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**Endoscopic management of complications to chronic pancreatitis**

**Dumonceau JM *et al*.** Endoscopy for CP-related complications

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**Abstract**

Pseudocysts and biliary obstructions will affect approximately one third of patients with chronic pancreatitis (CP). For CP-related, uncomplicated, pancreatic pseudocysts (PPC), endoscopy is the first-choice therapeutic option. Recent advances have focused on endosonography-guided PPC transmural drainage, which tends to replace the conventional, duodenoscope-based approach. Ancillary material is being tested to facilitate the endosonography-guided procedure. In this review, the most adequate techniques depending on PPC characteristics are presented along with supporting evidence. For CP-related biliary obstructions, endoscopy and surgery are valid therapeutic options. Patient co-morbidities (*e.g.*, portal cavernoma) and expected patient’s compliance to repeat endoscopic procedures are important factors when selecting the most adapted option. Malignancy should be reasonably ruled out before embarking in the endoscopic treatment of presumed CP-related biliary strictures. In endoscopy, the gold standard technique consists of placing simultaneous, multiple, side-by-side, plastic stents for a one-year period. Fully covered self-expandable metal stents are challenging this method and have provided 50% mid-term success.

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**Key words:** Biliary stricture; Chronic pancreatitis; Pseudocyst; Endoscopic retrograde cholangio-pancreatography; Endoscopic ultrasonography; Stent

**Core tip:** Endoscopy is the first-choice treatment of pancreatic pseudocysts. The transduodenal route may be preferable over the transgastric route. Two transmural double pigtail stents should be left for at least 2 mo. In the case of a disconnected pancreatic tail, secretin-enhanced magnetic resonance pancreatography should be obtained to decide about stent removal. Biliary strictures should be thoroughly investigated to rule out malignancy. To this aim, improved methods of biliary sampling have become available. Even with multiple biliary stents, potentially fatal cholangitis is frequent in the absence of regular stent revision. Fully covered self-expandable metal stents have provided 50% mid-term success.

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**INTRODUCTION**

Common local complications to chronic pancreatitis (CP) include pancreatic pseudocysts (PPCs) and biliary obstructions. These two complications develop in patients during the course of CP at a rate of 20%-40% for PPCs and 3%-23% for biliary obstructions[[1](#_ENREF_1),[2](#_ENREF_2)]. PPCs consist of a collection of pancreatic juice enclosed by a wall of fibrous granulation tissue, which may arise as a consequence of acute pancreatitis, pancreatic trauma or CP[[3](#_ENREF_3)]. Biliary obstruction may be caused by fibrosis, compression by a PPC or cancer. The present review covers the full spectrum of endoscopic management of local complications to CP; it is not an analysis of specific studies and it does not encompass the management of uncomplicated CP, which has recently been reviewed elsewhere[[4](#_ENREF_4)].

**METHODS**

Searches for relevant articles were conducted in Medline through PubMed on May 2013, without time limits, using the following search terms: ("pancreatitis, chronic"[MeSH Terms] OR ("pancreatitis"[All Fields] AND "chronic"[All Fields]) OR "chronic pancreatitis"[All Fields] OR ("chronic"[All Fields] AND "pancreatitis"[All Fields]) AND pseudocyst[All Fields] AND ("endoscopy"[MeSH Terms] OR "endoscopy"[All Fields]) OR (("pancreatitis, chronic"[MeSH Terms] OR ("pancreatitis"[All Fields] AND "chronic"[All Fields]) OR "chronic pancreatitis"[All Fields] OR ("chronic"[All Fields] AND "pancreatitis"[All Fields]) AND pseudocysts[All Fields] AND ("surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "surgery"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields]); ("pancreatitis, chronic"[MeSH Terms] OR ("pancreatitis"[All Fields] AND "chronic"[All Fields]) OR "chronic pancreatitis"[All Fields] OR ("chronic"[All Fields] AND "pancreatitis"[All Fields]) AND biliary[All Fields] AND ("endoscopy"[MeSH Terms] OR "endoscopy"[All Fields]). Articles written in English were selected for complete review on the basis of the abstract. Additional papers were identified by manually checking the reference lists of the articles selected for review.

