

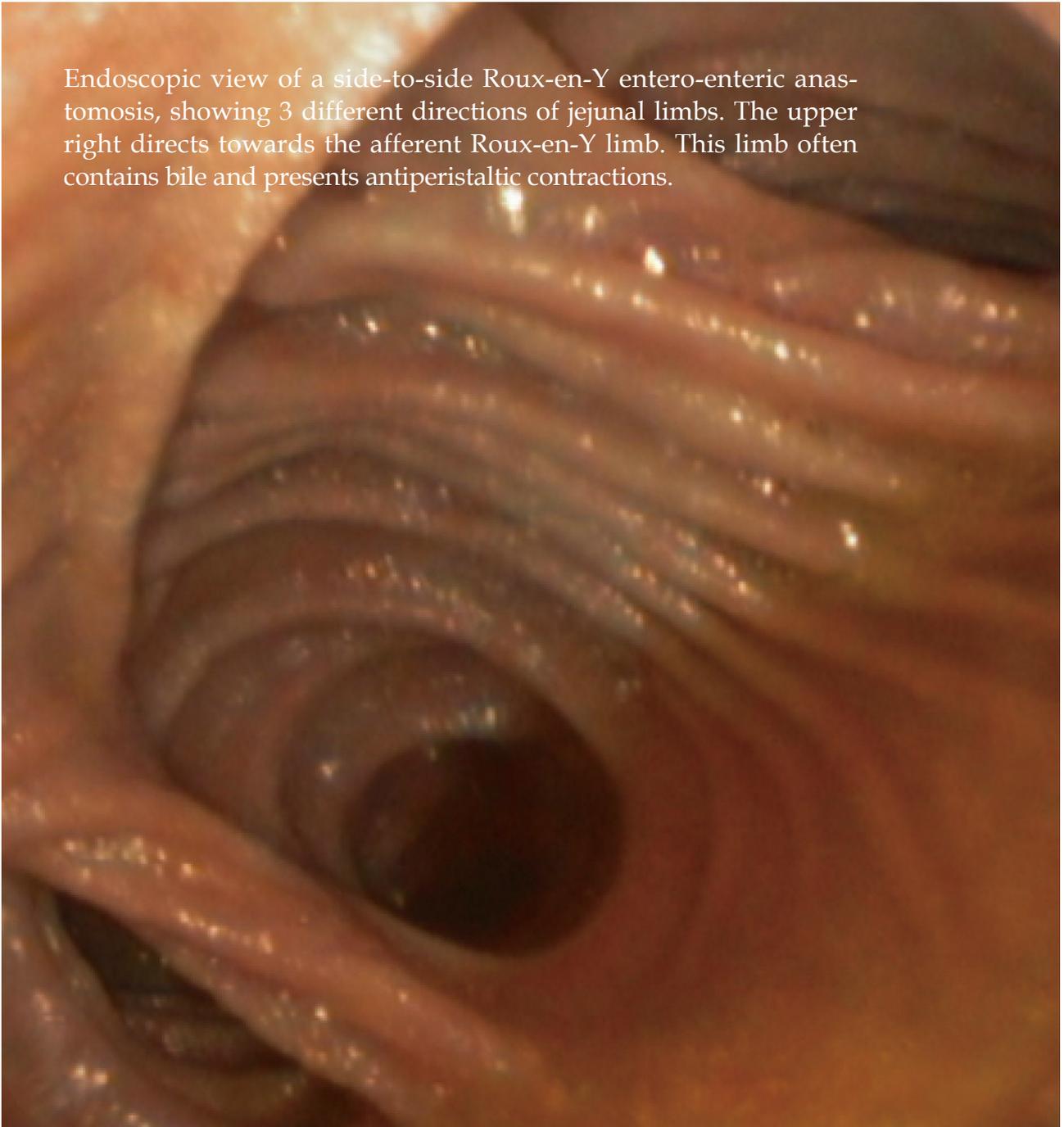
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Endoscopic view of a side-to-side Roux-en-Y entero-enteric anastomosis, showing 3 different directions of jejunal limbs. The upper right directs towards the afferent Roux-en-Y limb. This limb often contains bile and presents antiperistaltic contractions.



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## Endoscopic management of gastric dysplasia: Cutting edge technology needs a new paradigm

Seong Woo Jeon

Seong Woo Jeon, Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu 700-721, South Korea

Author contribution: Jeon SW solely contributed to this paper.  
Correspondence to: Seong Woo Jeon, MD, Assistant Professor of Gastroenterology, Kyungpook National University School of Medicine, Daegu 700-721, South Korea. [swjeon@knu.ac.kr](mailto:swjeon@knu.ac.kr)  
Telephone: +82-53-4205512 Fax: +82-53-4268773  
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### Abstract

There has been tremendous progress in endoscopic techniques for the management of premalignant or malignant gastric lesions. Gastric cancer remains the second most common cause of cancer related mortality worldwide. This means that there is a need for early detection and diagnosis of premalignant lesions or early cancer in clinical practice. Despite substantial development of endoscopic resection techniques, the management of gastric premalignant lesions is controversial because of the lack of consensus and accurate risk stratification. Future study of various aspects would clarify these issues but in the meantime we should reconsider the current algorithm approach for the management of gastric low grade dysplasia.

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**Key words:** Grade dysplasia; Endoscopic resection; Submucosal dissection

**Peer reviewer:** Philip Wai Yan Chiu, Associate Professor, Department of Surgery, Institute of Digestive Disease, Chinese University of Hong Kong, Prince of Wales Hospital, 30-32 Ngan Shing Street, Shatin, N.T., Hong Kong, China

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### INTRODUCTION

Gastric epithelial dysplasia (GED) is defined as noninvasive, neoplastic gastric epithelium. However, the term GED has become progressively complex and confusing because of differences in definitions and nomenclature that have been based on cytological, microscopic, endoscopic or gross features<sup>[1]</sup>. When the dysplastic lesion is flat or depressed the term dysplasia is used; if protruding from the mucosa, adenoma is used. These terms have been used for indicating the morphological type of the lesion and are considered as having same histology in clinical practice<sup>[2,3]</sup>.

There have been debates about the histological diagnostic criteria for gastric dysplasia or adenoma, especially between pathologists in Japan and the West<sup>[4]</sup>. The Vienna classification for gastric dysplasia was produced as a consensus for reducing the gap of the discrepancies between Western and Asian pathologists<sup>[5]</sup>. Ramification of the category according to the diagnostic criteria enabled us to reduce the gap in category 4 (high grade intraepithelial neoplasia, HGD) and 5 (carcinoma). However, discrepancy still exists in category 3 (low grade intraepithelial neoplasia, LGD). Although a designation of low-grade means a comparatively reduced risk of malignant transformation compared to high-grade, it should be kept in mind that a background intestinal metaplasia accompanying low grade dysplasia might be associated with an increased risk of malignancy<sup>[6]</sup>.

Endoscopic resection techniques have developed and there are almost no limits in endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) for the management of gastric neoplasia. The technical improvement in EMR/ESD procedures has enabled en bloc resection of the entire mucosal lesion regardless of its size and location in stomach<sup>[7]</sup>. The endoscopic management of HGD or carcinoma was well established with no controversy. However, EMR/ESD of gastric low grade adenoma may be controversial and resection of all these lesions demands costs and time. There are also patients

who are not candidates for ESD or EMR due to economic problems or physical limitations.

New techniques in therapeutic endoscopy demand an upgraded approach paradigm. So, taking into account all of this, the best management will be discussed.

## EPIDEMIOLOGY OF GASTRIC LGD

The prevalence of GED ranges widely according to region. In the region with the high risk of gastric cancer such as Korea and Japan, prevalence ranges from 9%-20% in contrast to the lower risk regions of up to 3.75%<sup>[8,9]</sup>. This difference can be explained by several factors such as genetics, incidence of helicobacter pylori infection and environmental factors<sup>[10]</sup>. Most of these gastric tumors are incidentally found during screening endoscopy in prevalent areas. GED has various morphologies on endoscopic findings: protruding or depressed; whitish or reddish; lobular or granular; and combining ulcer or not. These lesions might not be evident during endoscopy and repeat biopsy or EMR/ESD may be needed to confirm.

## NATURAL HISTORY OF GASTRIC EPITHELIAL DYSPLASIA

Proper management for GED needs the understanding of the natural course of this entity. GED (LGD or HGD) are regarded as precancerous lesions and the endoscopic management of HGD is uniform. However, the clinical course of LGD is variable and the transformation rate ranges from 0% to 23% (Table 1).

A recent study by Ruge *et al*<sup>[11]</sup> revealed that the risk of invasive gastric cancer increases with the histological grade of the non-invasive neoplasia. They included a total of 90 consecutive cases with LGD prospectively followed up. They excluded the patients in whom gastric cancer was detected within 12 mo from the initial diagnosis to rule out the chance of missed diagnosis at the initial endoscopy procedure. Of these cases, 78% of cases were no longer detected or unchanged; however, 17% (20/90) of cases evolved into gastric cancer. Evolution to invasive carcinoma was documented in 8 of 90 cases (8.9%) of LGD. This study is a prospective long-term follow up study of LGD, focusing on cancer risk. These results mean that although most of LGDs in stomach remain stable, during follow up they can progress in significant proportion.

However, this is not the case in a recent Japanese study<sup>[12]</sup>. This study included 48 lesions diagnosed as LGD or HGD on first biopsies. These lesions were followed for a median of 4.7 years. They reclassified the lesions according to the Vienna classification. Of the 38 cases of LGD, only 1 case showed progression to noninvasive carcinoma with the remaining cases unchanged. Even the HGD showed a stable course with only 1 case of intramucosal carcinoma. They insisted that LGD lesions have quite a low risk of progressing to HGD or noninvasive carcinoma and were never observed to progress to invasive

Table 1 Natural courses studies of low and high grade dysplasia progressing to carcinoma

	Low grade dysplasia	Mean interval to carcinoma	High grade dysplasia	Mean interval to carcinoma
Saraga <i>et al</i> <sup>[19]</sup>	2% (1/64)	4 yr	81% (7/21)	4 mo
Lansdown <i>et al</i> <sup>[20]</sup>	0% (0/7)	-	85% (11/13)	5 mo
Di Gregorio <i>et al</i> <sup>[21]</sup>	7% (4/73)	2 yr	60% (6/10)	11 mo
Kokkola <i>et al</i> <sup>[22]</sup>	0% (0/84)	-	67% (2/3)	1.5 yr
Rugge <i>et al</i> <sup>[11]</sup>	8.9% (8/90)	48 mo	69% (11/16)	30 mo
Yamada <i>et al</i> <sup>[12]</sup>	0% (0/38)	-	10% (1/10)	4.6 yr
Park <i>et al</i> <sup>[13]</sup>	11.5% (3/26)	3.7 yr	100% (1/1)	5.6 yr

carcinoma. Although this study is a long-term follow up study for gastric dysplasia, the diagnostic criteria should be considered and conclusions accepted with caution. As mentioned earlier, despite the efforts to overcome the gap between Western and Asian pathologists regarding the discrepancies in the concept of GED, there is still a lack of diagnostic pathological criteria. Overestimation of the pathological diagnosis could lead to the benign course of the lesion, especially in LGD.

Another Asian study revealed contrary results<sup>[13]</sup>. Twenty-six cases of gastric LGD were followed up for a median of 66 mo. Three cases out of 26 LGD progressed to invasive carcinoma. Four cases out of 26 LGD progressed to HGD. The author concluded that gastric intraepithelial neoplasia should be treated actively using recently advanced therapeutic endoscopic techniques, regardless of the degrees of dysplasia. Although this study is a small retrospective one, the proportion of progression to invasive carcinoma is similar to the study by Ruge *et al*<sup>[11]</sup>.

