speciality of Gastroenterology and Hepatology.

This section will systematically and periodically analyse all facets of the speciality.

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- 4° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents). If two or more originals have been chosen for the analysis, it is advisable to divide the section into sections at the authors' discretion.
- 5° Figure captions.
- 6° Tables and Figures in text.

Letters to the Editor: this section will be dedicated to comments on any manuscript published in RAPD Online. This section may also include comments of a more general nature, establishing the authors' own hypotheses and suggestions, within the scientific field of Gastroenterology. The length of the texts in this section of Letters to the Editor should not exceed 2 pages (850 words), including bibliographical references. Two figures or tables may be included and the number of authors should not exceed four.

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- 3° Centre(s) of origin (department, institution, city and country).
- 4° Full postal address of the responsible author, to whom correspondence should be addressed, including telephone, fax and e-mail address.
- 5° Declaration on the existence or non-existence of a source of funding for the work, or conflicts of interest.

- Basic body of the manuscript, containing:

1° Text of the manuscript.

2° Bibliography: According to the specifications set out in the common standards group (See common standards and other supporting documents).

B) Common standards and other supporting documents

This refers to the set of mandatory standards, both for uniformity in the presentation of manuscripts and for compliance with current legal regulations. In general, the style of manuscripts should follow the guidelines set out in the Vancouver Agreement of the International Committee of Medical Journal Editors. (<http://www.ICMJE.org>).

Units, generic names and abbreviations:

- Units. Biochemical and haematological parameters shall be expressed in International Units (SI), except haemoglobin which shall be expressed in g/dL. Length, height and weight measurements shall be expressed in decimal metric units and temperatures in degrees Celsius. Blood pressure shall be measured in millimetres of mercury.

There is an aid for the conversion of non-international (non-SI) units into international (SI) units. (<http://www.techexpo.com/techdata/techcntr.html>).

- Generic names. The generic names of medicinal products, clinical instruments and tools and software shall be used. When a brand name is the subject of research, the brand name and the name of the manufacturer, city and country shall be included in parentheses the first time the generic name is mentioned in the Methods section.

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Bibliographical references: bibliographical references should be presented in the order in which they appear in the manuscript, with a sequential number, which will appear in the appropriate place in the text, in brackets. This numbering will be maintained and will serve to order the list of all references at the end of the manuscript, as normal text and never as a footnote. Personal communications and unpublished data will not be included in the final list of bibliographical references, although they will be mentioned in the appropriate place in the text, in brackets, as appropriate, i.e. personal communication or unpublished data. When the bibliographic citation includes more than 6 authors, the first 6 authors should be cited, followed by the abbreviation et al.

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- Article already published in print and online journals Internet:

The authors (surname and initial of the first name, comma separation between authors), the full name of the manuscript, the abbreviation of the journal, the year of publication and after a semicolon the volume of the journal and after a colon the complete numbers of the first and last page of the paper.

Kandulsky A, Selgras M, Malferteiner P. Helicobacter pylori infection: A Clinical Overview. Dig Liver Dis 2008; 40:619-626.

Alvarez F, Berg PA, Bianchi FB, Bianchi L, Burroughs AK, Cancado EL, et al. International Autoimmune Hepatitis Group Report: review of criteria for diagnosis of autoimmune hepatitis. J Hepatol 1999; 31:929-938.

- Admitted article, published only on the Internet, but not yet included in a regular number of the journal: the authors, the full name of the manuscript, the abbreviation of the journal, the year and month since the article is available on the Internet and DOI will be noted. The original paper to which reference is made usually details how to cite the manuscript.

Stamatakis M, Sargedi C, Stefanaki C, Safi oleas C, Matthaopoulou I, Safi oleas M. Anthelmintic treatment: An adjuvant therapeutic strategy against Echinococcus granulosus. Parasitol Int (2009), doi:10.1016/j.parint.2009.01.002

Inadomi JM, Somsouk M, Madanick RD, Thomas JP, Shaheen NJ. A cost-utility analysis of ablative therapy for Barrett's esophagus. Gastroenterology (2009), doi: 10.1053/j.gastro.2009.02.062.

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Gurbulak B, Kabul E, Dural C, Citlak G, Yanar H, Gulluoglu M, et al. Heterotopic pancreas as a leading point for small-bowel intussusception in a pregnant woman. JOP (Online) 2007; 8:584-587.

Fishman DS, Tarnasky PR, Patel SN, Rajman I. Management of pancreaticobiliary disease using a new intra-ductal endoscope: The Texas experience. World J Gastroenterol 2009; 15:1353-1358. Available from: URL: <http://www.wjnet.com/1007-9327/15/1353.asp>. DOI: <http://dx.doi.org/10.3748/wjg.15.1353>

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Rossi CP, Hanauer SB, Tomasevic R, Hunter JO, Shafran I, Graffner H. Interferon beta-1a for the maintenance of remission in patients with Crohn's disease: results of a phase II dose-finding study. BMC Gastroenterology 2009, 9:22doi:10.1186/1471-230X-9-22.

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Klin M, Kaplowitz N. Differential susceptibility of hepatocytostoma TNF-induced apoptosis vs necrosis [Abstract]. Hepatology 1998; 28(Suppl):310A.

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Takada T. Medical Guideline of Acute Cholangitis and Cholecystitis. Tokyo: Igaku Tosho Shuppan Co; 2005.

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Siewert JR. Introduction. In: Giuli R, Siewert JR, Couturier D, Scarpignato C, eds. OESO Barrett's Esophagus. 250 Questions. Paris: Hors Collection, 2003; 1-3.

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U.S. positions on selected issues at the third negotiating session of the Framework Convention on Tobacco Control. Washington, D.C.: Committee on Government Reform, 2002. (Accessed March 4, 2002, at: http://www.house.gov/reform/min/inves_tobacco/index_accord.htm.)

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COMPLICATIONS IN THE FIRST MONTH AFTER AN ENDOSCOPIC PROCEDURE IN A TERTIARY CARE HOSPITAL

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Keywords: endoscopy, adverse effects.

Introduction and objectives

Endoscopic procedures are a fundamental and invaluable tool in the diagnostic and therapeutic repertoire of every gastroenterologist. This has led to an exponential increase in both the volume and technical difficulty of these tests. However, the prerequisite of quality and safety remains paramount, which has been reflected in the consensus documents of the various societies on quality indicators for gastrointestinal endoscopy¹⁻³.

The global incidence of complications in endoscopy ranges between 0.25-3%⁴, although the real rate is uncertain. Most of the published data correspond to intraprocedural adverse events or to deferred adverse events of a digestive nature^{5,6}; the difficulty of patient follow-up limits the knowledge of complications that occur in a deferred manner⁷. Furthermore, it is important to differentiate the rate of complications in specific groups such as anticoagulated/anti-aggregation patients^{8,9} or therapeutic procedures.

The aim of the present study is to determine the percentage of admissions secondary to complications within the first 30 days post endoscopic procedure, both diagnostic and therapeutic, in outpatients in a tertiary care hospital.

Material and methods

Retrospective descriptive observational study including all outpatients undergoing endoscopic digestive examinations (upper endoscopy, lower endoscopy, echoendoscopy, video capsule endoscopy and enteroscopy) between 1st October 2019 and 30th September 2022. Demographic, clinical and endoscopic procedure related data were collected from each patient. IBM-SPSSv.27.0 statistical software was used for statistical analysis.

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Results

35,327 digestive examinations were performed on 26,859 patients in the indicated period. 1,216 patients were admitted within 30 days (4.5%). 790 (65%) were admitted on a scheduled basis, 317 (26%) required admission for reasons unrelated to the examination and 112 (9.2%) due to a complication of the procedure (Figure 1).

Of the patients with a complication, 70 (62.5%) were male, with a median age of 69 years (SD 12.6). The most frequent cardiovascular factor (CVRF) was hypertension (80, 71.4%), followed by dyslipidaemia (57, 50.9%). More than half of the patients (67, 60%) were taking anticoagulant or antiplatelet medication. They had a high risk of thrombosis according to the CHADS2-VASc index (3+/-2) and a moderate risk of bleeding according to the HAS-BLED scale (2+/-1.5) (Table 1).

Characteristics of the patients	N= 112
Sex M/F, n (%)	70/42 (62.5%/37.5%)
Age, years (SD)	69 (±12.6)
Cardiovascular risk factors (CVRF)	
Hypertension, n(%)	80 (71.4%),
Diabetes mellitus, n(%)	34 (30.4%)
Dyslipaemia, n(%)	57 (50.9%)
None	15 (13.4%)
Usual treatment:	
Antiplatelet agents, n(%)	25 (22.32%)
Anticoagulants, n(%)	34 (30.35%)
Bleeding/thromboembolic risk	
CHADS2-VASc Score, median (+/-DE)	3 (+/-2)
HAS-BLED Score, median (+/-DE)	2 (+/-1.5)

Table 1. Baseline characteristics of patients admitted for a procedural complication within 30 days of the procedure.

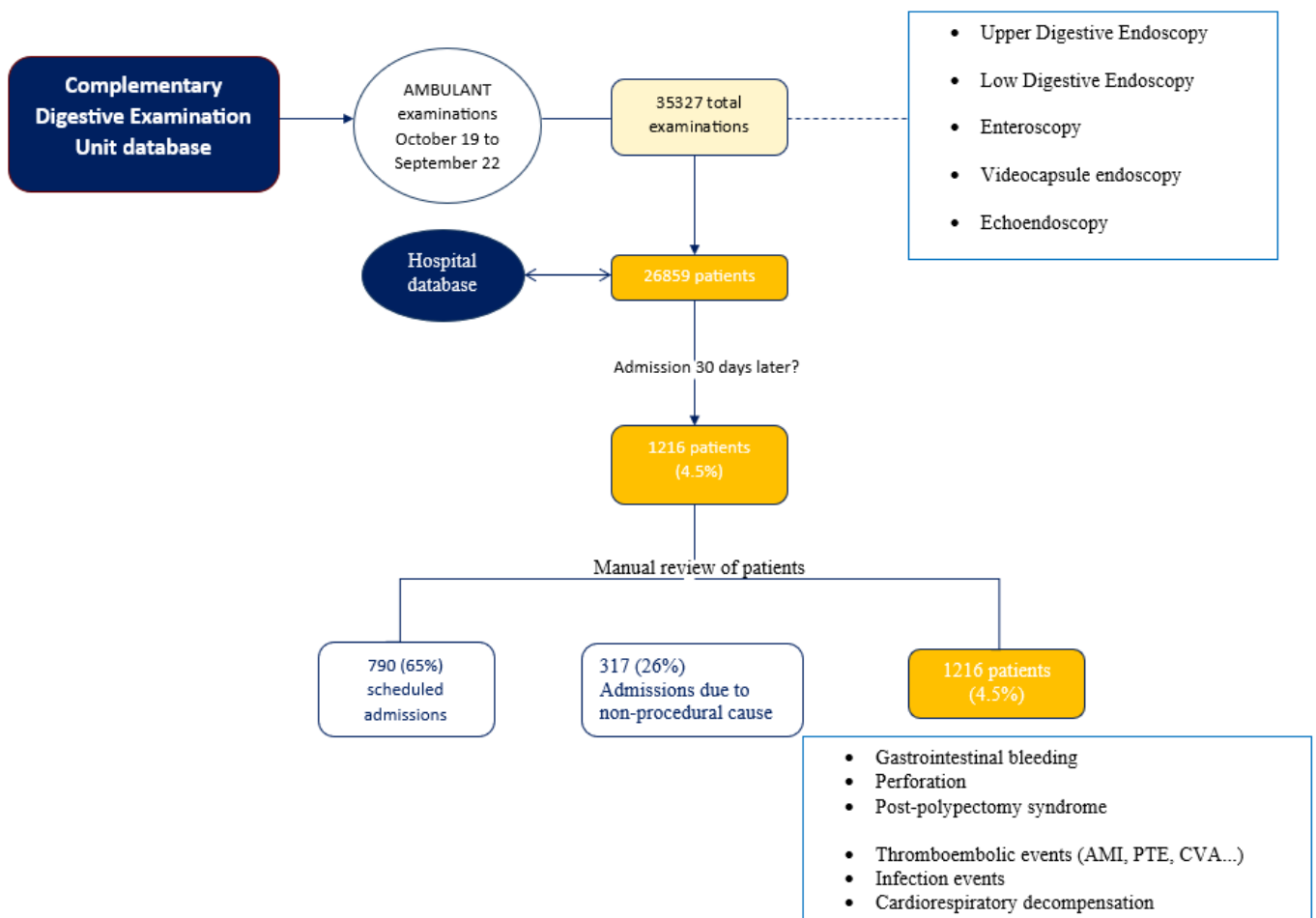


Figure 1. Flow chart for the selection of patients included in the study.