**PANCREATIC PSEUDOCYSTS**

***Differential diagnosis pseudocyst-cystic neoplasm***

Pseudocysts are the most frequent pancreatic fluid collections. The differential diagnosis between PPCs and cystic neoplasms or, less frequently, necrotized tumors, may be difficult in patients who present for the first time with a pancreatic fluid collection. Amongst the various cystic neoplasms that may affect the pancreas, mucinous cystic neoplasms and intraductal papillary mucinous neoplasms harbor a malignant potential; many of which require surgical resection[[5](#_ENREF_5)]. As only a few of the available tests provide a high degree of certainty, a diagnosis is usually made by analyzing a set of data, including demographic data and clinical history[[6](#_ENREF_6)], cross-sectional imaging[[7](#_ENREF_7)], and endosonography-guided sampling of the fluid content and of the wall of the lesion[[8](#_ENREF_8),[9](#_ENREF_9)]. Research has recently focused on the identification of new biomarkers and, on *in vivo* confocal microscopic examination of the cyst wall through a needle inserted under endosonographic guidance[[10](#_ENREF_10),[11](#_ENREF_11)].

***Indications for treatment***

Widely accepted indications for PPC treatment include the presence of symptoms such as abdominal pain, gastric outlet obstruction, early satiety, weight loss, jaundice, and infected or enlarging PPC[[12](#_ENREF_12)]. Some authors also recommend treating PPCs in asymptomatic patients to prevent potential PPC-related complications, although these occur only in a minority of patients[[13](#_ENREF_13),[14](#_ENREF_14)]. Other such debated indications include compression of major vessels, intracystic hemorrhage, pancreaticopleural fistula, and PPCs with a diameter greater than 5 cm without any regression after more than 6 wk and a cyst wall thickness larger than 5 mm[[15](#_ENREF_15)]. In patients with CP, PPCs rarely resolve spontaneously, particularly if their diameter is greater than 4 cm or if they have developed outside of the pancreas[[16](#_ENREF_16)].

***Results; choosing endoscopic vs surgical treatment***

Endoscopic drainage is recommended as a first-line treatment of accessible uncomplicated PPCs because it provides significantly better results compared to surgery in terms of cost, duration of hospital stay and quality of life up to three mo post-procedure, as demonstrated in a small randomized controlled trial (RCT)[[17](#_ENREF_17)]. Reviews of non-comparative historical series of endoscopic and of surgical treatments of PPCs have reported similar results for both modalities in terms of morbidity with 13% for endoscopic treatments and 16% for surgical treatments. A PPC recurrence during long-term follow-up has also been reported of 11% *vs* 10%, respectively for endoscopic and surgical treatments. An advantage was found in favor of the endoscopic method in terms of mortality (0.2% *vs* 2.5%)[[15](#_ENREF_15),[18](#_ENREF_18)].

Some, but not all, authors have reported that endoscopic PPC drainage yielded higher success rates in the setting of CP *vs* acute pancreatitis. For example, Baron et al. reported resolution of 92% of chronic pseudocysts *vs* 74% of acute pseudocysts in a series of 138 patients while Hookey et al. reported resolution of 94% of chronic pseudocysts *vs* 92% of acute pseudocysts in a series of 116 patients[[19](#_ENREF_19),[20](#_ENREF_20)].

A first-line surgical approach is usually adopted if necrosis has not yet liquefied and if treatment cannot be delayed. Endoscopy carries a lower success rate and higher morbidity rate in such instances; the reader is referred to a recent review for the comparison of currently available techniques in this particular indication[[21](#_ENREF_21)]. Pancreatic necrosectomy requires expert endoscopic skill, dedication and adequate patient selection.

***Endoscopic technique***

Access route:A direct communication between the PPC and the main pancreatic duct (MPD) may be demonstrated in 40%-66% of all PPCs[[22](#_ENREF_22)] Such a communication allows drainage of the PPC via a stent inserted into the PPC through the papilla (“transpapillary drainage”) as opposed to a stent being inserted into the PPC through the digestive wall (“transmural drainage”).

No RCT has compared the transpapillary *vs* the transmural drainage route but, in nonrandomized comparative studies, procedure-related morbidity was lower with the transpapillary route (2% *vs* 15%) and long-term success was similar[[20](#_ENREF_20),[22](#_ENREF_22),[23](#_ENREF_23)]. The transpapillary route is usually reserved for relatively small (diameter < 5 cm) PPC located in the head or the body of the pancreas.

***“Conventional” endoscopic-guided vs endosonography-guided technique***

Endosonography-guided PPC drainage tends to replace the “conventional” endoscopic approach that uses a duodenoscope or, in some cases, a gastroscope. A recent meta-analysis found that the single demonstrated advantage of the endosonography-guided technique is the possibility to drain non-bulging PPCs[[24](#_ENREF_24)], which represent approximately half of all PPCs[[22](#_ENREF_22)]. The most important limitations of the endosonography-guided technique reside in the thinner diameter of the working channel of the echoendoscope and in the lower maneuverability of the elevator. While the “conventional” approach is relatively standardized, new material is constantly being tested to make endosonography-guided PPC drainage a single-step, reliable, procedure. One of the most recent devices allows puncturing, dilating the puncture tract and inserting two guidewires into the PPC without any device exchange. The device is made of a catheter with two balloons, one to anchor it to inside the PPC and the other one to dilate the puncture tract[[25](#_ENREF_25)].