Although it requires years for a gastric LGD to progress into an invasive form and not all cases of LGD transform to advanced carcinoma, the recent advances in endoscopic resection can reduce the risk and cost of procedure and should be reconsidered as a first option for the management of gastric LGD. It may be sufficient to follow up the gastric neoplasia at a 1 year interval in cases of unavoidable observation.

## DISCREPANCY OF THE INITIAL BIOPSY WITH FINAL PATHOLOGY

When we consider EMR/ESD for gastric LGD or HGD, the concept of inaccuracy in a forceps biopsy should be kept in mind. Actually, the reactive changes may mimic the morphological appearance of GED and are well recognized as a pitfall in diagnosis<sup>[10]</sup>. Likewise, the pathological diagnosis of the gastric HGD by forceps biopsy probably means invasive carcinoma after EMR/ESD.

There are several studies regarding the discrepancy between forceps biopsy and final pathological diagnosis<sup>[7,14-18]</sup>. Park *et al* researched the possible risk factors of predicting malignant transformation of the gastric LGD. Eight of the 118 adenomas proved to have malignant foci. Univariate analysis revealed that location, histological

type, surface redness and degree of dysplasia of the lesion were significant predictors for malignant potential. In multivariate analysis, only the degree of dysplasia had significance. The author concluded that gastric HGD should be resected for possible malignancy.

Another large prospective study in a German group revealed that the size of tumor is important. They prospectively included 194 patients with 222 endoscopically removable gastric polyps ( $\geq 5$  mm) who underwent forceps biopsy and complete polypectomy. They excluded cases of fundic gland polyps and polyposis syndrome. Of the 222 polyps, histological examination of the polypectomy specimens revealed neoplasia in 19% (6% adenocarcinoma). The complete agreement was found in 124 cases (55.8%) and clinically important differentiation between tumor like lesions and neoplasia was possible in 90.5%. They insisted on complete removal by an experienced endoscopist of all epithelial gastric polyps larger than 5mm after thorough individualized risk benefit analysis. Most of the patients had no symptoms in this population. These results can be explained in two other aspects. The meticulous examination of the forceps biopsy samples by an experienced pathologist would be sufficient for a correct histological diagnosis without polypectomy. The other aspect is the problem of coexistence of malignant foci, as in 3.1% of the hyperplastic polyps in this study.

The recent study by Jung *et al* also mentioned the risk factors of malignant transformation in gastric LGD. This study included 114 patients with gastric LGD which was diagnosed at initial forceps biopsies. They divided these patients into two groups according to the post-EMR/ESD pathological diagnosis. The carcinoma group (63 cases) had distinct phenotypes such as depressed gross appearance, combined HGD, reddish surface and mucosal ulceration. In multivariate analysis, combined HGD was a significant independent predictor of carcinomas. Although all the gastric LGD could not be resected because of the patient's medical condition or equipment availability, these characteristics should be considered as an indication for endoscopic resection or be followed closely by available screening methods.

Contrary to the up-staging of the post-EMR/ESD diagnosis, one study mentioned down-staging after EMR/ESD<sup>[18]</sup>. Out of 633 patients treated with EMR or ESD, 20 patients (3.2%) were included in this study. The mean size of tumor was 6.4 mm. Sixty-five percent were LGD; the remainder was HGD or intramucosal carcinoma. Following endoscopic resection, no neoplasia was evident although only macroscopic lesions and no random biopsy cases were included in this study. The authors concluded that the tumors might have been small enough to be removed by the previous forceps biopsy.

All these studies regarding the discrepancy between the forceps biopsy and final pathological diagnosis are important in managing patients with gastric LGDs. When a forceps biopsy is performed on the lesion, more pieces mean more accuracy in diagnosis. However, it could hamper a procedure like ESD because of excessive scar formation resulting in the fibrosis. A few samples for for-

ceps biopsy diagnosis could not rule out sampling errors, like the hidden part of the iceberg. More validated studies using recently introduced instruments such as magnifying endoscopy, autofluorescence imaging and confocal endomicroscopy are needed to identify the high risk groups of hidden malignancy in lesions.

## CONCLUSION

EMR/ESD is gaining in popularity and substituted surgical policy on the management of early gastric cancer. More patients will benefit from screening programs for the early detection of gastric cancer and EMR/ESD is the leading technique at this point. Premalignant lesions would also be detected more during screening endoscopy. Assuming the progression of gastric LGDs to HGDs or carcinoma is not rare, close follow up strategies without informing the patients about endoscopic resection should be reconsidered. Given the availability of endoscopic management techniques and the problems of hidden malignancy in gastric LGDs, endoscopic management instead of an annual follow up strategy should be considered first in clinical practice. Future studies of molecular, genetic and morphological characteristics of gastric LGDs could be helpful in deciding management and stratifying the risk of progression.

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## Capsule endoscopy: Future horizons

Zvi Fireman

Zvi Fireman, Department of Gastroenterology, Hillel-Yaffe Medical Center, Hadera 38100, Israel

Zvi Fireman, Faculty of Medicine, The Technion - Institute of Technology, The Rappaport Faculty of Medicine, Haifa 31096, Israel

Author contribution: Fireman Z contributed solely to this paper.  
Correspondence to: Zvi Fireman, MD, Head, Department of Gastroenterology, Hillel Yaffe Medical Center, PO Box 169, Hadera 38100, Israel. [fireman@hy.health.gov.il](mailto:fireman@hy.health.gov.il)

Telephone: +972-4-6304480 Fax: +972-4-6304408

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Fireman Z. Capsule endoscopy: Future horizons. *World J Gastrointest Endosc* 2010; 2(9): 305-307 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v2/i9/305.htm> DOI: <http://dx.doi.org/10.4253/wjge.v2.i9.305>

### Abstract

Capsule endoscopy (CE) was launched at the beginning of this millennium and has since become a well established methodology for evaluating the entire small bowel for manifold pathologies. CE far exceeded early expectations by providing a tool for establishing the correct diagnosis for elusive gastrointestinal (GI) conditions such as obscure GI bleeding, Crohn's disease, polyposis syndrome and others. Contemporary CE, like radiology, gives results that can only be read, unlike conventional endoscopic procedures which enable concomitant biopsy when indicated. This is one of the major limitations of the technique. The ideal CE should improve the quality of the image and have a faster frame rate than the currently available one. There should be a therapeutic capsule capable of performing a biopsy, aspirating fluid, delivering drugs as well as measuring the motility of the small bowel wall. Another major leap forward would be the capability of remote control of the capsule's movement in order to navigate it to reach designated anatomical areas for carrying out a variety of therapeutic options. Technology for improving the capability of the future generation capsule is almost within grasp and it would not be surprising to witness the realization of these giant steps within the coming decade.

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### INTRODUCTION

Capsule endoscopy (CE) had been proven to be a safe and painless procedure that is superior to several other imaging modalities for diagnosing small bowel pathologies such as small bowel follow-through X-ray, colonoscopy with ileoscopy, computerized tomographic enterography, magnetic resonance enteroclysis and push-enteroscopy<sup>[1,2]</sup>. Since the emergence of CE, more than 1 000 000 capsules have been swallowed worldwide and nearly 1000 peer-reviewed publications have appeared in the literature. The ideal CE of the gastroenterologist's imagination should be capable of performing an ordinary biopsy as well as carry out an online analysis (an "optical" biopsy) and "stop" bleeding by an adrenaline injection, a heat probe, argon plasma coagulation, *etc.* The ultimate capsule would include special detectors for white blood cells and be capable of checking oncological markers (e.g. CEA, CA 19-9), perform serology tests (e.g. anti-endomysial, IgE) and measure various cytokines, pH, temperature and pressure, in addition to delivering drugs. The capsule's motility feature in the small bowel may open a window to study the pathophysiology of relatively elusive medical entities such as irritable bowel syndrome<sup>[3-7]</sup>. Finally, the optimal capsule

needs to contain a computerized system for automatic detection of pathologies such as the design of a Holter electrocardiographic recording in order to overcome the drawback of time-consuming viewing the video.

## IDEAL CAPSULE ENDOSCOPY

Solutions of fundamental problems in CE technology have not been forthcoming since its promising entrance into GI diagnostics. Has a technological plateau been reached? Probably not. Until the next breakthrough, however, CE remains a diagnostic tool that has yet to realize its potential. A look at the history of GI endoscopy reminds us that the first step had been limited to no more than viewing the organ. Only later did it develop into a tool for biopsy and then a conduit through which to perform therapeutic procedures such as polypectomy, sphincterotomy and others. Will the capsule of the future replace single or double balloon enteroscopy? According to a number of authors, the answer is probably yes<sup>[3,6,7]</sup>.

What, then, would be the ideal capsule of the gastroenterologist's wildest imagination? Would we prefer a single capsule that, in one "shot", can give us the entire view from the oral cavity to the anal canal, or are we hoping that some day there will be an "intelligent" capsule that specializes in each section of the GI tract? Unfortunately, the anatomical and physiological differences in the GI tract make it impossible to use the same capsule for both purposes. Small bowel, esophageal and colonoscopy capsules are now commercially available. The latter two are equipped with miniature cameras on both ends of two video cameras.

How we would love to be able to pinpoint drug deliveries in specific diseases such as Crohn's disease! The problem is that it would have to be done daily over a long period and this would be time consuming and costly. A pre-programmed non-viewing (i.e. no camera) capsule for drug delivery would be much cheaper and one can imagine a combination of viewing and non-viewing capsules that can be used to make this treatment efficient and cost-effective. This possibility of drug delivery would open enormous windows of opportunity to pharmaceutical companies. For clinicians, the capsule's motility feature in the small bowel would open a window to study the pathophysiology of relatively elusive medical entities such as irritable bowel syndrome. Malagelada *et al*<sup>[8]</sup> were the first to publish their findings on CE motility in the clinical setting and they found that CE was useful in diagnosing patients with irritable bowel syndrome.

Next in our dream of CE are zooming or magnification capabilities. Why not? Think of chromo-endoscopy, narrow band imaging, ultrasound imaging and the delivering of therapy including tissue coagulation and immunologically or chemically targeted optical recognition of malignancy as it exists in endoscopy, capable of spraying fluid (methylene blue, Lugol solution, *etc.*) in specific areas of the small bowel. At present, the capsule cannot obtain biopsies, aspirate fluid or brush lesions for cytology. These

techniques require real-time viewing as well as radio-controlled triggering and remote controlled capsule manipulation if they are to be used with precision. However, optical biopsy seems feasible<sup>[9]</sup>. We can easily visualize our capsule eventually becoming a complete miniature laboratory with the functions of bio-sensing luminal contents and biopsy (probably by optical technologies) as well.

## ENERGY SUPPLY

Technological advances, particularly in reducing the size of components and improving power management, will be needed before the next generation of capsule endoscopy devices can be developed. The quality of current CE images is inferior to that of conventional endoscopes and the solution awaits advances in microelectronics that will lead to image sensors with a smaller pixel size that enable higher resolution. In addition, current CE systems use image data compression which causes blurring at the edges of objects and leads to lower image quality, a major limitation of CE. In particular, depletion of the two silver oxide batteries used in current devices may prevent complete imaging of the small intestine if the pill remains in the stomach for too long. The problem becomes most apparent by the inability to view the cecum (the marker of a complete examination) in 10%-15% of CE examinations of the small bowel<sup>[1,2]</sup>. This will eventually be overcome by using power transfer methods from outside the body. In the short term, this problem can partly be solved by using more efficient power management algorithms that enable an 11 h recording time. There have been important "breakthroughs" in battery design with the advent of carbon nanotubes (Buckytubes) which have the intrinsic characteristics desired in the material used as electrodes in batteries and capacitors. Buckytubes have an enormous surface area (approximately 1000 m<sup>2</sup>/g) and good electrical conductivity. Their linear geometry makes the surfaces highly accessible to the electrolyte. It may be that their application will lead to enhanced battery design and better power management to give the capsule the power required for additional performance and functions for improving the quality of the image<sup>[7]</sup>.