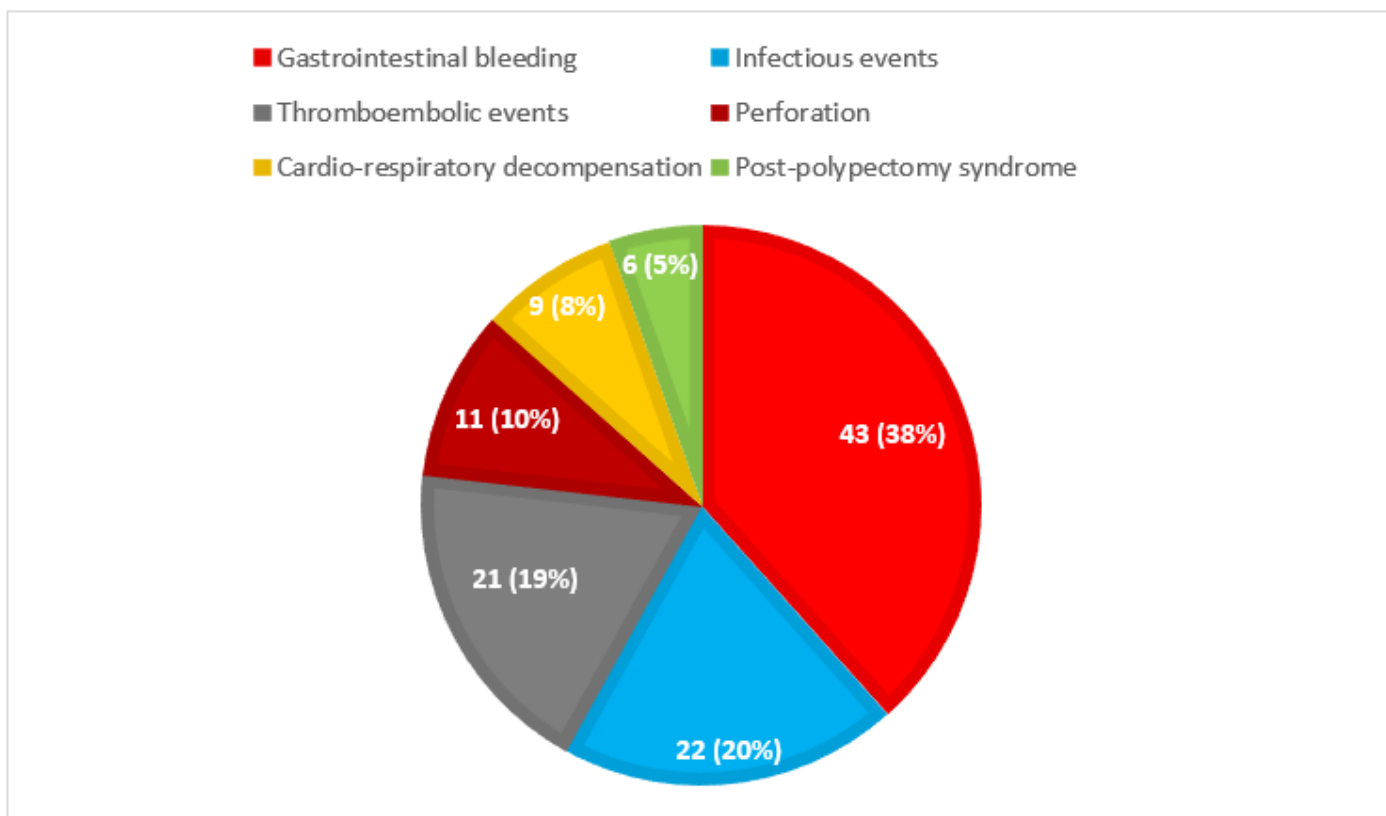


Figure 2. Complications requiring admission within 30 days post-procedure.

Colonoscopy was the most frequently performed digestive examination (83, 74%), followed by upper gastrointestinal endoscopy (22, 20%). Furthermore, most of the procedures were diagnostic (77, 69%), i.e. no or only low-complexity treatment was performed.

The most frequent complication was gastrointestinal bleeding (43, 38%) followed by infectious events (22, 20%), thromboembolic events (21, 19%), perforation (11, 10%), cardio-respiratory decompensation (9, 8%) and post-polypectomy syndrome (6, 5%) (Figure 2).

13 patients (0.036%) died during admission, with the development of a thromboembolic event being the most frequent cause of mortality.

Conclusions

Gastrointestinal endoscopy is a safe technique, with a low number of complications, most of them mild¹⁰. However, identifying which risk factors are associated with adverse events would allow the establishment of prevention protocols for their complete reduction¹¹. In our cohort, at least half of the admissions secondary to adverse events were for extra-

digestive complications. Thromboembolic events were the most frequent cause of death, which makes it necessary to be strict in the assessment of thromboembolic risk in all patients, as well as in the management of antiplatelet/anticoagulant medication.

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UPDATE ON THE MANAGEMENT OF PT1 COLORECTAL CANCER

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Abstract

With the implementation of CRC screening programs, the incidence of pT1 CRC has increased significantly: up to 40% of colon tumors detected in screening colonoscopies are pT1^{1,2}. Traditionally, the treatment of choice for CRC is surgery with lymph node resection, but pT1 CRC has a very good prognosis with 5-year disease-free survival rates greater than 90%³ and thanks to advanced endoscopy, it can be treated locally with a minimally invasive approach in many cases⁴⁻⁶. After resection of the lesion, an adequate histological description of the specimen will guide us to make the final decision in the management of pT1 CRC: whether endoscopic resection is considered curative or whether additional surgery will be required to prevent local recurrence, lymphatic dissemination and/or distant metastasis⁷. The decision to proceed with additional surgery or surveillance depends primarily on the estimated oncologic benefit of surgery, operative risk, and patient preferences. It must be taken into account that colorectal surgery carries a significant risk of morbidity and mortality for elderly patients⁸.

Currently we base our decisions on histological criteria, but the natural history of pT1 CRC resected by endoscopy is really unknown and there are not enough quality prospective studies with results after long-term follow-up of pT1 CRC non-surgically managed, especially in the case of high-risk pT1, which would explain the great variability in the management of these patients⁹.

In this thematic review we have analyzed the current state of management of pT1 CRC in the field of endoscopic diagnosis and treatment, histological evaluation and its prognostic implications. We have also reviewed the most recent evidence regarding surveillance: how to carry out adequate follow-up and determine the optimal frequency and the most appropriate surveillance method after local resection of pT1 CRC.

Keywords: colorectal cancer, pT1 CRC, colonoscopy, polyp, endoscopic resection, colorectal surgery, high risk histological factors.

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Update on the management of pT1 colorectal cancer
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Current management of pT1 CRC. Histological risk criteria.

Colorectal carcinoma (CRC) pT1 is the earliest form of CRC. It is defined as a tumour where neoplastic cells growing within a polyp invade the submucosa through the muscularis mucosae, but do not overgrow it. Endoscopic resection of a pT1 CRC is only oncologically safe if it is assumed that the malignant cells have not metastasised to locoregional nodes. Otherwise, surgical resection is considered necessary with the intention of preventing distant metastasis. Since in a local resection the lymph nodes are not removed and therefore cannot be analysed, a prediction of the risk of lymphatic metastasis (LM) is necessary and is based on the anatomical pathology report, where the presence or absence of the following histological criteria should be described:

- **Degree of differentiation:** this refers to the resemblance of the tumour cells to normal colonic epithelium and is defined according to the glandular structure content of the tumour¹⁰. Tumours with more than 50% of glands are well or moderately differentiated (G1 and G2), considered low grade and with a favourable prognosis. Those with less than 50% glandular formations are poorly differentiated (G3), this being an independent risk factor for poor prognosis^{11,12}.
- **Lymphovascular invasion:** the presence of tumour cells within the blood vessels of the submucosa, and especially the lymphatic vessels, is a known risk factor and is in fact the histological criterion that most strongly correlates with the presence of lymph node metastasis¹²⁻¹⁴.
- **Tumour budding (BT):** indicates the presence of a tumour cell or groups of up to four tumour cells aggregated at the invasive tumour front. There can be three grades of BT: low, intermediate and high. High grade BT has been shown to be a histological risk factor for ML in pT1 CRC^{15,16}, although it is only described in less than half of the published studies⁹.
- **Resection margins:** most Western guidelines recommend a margin of safety >1 mm to consider a curative resection (R0)^{17,18}, based primarily on the results of one study that observed residual invasive disease in 16% when the polypectomy margin was <1 mm, in 21% with an indeterminate margin

(Rx resection) and in 0% when the margin was ≥ 1 mm ($p=0.009$), but this was not a risk factor for ML¹⁹.

- **Depth of submucosal invasion:** the degree of submucosal invasion is categorised differently depending on the morphology of the polyp, according to the Haggitt and Kikuchi classifications (**Figure 1**):

- **Haggitt classification**²⁰, used for pedunculated polyps, classified into four levels according to the level of submucosal invasion: Haggitt 1: submucosal invasion at the head of the polyp; Haggitt 2: invasion up to the junction of the head with the stalk; Haggitt 3: invasion up to the stalk of the polyp; and Haggitt 4: invasion into the deep submucosa, below the stalk into the underlying colonic wall, which is considered a risk factor for lymphatic metastasis.

- **Kikuchi classification**²¹, for non-pedunculated lesions: the submucosa is divided into three levels according to the degree of submucosal infiltration: SM-1 (<1,000 μm), SM-2 and SM-3 (>1,000 μm). The Kikuchi level can only be reported when *muscularis propria* is included in the resection specimen, which is not the case in many cases.

A polyp has superficial submucosal invasion if the invasion is <1,000 μm (Kikuchi SM-1) or, in case of pedunculated polyps, Haggitt level 1-2-3. Deep submucosal invasion of >1,000 μm (Haggitt 4 or SM 2-3) has been associated with a higher risk of lymph node invasion, and therefore worse prognosis. This relationship is based on results from historical surgical series²².

Surgery or follow-up? The great dilemma

The final decision on whether a patient should be referred for further surgery after local resection of a pT1 CRC or follow-up depends mainly on the histological criteria described above. As recommended in clinical practice guidelines²³⁻²⁶, a pT1 CRC is considered high-risk, and therefore an indication for salvage surgery, when one or more of the histological risk criteria are present. The surgical technique varies depending on the location of the tumour, but always includes resection of the corresponding meso, with the vascular pedicle and the lymphatic drainage system that includes the locoregional lymph nodes of the resected segment.

The scientific evidence supporting this recommendation to date is based on the results of previous studies showing that, in the absence of these histological criteria, the risk of residual local neoplasia is 0.7%, the risk of lymphatic metastasis is less

than 1%, and the risk of distant metastasis is around 0.7%. In contrast, in the presence of any of these, the risk was 4-11%, 10-16% and 1.3-6%, respectively^{24,27}. These estimates do not take into account the different relative risk that histological criteria show in the series, nor the possible effect of combining these criteria with each other.

"Sub-optimal" histological criteria:

Using current histological criteria, more than 80% of patients with pT1 CRC are classified as high risk³¹. However, after histological analysis of surgical resection specimens, only 2-10.5% have lymph node invasion and less than 20% have residual lesion^{29,32-37}. Therefore, there seems to be a risk of overtreatment by relying exclusively on histological criteria for our decision making, as we are referring many pT1 CRC to surgical rescue that could have been optimally treated endoscopically. On the other hand, there are a number of limitations that may hinder decision-making, such as the lack of information in the anatomopathological description or inter-observer variability between pathologists. Thus, in the work of Lugli et al³⁸, 67 histological reports after local resection of pT1 CRC were reviewed, showing that histological grade was only reported in 31% of cases, tumour budding was not reported in 97% and lymphovascular invasion was not described in 81%. On the other hand, regarding inter-observer variability, Rampioni et al³⁹ retrospectively analysed 82 endoscopically resected pT1 CRCs: in 9.7% of the cases there was a change in the classification of the risk of the lesions after review by a second pathologist, 7.3% were reclassified as high risk and 2.4% as low risk after a 2nd assessment.

There is a general consensus in clinical practice guidelines to consider the presence of lymphovascular invasion, the degree of histological differentiation and tumour budding as independent risk factors for lymphatic spread. However,

recent evidence questions the other criteria: deep submucosal invasion and resection margin:

- **Deep submucosal invasion:** in a retrospective population-based cohort study¹² that prospectively collected data from 1,439 patients with T1 CRC resected locally by surgery from two populations (Sweden, between the years 2009-2017 and Denmark, between 2016-2018) it was observed, in contrast to that reported in previous studies, that differences in the risk of LM in patients with superficial submucosal invasion (SM-1) versus deep submucosal invasion (SM-3) were very limited, concluding that deep submucosal invasion is not an independent risk factor for lymphatic invasion. In 2022, the Dutch group led by Evelyn Decker, published a meta-analysis⁴⁰ that included 67 studies with 21,238 patients where it was also shown that deep submucosal invasion, when appearing as the only risk factor, has an absolute risk of LM of only 2.6%, and in multivariable analysis was not a significant predictor of LM (odds ratio [OR] 1.73; 95% confidence interval [CI] 0.96-3.12), compared to the presence of the other factors that did show significant association: poorly differentiated histology (OR 2.14; 95% CI 1.39-3.28), lymphovascular invasion (OR 3.16, 95% CI 1.88-5.33), high-grade tumour budding (OR 2.83, 95% CI 2.06-3.88).

The question we should be asking is whether a 2.6% absolute risk of lymphatic metastasis is sufficient to refer a patient for surgery. We should bear in mind that oncological surgery does not prevent mortality and recurrence 100%: in the retrospective study by Tamaru et al⁴¹, a recurrence rate of 3.8% was observed, and CRC-associated mortality was 1.2% in cases of pT1 CRC treated with primary surgery alone. Surgical treatment for non-malignant colorectal polyps has been associated with 1% mortality and high morbidity rates, especially in the elderly population, in whom endoscopic treatment could ensure a better quality of life compared to surgery⁴².