***Transgastric vs transduodenal transmural route***

Some PPCs may be accessed through either the gastric or the duodenal wall. In such cases, the transduodenal route may be preferable as long-term success has been reported more frequently with the transduodenal *vs* the transgastric route (83% *vs* 64%); procedure-related morbidity was 10% with both routes[[26](#_ENREF_26)]. The difference in long-term success may be related to the longer durability of cystoduodenal compared with cystogastric fistulas (the latter ones typically close a few days after stent removal).

***Number and type of stents***

Two double pigtail stents are usually inserted for transmural drainage; a naso-cystic catheter may be left in place to rinse the PPC cavity with saline if debris are present. In a large retrospective series, the insertion of a single *vs* multiple stent was independently associated with the failure of endoscopic PPC drainage, defined as severe procedure-related complication or need for another treatment modality[[27](#_ENREF_27)]. In that series, straight stents were used and they were associated with frequent bleeding (7% of patients, with surgery required in two thirds of them) and stent migration.

***Stenting duration***

Enterocystic transmural stents should not be retrieved before PPC resolution and not before at least 2 mo of stenting. This recommendation is mostly based on a RCT that allocated 28 patients (including 15 with CP) who had PPC resolution after transmural drainage to either stent maintenance or early stent retrieval; in the latter allocation group, stent retrieval was performed at a median of 2 mo post stent insertion)[[28](#_ENREF_28)]. PPC recurrence was more frequent in the early stent retrieval group (38% vs 0%) and, in another, retrospective, series, a stenting duration of 6 weeks or less was independently associated with the failure of endoscopic PPC drainage[[27](#_ENREF_27)].

***Procedure-related complications***

Reported figures largely vary from center to center with average morbidity rates of 13% and average mortality rates of 0.3%[[15](#_ENREF_15),[29](#_ENREF_29)]. Major complications include hemorrhage, perforation and infection. Most of these can be managed by non-operative means, including endoscopic coagulation, arterial embolization, repeat endoscopic drainage in the case of secondary infection and antibiotics in the case of retroperitoneal perforation. The following measures may help preventing procedure-related complications:

**Secondary infection:** Although no data on the efficacy of antibiotic prophylaxis for endoscopic PPC drainage is available, antibiotic administration has been recommended immediately before transmural or transpapillary PPC drainage[[30](#_ENREF_30)]. The decision whether to continue antibiotics or not after the procedure should be based on drainage adequacy and on the presence or absence of necrosis[[12](#_ENREF_12)].

**Bleeding:** Severe bleeding usually arises from dilated arteries or veins. Pseudoaneurysms of the splenic artery may develop in the vicinity of PPCs. Imaging preceding the endoscopic drainage of PPCs should look for pseudoaneurysms and, in the case that one is discovered, have its prophylactic embolization discussed if the transmural route is elected.Extrahepatic portal hypertension develops during the course of CP in 15% or more of patients. It is frequently associated with PPC as well as higher morbidity in patients who undergo pancreatic surgery[[31](#_ENREF_31)]. The endosonography-guided technique of PPC drainage has been recommended in such patients although it has not been demonstrated to decrease the risk of bleeding[[32](#_ENREF_32)].

***In the case of infected PPC, should the strategy be different?***

Primary infection is a rare complication of CP-related PPCs; secondary infection following stent occlusion or endoscopic attempt at draining pancreatic necrosis is more frequent[[33](#_ENREF_33)].

Infected PPCs present a thick content that may not drain adequately through one or two thin plastic stents. Traditionally, in such cases, more large-bore stents are inserted together with a nasocystic catheter that is used for PPC irrigation. These additional interventions have resulted in similarly high success rates in patients with infected PPCs as compared with those who present uncomplicated PPC[[20](#_ENREF_20),[34](#_ENREF_34)]. As inserting multiple stents plus a nasocystic catheter requires time and may be technically challenging, fully covered self-expandable metal stents (FCSEMSs) seem to be a promising alternative for draining PPCs with a thick content. In a series of 20 patients with an infected PPC that was drained by endosonography-guided FCSEMS transmural insertion alone, clinical success was achieved in 17 patients[[35](#_ENREF_35)]. The authors suggested that using FCSEMS rather than plastic stents plus nasocystic drains in patients with infected PPCs may decrease the number of endoscopic procedures, increase the final success rate, and reduce the time required for PPC resolution. FCSEMSs specifically designed for PPC drainage have become available from various manufacturers; they present a short length, a large lumen, and a diabolo shape aimed at preventing stent migration[[25](#_ENREF_25),[36](#_ENREF_36)].