Other methods that are under consideration for development for solving imaging issues include control units that vary the frame rate. One example is the OMOM capsule, developed at Chongqing Jinshan Science and Technology Group (Chongqing, China), which can switch from 0.5 frames per second (fps) inside the stomach to 2 fps after entering the pylorus<sup>[9]</sup>. In a well-conducted randomized prospective study of 50 patients in China, the cecum was visualized in the 25 subjects who ingested the capsule in the switching frame rate mode compared with 18 of 25 in whom the pill functioned at a steady frame rate of 2 fps<sup>[10]</sup>.

The benefit from size reduction and power efficiency is best exemplified by MiroCam by Intromedic (Seoul, South Korea). This is the first endoscopic capsule that uses the human body instead of radiofrequency to trans-

mit data, reducing power consumption. In the first clinical trial on 45 patients in South Korea, MiroCam captured images from the whole small intestine as far as the cecum in all the subjects. Because the device does not use image compression, the bowel mucosa was viewed without blurring or distortion in over 90% of patients<sup>[11]</sup>. This system also uses fewer components for remote transmission, thus saving space for the possible addition of modules for biopsy or locomotive guidance<sup>[11]</sup>.

All in all, the technical shortcomings are quite straightforward and so we have every reason to believe that CE will be able to exploit the energy and enthusiasm of modern technology to deal with them. It is only a matter of time.

## PROPELLING THE CAPSULE

We eagerly look forward to the day that we will be able to “control and steer” the CE as endoscopists are able to do in standard endoscopy. This would give us control in maintaining the capsule steady in a selected area and hold the view in order to have more time to examine the opposite wall of the bowel. Miniaturization of capsule components and power consumption are also pivotal to tackling the biggest challenge of all, that of active capsule locomotion. Two research projects supported by the European Union are currently pursuing this goal. One is VECTOR (Versatile Endoscopic Capsule for gastrointestinal TumOr Recognition and therapy) and the other is NEMO (Nano-based capsule-Endoscopy with Molecular Imaging and Optical biopsy). The former aims to develop a self-propelled miniaturized robotic pill for advanced diagnostics and treatment in the digestive tract. Over the last few months, the topic of the feasibility and effectiveness of the combined use of external static magnetic fields to achieve wirelessly controllable and precise camera steering has been published<sup>[12-14]</sup>. In addition to investigating capsule maneuvering, the second study is looking into the detection of surface and deep-seated pathology by photonic technologies that enable optical biopsies. This would eliminate the need to take biopsy specimens and perform histological examination<sup>[7]</sup>. Goals such as these make it somewhat difficult to contain our impatience for their realization!

## CONCLUSION

Technological advances together with improving power management will be needed before the next generation of CE devices can be developed. Advances in microelectronics will produce image sensors with smaller pixel sizes and resultant higher resolution to considerably enhance the image quality provided by CE which is cu

rrently inferior to that of conventional endoscopes. Future gastroenterologists will have a number of types of capsules from which to choose according to whether the purpose of the evaluation is diagnostic and/or therapeutic. We are confident that our expectations of CE will soon become a reality and that CE will enrich the gastroenterologist’s armamentarium, providing “Star Wars” patient care in which almost all things are possible.

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## ERCP in acute pancreatitis: What takes place in routine clinical practice?

Armando Gabbrielli, Raffaele Pezzilli, Generoso Uomo, Alessandro Zerbi, Luca Frulloni, Paolo De Rai, Laura Castoldi, Guido Costamagna, Claudio Bassi, Valerio Di Carlo

Armando Gabbrielli, Luca Frulloni, Claudio Bassi, Department of Surgical and Gastroenterological Sciences, University of Verona, Verona 37100, Italy

Raffaele Pezzilli, Department of Digestive Diseases and Internal Medicine, S. Orsola-Malpighi Hospital, Bologna 40138, Italy

Generoso Uomo, Department of Internal Medicine, Ospedale A. Cardarelli, Naples 80100, Italy

Alessandro Zerbi, Department of Surgery, Humanitas Hospital, Milan 20100, Italy

Paolo De Rai, Laura Castoldi, Department of Emergency Surgery, Fondazione IRCCS Maggiore, Mangiagalli and Regina Elena Hospital, Milan 20100, Italy

Guido Costamagna, Digestive Endoscopy Unit, "Agostino Gemelli" University Hospital, Catholic University of Rome, Rome 00100, Italy

Valerio Di Carlo, Department of Surgery, University Vita e Salute, IRCCSS. Raffaele, Milan 20100, Italy

**Author contributions:** Gabbrielli A, Pezzilli R, Uomo G, Zerbi A, Frulloni L, De Rai P, Castoldi L, Costamagna G, Bassi C and Di Carlo V designed the study, coordinated and collected all the human material and revised the data; Pezzilli R and Gabbrielli A analyzed the data and interpreted the results; and Pezzilli R and Gabbrielli A wrote the manuscript.

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**Correspondence to:** Raffaele Pezzilli, MD, Department of Digestive Diseases and Internal Medicine, Sant'Orsola-Malpighi Hospital, University of Bologna, Via Massarenti, 9, Bologna 40138, Italy. [raffaele.pezzilli@aosp.bo.it](mailto:raffaele.pezzilli@aosp.bo.it)

Telephone: +39-51-6364148 Fax: +39-51-6364148

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### Abstract

**AIM:** To evaluate the data from a survey carried out in Italy regarding the endoscopic approach to acute pancreatitis in order to obtain a picture of what takes place after the release of an educational project on acute pancreatitis sponsored by the Italian Association for the Study of the Pancreas.

**METHODS:** Of the 1 173 patients enrolled in our survey, the most frequent etiological category was biliary forms (69.3%) and most patients had mild pancreatitis (85.8%).

**RESULTS:** 344/1 173 (29.3%) underwent endoscopic retrograde cholangiopancreatography (ERCP). The mean interval between the onset of symptoms and ERCP was  $6.7 \pm 5.0$  d; only 89 examinations (25.9%) were performed within 72 h from the onset of symptoms. The main indications for ERCP were suspicion of common bile duct stones (90.3%), jaundice (44.5%), clinical worsening of acute pancreatitis (14.2%) and cholangitis (6.1%). Biliary and pancreatic ducts were visualized in 305 patients (88.7%) and in 93 patients (27.0%) respectively. The success rate in obtaining a cholangiogram was statistically higher ( $P = 0.003$ ) in patients with mild acute pancreatitis (90.6%) than in patients with severe disease (72.2%). Biliary endoscopic sphincterotomy was performed in 295 of the 305 patients (96.7%) with no difference between mild and severe disease ( $P = 0.985$ ). ERCP morbidity was 6.1% and mortality was 1.7%; the mortality was due to the complications of acute pancreatitis and not the endoscopic procedure.

**CONCLUSION:** The results of this survey, as with those carried out in other countries, indicate a lack of compliance with the guidelines for the indications for interventional endoscopy.

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**Key words:** Acute pancreatitis; Epidemiology, Endoscopic retrograde cholangiopancreatography; Data collection

**Peer reviewer:** Majid A Almadi, MD, Department of Gastroenterology Division, McGill University, McGill University Health Center, Montreal, H3A 1A1, Canada

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## INTRODUCTION

The pathogenesis of acute biliary pancreatitis (ABP) is still unknown; several hypotheses have been made such as transient obstruction of both the common bile duct and the pancreatic duct, reflux of bile and duodenal content into the pancreatic duct and, finally, increase in the hydrostatic pressure in the pancreatic duct<sup>[1,2]</sup>. The severity of biliary pancreatitis probably depends on individual predisposition but the duration of bile duct obstruction seems to be the main factor contributing to the development of the severity of pancreatitis, as suggested by animal models and human studies<sup>[3-6]</sup>. The decision for the management of patients with predicted severe acute biliary pancreatitis is still a matter of debate; even if endoscopic treatment appears to be safe and effective and may be the definitive treatment in patients with acute pancreatitis with a high anesthesiological risk<sup>[7]</sup>. Several guidelines on acute pancreatitis recommend that urgent therapeutic endoscopic retrograde cholangiopancreatography (ERCP) be performed within 72 h of admission for all patients with predicted severe ABP, whether or not cholangitis is present<sup>[8-10]</sup>. However, two recent meta-analyses<sup>[11,12]</sup> suggested that early ERCP, with or without endoscopic sphincterotomy (ES), had no beneficial effect in patients with predicted mild or severe acute biliary pancreatitis without cholangitis or persistent biliary obstruction; this point of view has also been supported by two position papers<sup>[10,13]</sup>. However, what happens in clinical practice is not completely known. The majority of studies come from the United Kingdom; Mofidi *et al.*<sup>[14]</sup> have reported that physicians complied with all the UK guidelines except for urgent ERCP for severe acute pancreatitis because only 48% of patients underwent ERCP within 72 h due to difficulties in transferring patients to specialized centers capable of performing and providing ERCP outside normal weekday working hours. The two above-mentioned factors may have contributed to these results and these results were also confirmed by another study carried out in England<sup>[15]</sup>. For this reason, we believe the data from an observational study on acute pancreatitis carried out in Italy to be of particular interest; the results on the diagnosis and treatment of acute pancreatitis were published in 2007<sup>[16,17]</sup>. Complete data on the endoscopic approach to the disease have never been reported; of importance, the study was carried out after the release of the recommendations of the Italian Association of the Study of the Pancreas (AISP) in 1999<sup>[18]</sup> and before the release of the new position statement of the same Society in 2008<sup>[10]</sup>. Thus, these data represent a picture

of what takes place during the course of this educational project on acute pancreatitis sponsored by the AISP.

## MATERIALS AND METHODS

The present study involved 56 Italian public hospitals, equally distributed throughout Italy and almost all of them had access to the same facilities. *Ad hoc* software including 530 items designed by the scientific committee of the study was furnished to each participating center. Of these 530 items, 64 (12%) regarded specific questions about endoscopic treatment. All cases of acute pancreatitis consecutively observed in the various centers during the period from December 2001 to November 2003 were included in the study.

The diagnosis of acute pancreatitis was based on clinical (onset of pancreatic-type pain), biochemical (a three-fold increase of amylase and/or lipase) and radiological (ultrasonography, computer tomography scan, magnetic resonance) findings<sup>[16]</sup>. The disease was classified into mild and severe forms according to Atlanta criteria<sup>[19]</sup>. The etiological classification of the disease was made according to the United Kingdom guideline<sup>[8]</sup>.

Data were collected and tabulated centrally; a careful monitoring process was carried out during the period of the study. At the end of the study, additional quality control regarding the completeness and congruence of each single chart was carried out in order to exclude cases with incomplete and/or inconsistent charts. One of the endpoints of the study was to evaluate, in detail, the endoscopic approach in patients with acute pancreatitis in Italy.

### Statistical analysis

Data are presented as mean  $\pm$  SD and frequencies. Statistical analysis was carried out using the chi-square test and Fisher's exact test. Data were run on SPSS version 10. Differences with a *P* value of less than 0.05 were considered significant.