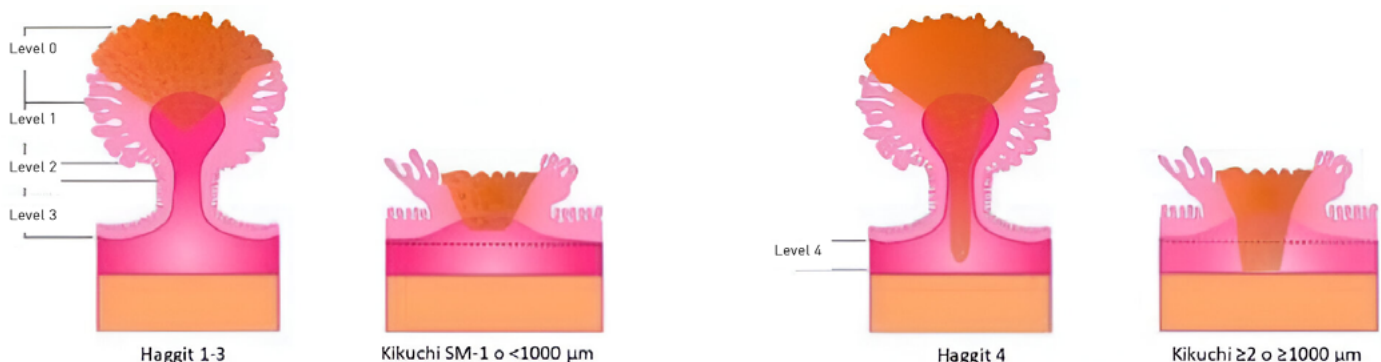


Figure 1. Haggitt and Kikuchi Classification.

- **Deep resection margin <1 mm:** the most accepted definition of an affected resection margin or incomplete resection (R1) is one in which the distance to diathermy-induced histological change is less than 1 mm⁴³, based on results from several studies⁴⁴⁻⁴⁷ showing an increase in residual disease (7-17%). But recent evidence is beginning to question this: A retrospective study from the Dutch pT1 CRC group⁴⁸ showed that a free resection margin <1 mm (between 0.1 and 1 mm), in the absence of other risk factors (high-grade budding, lymphovascular invasion and poorly differentiated histology) has a risk of residual neoplasia of only 2.9% (95% CI 1.0-6.7), with no significant difference compared to lesions with margins >1 mm. Furthermore, analysing lesions with resection margins <1 mm and with residual disease, the presence of tumour budding was also demonstrated in 80% of them.

The European Society of Gastrointestinal Endoscopy (ESGE) clinical practice guideline on endoscopic submucosal dissection states that there is no evidence to support the concept that a tumour-free margin of less than 1 mm should be considered a risk factor and, therefore, an indication for surgery, recommending the concept of "preferably >1 mm" to define R0 resection, taking into account that if it is <1 mm but free of tumour and without other risk factors, "close follow-up could be considered"⁴⁹.

On the other hand, it seems that the risk of residual disease is more related to incomplete resection than to the status of the margins. Thus, studies that had reported high rates of residual disease (>15%) after endoscopic resection of pT1 CRC had included incomplete endoscopic resection techniques in >10% of them. In contrast, studies with low rates of residual disease mostly excluded incomplete resections⁴³. In addition, fragmented endoscopic resection, which is often performed to resect polyps >20 mm in size, is often reported as an indeterminate resection margin (Rx resection) even though it is a complete resection, which may result in a referral for surgery as it is erroneously considered an incomplete resection⁴³.

Does surgery really improve the prognosis of pT1 CRC?

pT1 CRC generally has an excellent prognosis, with 5-year overall survival rates of 94%³⁵, so surgery may have a potential beneficial effect only in a small group of patients. We therefore wonder what is the best therapeutic strategy in patients with pT1 CRC, whether the treatment modality (endoscopic or surgical) influences prognosis. In the meta-analysis by Dang et al³⁰, recurrence and mortality related to pT1 CRC were analysed: 71 studies with 5,167 patients with pT1 CRC treated with endoscopy alone were included and an overall recurrence

risk after endoscopic resection of 3.3% after 72 months of follow-up, with the cumulative incidence of recurrence in patients with low-risk pT1 CRC being 0.7% (0.4-1.2%) and 7% (4.9-9.9%) for patients with high-risk pT1 CRC. These figures are similar to those reported for patients with surgically treated pT1 CRC: in the meta-analysis by Yeh et al.³⁵ there was no significant difference in overall survival rates, recurrence-free survival or CRC-specific survival between patients with high-risk pT1 CRC treated with endoscopy versus those treated with surgery alone. Therefore, it appears that neither endoscopic treatment nor surgery will change the unfavourable prognosis in high-risk pT1 CRC. One possible reason for this is that the likelihood of an unfavourable prognosis may be more related to the aggressiveness of the tumour itself than to the treatment performed⁴³. Prospective long-term studies are needed to provide more data and to help us make decisions about follow-up in patients with high-risk pT1 CRC treated endoscopically.

Another important aspect to consider in our decision-making is the risk of adverse events (AE) of the treatment offered to patients with pT1 CRC. It is estimated, based on data from European screening programmes, that the percentage of pT1 CRC treated with surgery is currently between 38-55%^{36,50,51}). An otherwise healthy patient who has had a potentially curable malignant polyp resected endoscopically will be highly likely to be referred for surgery, with the risk of AE that this entails, as well as the added costs.

Table 1 summarises the main AE's of endoscopic treatment, with an overall percentage of 5.5%, which is much lower than the 20% morbidity related to surgical treatment, and which is similar to that observed in more advanced stage CRC surgery^{35,51,52-54}.

	Adverse events	Mortality
Endoscopic treatment	5.5% Bleeding 3.78% Perforation: 1.2% Postpolypectomy 0.6%	0-1.4%
Surgery	20% Severe AEs 8% Anastomotic leak 4%	3.2%

Table 1. Morbidity and mortality of endoscopic treatment vs surgical treatment of pT1 CRC.

The meta-analysis by Yeh et al. also reported a much lower AE rate among patients treated with endoscopic resection (2.3%) compared to those treated with primary surgery (10.9%), with the differences being statistically significant (p<0.001)³⁵. With respect to mortality, differences are also evident: in the study

by Belderbos *et al.*⁵³, mortality in patients treated with surgery was 3.2%, which contrasts with 1.4% in the group treated with endoscopy, taking into account that in many studies mortality in these is around 0%^{32,53,54}.

Endoscopic evaluation

Endoscopic evaluation of any colorectal lesion is considered a fundamental element in deciding the most appropriate resection technique⁵⁵. Optical diagnosis allows us to estimate the probability of submucosal invasion of a colorectal lesion, as well as the depth of this invasion. If pT1 CRC is suspected during colonoscopy, en bloc resection should be performed, which will then allow adequate histological evaluation and optimal staging. In the endoscopic evaluation of a colorectal polyp, we must take into consideration the following characteristics that may suggest the suspicion of occult carcinoma:

- **Size:** the risk of invasive cancer increases progressively the larger the size of the lesion. According to a meta-analysis of more than 5,000 adenomas, this risk is 9.2% for lesions between 20 and 30 mm, and increases to 16.5% for lesions larger than 30 mm in diameter⁵⁶.
- **Location:** several studies have shown that location in the left colon, and especially in the sigma and rectum, is an independent risk factor for developing pT1^{57,58}.
- **Morphology:** the Paris⁵⁹ and Kudo classifications of lateral spreading tumours (LST)⁶⁰ are very useful for estimating the risk of malignancy of a lesion: homogeneous granular LSTs have a very low risk of only 0.5%. LSTs with mixed granular surface (with dominant nodule or non-granular areas) the risk of malignancy increases to 10.5%⁵⁶ (Figure 2). Non-granular LSTs (nongranular LST-NG) have a higher risk of deep submucosal invasion and, if they have a pseudodepressed area, the risk increases to 31.6%; 95% CI 19.8%-43.4%⁵⁶, (Figure 3).
- **Macroscopic features:** as a colorectal polyp becomes more dysplastic, angiogenesis increases and changes occur in the microvasculature that we can identify and thus estimate a possible deep submucosal invasion: presence of surface erythema or spontaneous bleeding⁶¹, erosions, ulcerations or exudate on the surface of the polyp^{62,63}. Other signs of malignancy may include retraction/convergence



Figure 2. Granular LSTs and risk of deep submucosal invasion

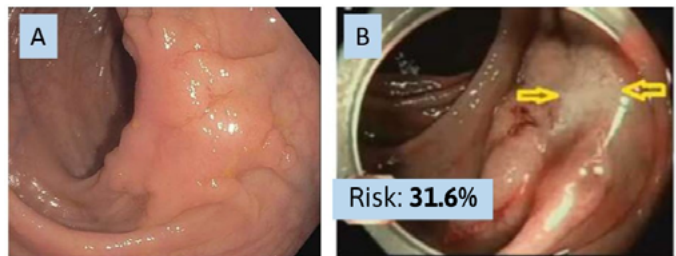


Figure 3. Non-granular lateral spreading lesions (LST-NG). A): Flat-elevated LST-NG (0-IIa). B): LST-NG with a pseudo-depressed area: the risk of deep invasion increases up to 31.6%⁵⁶.

of folds, the presence of so-called "chicken skin" and the "no-lifting sign", which can be observed when the lesion does not rise after submucosal injection, although these alone lack specificity^{64,65}.

- **Glandular and vascular pattern:** unlike the other features, which can be assessed by white light endoscopy, assessment of the distribution pattern of glandular crypts and vessels on the surface of the lesion requires the use of virtual chromoendoscopy. The NICE classification allows differentiation of three types of lesions: serrated or hyperplastic (NICE 1), adenomatous (NICE 2) and/or deep invasive lesions (NICE 3)^{66,67}, which allows the endoscopist to decide whether a lesion is a candidate for endoscopic treatment (NICE 1 or 2) or would require surgical oncological resection (NICE 3), with good confidence in up to 87.5% of lesions⁶⁸; but for the rest, other advanced imaging techniques would be needed, such as optical magnification, with which we can apply other classifications: JNET, Kudo or Sano⁶⁹⁻⁷¹: the presence of an irregular vascular and crypt pattern (JNET 2B, Kudo Vi, Sano IIIA) suggests superficial submucosal invasion, which could be treated by endoscopic resection (en bloc). When this pattern is completely lost (JNET 3, Kudo Vn, Sano IIIB), it is most likely an infiltrative lesion⁶⁹⁻⁷¹ (Table 2).

Despite advances in optical diagnosis, evidence shows that in actual practice around 42% of endoscopically resected pT1 CRC are unexpected histological diagnoses⁷².

	Classification	Benign/non-invasive	High grade dysplasia/ superficial pT1	≥ Deep invasive/CCR pT1
Crypt and surface pattern	Kudo	Kudo I-IV	Kudo Vi	Kudo Vn
(Micro)vascular pattern	Sano	Sano I-II	Sano IIIa	Sano IIIb
Crypt/surface and (micro)vascular pattern	JNET	JNET 1-2a	JNET 2b	JNET 3
	NICE	NICE 1 and 2	NICE 2	NICE 3

Table 2. Advanced imaging classification systems and the different subtypes/categories associated with the presence of pT1 CRC with deep or superficial invasion.

In scans performed by expert endoscopists, this rate drops to around 10-15%⁶⁵, and in some studies performed in non-expert endoscopists, the percentage of unidentified T1 CRC can be as high as 80%. Inadequate assessment of the risk of invasion of a lesion may have negative repercussions for the patient, such as fragmented resection of a malignant lesion and subsequent inability for adequate histological examination, which may lead to surgery and loss of the opportunity for local, organ-sparing, curative resection⁷³. Another consequence of a failed endoscopic assessment may be the need for repeat colonoscopy to tattoo the resection site of a malignant lesion or the erroneous indication of surgery for benign lesions.

The case of pT1 in the rectum

Lesions located in the rectum present a higher risk of occult submucosal invasion than in the rest of the colon. This risk is especially significant in the case of non-granular or mixed surface LSTs with a sessile component⁵⁸. For large mixed granular LSTs larger than 4 cm, the risk of occult submucosal invasion is three times higher in the rectum than in the rest of the colon⁵⁷. Furthermore, rectal location appears to confer a higher risk of lymphatic metastasis, and is a risk factor for recurrence after local resection, the more distal the lesion is located, the higher the risk^{74,75}.

On the other hand, rectal surgery has a greater impact on patients, given the greater likelihood of complications and sequelae that negatively affect the patient's quality of life, such as the possibility of faecal or urinary incontinence, temporary or permanent stoma, or sexual dysfunction⁷⁶.

In summary, the consequences of unnecessary surgery in the particular case of the rectum may be worse, which, together with a greater risk of hidden deep submucosal invasion and its greater anatomical accessibility, would tip the balance in favour of local en bloc resection techniques in lesions where the risk of invasion is not negligible.

Local resection techniques

There are several local and minimally invasive methods that allow curative treatment of pT1 CRC. The choice of the most appropriate one may vary according to its capacity to resect the lesion en bloc, as well as its complication rate, its cost and duration, and its availability, among others.