## RESULTS

One thousand one hundred and seventy-three patients (581 females and 592 males; mean age  $\pm$  SD: 62.0  $\pm$  18.2 years) were considered for the present study. Biliary forms represented the most frequent etiology (813 cases, 69.3%) while alcoholic forms occurred in only 77 cases (6.6%); the remaining etiologies (post-surgical, post-endoscopic cholangiopancreatographic, traumatic, hyperlipemic, drug-induced and from pancreas divisum) accounted for 83 cases (7.1%). Two hundred cases (17.1%) remained without a definite etiological factor (idiopathic forms).

One thousand and six patients (85.8%) had mild pancreatitis and 167 (14.2%) had the severe form. The mean interval between the onset of pain and hospital admission was not statistically significant (*P* = 0.374) between patients with mild (14.9  $\pm$  37.2 h) and those with severe pancreatitis (17.8  $\pm$  39.1 h). Of the 1 173 patients, 344 (29.3%; males 140, females 204, mean age  $\pm$  SD: 65.7  $\pm$

**Table 1** Indications for endoscopic retrograde cholangiopancreatography in the 344 patients with acute pancreatitis according to the etiology of the disease<sup>1</sup>

	Biliary acute pancreatitis (N = 320)		Non-biliary acute pancreatitis (N = 24)		Overall (N = 344)	
	n	Frequency	n	Frequency	n	Frequency
Suspicion of common bile duct stones	289	89.4	17	70.8	306	89
Jaundice	153	47.8	-	-	153	44.5
Clinical worsening of acute pancreatitis	45	14.1	4	16.7	49	14.2
Cholangitis	21	6.6	-	-	21	6.1
Disruption of the main pancreatic duct	-	-	2	8.3	2	0.6
Suspicion of malignancy	-	-	1	4.2	1	0.3

<sup>1</sup>More than one indication may be present in the same patient.

**Table 2** Distribution of different techniques used for biliary sphincterotomy according to the severity of the acute pancreatitis

	Mild acute pancreatitis (N = 269)		Severe acute pancreatitis (N = 26)		P value
	n	Frequency	n	Frequency	
Standard sphincterotomy	219	81.4	23	88.5	0.531
Precut	21	7.8	2	7.7	
Standard sphincterotomy + Precut	29	10.8	1	3.8	

16.2 years) underwent ERCP. The mean interval between the onset of symptoms and ERCP was  $6.7 \pm 5.0$  d and the mean interval between hospital admission and ERCP procedure was  $5.7 \pm 5.0$  d. Eighty-nine examinations (25.9%) were performed within 72 hours from the onset of symptoms.

Of the 344 patients, 320 (93.0%) patients had biliary pancreatitis (288, 90.0% had mild acute pancreatitis; 32, 10.0% had the severe form). As reported in Table 1, the main indication for ERCP was radiological and/or biochemical suspicion of common bile duct stones in 90.3% followed by jaundice (47.8%), clinical worsening of acute pancreatitis (14.1%) and cholangitis (6.6%). In 24 patients suffering from non-biliary pancreatitis (4 with severe disease), the indications for the procedure were suspicion of common bile duct stones in 17 patients, worsening of the disease in 4, disruption of the main pancreatic duct in 2 and suspicion of malignancy in the remaining one.

The endoscopic aspect of the papilla was reported in 303 of the 344 patients (88.1%) and appeared pathological in 62 cases (20.5%). In particular, in 41 patients (66.1%) there was an aspect of recent stone migration while, in the remaining 21 (33.9%), an impacted stone was found.

Biliary and pancreatic ducts were visualized in 305 (88.7%) and in 93 patients (27.0%) respectively. A pathological cholangiogram was reported in 236 of the 305 patients (77.4%). The main findings reported in 222 of the 236 patients (94.1%) were: common bile duct stones in 172 (77.5%) patients (5 of whom had intrahepatic stones) and dilation of the common bile duct in 50 (22.5%). The rate of success in obtaining a cholangiogram was statistically higher ( $P = 0.003$ ) in patients with mild acute pancreatitis (279/308; 90.6%) than in patients with severe disease (26/36; 72.2%).

In the 93 patients in whom the main pancreatic duct was visualized, two patients had pancreas divisum and three had a disruption of the Wirsung duct associated with necrotizing pancreatitis while the majority of patients had a normal main pancreatic duct (88/93; 94.6%).

Biliary endoscopic sphincterotomy was performed in 295 of the 305 patients (96.7%) in whom the common bile duct was visualized: in 269 cases out of 279 (96.4%) with mild pancreatitis and in all 26 patients with severe disease ( $P = 0.985$ ).

Biliary endoscopic sphincterotomy was performed for the following reasons (more than one indication may be present in the same patient): common bile duct stones in 168/295 patients (57.0%), biliary sludge in 173/295 (58.6%), cholangitis in 16/295 (5.4%) and high surgical risk in order to prevent further attacks of pancreatitis in 3/295 (1.0%).

The technique of biliary sphincterotomy was standard in 242/295 (82.0%), precut in 23/295 (7.8%) and precut associated with standard 30/295 (10.2%). The distribution of these different techniques did not differ ( $P = 0.531$ ) in mild and severe pancreatitis (Table 2).

Complete clearance of the common bile duct was achieved in all 168 patients with biliary stones; in 161 of the 168 (95.9%), patient clearance was obtained at the first attempt. A nasobiliary drain was inserted in 28 of the 295 patients (9.5%) for retained stones or transient distal stenosis of the common bile duct due to pancreatic head edema.

Morbidity of the endoscopic procedure was 6.1% (11/344): nine bleeds, one retroperitoneal perforation and one acute cholecystitis. The complications were equally distributed between mild and severe disease and all were treated conservatively.

Mortality in the patients who underwent operative endo

**Table 3** Number of cases and respective frequency of patients who underwent endoscopic retrograde cholangiopancreatography in the two Italian surveys

	Survey 1996-2000 <sup>21</sup>			Present survey 2001-2003		
	Overall population (N = 1005)	Mild AP (n = 753)	Severe AP (n = 252)	Overall population (N = 1173)	Mild AP (N = 1006)	Severe AP (N = 167)
	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Interventional ERCP	646/1005 (64.3%)	482/753 (64.0%)	164/252 (65.1%)	344/1173 (29.3%)	308/1006 (30.6%)	36/167 (21.6%)
Interventional ERCP within 72 h	293/646 (45.4%)	227/482 (47.1%)	66/164 (40.2%)	89/344 (25.9%)	69/308 (22.4%)	20/36 (55.6%)

ERCP: endoscopic retrograde cholangiopancreatography; AP: acute pancreatitis.

scopy was 1.7% (6 out of 344). All the patients who died had severe pancreatitis and mortality was due to the complications of acute pancreatitis and not to the endoscopic procedure.

Eighty-three patients underwent ERCP and cholecystectomy (laparoscopic or open cholecystectomy) during the same hospitalization; ERCP and cholecystectomy were performed within  $5.7 \pm 5.3$  d and  $10.4 \pm 5.8$  from hospital admission respectively.

## DISCUSSION

### Practical and technical considerations

Firstly, it should be pointed out that, of the 344 patients who underwent ERCP, only relatively few examinations were performed within 72 h from the onset of symptoms and this represents a clear deviation from the largely accepted guidelines (Table 3)<sup>[18,20]</sup>. Furthermore, comparing the data of the present survey with those previously published<sup>[21]</sup>, we found that the number of ERCPs carried out was lower in the period from 2001 to 2003 (29.3%) than the number carried out from 1996 to 2000 (64.3%) and the number of interventional ERCPs carried out within 72 h, especially in patients with the severe form, was also equally low (Table 3). These data are similar to those reported in UK studies in which a check on the adherence of clinicians to the published guidelines was carried out<sup>[14,15,22-24]</sup>. These data clearly represent a deviation from the national recommendations or guidelines released in Italy and in the United Kingdom<sup>[18,20]</sup>. From a practical point of view, common bile duct visualization was obtained in about 90% of patients and biliary sphincterotomy was carried out in 96.7% of the patients. However, these findings should not fool us because the rate of success in obtaining a cholangiogram was significantly higher (90.6%) in patients with mild acute pancreatitis than in those with severe disease (72.2%), even if the rate of biliary endoscopic sphincterotomy was not different in patients with mild and severe pancreatitis. The high rate of success of endoscopic sphincterotomy may be due to the skill of the endoscopists who were able to perform not only the standard technique but also the precut in about 20% of the examinations. The skill of the endoscopists is also demonstrated by the low morbidity (6.1%) rate of the procedure (equally distributed between mild and severe disease).

### Clinical considerations

As suggested by Petrov *et al.*<sup>[25]</sup>, the trials considered for their meta-analysis in assessing the benefit of ERCP in acute biliary pancreatitis used different definitions for acute cholangitis and included different subgroups of patients with acute biliary pancreatitis. Folsch *et al.*<sup>[26]</sup> excluded all patients with a bilirubin greater than 5 mg per deciliter who might theoretically benefit from interventional endoscopy, Neoptolemos *et al.*<sup>[27]</sup> included all patients with acute pancreatitis and presented separate data on patients without acute cholangitis and Oria *et al.*<sup>[28]</sup> included only patients with acute biliary pancreatitis and clinical evidence of bilio-pancreatic obstruction with out acute cholangitis. The same problems of the above-mentioned randomized studies were observed in our survey; only a minority of patients underwent interventional endoscopy for cholangitis (6.6%) and 50% of subjects underwent ERCP for the presence of jaundice (a clear sign of cholestasis) whereas the most frequent indication for ERCP (90%) was suspicion of common bile duct stones. We believe that this situation reflects the fact that, at the time of the survey, the indications for ERCP in acute pancreatitis were probably misleading for several physicians<sup>[18]</sup>; in fact, they have been revised in the recent AISP position statement<sup>[10]</sup>.

### Endoscopic and surgical approaches in patients with gallstones

As suggested by a number of guidelines<sup>[8-10,13,18]</sup>, a combined approach (ERCP plus laparoscopic/open cholecystectomy) seems to be the most logical and it was proven suitable in mild pancreatitis. The delay of 4 d between endoscopy and surgery observed in our survey appears slightly too long and reflects some difficulties in planning early surgical procedures in Italy and in transferring patients from medical to surgical departments. Another important fact is that the majority of patients with mild acute pancreatitis do not have their gallbladder removed during the same hospitalization after the attack of acute pancreatitis. It should be pointed out that the endoscopic approach may be the only and definitive treatment in patients with a high anesthesiological risk and in those with advanced age for preventing further attacks of acute pancreatitis.

### Suggestions for the future

More effort needs to be made by national and interna-

tional scientific societies and by the National Health Services to apply the guidelines released in order to decrease the number of unnecessary ERCP examinations, thus saving resources. However, we should also emphasize that the guidelines should be revised for the endoscopic treatment of acute biliary pancreatitis. In fact, endoscopic ultrasonography (EUS) has emerged as an accurate diagnostic alternative to ERCP and, as demonstrated by the results of recent meta-analyses<sup>[29]</sup>, the use of EUS significantly reduced the risk of overall complications of interventional ERCP; by performing EUS first, ERCP may be safely avoided in two-thirds of patients with suspected common bile duct stones.

In conclusion, the results of various surveys carried out in Europe indicate a lack of compliance with the guidelines regarding the indications for interventional endoscopy. We believe that further effort should be made by scientific societies and by the National Health Services to release updated guidelines and evaluate their correct application in clinical practice.

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## COMMENTS

### Background

The decision for the management of patients with predicted severe acute biliary pancreatitis is still a matter of debate, even if endoscopic treatment appears to be safe and effective and may be the definitive treatment in patients with acute pancreatitis with a high anesthesiological risk.