- **Endoscopic Mucosal Resection (EMR) or Mucosectomy:** allows resection of low-risk lesions in fragments, such as homogeneous granular LSTs located in the right colon. However, for lesions with risk of deep invasion and that, therefore, would require en bloc resection, this technique is only effective in lesions <20 mm in diameter. There are other derivative techniques, such as underwater EMR or partial or total mucosal precutting, which in expert hands, increase en bloc resection rates in lesions up to 25-30 mm. Its better safety profile, as well as its lower time and resource consumption, makes EMR available in almost all centers⁷⁷.
- **Endoscopic Submucosal Dissection (ESD):** unlike EMR, it allows en bloc resection (R0) regardless of the size and location of the lesion, obtaining a high quality histological specimen and considerably reducing recurrences and the need for revision and retreatment endoscopies⁴⁹. In lesions with superficial submucosal invasion, ESD achieves en bloc resection rates of over 90%. When performed in lesions with deep submucosal invasion the R0 resection rate drops to 47-64%^{78,79}. It is necessary to take into account the complication rates with the need for additional surgery, such as perforation (around 5%) or delayed hemorrhage, which occurs in up to 20% of cases⁸⁰⁻⁸⁵. Furthermore, theoretical and technical training in ESD requires a high degree of specialization and its learning curve is slower than that of other techniques, which, together with the fact that it is a procedure of prolonged duration, means that in Western countries its availability is heterogeneous⁸⁶.

- **Intermuscular dissection:** variant of ESD where the dissection plane is not located in the submucosa, but in the connective tissue that separates the longitudinal and circular layer from the muscular layer, including the external, circular layer in the specimen. It has only been shown to be technically possible in the rectum, where it could exceed 80% en bloc resection of lesions with deep submucosal invasion⁸⁷.
- **Transmural endoscopic resection (full-thickness resection: FTR):** allows obtaining an optimal histological specimen by including the complete muscular layer, which in turn allows resection en bloc of lesions with deep submucosal invasion. This is a device-assisted technique with an ovesco and a pre-loaded loop that is attached to the tip of the endoscope, which with a short learning curve allows R0 resections in approximately 90% of lesions up to 15 mm in diameter⁷². Above 20 mm the ability of this technique to resect en bloc drops drastically. The AE rate is 8-14%, including 2-3% of deferred perforations due to premature opening of the ovesical clip⁷³. With the new evidence available, the involvement of the resection margins tends to be considered more a risk factor for local recurrence than a criterion for high risk of LM, which favors the possibility of using this technique to perform an additional resection on the eschar of a previously resected invasive lesion with affected margins or margins that cannot be assessed by fragmentation. This has been the most frequent indication for transmural resection in the Dutch T1 CRC cohort, where 77.6% of eschar resected by this technique showed no residual tissue. Further analysis suggests that when this is the case, the probability of LM and/or recurrence is similar to that of those patients who undergo surgery⁷⁴, and may therefore be considered an alternative to surgery in the absence of other risk factors.
- **Transanal Minimally Invasive Surgery (TAMIS),** with the aid of a single port placed in the anus, laparoscopic instruments can be used to resect lesions located in the middle and proximal rectum, including the muscular layer, and can therefore be useful in cases of suspected deep invasion or for the resection of eschar. TEM (Transanal Endoscopic Microsurgery) is another local resection technique comparable to TAMIS, although it uses different surgical instruments. The en bloc resection and complication rates of TAMIS/TEM may be similar

to those of ESD. There is currently an ongoing randomized clinical trial (TRIASSIC) to compare both techniques in the rectum⁹¹.

In summary, when a lesion is suspicious or presents a significant risk of being a pT1 CRC, we have several minimally invasive local resection techniques with the main objective of organ preservation, especially in the rectum, and also with an acceptable safety profile, which allow en bloc resection of the tumor and an adequate assessment of the histologic risk of LM. The patient's characteristics and preferences, as well as the size and location of the tumor and local availability and experience will determine the most appropriate strategy in each case.

Decision-making after local resection of pT1 CRC

The main objective in the follow-up of endoscopically resected pT1 CRC is to identify local recurrence or metachronous lesions at a time when additional treatment could extend the patient's survival or improve his quality of life. When faced with a patient who has had a pT1 CRC resected, in order to make the decision to follow up or, on the contrary, to refer the patient for surgical rescue, three factors must be taken into consideration:

1. Risk of LM, established by histologic criteria. The limitations of the considered suboptimal criteria (deep submucosal invasion and resection margin <1 mm) should be taken into account as independent risk factors for LM, according to current evidence.
2. Comorbidities, patient's physical condition and risk of adverse events.
3. Patient preferences and impact on quality of life.

It is essential that decision making be discussed within a multidisciplinary committee, where these factors, especially the individual perioperative risk of each patient, will be taken into account to help us decide who will really benefit from additional surgical treatment. Scales developed to assess the risk of AE according to a patient's comorbidities and life expectancy are very useful. The most widely used is the Charlson Comorbidity Index (CCI)⁹². Age older than 79 years and a CCI >3 points are associated with shorter survival⁹³. On the other hand, according to the Modified Frailty Index (FI), frail patients with a FI ≥ 2 points present increased morbidity-mortality rates, fewer discharges, more readmissions and lower disease-free survival and overall survival rates⁹⁴.

In the following sections we will summarize the main recommendations for follow-up after endoscopic resection

of pT1 CRC that have been developed by the main scientific societies of digestive endoscopy in Europe (ESGE)^{26,49} and the American Gastroenterological Association (AGA)⁹⁵ to help us define under what circumstances additional treatment would improve patient survival. Its low level of evidence must be taken into account, so we also add the recommendations of the latest studies and meta-analyses with the most recent evidence.

- **Low risk pT1 CRC:** it is considered curative resection and does not require additional procedure or treatment.

- There is no evidence to support the periodic determination of carcinoembryonic antigen (CEA) or imaging tests, neither for initial staging nor during follow-up. The National Comprehensive Cancer Network (NCCN) guidelines specify, in relation to stage I CRC, that *"imaging is not routinely indicated, and should only be based on symptoms and/or clinical concern for recurrent/metastatic disease"*⁹⁶.

- Endoscopic follow-up is indicated (always based on a quality baseline colonoscopy, complete up to the cecum and with adequate cleaning):

The ESGE recommends²⁶: 1st colonoscopy at one year, then at three years and at five years after the previous one. In the case of a non-pedunculated lesion resected in fragments, the first endoscopic revision should be performed between 4-6 months. The AGA recommends⁹⁵: 1st colonoscopy in 3-6 months. 2nd colonoscopy: six months after the previous one. 3rd colonoscopy: one year after the previous one. Continue thereafter according to post-polypectomy recommendations.

- **High risk pT1 CRC:**

In a recent meta-analysis by Dang *et al.*³⁰ that included 71 studies with more than 5,000 endoscopically treated pT1 CRC, an overall recurrence risk of 3.3% was established, with most cases of recurrence (95.6%) occurring in the first 72 months (six years). When categorizing pT1 into two groups, high and low risk, a recurrence of 7.7% was observed in the high risk group and only 0.7% in the low risk group. These findings suggest that histologic status is the most important factor in establishing follow-up recommendations.

However, in contrast to low-risk pT1 CRC in which clinical practice guidelines do give more specific follow-up recommendations, in the case of high-risk pT1 CRC it is more difficult to establish more specific follow-up guidelines, mainly due to the heterogeneity of this group of patients. Moreover, not

all histologic criteria have the same weight in determining risk stratification, as is the case with the so-called "non-consensus" criteria that we have discussed in this article: deep submucosal invasion^{12,40} or distance to the deep margin of <1 mm⁴⁸.

In view of the lack of quality prospective studies with long-term follow-up periods in patients with high-risk pT1 endoscopically resected, we will continue to base our decisions on histological criteria, but it is also important to pay attention to other relevant clinical characteristics that would increase the risk of recurrence³⁵: rectal location, non-pedunculated lesion morphology, fragmented resection not en bloc (EMR more risky than ESD).

We can conclude that in the case of patients who have undergone resection of a high-risk pT1 CRC, we should try to carry out the most personalized follow-up possible, with colonoscopies, imaging tests and periodic CEA determination, with the aim of detecting local and distant recurrence, at least during the first six years, the period in which most cases of recurrence have been shown to occur³⁰. There is no consensus in the guidelines on the periodicity with which the different tests should be requested. It has not been demonstrated that "intensive" follow-up improves survival⁹⁷⁻⁹⁹ and, in addition, there is the probability of incidental findings in imaging tests that in many cases may be clinically irrelevant and cause more anxiety in patients, as well as increased costs. A recently published study¹⁰⁰ showed a 5-year cumulative incidence of benign incidental findings of 18.3%, which contrasts with a 2.5% 5-year cumulative incidence of malignant incidental findings during follow-up.

- **pT1 resected in the rectum:**

The risk of recurrence after local resection is higher for rectal pT1s, standing at 7.7%¹⁰¹, much higher than the 3.3% for pT1s of any other colon location treated endoscopically³⁰. Stratifying according to histologic status, the risk of recurrence of high-risk rectal pT1 is significantly increased after local resection: 12.5% (if resected endoscopically) and 29.7% (if resection is via TEM/TAMIS). With these results we could think that the best solution is surgical rescue. But we must also take into account the negative impact that oncologic surgery on the rectum can have: risk of incontinence/sexual dysfunction, consequences of a possible low anterior resection syndrome or abdomino-perineal amputation. We will differentiate between these situations:

1. **pT1 in low-risk rectum:** close follow-up should be offered, preferable to surgery, since *a priori* the

negative consequences of oncological surgery would outweigh the possible benefits. The Dekkers meta-analysis¹⁰¹ proposes a 5-year follow-up strategy: Rectoscopies every six months for the first two years, then annually for the following five years, with annual CEA determination.

2. **pT1 in high-risk rectum:** the patient should be offered complete surgery with total excision of the mesorectum, as indicated in most clinical practice guidelines^{49,95,102}. If oncologic surgery is not possible (the patient refuses surgery or is at high surgical risk), intensive follow-up should be performed for at least 5-6 years in order to detect endoluminal recurrence, locoregional lymphatic metastases and/or recurrence or distant metastatic disease. As an example of a follow-up strategy, the one proposed by Dekkers et al.¹⁰¹ is proposed: Rectoscopies every six months for the first two years, then annually for the following five years, and annual CEA determination. In addition, add annual MRI or echoendoscopy and chest/abdominal CT in the first year, then at three and five years.
3. **pT1 in the rectum, with deep submucosal invasion (>SM-1) as the only risk factor:** the European ESGE guidelines also propose a more conservative approach in this case⁴⁹: close surveillance and/or chemo-radiotherapy, without ruling out surgery, always after individualizing each case and within a multidisciplinary committee.

Conclusions and areas for improvement

With the current histological criteria, more than 70% of patients with pT1 CRC meet high-risk criteria and, therefore, with a theoretical indication for surgical rescue. But most of them will not have lymphatic metastases or residual tumor after endoscopic resection^{32,33,37}. There is therefore a risk of overtreatment by relying exclusively on histological criteria.

There is a need to "redefine" the histological criteria, especially deep submucosal invasion and the distance to the resection margin in order to consider an R0 resection. We may see changes in this regard in clinical practice guidelines in the coming years, although prospective studies with long-term follow-up are necessary, especially in the case of patients with high-risk pT1 CRC who do not undergo surgery.

In selected cases, close clinical follow-up may be indicated instead of surgery, especially in patients with comorbidities or frail elderly. Special mention should be made of rectal pT1, where a higher risk of recurrence and lymphatic metastasis has been demonstrated, but the negative consequences of surgery in this location must also be considered.

Therefore, it is essential to develop and learn endoscopic resection techniques with a minimally invasive approach to obtain higher R0 resection rates, which will help to improve the histological evaluation of lesions, with the aim of achieving organ preservation and avoiding the dreaded adverse events of surgery (especially in the rectum).

The future lies in the development of artificial intelligence, which will improve optical endoscopic diagnosis and histological evaluation of lesions. The use of predictive models with new molecular biomarkers will also make it possible to make more precise estimates of the individual risk of each patient and facilitate the decision-making process.

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ENDOSCOPIC TREATMENT OF GASTRIC VARICES: WHEN AND HOW?

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Abstract

Bleeding from gastric varices is less common than from esophageal varices, but when it occurs, it does so more rapidly and profusely, with higher rates of rebleeding and mortality. Therefore, understanding their complex pathophysiology and vascularization is essential, posing a significant endoscopic and therapeutic challenge.

To classify them, the Sarin classification must be used, with fundic varices posing the greatest risk of bleeding and being the focus of this controversy.

When there is active bleeding from fundic varices, treatment must be applied; however, high-quality data to choose the optimal strategy remain limited. Nonetheless, clinical practice guidelines strongly recommend treatment with cyanoacrylate via conventional gastroscopy, as it is an effective, relatively easy, and safe technique to apply in an emergency.

Special precautions must be taken when applying cyanoacrylate due to its complications, the most feared

being systemic embolisms. To minimize or even eliminate complications, the combined technique (cyanoacrylate + coils) guided by endoscopic ultrasound was developed. This treatment modality could be considered the most effective and safe technique, and although it is not yet the preferred choice for acute bleeding, it plays a fundamental role in secondary prophylaxis. It is endorsed by the ESGE guideline and has been included in the research agenda for the upcoming Baveno consensus.

Keywords: gastric varices, treatment, cyanoacrylate, combined technique.

Introduction

Gastric varices (GV) are present in approximately 20% of cirrhotic patients with portal hypertension (PH), with GV bleeding being less frequent than oesophageal variceal (EV) bleeding. However, when GVs bleed, they bleed more rapidly and profusely, leading to higher mortality (mortality rates of up to 45%), higher rates of treatment failure and thus rebleeding

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(rebleeding rates 35-90%)¹. All this, added to the complexity of its pathophysiology and vascularisation, presents us with a diagnostic and, above all, therapeutic challenge.

In general, the risk factors for GV bleeding are: advanced liver disease (Child B-C), GV >5 mm, GV with red dots and their location, fundic varices (FV) have a higher risk of bleeding than the rest².

As for their pathophysiology, GVs are made up of an afferent, nutritive or inflow vein and an efferent or outflow vein. This efferent vein, in 85% of cases, is formed by a decompressive portosystemic shunt, to which the systemic complications of the most widely used treatment at present, the injection of cyanoacrylate, are attributed^{3,4} (Figure 1).

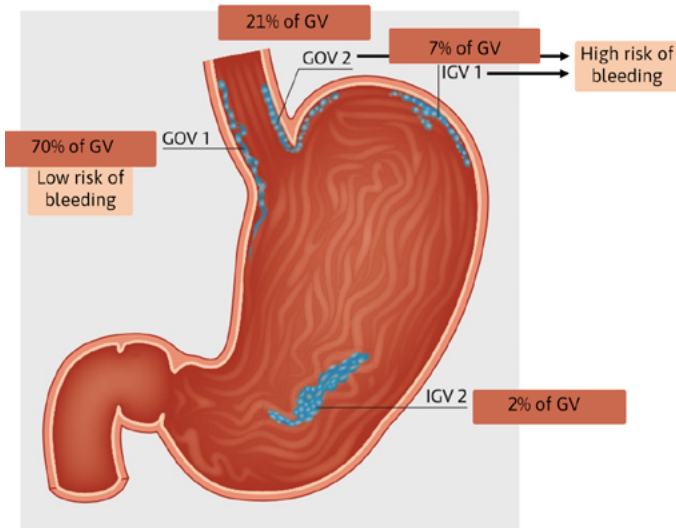


Figure 1. Sarin Classification of Gastric Varices (GV: Gastric Varices. GOV: Gastroesophageal Varices. IGV: Isolated Gastric Varices).

Classification

In order to be able to treat them correctly, it is essential to define and characterise them with criteria. There are several classifications^{5,6}, but the one used in endoscopy and endorsed by Baveno VII⁷, is the Sarin classification¹. It divides them according to their location into oesophagogastric or "junctional" varices, type GOV-1 (extending towards the lesser curvature) and GOV-2 (extending towards the fundus); on the other hand, isolated gastric varices type IGV-1 (in the fundus) and IGV-2 elsewhere. The most frequent are GOV-1 (70% of GVs) and have a lower risk of bleeding. In contrast, IGV-1 and GOV-2 are less frequent but have a high risk of bleeding, and are the origin of GV bleeding in 60-70% of cases^{7,8} (Figure 2). These FVs are the focus of this controversy.

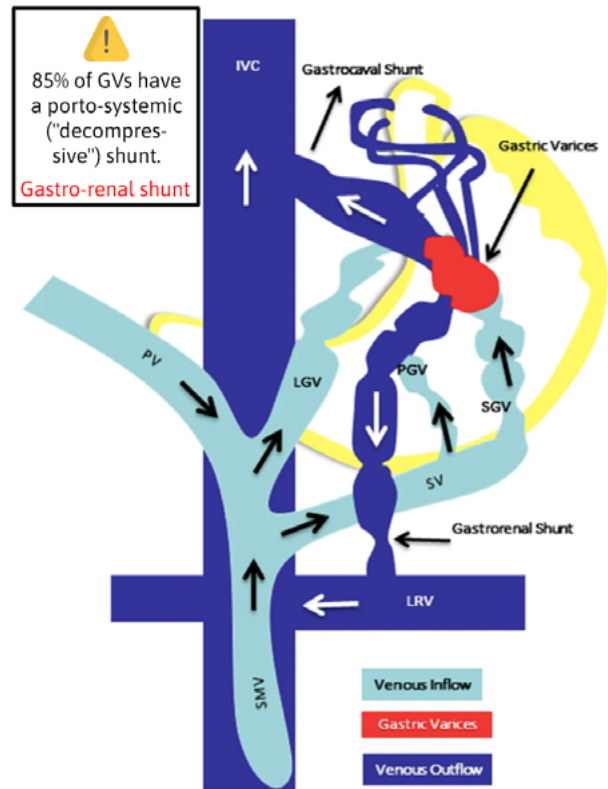


Figure 2. Vascularization of Gastric Varices (GV). Phillips et al. Figure, BMC Gastroenterol (2020). IVC: Inferior Vena Cava. LRV: Left Renal Vein. PV: Portal Vein. SMV: Superior Mesenteric Vein. SV: Splenic Vein. LGV: Left Gastric Vein. SGV: Short Gastric Vein. PGV: Posterior Gastric Vein.

Available treatments

Depending on the scenario and the techniques available in each centre, we can apply one treatment or another.

1. CONVENTIONAL GASTROSCOPY
 - Elastic bands.
 - Cyanoacrylate injection.
 - Sclerotherapy (ethanol, ethanolamine or polidocanol).
2. ECOENDOSCOPY
 - Cyanoacrylate injection.
 - Coil release.
 - Coil release + cyanoacrylate injection.
3. INTERVENTIONAL RADIOLOGY
 - TIPS (trans-jugular intrahepatic portosystemic shunt).

- BRTO (Balloon-occluded retrograde transvenous obliteration).

Different clinical scenarios

1. Gastric varicose veins with active bleeding. Treatment is always necessary.
2. Gastric varices that have bled, but at the time of gastroscopy there is no active bleeding. The treatment to be applied is secondary prophylaxis.
3. Gastric varices that have never bled. The treatment we decide on is primary prophylaxis.

Treatment of active bleeding from gastric varices

Initial assessment, resuscitation and general measures

Management of these patients should be carried out in critical or intermediate care units, at least during the first hours.

Baveno VII supports a conservative transfusion strategy, aiming for a haemoglobin of 7-8 g/dL; and avoid routine transfusion of fresh frozen plasma or platelets.

Specifically, routine orotracheal intubation prior to endoscopy is discouraged, reserving the latter for patients with altered level of consciousness or active haematemesis.

Prevention of bacterial infection remains a priority objective and intravenous ceftriaxone (1 g/24 hours) remains the most commonly used option in clinical practice. Withdrawal of proton pump inhibitors is recommended once endoscopy confirms the variceal origin of the bleeding.

Specific pharmacological haemostatic therapy of acute bleeding consists of early administration of vasoactive drugs (terlipressin, somatostatin or octreotide) as early as possible, to be maintained for 2-5 days, in addition to endoscopic treatment in the first 12 hours after stabilisation of the patient (or as soon as it is safe if instability persists). For these reasons it is considered essential that hospitals caring for patients with acute variceal haemorrhage have a gastroenterologist with experience in endoscopy available 24 hours a day⁹.

Specific endoscopic treatment

Whenever there is active bleeding at the time of gastroscopy, some endoscopic treatment should be applied.

Endoscopic options currently available to treat acute GV bleeding include sclerotherapy, endoscopic band ligation (EBL) and cyanoacrylate injection. However, high-quality data for choosing the optimal strategy remain limited, with inconsistencies between trials regarding mortality, incidence of rebleeding and adverse events.

Several systematic reviews/meta-analyses¹⁰⁻¹³ have evaluated the efficacy of cyanoacrylate injection for the treatment of GV bleeding and compared it with other endoscopic methods (sclerotherapy or EBL), with cyanoacrylate being superior in most outcomes, achieving better rates of immediate haemostasis and prevention of rebleeding.

Based on current evidence, clinical practice guidelines (ESGE and Baveno VII⁹) recommend:

1. GOV-1 and IGV-2 type GVs can be treated the same as EVs with EBL.
2. GOV-2 and IGV-1 type GVs should be treated with cyanoacrylate injection by conventional gastroscopy, achieving high rates of immediate haemostasis and low rates of rebleeding. In addition to being effective, it is easy and safe to apply in an emergency.

Cyanoacrylate is a tissue adhesive that polymerises rapidly on contact with blood and becomes a hard, acrylic material that will obliterate the varicose vein^{3,14}. In the United States it was approved by the FDA in 1998, but its use is restricted and few authorised centres are allowed to use it. Although it was first described in 1986 for the treatment of GVs by Soehendra, there are several ways of doing it and this is what makes the technique somewhat confusing and complex for endoscopists. For this reason, the endoscopy service of our hospital (Virgen Macarena University Hospital) together with the nursing staff, have developed a protocol according to our availability and experience, explaining the whole process step by step (Figure 3).

1. Lubricate the channel with acetone/silicone/lipiodol.
2. Disconnect suction.

3. Flush the injector with saline solution (SS) (approx. 1.5-2 ml).
4. Load 2 ampoules of Histoacryl (0.5 ml+ 0.5 ml) mixed with 1 ml lipiodol in a 5 ml syringe.
5. Inject the glue and rapidly push in 1.5-2 ml of SS.
6. Keep the needle inside the catheter to avoid tissue impaction (adhesive).
7. Remove the gastroscope without keeping the catheter inside the channel and then cut off the tip of the catheter so that the catheter can be removed.

severe embolism. Lipiodol is used to control the polymerisation time and, very importantly, as a contrast medium, a particularly useful advantage in cases of suspected embolisation. Although in most cases systemic emboli are asymptomatic, some studies describe up to 50% of these¹⁵⁻¹⁷.

Other complications of this technique are the formation of post-injection ulcers or fistulas, as well as systemic infections. Special mention should be made of complications related to the equipment, such as adhesion of the glue to the lens or to the gastroscope channel.

All these drawbacks of direct injection of cyanoacrylate by gastroscopy can be minimised or even eliminated by echoendoscopically guided administration, which would also allow for coil release^{15,17}.

The first time the echoendoscopy-guided coils release technique was performed to treat acute bleeding due to gastric varices was at Virgen Macarena University Hospital in Seville in 2010, by Romero-Castro *et al.*¹⁵. In 2011, Binmoeller *et al.*¹⁸ described this same technique, combined with cyanoacrylate, achieving a 96% obliteration rate of gastric varices in a single treatment session, without clinical signs of embolization with cyanoacrylate. Since this initial study, multiple retrospective studies, two randomised clinical trials and systematic reviews/analyses have been published on this topic^{19,20}, concluding that the treatment of acute GV bleeding is more effective and safe under endoscopic guidance and in combination (coils + cyanoacrylate).

Despite this evidence in the literature, for the moment, clinical practice guidelines^{7,8} do not strongly recommend this combined technique guided by echoendoscopy as the treatment of choice for acute GV bleeding. This may be due to the complexity of applying it in an emergency; these techniques are safer but only performed by expert personnel and are more expensive.

Where the recommendation for the combined echoendoscopy-guided technique is strong, on a par with the other options, is in secondary prophylaxis, which we will see later.



Cyanoacrylate injection technique. Treatment of gastric varicose veins




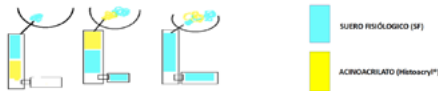
1. Eye protection for healthcare personnel and patient.
 
2. Disconnect suction.
3. Lubricate the channel with acetone/silicone/lipiodol.
4. Flush the injector with saline solution (SS) (approx. 1.5-2 ml).
 
5. Load 2 ampoules of Histoacryl (0.5 ml+ 0.5 ml) mixed with 1 ml lipiodol in a 5 ml syringe.
 
6. Inject the glue and rapidly push in 1.5-2 ml of SS.
 
7. Remove the gastroscope without keeping the catheter inside the channel and then cut off the tip of the catheter so that the catheter can be removed.

Figure 3. Cyanoacrylate Injection Technique. Virgen Macarena University Hospital.

In addition to the preparation and care during injection, special precautions must be taken with cyanoacrylate, such as in large portosystemic shunts, cardiac septal defects or hepatopulmonary syndrome, due to the risk of symptomatic and

Persistent bleeding or early rebleeding of gastric varices

When endoscopic primary haemostasis fails or we have early recurrent bleeding we have to resort to the urgent

salvage radiological techniques, TIPS or BRTO. There are very limited high level data comparing TIPS and BRTO in these situations^{21,22}. BRTO and TIPS have similar rates of technical success and adverse effects. TIPS is associated with higher rates of hepatic encephalopathy and BRTO with long-term aggravation of oesophageal varices. Due to the limited quality of comparative data, no specific selection criteria are currently available, therefore individualisation according to patient and centre experience is necessary.

Primary and secondary prophylaxis of gastric varices

Primary prophylaxis (GVs that have never bled) is performed in the same way and with the same criteria as EVs. When patients cannot receive non-selective beta-blockers (BBNS) (due to intolerance or contraindication), in the case of GOV-1 type GV, they should be treated like EVs with EBL. However, in the case of FVs, type GOV-2 or IGV-1, to date there are no firm recommendations on the endoscopic treatment of FVs in patients with intolerance to BBNS. In fact, the ESGE suggests, with a weak recommendation and low evidence, that it is equally valid not to perform any treatment or to treat them, either with cyanoacrylate injection by gastroscopy or treatment by echoendoscopy with coils + cyanoacrylate, on a case-by-case basis, and if treated, in centres with experience in the technique⁸.