### Research frontiers

To evaluate the data of a survey carried out in Italy regarding the endoscopic approach to acute pancreatitis in order to obtain a picture of what takes place after the release of an educational project on acute pancreatitis sponsored by the Italian Association for the Study of the Pancreas.

### Innovations and breakthroughs

The results of the Italian nation-wide survey indicate a lack of compliance with the guidelines for the indications for interventional endoscopy.

### Applications

Further effort should be made by scientific societies and by the National Health Services to release updated guidelines and evaluate their correct application in clinical practice.

### Terminology

The trials considered for the meta-analyses in assessing the benefit of endoscopic retrograde cholangiopancreatography (ERCP) in acute biliary pancreatitis used different definitions with respect to acute cholangitis and included different subgroups of patients with acute biliary pancreatitis; thus definitive conclusions cannot be drawn from what happens in routine clinical practice.

### Peer review

This study addresses an important issue for endoscopic practice although the current literature does not provide definitive conclusions on the utility of ERCP in acute biliary pancreatitis. The number of events in this study is large and this adds further value to the conclusions.

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## Comparison between double-balloon and single-balloon enteroscopy in therapeutic ERC after Roux-en-Y entero-enteric anastomosis

Tom G Moreels, Paul A Pelckmans

Tom G Moreels, Paul A Pelckmans, Division of Gastroenterology and Hepatology, Antwerp University Hospital, Wilrijkstraat 10, Antwerp B-2650, Belgium

Author contributions: Moreels TG contributed solely to this paper under the direct supervision of Pelckmans PA.

Correspondence to: Tom G Moreels, MD, PhD, Division Gastroenterology and Hepatology, Antwerp University Hospital, Wilrijkstraat 10, Antwerp B-2650,

Belgium. tom.moreels@uza.be

Telephone: +32-3-8213323 Fax: +32-3-8214478

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### Abstract

**AIM:** To compare the efficacy of double-balloon enteroscopy (DBE) and single-balloon enteroscopy (SBE) in therapeutic endoscopic retrograde cholangiography (ERC) in patients with Roux-en-Y entero-enteric anastomosis.

**METHODS:** Retrospective analysis of our patient cohort revealed 4 patients with enterobiliary anastomosis and Roux-en-Y entero-enteric anastomosis who underwent repeated ERC with DBE and SBE because of recurrent cholangitis.

**RESULTS:** A total of 38 endoscopic retrograde cholangiopancreatography procedures were performed in 25 patients with Roux-en-Y entero-enteric anastomosis. DBE was used in 29 procedures and SBE in 9. The 4 patients who underwent repeated ERC with DBE and SBE suffered from recurrent cholangitis due to stenosis of the enterobiliary anastomosis. ERC was performed repeatedly to achieve balloon dilation with/without biliary stone extraction and multiple stent placement at the level of the enterobiliary anastomosis. In all 4 patients DBE and SBE were equally successful. Compared to DBE, SBE was equally effective in passing the Roux-

en-Y entero-enteric anastomosis, reaching the enterobiliary anastomosis and performing therapeutic ERC.

**CONCLUSION:** This retrospective comparison shows that DBE and SBE are equally successful in the performance of therapeutic ERC at the level of the enterobiliary anastomosis after Roux-en-Y entero-enteric anastomosis.

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**Key words:** Roux-en-Y; Double-balloon enteroscope; Single-balloon enteroscope; Endoscopic retrograde cholangiopancreatography

**Peer reviewers:** David Friedel, MD, Gastroenterology, Winthrop University Hospital, 222 Station Plaza North, Suite 428, Mineola, NY 11501, United States; C Mel Wilcox, MD, Professor, Director, UAB Division of Gastroenterology and Hepatology, 703 19th Street South, ZRB 633, Birmingham, AL 35294-0007, United States

Moreels TG, Pelckmans PA. Comparison between double-balloon and single-balloon enteroscopy in therapeutic ERC after Roux-en-Y entero-enteric anastomosis. *World J Gastrointest Endosc* 2010; 2(9): 314-317 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v2/i9/314.htm> DOI: <http://dx.doi.org/10.4253/wjge.v2.i9.314>

### INTRODUCTION

Roux-en-Y entero-enteric anastomosis of the small bowel is a standard surgical technique for draining the biliary system *via* an afferent jejunal limb<sup>[1]</sup>. However, the enterobiliary anastomosis is excluded from conventional endoscopic access. Therefore, biliary complications such as stenosis or stones are often dealt with surgically.

The recently developed technique of balloon-assisted enteroscopy allows deep and even complete intubation of

the small bowel<sup>[2,3]</sup>. Fujinon double-balloon enteroscopy (DBE) has been commercially available since 2003 and Olympus single-balloon enteroscopy (SBE) since 2007. Both types of balloon-assisted enteroscopes also allow intubation of the Roux-en-Y afferent limb to perform endoscopic retrograde cholangiopancreatography (ERCP) although with variable success rates<sup>[4-12]</sup>. However, due to the complex nature of these procedures, head to head comparison studies of DBE and SBE to perform ERCP after Roux-en-Y is not available.

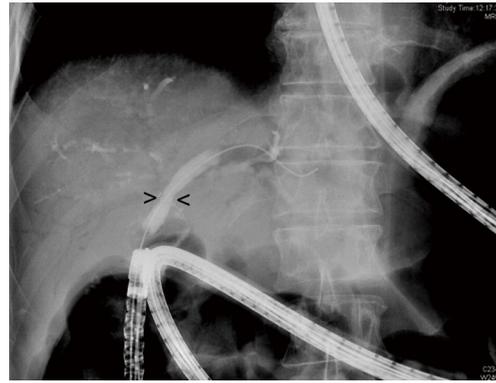
We present a case series of 4 patients who underwent successful ERC using DBE, and successful repeated ERC using SBE. All procedures were performed because of cholangitis due to stenosis with/without biliary stones at the level of the enterobiliary anastomosis with Roux-en-Y reconstruction. Endoscopic treatment consisted of balloon dilation of the enterobiliary anastomosis and multiple stent placement.

## MATERIALS AND METHODS

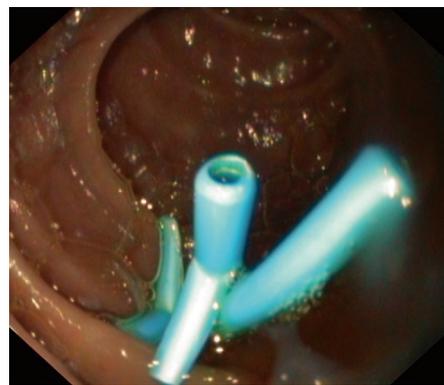
From 2006 to 2009 a total of 25 patients with previous Roux-en-Y reconstruction underwent 38 ERCP procedures using either DBE or SBE. 29 procedures were performed with DBE and 9 with SBE. Retrospective analysis revealed that 4 patients underwent repeated procedures with DBE and SBE, allowing comparison of the two types of enteroscopes in the same patient. The 4 patients had previously undergone hepatobiliary surgery with enterobiliary anastomosis and Roux-en-Y entero-enteric anastomosis. They were referred for ERC because of recurrent cholangitis due to stenosis of the enterobiliary anastomosis. All procedures were performed under general anesthesia with endotracheal tube ventilation and the patient in supine position. Fluoroscopic control was available in all procedures. We used the therapeutic Fujinon DBE EN-450T5 (since 2005) and the Olympus SIF Q180 (since 2009) with a working length of 200 cm and a working channel of 2.8 mm diameter, allowing introduction of all conventional accessory tools and provided the length is at least 230 cm. Both endoscopes are readily available in our endoscopy department and are equally used without preference. Cannulation catheters (PR-Y0001), guidewires (G-Y0001), extraction balloons (B-Y0003) and stent pushers (MAJ-Y0025-1) were Olympus prototypes (Olympus Medical Systems Corp., Japan), dilation balloons were conventional esophageal dilation balloons (CRE Microvasive, Boston Scientific, Ireland), plastic stents were conventional 7 Fr biliary stents (Cook Medical, Ireland). Procedures were performed according with the Helsinki Declaration and all patients signed informed consents.

## RESULTS

The first patient was a 73-year old male with a right hepatectomy because of a Klatzkin tumor. An enterobiliary anastomosis was constructed at the level of the left hepatic duct with a Roux-en-Y entero-enteric anastomosis. The patient was referred because of recur-



**Figure 1** Radiologic view of a balloon dilation of a stenotic hepaticojejunostomy. The arrows indicate the stenosis.



**Figure 2** Three 7 Fr stents were placed through the enteroscope in the enterobiliary anastomosis after balloon dilation of the postoperative stenosis. Bile is spontaneously evacuated through and between the stents.

rent cholangitis 2 years after surgery. The initial DBE procedure consisted of balloon dilation (6 mm) of the stenotic enterobiliary anastomosis and removal of sludge and biliary stone fragments (Figure 1). Because of recurrent cholangitis a second DBE procedure was performed with placement of 3 biliary 7 Fr stents (Figure 2). Afterwards SBE was used to remove the biliary stents and to perform a control cholangiogram. SBE was found to be as effective as DBE for passing the entero-enteric Roux-en-Y anastomosis and proceeding in the afferent limb to reach the enterobiliary anastomosis and then performing ERC.

The second patient was a 62-year old female with a Billroth II gastrectomy and an enterobiliary anastomosis with a Roux-en-Y entero-enteric anastomosis performed because of congenital common bile duct duplication cysts. She suffered from recurrent cholangitis in the left liver lobe. The initial DBE procedure consisted of balloon dilation (7 mm) of the stenotic enterobiliary anastomosis at the level of the left hepatic duct. Three months later a further balloon dilation (8 mm) was performed using the SBE, which was equally effective.

The third patient was a 31-year old female with an enterobiliary anastomosis with a Roux-en-Y entero-enteric anastomosis carried out after complicated cholecystectomy. She was referred for recurrent cholangitis. Initial DBE

encountered difficulties in manoeuvring the endoscope beyond the Roux-en-Y anastomosis. However, the stenotic enterobiliary anastomosis was reached, balloon dilation (8 mm) was performed and 3 biliary 7 Fr stents were successfully placed. The stents spontaneously dislocated after 2 wk and 4 mo later a second balloon dilation (8 mm) was performed using the SBE. Similar difficulties in passing the entero-enteric Roux-en-Y anastomosis were encountered.

The last patient was a 71-year old male with a resected Klatzkin tumor with enterobiliary anastomosis and a Roux-en-Y entero-enteric anastomosis. Shortly after the initial surgery, cholangitis with intrahepatic abscess formation occurred. Percutaneous transhepatic cholangiography was performed in order to dilate the stenotic enterobiliary anastomosis. This procedure was complicated by a perforation of the anastomosis and intraperitoneal bile leak. The patient was then referred for ERC using DBE. With the DBE the stenotic and inflammatory enterobiliary anastomosis was easily reached. Because of the inflammatory oedema and the recent perforation, no balloon dilation was performed before 2 biliary 7 Fr stents were placed. One mo later cholangitis re-occurred and ERC was repeated, this time using SBE. The stents were occluded and removed. Using an extraction balloon the intrahepatic bile ducts were cleared of sludge. Progressive balloon dilation (8 mm) of the anastomosis was successfully performed.

In order to prevent cholangitis, 3 out of these 4 patients were treated with oral ursodeoxycholic acid on a continuous basis.

## DISCUSSION

The concept of balloon-assisted endoscopy was developed by the Japanese endoscopist Hironori Yamamoto in 2001<sup>[2,13]</sup>. It was designed for deep and even complete intubation of the small bowel. Nowadays, both DBE and SBE are commercially available. Both techniques have been shown effective to perform ERCP after Roux-en-Y reconstructive surgery of the small bowel<sup>[4-12]</sup>. However, head to head comparison of DBE and SBE is not available, because of the complex nature of these time-consuming procedures. In the present report we describe a case series of repeated ERC using both DBE and SBE in the same patients. This offers a unique comparative insight into the quality performance of DBE and SBE.