In secondary prophylaxis (GVs that have bled at some point), GOV-1s are treated the same as EVs. For FVs, type GOV-2 and IGV-1, it is difficult to provide solid evidence-based recommendations due to the heterogeneity of previous research and the lack of uniform definitions or standardised outcomes. The available literature consists of case series, restricted cohort studies and a few small randomised trials, with significant selection biases²³. Therefore, the ESGE recommends an individualised approach, based on patient factors and local experience for FV eradication therapies, considering endoscopic injection of cyanoacrylate +/- BBNS, combined treatment with coils + cyanoacrylate guided by echoendoscopy, TIPS placement or BRTO⁸. A recently published network meta-analysis²⁴ suggested that BRTO may be the best intervention to prevent FV rebleeding (secondary prophylaxis), while BBNS monotherapy cannot be recommended; however, direct comparative studies are much needed.

With regard to treatments guided by endoscopic ultrasound, the target is to puncture the nutrient vessel, the perforating vein, or, failing that, the varicose vein directly. In addition, this allows us to perform it when endoscopic vision is limited by bleeding, since with Doppler we can locate the vessels and the flow, and

Doppler also allows us to check the cessation of flow when the varicose vein is obliterated (Figure 4). This can be done with different methods of obliteration: with cyanoacrylate alone, with coils alone, or with a combination of both. After a first GV treatment session, the next revision is recommended after 4-6 days and thereafter, as with EVs, every 2-4 weeks until complete GV obliteration is achieved²⁵. The steps for cyanoacrylate injection and echoendoscopically guided coil placement are explained below.

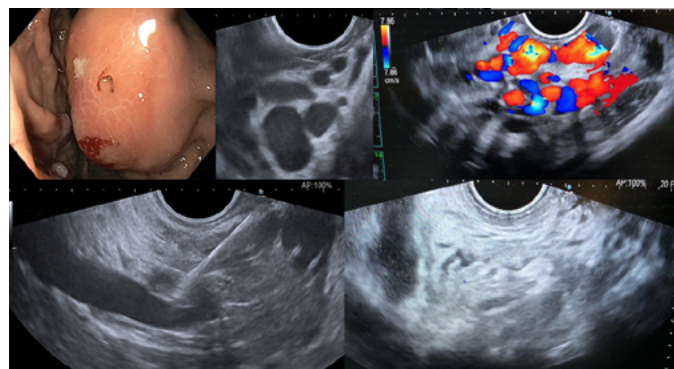


Figure 4. Example Clinical Case Dr. Romero. Placement of coils in GOV-2 varix. Gastric varix with intense Doppler flow (figure 3). Injection of 6 coils (figure 4). Complete cessation of intravariceal flow (figure 5).

Echoendoscopy-guided cyanoacrylate injection technique:

1. 22G needle purged by glucosmon.
2. Cyanoacrylate with lipiodol 1:1.
3. Avoid lateral movements with the needle inside the varicose vein.
4. Check afferent perforator: contrast or Doppler.
5. Inject 1 ml of cyanoacrylate above the muscle layer.
6. Check occlusion of the varicose vein with Doppler.

Echoendoscopy-guided coil placement technique:

1. 19 G needle.
2. Coils diameter 20% larger than the varicose vein: 8-20 mm.
3. Remove stylet and push coil with it.
4. Check intravaricose insertion of the coil.

5. As many coils as necessary.

As with EVs, patients with GV and high risk of failure to standard treatment would benefit from placement of a preventive TIPS in the first 72 hours^{7,8}.

Conclusions

1. The treatment of choice in acute bleeding of fundic varices (GOV-2 and IGV-1) is cyanoacrylate injection by conventional endoscopy.
2. Echoendoscopy-guided therapy may be particularly useful in specific situations: poor visibility and retreatment. It reduces cyanoacrylate complications and allows coil release.
3. Combined echoendoscopy-guided treatment (coils + cyanoacrylate) appears to be the most effective and safe strategy today, but well-designed controlled studies are needed to position it as the treatment of choice. This will ensure that in the coming years there will be a stronger position in the recommendations.

Finally, and by way of conclusion, the algorithm of action we follow when there is an active VG haemorrhage in the Virgen Macarena University Hospital is shown graphically (Figure 5).

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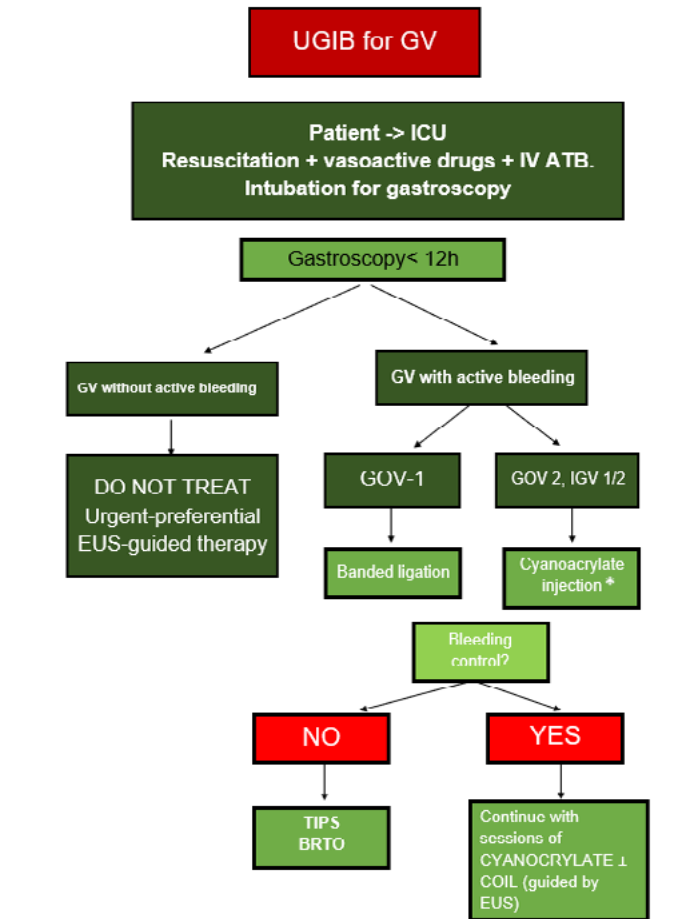


Figure 5. Algorithm for Acute Hemorrhage from Gastric Varices (GV: Gastric Varices. ICU: Intensive Care Unit. IV ATB: Intravenous Antibiotic Therapy. BRTO: Balloon-occluded Retrograde Transvenous Obliteration). * By standard endoscopy only in case of emergency without an experienced echoendoscopist available. Echoendoscopy-guided treatment (coils+/-cyanoacrylate) is preferable.

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INTRADUODENAL AND RETROPERITONEAL HEMATOMA AFTER DUODENAL BIOPSIES

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Abstract

We present the case of a 20-year-old male with no previous history of interest who developed an intraduodenal and retroperitoneal hematoma in the context of an oral endoscopy with duodenal biopsies due to abdominal pain and chronic diarrhea. The evolution with conservative treatment was favorable and ultrasound controls were performed until resolution. Intraduodenal hematomas are lesions that are usually observed in children after blunt abdominal trauma or in patients with risk factors, being infrequent as a complication after diagnostic or therapeutic endoscopic procedures. Their management is mainly conservative and in case of absence of improvement or perforation, surgery is indicated.

Keywords: intraduodenal hematoma, retroperitoneal hematoma, duodenal biopsies.

Introduction

Intramural duodenal haematomas (IDH) are infrequent lesions that are usually seen in children after blunt abdominal trauma or in patients with underlying risk factors such as

coagulation disorders or anticoagulant therapy^{1,2}. They can also, but rarely, occur as a complication of endoscopic diagnostic and therapeutic procedures, even in the absence of these risk factors^{2,3}.

Clinical case

The patient was a 20-year-old male with no previous history of interest who began an outpatient study due to abdominal pain and chronic diarrhoea, for which reason oral endoscopy was performed and duodenal biopsies were taken with standard forceps. However, approximately 8-12 hours after the endoscopy, he began to experience intense epigastralgia which required an urgent abdominal CT scan and a collection measuring 12x6x10 cm compatible with haematoma was found in the duodenum and right retroperitoneum. During hospitalisation, an abdominal ultrasound scan was performed (**Figure 1**) with views to subsequent check-ups. A conservative treatment was decided in conjunction with surgery and the clinical, analytical and ultrasound evolution was favourable with this treatment. Finally, he was assessed by haematology,

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Intraduodenal and retroperitoneal hematoma after duodenal biopsies
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CLINICAL CASE

ruling out haematological disease or underlying coagulation disorder.

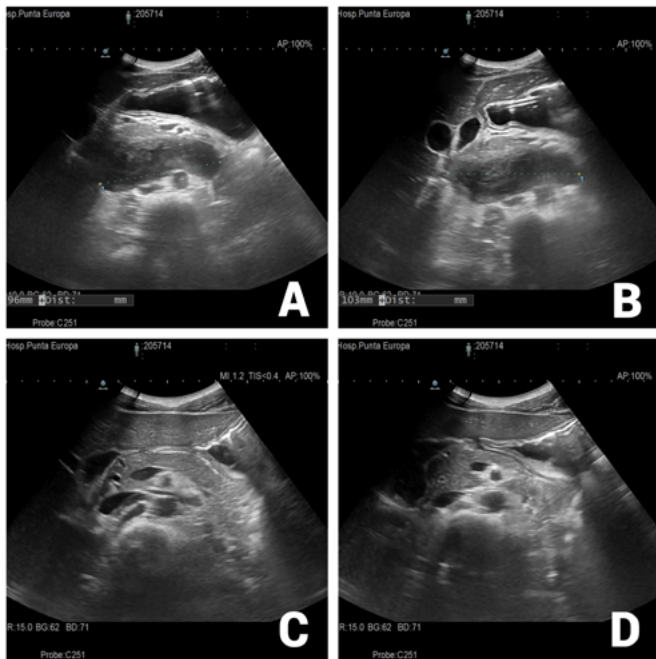


Figure 1. A and B correspond to ultrasound images obtained during admission where a dilated gastric chamber is identified, as well as a mass with heterogeneous and hyperechogenic content, bean-shaped morphology and caudal location to the pancreas compatible with retroperitoneal haematoma. C and D are the outpatient controls after discharge where the haematoma is no longer identified.

Discussion

Upper endoscopy is a common procedure with few complications, most commonly bleeding, perforation and sedation-related complications, with the occurrence of IDH being very rare². Traction of the duodenal mucosa with the endoscopic forceps during biopsy may separate a considerable area of the duodenal mucosa from the duodenal wall, tearing the intramural vessels. Therefore, it has been suggested that the endoscopic forceps should not be advanced more than 3 cm beyond the tip of the endoscope to grasp the mucosa in order to minimise shearing^{2,4}.

Symptoms of IDH include abdominal pain and vomiting which usually appear within 48 hours of biopsies, although they can appear up to seven days later^{1,2}. It can also lead to cholestasis or acute pancreatitis due to obstruction of the duodenal papilla¹.

Laboratory findings are non-specific and show decreased haemoglobin concentration¹. A summary diagnosis can be made by imaging (ultrasound, CT or MRI) or endoscopy^{1,2}. Ultrasound

findings are variable and include a thickened hypoechoic duodenal wall, a mass close to the duodenum of variable echogenicity, a paravertebral cystic lesion simulating a pancreatic pseudocyst and a polypoid lesion within a distended loop of bowel, sometimes making it difficult to diagnose this entity by this technique. In addition, the echogenicity of the haematoma changes substantially over time and may resemble an abscess, showing internal echoes in some cases^{3,5}. However, once the diagnosis has been made, ultrasound may be used for the follow-up of patients with IDH, as it is available in most centres and avoids the use of ionising radiation^{1,5}.

Treatment is conservative in most cases, consisting of fasting, serotherapy and nasogastric aspiration^{1,2}, with resolution of IDH occurring one to three weeks after onset^{1,6}. In the event of perforation or lack of improvement with conservative management, surgery is indicated^{1,2}.

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MESO-ILEAL ECTOPIC VARICOSE VEIN WITH UTERINE SYSTEMIC SHUNT AS AN UNCOMMON CAUSE OF SEVERE LOWER GASTROINTESTINAL BLEEDING IN PATIENT WITH MILD PORTAL HYPERTENSION

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Abstract

Ectopic varicose veins of the small intestine are an uncommon cause of gastrointestinal bleeding in patients with portal hypertension. We present the case of a 52-year-old female patient with mild portal hypertension and repeat episodes of lower gastrointestinal bleeding because of meso-ileal ectopic varicose vein with systemic uterine shunt secondary to previous pelvic surgery, radiological findings and treatment performed.

Keywords: gastrointestinal hemorrhage, varicose vein, systemic uterine shunt, portal hypertension, computed tomography angiography.

Introduction

Lower gastrointestinal bleeding secondary to ectopic varices in patients with mild portal hypertension without other stigmata of chronic liver disease is a rare scenario.

The development of a meso-ileal ectopic varicose vein with uterine systemic shunt secondary to previous pelvic surgery for removal of an intrauterine device in a patient with mild portal hypertension without oesophagogastric varices and which causes bleeding in the transfusion range is a form of bleeding not described in the literature, so we present this case for its originality and relevance in the form of presentation, management and treatment.