Retrospective analysis of our patient cohort revealed 4 patients who had undergone repeated ERC using both DBE and SBE. They were all patients with a history of hepatobiliary surgery resulting in enterobiliary anastomosis and Roux-en-Y entero-enteric anastomosis. The reason for referral was recurrent cholangitis with/without biliary stones because of stenosis at the level of the anastomosis. Because of the Roux-en-Y entero-enteric anastomosis, ERC with a conventional duodenoscope was not possible.

The balloon-assisted enteroscopy allows deep intubation of the small bowel, and usually successful progression of the endoscope beyond the Roux-en-Y anastomo-



**Figure 3** Endoscopic view of a side-to-side Roux-en-Y entero-enteric anastomosis, showing 3 different directions of jejunal limbs. The upper right directs towards the afferent Roux-en-Y limb. This limb often contains bile and presents antiperistaltic contractions.

sis into the afferent limb. These are mostly constructed side-to-side, which makes it difficult to differentiate the afferent limb (Figure 3). In our series, DBE and SBE were equally effective in reaching the enterobiliary anastomosis. Apparently, the additional inflatable balloon at the tip of the enteroscope is not a prerequisite for these procedures. In contrast, the balloon-loaded overtube is of great help in allowing the enteroscope to proceed into the small bowel, for straightening the enteroscope into a short position and for keeping the enteroscope in position in front of the enterobiliary anastomosis. However, since both DBE and SBE are forward looking endoscopes without steerable lifting, local control of the accessory ERC material at the level of the enterobiliary anastomosis is less effective as compared to ERC with a conventional side-viewing duodenoscope. In addition, the length of the accessory equipment must exceed 230 cm and the width must be less than 2.8 mm.

Therefore, both DBE and SBE seem to be valuable for therapeutic ERCP in selected patients with postoperative complications which are usually dealt with surgically. However, these procedures are complex and time-consuming and the local control of the accessory equipment is not ideal. Although few data are available on the performance of SBE, the present case series shows equal efficacy of DBE and SBE in performing ERC of the enterobiliary anastomosis with Roux-en-Y entero-enteric anastomosis. However, the small number of subjects precludes clear recommendation of one enteroscope system over the other. Moreover, the potential use of alternative therapeutic methods such as interventional radiology and the newly developed spiral Discovery SB overtube should also be studied in order to determine the optimal procedure for dealing with postoperative biliopancreatic problems in patients with Roux-en-Y entero-enteric anastomosis<sup>[13]</sup>.

## COMMENTS

### Background

Small bowel reconstructive surgery may render parts of the gastrointestinal tract inaccessible for conventional endoscopy techniques. Therefore, postoperative

problems occurring in these excluded segments are often dealt with surgically. With the development of balloon-assisted enteroscopy, complete endoscopic visualisation of the small bowel is nowadays feasible. Both double- (DBE) and single-balloon enteroscopy (SBE) are available. However, comparative studies of the two techniques are scarce. We present a case series of 4 patients who underwent repeated therapeutic endoscopic retrograde cholangiography after a Roux-en-Y reconstruction of the small bowel, using both DBE and SBE.

### Research frontiers

The recently developed balloon-assisted enteroscopy may avoid the need for rescue surgery in case of biliopancreatic problems after Roux-en-Y reconstructive surgery of the small bowel. This is an important endoscopic breakthrough for the therapeutic management of the conventionally inaccessible biliopancreatic ducts.

### Innovations and breakthroughs

We illustrate that DBE and SBE have comparable accuracy in performing therapeutic endoscopic retrograde cholangiography after Roux-en-Y reconstruction of the small bowel. Although these are time-consuming and technically challenging procedures, we show that both DBE and SBE may avoid the need for rescue surgery in case of biliary tract obstruction. The fact that DBE and SBE were repeated in the same patients provides a unique comparison, showing the equal accuracy of the two techniques.

### Applications

We show that DBE and SBE are both suitable for performing ERC after Roux-en-Y reconstruction of the small bowel. This opens the door for new endoscopic indications for balloon-assisted enteroscopy and further development of accessory equipment to perform endoscopic retrograde cholangiopancreatography (ERCP). With the global obesity endemic which is often treated surgically by means of Roux-en-Y gastric bypass, indications for these balloon-assisted ERCP procedures are likely to increase in the future.

### Terminology

Roux-en-Y reconstruction of the small bowel is an often used surgical technique in gastrointestinal oncology surgery, hepatobiliary and pancreatic surgery and bariatric surgery. However, this technique renders specific parts of the gastrointestinal and biliopancreatic tract inaccessible for conventional endoscopy.

### Peer review

The current manuscript illustrates that SBE seems to be as accurate as DBE for performing therapeutic ERC after Roux-en-Y reconstruction. This is a descriptive case series of patients who underwent both procedures successfully. Further comparative studies with larger numbers of patients and procedures are necessary. This manuscript is a first encouraging step towards a larger comparative head-to-head study of the two balloon-assisted enteroscopy techniques.

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## Duodenal duplication cyst and pancreas divisum causing acute pancreatitis in an adult male

Eduardo Redondo-Cerezo, Julio Pleguezuelo-Díaz, Mercedes López de Hierro, José F Macías-Sánchez, Cristina Viñolo Ubiña, María Del Mar Martín-Rodríguez, Javier De Teresa-Galván

Eduardo Redondo-Cerezo, Julio Pleguezuelo-Díaz, Mercedes López de Hierro, José F Macías-Sánchez, Cristina Viñolo Ubiña, María Del Mar Martín-Rodríguez, Javier De Teresa-Galván, Endoscopy Unit, Gastroenterology Department, Hospital Universitario Virgen de las Nieves, Avenida de las Fuerzas Armadas 2, Granada 18014, Spain

**Author contributions:** Redondo-Cerezo E and Pleguezuelo-Díaz J were the endoscopists in this case, and prepared the definitive version of this manuscript; and López de Hierro M, Macías-Sánchez JF, Viñolo Ubiña C, Martín-Rodríguez MM, and De Teresa-Galván J contributed equally to this work, responsible for designing, drafting and revising.

**Correspondence to:** Eduardo Redondo-Cerezo, MD, PhD, Digestive Endoscopy Unit, Department of Gastroenterology, Hospital Universitario Virgen de las Nieves, Avenue of the Armed Forces 2, Granada 18006, Spain. [eredondoc@yahoo.es](mailto:eredondoc@yahoo.es)

Telephone: +34-95-8020146 Fax: +34-95-8020000

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**Peer reviewer:** Everson Luiz de Almeida Artifon, MD, PhD, FASGE, University of Sao Paulo School of Medicine, Rua Guimaraes Passos, Sao Paulo 04107030, Brazil

Redondo-Cerezo E, Pleguezuelo-Díaz J, López de Hierro M, Macías-Sánchez JF, Viñolo Ubiña C, Martín-Rodríguez MM, De Teresa-Galván J. Duodenal duplication cyst and pancreas divisum causing acute pancreatitis in an adult male. *World J Gastrointest Endosc* 2010; 2(9): 318-320 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v2/i9/318.htm> DOI: <http://dx.doi.org/10.4253/wjge.v2.i9.318>

### Abstract

Duodenal duplication cysts are rare congenital abnormalities which are more commonly diagnosed in infancy and childhood. However, in rare cases, these lesions can remain asymptomatic until adulthood. The combination of duplication cyst and pancreas divisum is extremely rare and both conditions have been linked with acute recurrent pancreatitis. We present the case of a 37 years-old patient who presented with repeated episodes of acute pancreatitis. By means of magnetic resonance imaging and endoscopic ultrasonography we discovered a duplication cyst whose cavity received drainage from the dorsal pancreas. After opening the cyst cavity to the duodenal lumen with a needle knife the patient presented no further episodes in the clinical follow-up. Comparable literature findings and therapeutic options for these abnormalities are discussed with regard to the presented case.

### INTRODUCTION

Recurrent idiopathic pancreatitis is defined as repeated episodes of pancreatitis in a patient in which the cause has not been identified by the usual diagnostic workup. Nevertheless, after a single episode of acute pancreatitis of unexplained origin, a repeated attack is unlikely<sup>[1]</sup>. However, a variety of additional investigations have been advocated before considering the pancreatitis as idiopathic, and they offer the possibility of finding a probable cause in the vast majority of these patients<sup>[2]</sup>. Duodenal duplication cysts are rare congenital abnormalities which are more commonly diagnosed in infancy and childhood. However, in exceptional cases, the lesion can remain asymptomatic until adulthood<sup>[3]</sup>. We present a singular case of the coincident occurrence of a duplication cyst with pancreas divisum, and drainage of the dorsal pancreas inside the cyst, causing recurrent acute pancreatitis in a 37 years-old male. There are a few similar cases in the previous literature but none with the features we found,

and with such a simple and successful endoscopic treatment.

## CASE REPORT

A 37 year-old male with a previous history recurrent acute pancreatitis came to the emergency room because of a new episode of acute pancreatitis. He had presented with attacks of abdominal pain attributable to pancreatitis and biliary colic in the previous three years, with repeated admission to the ER. He did not drink or smoke and had no medical intolerances. No previous surgeries were reported. He had undergone multiple abdominal ultrasound procedures with no significant findings. Abdominal exam showed a mild tenderness in epigastrium with neither masses nor peritoneal signs. Laboratory analysis revealed elevated amylase levels (861 U/L) with no other abnormalities.

Abdominal ultrasonography was once again normal. An magnetic resonance imaging (MRI) (Figure 1) indicated a normal gallbladder with a cystic dilatation at the distal, periampullary common bile duct, protruding in the duodenal lumen, that was considered by the radiologist to be a choledocoloce or Todany's type III choledocal cyst.

The patient was sent to the endoscopy unit for an ERCP under general anesthesia. From the second duodenal portion a protruding duodenal mass, with normal overlying mucosa, was seen cranial and slightly lateral to the choledocal fold. Cholangiography was normal, but pancreatography showed a blockage in the first third of the pancreatic duct highly suggestive of pancreas divisum (Figure 2). Minor papilla could not be found even after careful examination. Taking into account these findings, a linear endoscopic ultrasound (EUS) probe was inserted. The procedure revealed a cystic cavity, with a small amount of debris inside, and a wall in which three layers could be identified (Figure 3). With the endosonographic diagnosis of duplication cyst and the absence of an evident minor papilla we inserted a needle knife inside the cyst, injecting contrast medium into the cystic cavity, which showed no communication with the duodenal lumen (Figure 4). We then opened the cyst into the duodenal lumen with the same needle knife, achieving a complete drainage of its content.

A repeat radial EUS, one month later, failed to find the cyst, indicating that it was completely drained. A repeat MRI confirmed the presence of a pancreas divisum, after consultation with the radiologist.

The patient is now doing well, with no recurrent episodes of acute pancreatitis, three months after the procedure.

## DISCUSSION

Duplication cysts are benign, rare anomalies that arise during early embryonic development<sup>[4]</sup>. Usually, these cysts present in childhood with obstructive or bleeding symptoms. Clinical findings of this entity may be non-specific,

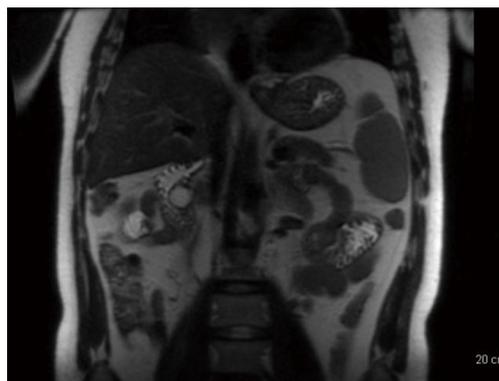


Figure 1 A cystic lesion in the area of the distal common bile duct, bulging into the duodenal lumen is seen in the magnetic resonance imaging.

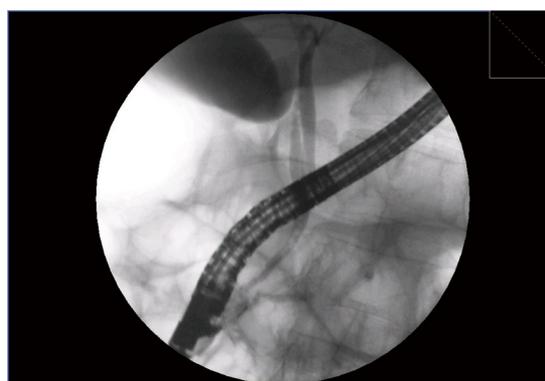


Figure 2 Pancreatography showed a blockage in the main pancreatic duct suggestive of pancreas divisum.

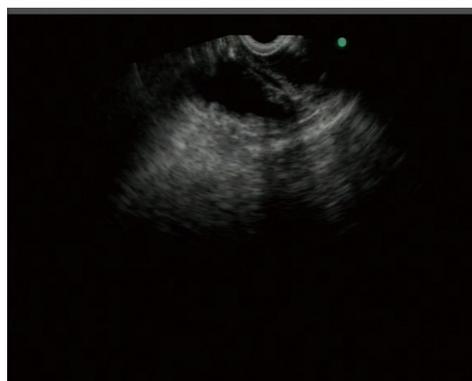
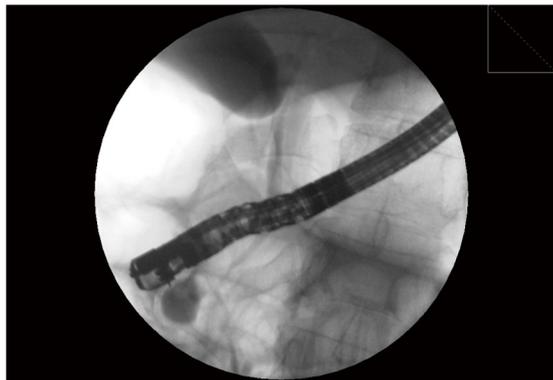


Figure 3 A cystic lesion found in the second duodenal portion, with three layer walls and debris inside the cystic cavity.

such as mild abdominal pain, or more specific, such as acute or chronic pancreatitis. A variety of possible mechanisms might be responsible for pancreatitis: a transitory and mobility-related duodenal obstruction of the major papilla outflow by the cyst; the migration of biliary sludge and/or microstones from the cyst to the biliary tree, as observed in biliary pancreatitis; the communication of the dorsal pancreatic duct with the cystic cavity<sup>[5-6]</sup>. Diagnosis can be made without ERCP in most cases, given the increased availability of MRCP and EUS<sup>[7]</sup>.



**Figure 4** Contrast media is injected inside the cystic cavity with a needle knife.

These cysts are lined with stratified, ciliated, or columnar epithelium and contain a mucoïd fluid<sup>[8,9]</sup>. They are typically discovered incidentally on endoscopy or radiologic imaging since they only rarely cause symptoms. Complications are rare but may include pancreatitis when cysts are located near the ampulla of Vater<sup>[8]</sup>. While they are believed to have a low malignant potential, case reports have described malignant transformation<sup>[10]</sup>. The endoscopic exam may reveal a bulge with normal overlying mucosa, or a diverticulum. Cysts have a regular appearance without mucosal irregularities. On EUS, duplication cysts are usually anechoic homogeneous lesions with regular margins arising from the submucosa (third layer) or extrinsic to the gastrointestinal wall. Their wall can be characterized by three- to five-layer structures. They may contain septae, fluid, or echogenic material consisting of layering debris or mucin. EUS is helpful in discriminating a duplication cyst from a solid mass. The diagnosis can usually be made by the characteristic endoscopic and endosonographic appearance. Management of asymptomatic cysts is usually expectant. Nevertheless, prospective studies evaluating the natural history of duplication cysts are lacking. When symptomatic, duplication cysts can be treated surgically or endoscopically<sup>[7,11]</sup>. Although therapy has classically involved surgical resection, different endoscopic methods, such as resection of the cystic roof by using a standard polypectomy snare, or a large incision of the roof, are probably sufficient to cure the patient. Additional sphincterotomy is not necessary, because the sphincter area is intact in cases of duodenal duplication, in contrast to what happens with choledocoele, in which biliary sphincterotomy is the treatment of choice<sup>[12]</sup>. Con-

cerns may arise around the potential of malignant transformation of duplication cysts but, although endoscopic therapy does not achieve a complete mucosal resection, it avoids stasis of secretions inside the cyst with a potential protective effect<sup>[7,10,12]</sup>. Indeed, some authors recommend an endoscopic review of the area with follow up biopsies, after endoscopic therapy<sup>[7]</sup>.

In summary, we present an extraordinarily infrequent case of recurrent pancreatitis caused by a duplication cyst connected with the minor papilla in a patient with pancreas divisum.

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## Ileal gallstone obstruction: Single-balloon enteroscopic removal

Hauke Sebastian Heinzow, Tobias Meister, Johannes Wessling, Wolfram Domschke, Hansjoerg Ullerich

Hauke Sebastian Heinzow, Tobias Meister, Wolfram Domschke, Hansjoerg Ullerich, Department of Medicine B, University of Muenster, Muenster D48149, Germany

Johannes Wessling, Department of Radiology, University of Muenster, Muenster D48149, Germany

**Author contributions:** Heinzow HS and Ullerich H contributed equally to this work; Heinzow HS, Meister T, Wessling J, Domschke W and Ullerich H designed and performed the research and analyzed the data; and Heinzow HS, Meister T, Domschke W and Ullerich H wrote the paper.

**Correspondence to:** Hauke Sebastian Heinzow, MD, Department of Medicine B, University of Muenster, Albert-Schweitzer-Str. 33, Muenster D48149,

Germany. [hauke.heinzow@ukmuenster.de](mailto:hauke.heinzow@ukmuenster.de)

Telephone: +49-251-8347661 Fax: +49-251-8347576

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### Abstract

Gallstone-induced ileus is a rare complication of cholelithiasis. Since localization of gallstones impacted in the small bowel, especially in the ileum, prevents access by conventional endoscopy in most cases, the mainstay of treatment remains surgical. Recent invention of double- and single-balloon enteroscopy has added much to the ability of imaging the small bowel and enables endoscopically directed therapy. Herein, for the first time, we report a successful endoscopic calculus removal *via* peroral single-balloon enteroscopy in an 81-year-old woman suffering from gallstone ileus of the ileum.

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**Key words:** Gallstone ileus; Small bowel obstruction; Single-balloon enteroscopy; Cholelithiasis

**Peer reviewers:** Sherman M Chamberlain, MD, FACP, FACG, AGAF, Associate Professor of Medicine, Section of Gastroen-

terology, BBR-2538, Medical College of Georgia, Augusta, GA 30912, United States; Iruru Maetani, MD, Professor and Chairman, Division of Gastroenterology, Department of Internal Medicine, Toho University Ohashi Medical Center, 2-17-6 Ohashi Me-guro-ku, Tokyo 153-8515, Japan

Heinzow HS, Meister T, Wessling J, Domschke W, Ullerich H. Ileal gallstone obstruction: Single-balloon enteroscopic removal. *World J Gastrointest Endosc* 2010; 2(9): 321-324 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v2/i9/321.htm> DOI: <http://dx.doi.org/10.4253/wjge.v2.i9.321>

### INTRODUCTION

Although rarely reported, gallstone ileus is an important cause of mechanical bowel obstruction, resulting from impaction of a gallstone in the jejunum or ileum after being passed through a biliary-enteric fistula<sup>[1]</sup>. It was first described by Leon Bouveret in 1896. The diagnosis in mainly elderly patients who not infrequently have other significant medical conditions is often delayed since symptoms may be intermittent and investigations fail to identify the cause of obstruction<sup>[2]</sup>. Patients may present with nausea, vomiting and epigastric pain. Hematemesis can sometimes also occur due to erosion at the site of the biliary-enteric fistula<sup>[3]</sup>. Diagnostics usually include endoscopy, computed tomography (CT) and more recently magnetic resonance cholangiopancreatography. The diagnosis may be suggested by fulfilment of the Rigler triad: bowel obstruction, pneumobilia and ectopic gallstone. Since the reported mortality rate has is high at 12%, early diagnosis and treatment of gallstone-induced ileus remain crucial. So far, surgery has had the pivotal role in managing this condition. Enterolithotomy, cholecystectomy, and fistula division, with or without common bile duct exploration are the surgical options considered<sup>[1,4]</sup>. In high-risk patients, however, non-surgical treatment of gallstone ileus is desirable. Accordingly, successful electrohydraulic litho-

tripsy and extracorporeal shockwave lithotripsy (ESWL) of stones obstructing the jejunum, stomach, and colon has been reported in some cases<sup>[5-8]</sup>. Removal of gallstones from the upper small intestine *via* conventional endoscopy has also been described<sup>[9]</sup>.

## CASE REPORT

A febrile and slightly dehydrated 81-year-old woman was admitted due to a three day history of diffuse abdominal pain, nausea and hematemesis. On admission physical examination revealed mild tenderness of the upper abdominal quadrants and signs of subileus. There was no jaundice observed. Leukocytes and C-reactive protein were slightly elevated. Abdominal ultrasound showed pneumobilia. Upper gastrointestinal endoscopy revealed a deep ulcer of the duodenal bulb (Figure 1). Small bowel ileus was confirmed by plain abdominal X-ray and CT-scan showing the typical image of mechanical small bowel obstruction. Moreover, pneumobilia of the central biliary tract was observed (Figure 2A). Abdominal CT-scan (Figure 2B) also detected a fistulous structure extending from the duodenum to the gallbladder and, in addition, showed a calcified mass of 5 cm in diameter in the distal small bowel, thus establishing the diagnosis of bilioduodenal fistula and gallstone ileus of the ileum.

Because of the poor physical condition and underlying comorbidities of the patient, surgery was considered to carry too high a risk. Therefore, single-balloon enteroscopy (SBE, SIF-100 enteroscope, Olympus, Japan) *via* the oral route was performed revealing a calculus about 450 cm distant from the pylorus, completely occluding the intestinal lumen (Figure 3). Under endoscopic guidance the calculus was captured with a Dormia basket but could not be retracted due to intestinal incarceration. Therefore the endoscope was withdrawn leaving the captured calculus in situ and leading out the basket wire pernasally. In order to facilitate calculus removal three sessions of ESWL (4000 pulses each session) were performed. Thereafter, the single-balloon enteroscope was reinserted *via* the oral route guided by the wire of the Dormia basket. This time, under fluoroscopic control (Figure 4) the partially disintegrated calculus could be endoscopically retrieved up to the stomach. Since the size of the calculus did not allow retraction through the lower esophageal sphincter, endoscopically guided laser lithotripsy (Calculase 27750120 Desktop Holmium YAG Laser, Karl Storz, Germany) and mechanical fragmentation were performed permitting safe peroral endoscopic removal of all gallstone fragments (Figure 5). 3 d later the patient was discharged in good health. Endoscopic follow-up at 4 wk after discharge revealed the deep duodenal bulb ulcer to be healed. Neither pneumobilia nor any fistulous structure could be observed radiographically.