For this reason, we present the clinical case of a 52-year-old patient with the previously described background to visualise this unpublished case, providing the clinical management and diagnostic imaging where the varicose vein was visualised and the endovascular treatment that allowed its embolisation in a safe and effective manner.

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Fernández Calzado LM, Lombardo Galera MS, Mesa Quesada J, Alañón Martínez PE. Meso-ileal ectopic varicose vein with uterine systemic shunt as an uncommon cause of severe lower gastrointestinal bleeding in patient with mild portal hypertension. *RAPD* 2024;47(3):125-129. DOI: 10.37352/2024473.5

Clinical case

52-year-old woman, smoker, drinker and with a previous history of three pregnancies (two vaginal deliveries and one caesarean section). She underwent surgery due to a complication in the removal of an intrauterine device (Essure®) with salpingectomy and partial hysterectomy four years ago.

She came to the emergency department for intermittent rectorrhagia of three days duration, although on the last day it was continuous with clots. She presented with mucocutaneous jaundice, stigmata of chronic liver disease with telangiectasias and palmar erythema, hepatomegaly without signs of ascites, hypotension of 77/66 mmHg well tolerated with a heart rate of 100 bpm and a positive rectal examination for red blood.

Complete blood count of $1.24 \times 10^6 \mu/L$ (reference 4.20-6.10 μ/L), haemoglobin of 4.5 g/dL (reference 12-16 g/dL) with normal urea and activated partial thromboplastin time of 24.9 s (reference 26-39 s).

Biochemistry showed total bilirubin of 2.40 mg/dL (reference 0.3-1.20 mg/dL), GGT of 404 U/L (reference 5-38 U/L), ALT of 53 U/L (reference 10-49 U/L) and alkaline phosphatase of 667 U/L (reference 46-116 U/L).

Upper gastrointestinal endoscopy was performed and no oesophagogastric varices or other potentially bleeding lesions were identified. Colonoscopy was also performed with no relevant findings. Abdominal ultrasound showed signs of chronic liver disease and mild ascites. This episode resolved with transfusion of red blood cell concentrates.

Twelve days later, she came to the emergency department for a new episode of rectorrhagia with severe anaemia in transfusion range. Contrast-enhanced magnetic resonance enterography showed a hypervascular structure with submucosal arrangement in the wall of the pelvic ileum communicating with the prominent superior mesenteric vein and with right periuterine branches (**Figure 1**), and subsequently non-contrast and contrast-enhanced computed tomography of the abdomen and pelvis in arterial and venous phases, which corroborated the vascular finding (**Figure 2**).

To confirm portal hypertension and the findings of the imaging tests, manometry of the suprahepatic veins was performed through the right internal jugular vein, obtaining a transhepatic gradient of 8 mmHg compatible with mild portal hypertension. Venography of the ovarian and hypogastric veins was also performed, without identifying any communication between them and the ileal veins. Subsequently, indirect

portography was performed by catheterising the superior mesenteric artery, showing a dilated ileal vein in the venous phase that reached the wall of an ileal loop and opacified part of the uterine body and uterine veins.

In a second stage, direct portography was performed by transhepatic puncture with a 21G needle through a 6F introducer, 4F catheter and Terumo® hydrophilic guide, and the distal ileal branch was catheterised with venographic series confirming the presence of dilated ileal varicose veins with fistula to the uterine veins and early opacification of both hypogastric veins. These branches were selectively catheterised with a Marathon® microcatheter and embolised with Onyx® 34. In the final control, embolisation of the branches at the level of the loop and the origin of the fistula with the uterine veins is observed (**Figure 3**). Finally, the transhepatic tract was embolised with Espongostan® Film. More than six months after the procedure, the patient has had no new episodes of lower gastrointestinal bleeding.

Discussion

Ectopic variceal bleeding in patients with portal hypertension is rare and few cases have been reported in the literature. In the published cases, the most common is the history of an abdominal surgical procedure that has triggered the formation of new spontaneous and ectopic portosystemic shunts through postoperative scar tissue, with enterectomy being the most commonly described procedure¹. The development of a meso-ileal ectopic variceal shunt with systemic-uterine shunt secondary to a previous surgical procedure of salpingectomy and partial hysterectomy leading to repeated lower gastrointestinal bleeding and its diagnosis and treatment has not been described.

Gastrointestinal bleeding is defined as blood loss from the digestive tract and may constitute an emergency requiring urgent admission in order to treat or prevent hypovolemic shock, identify the bleeding lesion and treat it for haemostatic or curative purposes^{2,3}.

Oesophagogastric varices are the most frequent cause of upper gastrointestinal bleeding in patients with liver cirrhosis and are a consequence of the development of portal hypertension, with a risk of bleeding when the pressure gradient exceeds 12 mmHg.

Cirrhotic patients with portal hypertension may also develop varices in other locations. These are called ectopic varices and are defined as portosystemic venous collaterals that can occur anywhere except in the cardio-oesophageal

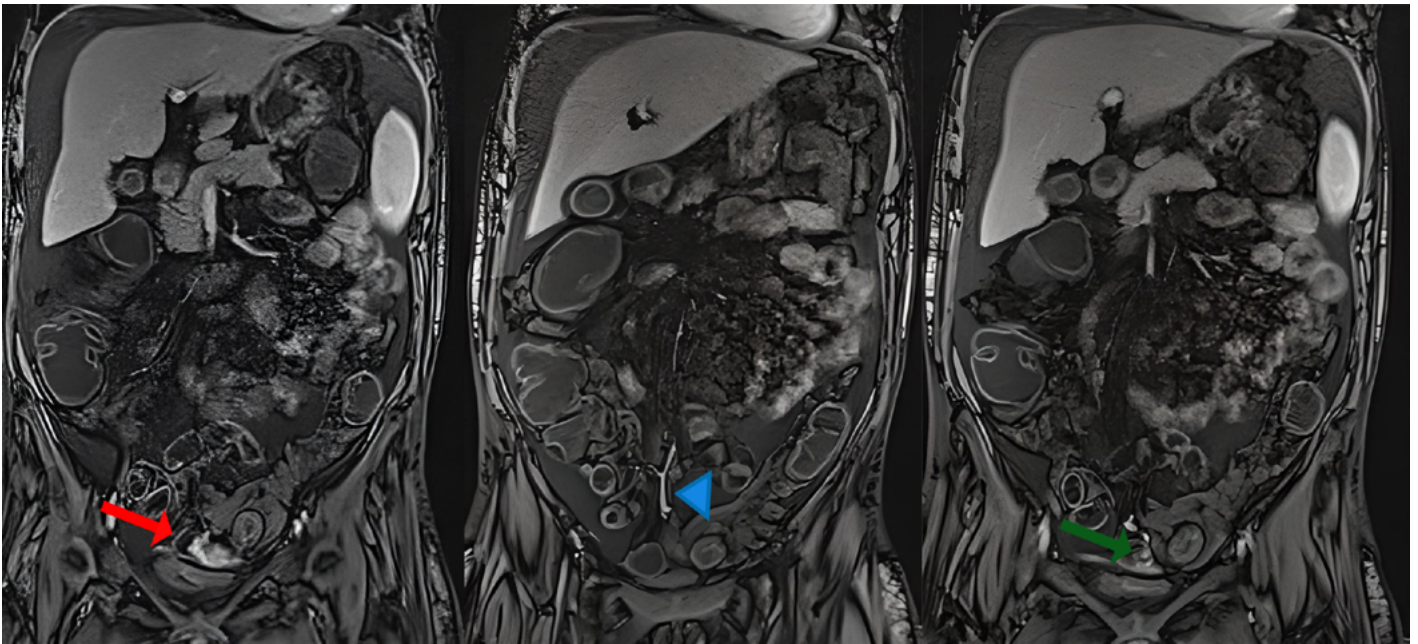


Figure 1. Magnetic resonance enterography T1 sequences with fat saturation and contrast, showing a hypervascular structure with submucosal disposition in the wall of the pelvic ileum (red arrow) that communicates with the prominent superior mesenteric vein (blue arrow) and with periuterine branches (green arrow).

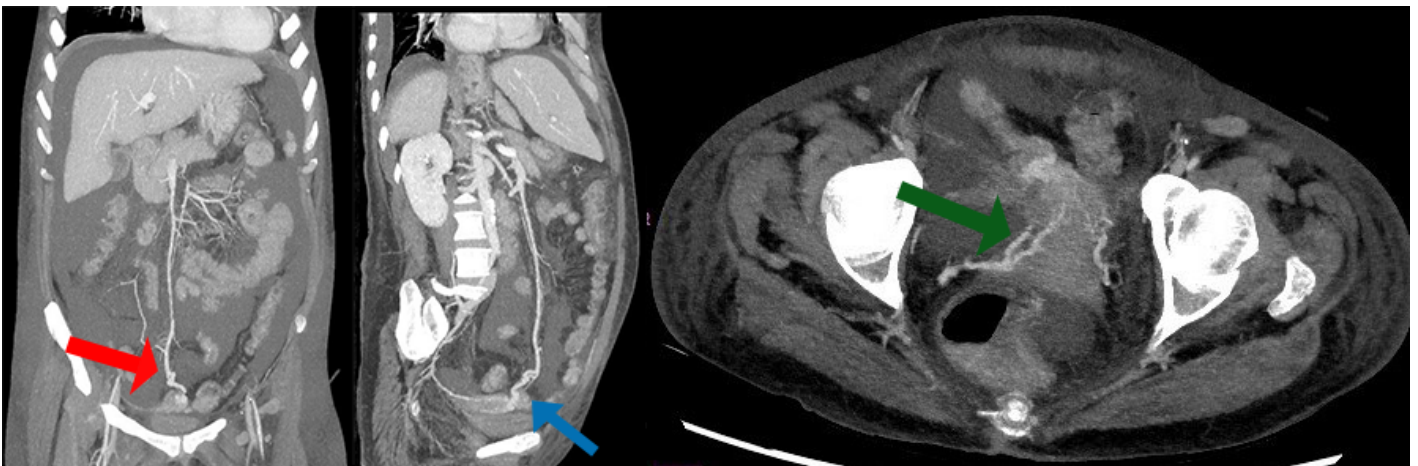


Figure 2. Computed tomography angiography of the abdomen and pelvis, maximum intensity projections with contrast and in the venous phase, in coronal, oblique sagittal, and axial planes. Ectopic meso-ileal varix with systemic-uterine shunt. Enlarged superior mesenteric vein continuing into the ileal vein (red arrow) protruding over the submucosa of the pelvic ileum (blue arrow) and opacifying the uterine veins (green arrow).

region⁴. Ectopic varices include isolated type II gastric varices (antrum, body and around the pylorus), those of the abdominal wall and peritoneal space. It has been reported that up to 8% of patients with portal hypertension may present them, with the most frequent location being the duodenum followed by the jeuno-ileum, colon, rectum, biliary tree, ovarian circulation and peritoneum⁵.

They can develop anywhere in the intestinal or biliary circulation as a result of short circuits of the portal system due to high pressure in this system, because this hypertension and congestion in the splanchnic circulation increase the susceptibility to damage by impaired oxygenation and

ischaemia, being greater in portal hypertension of extrahepatic origin⁶.

In patients without portal hypertension, the occurrence of ectopic varices has been explained in several ways. Firstly, it has been suggested that they may be related to intestinal surgeries in which systemic drains are anastomosed to portal draining structures. In strictures of intestinal surgeries or in adhesion tissues, arteriovenous fistulas secondary to trauma are also thought to be factors facilitating the development of ectopic varices. The risk of developing ectopic varices is higher if there is a surgical history, whether or not it involves the portal circulation, stenosis of the stoma, or in patients with a



Figure 3. Digital subtraction angiography. Meso-ileal varix with systemic-uterine shunt (red arrow) and subsequent embolization with Onyx® (blue arrow).

surgical history who subsequently develop cirrhosis and portal hypertension. The likelihood of developing bleeding is greater the larger the size of the ectopic varices⁷.

Contrast-enhanced computed tomography is a good alternative for the diagnosis of intestinal varices⁸. Radiological findings of small bowel varices have been rarely described in the literature. The presence of an intestinal intramural lesion with no enhancement in the arterial phase and homogeneous enhancement in the venous phase in a patient with intestinal bleeding should raise suspicion. Differential diagnosis should be established mainly with small bowel tumours, including haemangioma and GIST (gastrointestinal stromal tumours). Therapeutic possibilities include percutaneous embolisation and surgery⁹.

Endovascular treatment of bleeding from ectopic varices allows surgery to be dispensed with, avoiding major bowel resections, and is a minimally invasive curative technique.

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A “C” TRIAD: CIRRHOSIS AND CHOLANGITIS DUE TO CAROLI DISEASE.

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Abstract

Caroli disease (CD) is a rare congenital pathology of probable autosomal recessive inheritance, it is part of the fibrocystic liver diseases and is included in group V of the Todani classification. It is characterized by saccular or cystic dilations of the intrahepatic bile ducts, sometimes associated with congenital liver fibrosis, and is then called Caroli syndrome (CS). The usual clinical manifestation is recurrent abdominal pain secondary to intrahepatic or vesicular stones, and acute cholangitis crises with the consequent formation of intrahepatic abscesses.

Keywords: caroli disease, liver cirrhosis, acute cholangitis.