## DISCUSSION

Gallstone-induced ileus is a rare complication of cho-



Figure 1 Upper gastrointestinal endoscopy showing a deep ulcer of the duodenal bulb.

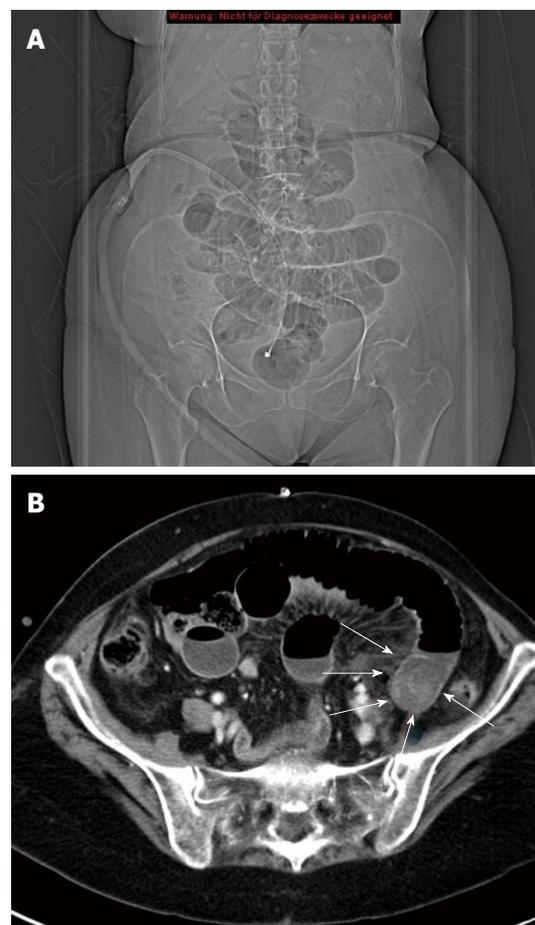
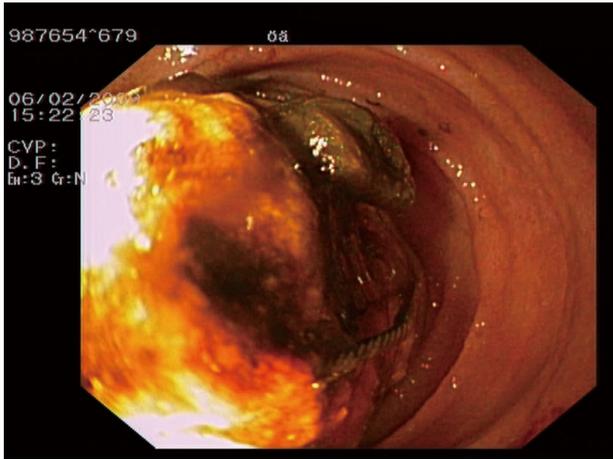


Figure 2 Abdominal computed tomography-scan. A: The typical image of mechanical small bowel obstruction with distended small bowel loops reaching to the mid ileum as well as pneumobilia of the central biliary tract; B: A calcified mass of 5 cm in diameter located in the distal small bowel.

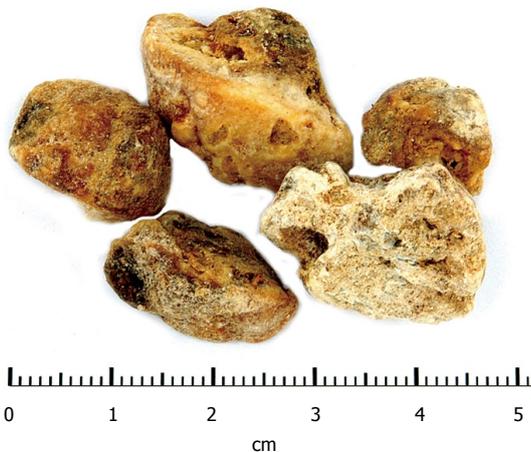
lelithiasis and is associated with relatively high rates of mortality<sup>[2]</sup>. Endoscopic removal of gallstones from the upper jejunum has been described<sup>[9]</sup>. However, since localization of gallstones impacted in the small bowel pre-



**Figure 3** Single-balloon enteroscopy *via* the oral route revealing a calculus, about 450 cm distant from the pylorus, completely occluding the intestinal lumen.



**Figure 4** Plain X-ray showing an ileal calculus endoscopically captured with a dormia basket guided by single-balloon enteroscopy.



**Figure 5** Removed gallstone fragments.

vents access of conventional endoscopy in most cases, such situations usually require surgical treatment<sup>[1-3]</sup>.

Recent invention of double- and single-balloon enteroscopy<sup>[10,11]</sup> has added much to the ability of imaging the small bowel and enables endoscopically directed therapy such as polypectomy, extraction of foreign bodies and arrest of bleeding. In a study by Ramchandani and colleagues with 106 patients the mean insertion depth *via* SBE was 255.8 cm  $\pm$  84.5 cm beyond the duodenojejunal flexure by the oral route and 163 cm  $\pm$  59.3 cm proximal to the ileocecal valve by the peranal approach<sup>[12]</sup>. Pan-enteroscopy is possible in 25% to 60% of cases combining peroral and peranal access<sup>[11,12]</sup> and is a highly useful diagnostic and therapeutic tool in endoscopy<sup>[12]</sup>. Therefore, the use of SBE to detect jejunal or ileal gallstones appears promising.

Consequently, in the present setting, single-balloon enteroscopy was performed and proved to be a successful minimally-invasive and safe method for calculus removal.

This report for the first time demonstrates the beneficial role of single-balloon enteroscopy in treating small bowel gallstone ileus, potentially obviating the necessity of surgical intervention. Therefore, in cases similar to that reported here minimal invasive SBE should be the primary therapeutic approach with the surgical option still remaining in case of failure. The development of special probes for laser lithotripsy *via* SBE would be ideal. As long as such probes are not available, however, we recommend the combined procedure of SBE and ESWL.

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**Majid A Almadi, MD**, Department of Gastroenterology Division, McGill University, McGill University Health Center, Montreal, H3A 1A1, Canada

**Everson Luiz de Almeida Artifon, MD, PhD, FASGE**, University of Sao Paulo School of Medicine, Rua Guimaraes Passos, Sao Paulo 04107030, Brazil

**Carlo Calabrese, MD, PhD**, Department of Clinical Medicine, University of Bologna, Via Massarenti 9, Bologna 40138, Italy

**Sherman M Chamberlain, MD, FACP, FACC, AGAF, Associate Professor of Medicine**, Section of Gastroenterology, BBR-2538, Medical College of Georgia, Augusta, GA 30912, United States

**Philip Wai Yan Chiu, Associate Professor**, Department of Surgery, Institute of Digestive Disease, Chinese University of Hong Kong, Prince of Wales Hospital, 30-32 Ngan Shing Street, Shatin, N.T., Hong Kong, China

**David Friedel, MD**, Gastroenterology, Winthrop University Hospi-

tal, 222 Station Plaza North, Suite 428, Mineola, NY 11501, United States

**Lesur Gilles, MD**, Hopital Ambroise Paré, 9 avenue Charles de Gaulle, Boulogne 92100, France

**Carlo M Girelli, MD**, 1st Department of Internal Medicine, Service of Gastroenterology and Digestive Endoscopy, Hospital of Busto Arsizio, Via Arnaldo da Brescia, Busto Arsizio, VA 121052, Italy

**Dimitris K Iakovidis, Professor**, Department of Informatics and Computer Technology, Technological Educational Institute of Lamia, 3rd km Old National Road Lamias Athinas, Lamia, GR 35100, Greece

**Dimitrios Kapetanios, MD**, Gastroenterology Department, George Papanikolaou Hospital, Exohi, Thessaloniki 57010, Greece

**Iruru Maetani, MD, Professor and Chairman**, Division of Gastroenterology, Department of Internal Medicine, Toho University Ohashi Medical Center, 2-17-6 Ohashi Meguro-ku, Tokyo 153-8515, Japan

**Nobumi Tagaya, MD, PhD**, Second Department of Surgery, Dokkyo Medical University, 880 Kitakobayashi, Mibu, Tochigi 321-0293, Japan

**C Mel Wilcox, MD, Professor, Director**, UAB Division of Gastroenterology and Hepatology, 703 19th Street South, ZRB 633, Birmingham, AL 35294-0007, United States

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 Negligence and Litigation in Medical  
 Practice

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 Waikoloa, HI, United States  
 Selected Topics in Internal Medicine

January 26-27  
 Dubai, United Arab Emirates  
 2nd Middle East Gastroenterology  
 Conference

February 11-13  
 Fort Lauderdale, FL, United States  
 21th Annual International Colorectal  
 Disease Symposium

February 26-28  
 Carolina, United States  
 First Symposium of GI Oncology at  
 The Caribbean

March 05-07  
 Peshawar, Pakistan  
 26th Pakistan Society of  
 Gastroenterology & Endoscopy  
 Meeting

March 12-14  
 Bhubaneswar, India  
 18th Annual Meeting of Indian  
 National Association for Study of  
 the Liver

March 25-28  
 Beijing, China  
 The 20th Conference of the Asian  
 Pacific Association for the Study of  
 the Liver

March 27-28  
 San Diego, California, United States  
 25th Annual New Treatments in  
 Chronic Liver Disease

April 07-09  
 Dubai, United Arab Emirates  
 The 6th Emirates Gastroenterology  
 and Hepatology Conference, EGHC  
 2010

April 14-17  
 Landover, Maryland, United States  
 12th World Congress of Endoscopic  
 Surgery

April 14-18  
 Vienna, Austria  
 The International Liver Congress™  
 2010

April 28-May 01  
 Dubrovnik, Croatia  
 3rd Central European Congress  
 of surgery and the 5th Croatian  
 Congress of Surgery

May 01-05  
 New Orleans, LA, United States  
 Digestive Disease Week Annual  
 Meeting

May 15-19  
 Minneapolis, MN, United States  
 American Society of Colon and  
 Rectal Surgeons Annual Meeting

June 04-06  
 Chicago, IL, United States  
 American Society of Clinical  
 Oncologists Annual Meeting

June 16-19  
 Hong Kong, China  
 ILTS: International Liver  
 Transplantation Society ILTS Annual  
 International Congress

June 20-23  
 Mannheim, Germany  
 16th World Congress for  
 Bronchoesophagology-WCBE

August 28-31  
 Boston, Massachusetts, United States  
 10th OESO World Congress on  
 Diseases of the Oesophagus 2010

September 10-12  
 Montreal, Canada  
 International Liver Association's  
 Fourth Annual Conference

September 11-12  
 La Jolla, CA, United States  
 New Advances in Inflammatory  
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 Prague, Czech Republic  
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Symposium of Society of  
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October 29-November 02  
 Boston, Massachusetts, United States  
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November 13-14  
 San Francisco, CA, United States  
 Case-Based Approach to the  
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- 3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

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- 4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

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- 5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

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- 6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

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- 9 Outreach: Bringing HIV-positive individuals into care. *HRS-A Careaction* 2002; 1-6 [PMID: 12154804]

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- 10 **Sherlock S**, Dooley J. Diseases of the liver and biliary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

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- 11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

Author(s) and editor(s)

- 12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wicczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

Conference proceedings

- 13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

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- 14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

Electronic journal (list all authors)

- 15 Morse SS. Factors in the emergence of infectious diseases. *Emerg Infect Dis* serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: <http://www.cdc.gov/ncidod/eid/index.htm>

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- 16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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