Introduction

Caroli syndrome (CS) is a rare congenital pathology of probable autosomal recessive inheritance characterised by saccular or cystic dilatations of the intrahepatic bile ducts associated with congenital hepatic fibrosis and development of portal hypertension. A common form of presentation is recurrent cholangitis associated with hepatic abscesses as in the present case.

Clinical case

A 46-year-old woman from Romania with cirrhosis of the liver of unrelated aetiology since childhood associated with subsequent alcohol consumption, in abstinence more than one

year. Previous admissions for edemascitic decompensation and varicose ADH, carrier of TIPS. During the last year she has required five admissions following an episode of acute cholangitis with endoscopic biliary drainage and subsequent development of persistent liver abscesses/phlegmons despite multiple antibiotic therapies aimed at microbiological isolation, opting for chronic antibiotic treatment. She attended the emergency department for fever and pain in the right hypochondrium and was started on intravenous antibiotics. A follow-up CT scan showed resolution of the residual phlegmonous area and described multiple millimetric cystic liver areas.

In view of the suspicion of CD, magnetic resonance cholangiography (MR cholangiography) was performed, confirming the presence of these cystic areas which communicate with the biliary tract, giving rise to fusiform dilatations of the smaller biliary radicals located mostly towards the periphery of the liver parenchyma, compatible with CD. Finally, the patient was discharged and it was decided to evaluate the patient for liver transplantation.

Discussion

CS is a congenital biliary pathology resulting from a defect in the remodelling of the ductal plate during embryogenesis. The clinical manifestations may appear during childhood or in adulthood, and are often diagnosed late.

The main symptom is recurrent abdominal pain secondary to intrahepatic stone formation. Acute cholangitis crises are also common, occurring spontaneously or after manipulation of the bile duct, with usual microbiological isolation of gram-

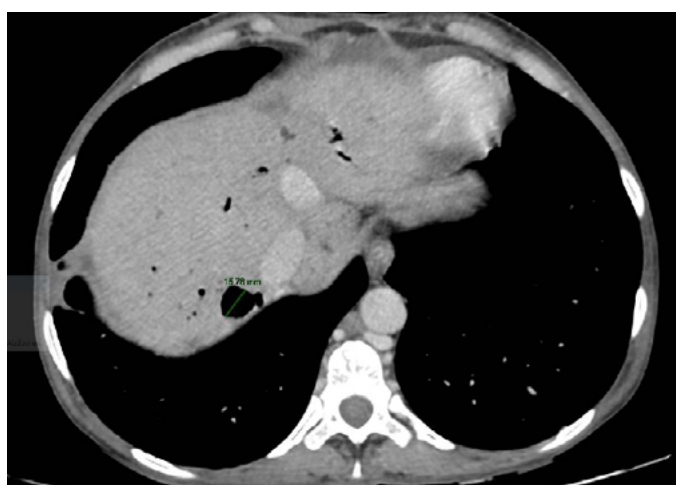


Figure 1. Cystic dilatation of the bile duct in the dome of segment VII in proximity to the intrahepatic cava.

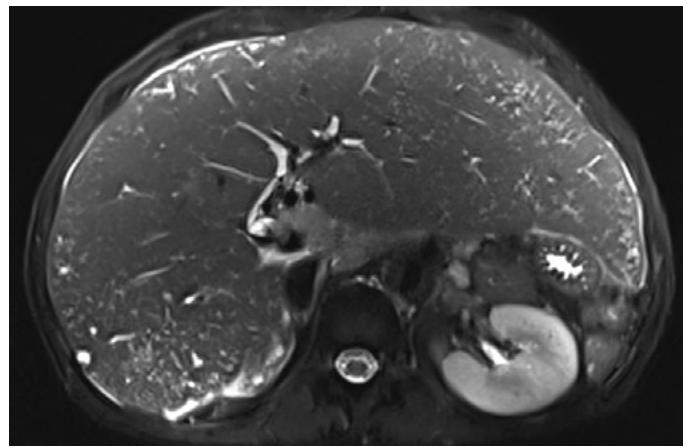


Figure 2. Axial section. Spindle-shaped dilatations of the smaller biliary radicals predominantly towards the periphery of the liver parenchyma, secondary to communication between the multiple millimetric cystic areas and the bile duct.

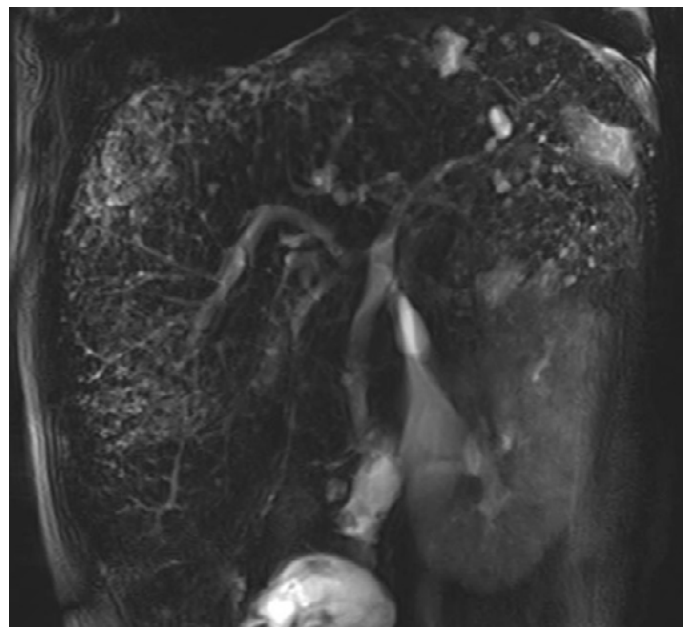


Figure 3. Coronal section. Spindle-shaped dilatations of the smaller biliary radicals predominantly towards the periphery of the liver parenchyma, secondary to communication between the multiple millimetric cystic areas and the bile duct.

negative germs, and often leading to the formation of liver abscesses as in the case described.

Diagnosis is mainly radiological, with MR cholangiography confirming findings of cystic areas communicating with the biliary tree and presenting saccular dilatations of monolobular or diffuse distribution. Control of the focus with antibiotic therapy is complicated, usually requiring partial lobectomy or liver transplantation depending on the extent of the disease. For the treatment of abdominal pain secondary to hepatolithiasis and mild disease, ursodeoxycholic acid at high doses has proved beneficial.

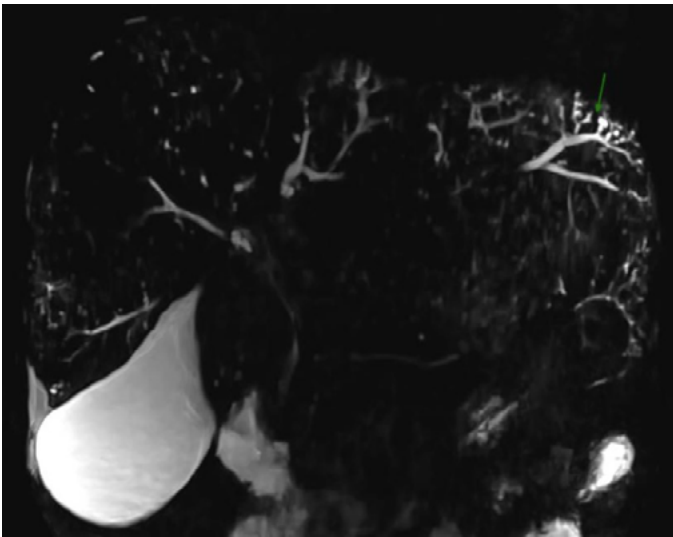


Figure 4. Multiple saccular dilatations involving intrahepatic bile ducts throughout the liver parenchyma.

Thus, CS is a rare pathology to be taken into account in patients with liver disease of non-filial origin with recurrent episodes of acute cholangitis because of its enormous significance in the need for liver transplantation.

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ATYPICAL CHARACTERISTICS AND BEHAVIOR OF GIST

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Abstract

Gastrointestinal stromal tumors (GISTs), constituting digestive neoplasms, typically have a favorable prognosis, although occasional distant extension can occur. The main prognostic factors associated with GISTs are described as lesion size and the number of mitoses per field. These lesions primarily metastasize to the liver, omentum, and peritoneum, with lymphatic dissemination being exceptionally rare. Although the presence of lymph node involvement has been identified as an independent predictor of mortality, since it is an infrequent finding, further studies are needed to understand its prognostic and therapeutic implications. This clinical case describes the approach to a 75-year-old patient with no significant medical history presenting with gastric GIST, who notably had multiple tumor-associated lymph nodes on staging studies, requiring treatment with Imatinib.

Keywords: GIST, metastases, adenopathy.

Introduction

GIST (gastrointestinal stromal tumours) are digestive neoplasms with a usually favourable prognosis, although they can present an aggressive clinical course with distant extension. The incidence in Spain is 1.24 cases each 100,000 inhabitants, with the main site being the stomach and causing epigastralgia, abdominal distension or gastrointestinal bleeding when symptomatic¹. The endoscopic and radiological images of a GIST characterised by distant dissemination exclusively by the lymphatic route are presented below.

Clinical Case

A 75-year-old patient with no personal history of interest was referred for oral intolerance and constitutional syndrome and underwent gastroscopy, where a subcardial lesion with a submucosal appearance and an ulcerated surface was found, which appeared to be malignant (**Figure 1**).

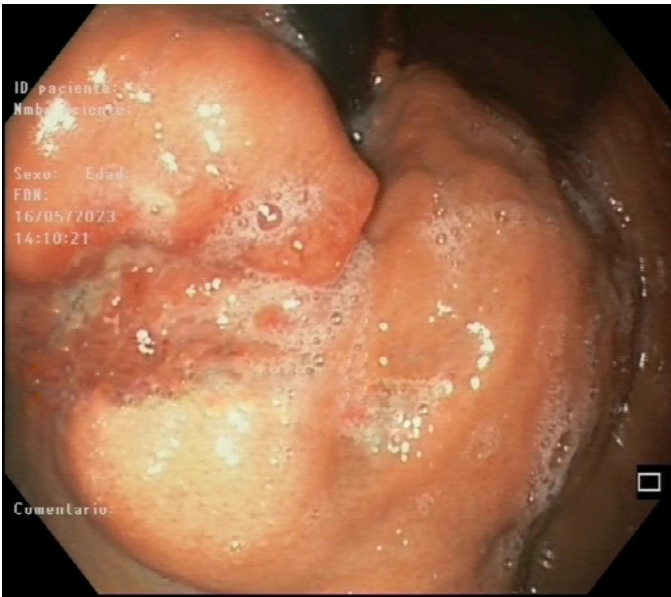


Figure 1. Gastroscopy . At the subcardial level, in the upper body towards the greater curvature, a submucosal lesion of about 25 mm, friable to friction and with an ulcerated centre covered by fibrin, can be identified.

In the extension study performed by Computerised Axial Tomography (Figures 2 and 3) a stenosing lesion compatible with GIST was identified, with an approximate size of 16x11x14 cm (craniocaudal, transverse and anteroposterior diameters respectively). Adenopathies of tumour origin were observed in the left common and external iliac, celiac trunk, retroperitoneum and interaortocaval space, as well as contiguous infiltration of the upper pole of the spleen and left adrenal gland.



Figure 2. Abdominal CT scan. Bulky ulcerated submucosal gastric tumour with dependence on the cardia-fundus region compatible with gastrointestinal stromal tumour (GIST). Approximate maximum dimensions of 16x11x13.7 cm (cc x t x ap).



Figure 3. Abdominal CT scan. Left common and external iliac and left external iliac adenopathies of 13 and 10 mm, respectively.

Biopsies obtained by endoscopy confirmed positivity for CD34, DOG1 and CD117, and six high magnification mitoses/field were counted. The study was completed by requesting PET-CT (Figure 4) and mutational analysis was also performed, identifying deletion 558 in exon 11 of the KIT gene. The patient was referred to Oncology and treatment with Imatinib was started and has continued for a year with adequate response



Figure 4. PET-CT scan. Large hypermetabolic mass in the hypochondrium and left flank, dependent on the gastric chamber, with invasion of the spleen and left adrenal gland. It has a SULmax of 15.19.

and tolerance, with the only notable finding being the appearance of massive post-treatment necrosis two months after starting this therapy.

Discussion

Gastrointestinal stromal tumours (GIST) are the most common digestive neoplasm of mesenchymal origin, and are characterised by the presence of a mutation in the C-Kit protein (CD117) in up to 95% of cases². Our patient had some features that have been identified as risk factors for distant involvement, such as a size greater than 10 cm and a mitosis count greater than five mitoses per field³. In these neoplasms, mutational analysis prior to initiation of Imatinib treatment is recommended as it provides prognostic information and predicts the likelihood of response to tyrosine kinase inhibitor drugs. Mutations in exon 11 of the KIT gene, such as the one in our patient, are usually associated with a good response to Imatinib⁴.

Regarding distant extension, GIST tumours mainly metastasise to the liver, omentum and peritoneum, with lymphatic spread being exceptional, unlike what was reported in the present case. A higher probability of adenopathy has been described in paediatric patients or when it occurs in association with Carney syndrome, but it is very rare in sporadic tumours that appear in adulthood. A study by Zachary E Stiles et al⁵ included 5,018 patients with gastrointestinal GIST, of whom 301 (6%) had lymphatic involvement. In this study, the presence of lymph node metastases was associated with increased mortality, although given that this is an infrequent finding, further studies are needed to define its prognostic and therapeutic implications.

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