***In the case of complete MPD rupture, should the strategy be different?***

If complete MPD rupture occurs, the disconnected pancreatic tail may keep secreting pancreatic juice that, in the absence of effective drainage, will lead to prolonged fluid accumulation. Bridging of complete MPD ruptures should be attempted and a combination of transmural PPC drainage plus a transpapillary stent bridging the MPD rupture should be considered[[37](#_ENREF_37),[38](#_ENREF_38)]. The stent should be left in place for a long duration, at least as long as secretin-enhanced magnetic resonance pancreatography demonstrates juice outflow from the pancreatic tail[[39](#_ENREF_39)].

**BILIARY STRICTURES**

***Differential diagnosis***

It is of paramount importance to reasonably rule out malignancy before embarking in the endoscopic treatment of presumed CP-related biliary strictures as such a treatment usually lasts for one year and the course of pancreatic cancer is rapid. Particular attention should be paid to patients who present risk factors for pancreatic cancer; these include patients over 50 years of age, female gender, white race, or an absence of pancreatic calcifications and presence of exocrine insufficiency[[40](#_ENREF_40),[41](#_ENREF_41)]. Patients with hereditary pancreatitis present a very high risk of pancreatic cancer.

The accuracy of standard CT scanning and of endosonography for disclosing pancreatic cancer is limited in patients with CP[[42](#_ENREF_42),[43](#_ENREF_43)]. Endosonography, supplemented by fine needle aspiration (FNA) plus biliary endoluminal sampling and dosage of malignancy biomarkers are part of the standard work-up of a biliary stricture detected in the setting of CP. Other examination modalities such as probe-based endoluminal real-time microscopy are investigational. It should be kept in mind that endosonography-guided FNA is less accurate in the presence, than in the absence of CP[[41](#_ENREF_41),[44](#_ENREF_44)], although this decrease in accuracy has been suggested to be confined to a subset of patients who present with obstructive jaundice and a biliary stent[[45](#_ENREF_45)]. Furthermore, in the community, the accuracy of endosonography-guided FNA for diagnosing pancreatic cancer is likely to be much lower than the 90% figure that is widely reported in the literature (latter reports originate from tertiary centers and use per-protocol analysis)[[46](#_ENREF_46),[47](#_ENREF_47)]. The technical details of the sampling procedure and of the sample processing are extremely important to reach a high accuracy; they have recently been reviewed elsewhere for endosonography-guided FNA and for endoluminal biliary sampling[[48-50](#_ENREF_48)]. Recent improvements in the field of endoluminal biliary sampling include the development of more effective sampling devices and the use of rapid on-site examination for smears as well as for tissue biopsies[[48](#_ENREF_48),[51](#_ENREF_51),[52](#_ENREF_52)].

***Indications for treatment***

Generally accepted indications for the treatment of CP-related biliary strictures include symptoms such as secondary biliary cirrhosis, biliary stones, progression of biliary stricture, and asymptomatic elevation of serum alkaline phosphatase (greater than 2 or 3 times the upper limit of normal values) or of serum bilirubin or both for longer than one month.

***Results: Choosing endoscopic vs surgical treatment***

A Guideline recently issued by the European Society of Gastrointestinal Endoscopy proposed that the choice between endoscopic and surgical treatment should rely on local expertise, loco-regional or systemic patient co-morbidities and expected patient compliance with repeat endoscopic procedures[[53](#_ENREF_53)]. No strong recommendation could be made about the choice between the endoscopic and the surgical approach to CP-related biliary strictures due to the lack of comparative studies. In conditions different from CP, two comparative nonrandomized studies that included 143 patients with biliary strictures related to a traumatism have found that long-term success was similar (77%-83%) with the endoscopic and the surgical approaches[[54](#_ENREF_54),[55](#_ENREF_55)]. However, the endoscopic techniques used in these studies are not current anymore and the endoscopic treatment is more effective in post-traumatic compared with CP-related biliary strictures[[29](#_ENREF_29)]. Another study has compared the endoscopic *vs* the surgical drainage of CP-related biliary strictures, however surgery was performed in only 6 patients, of whom five also had a pancreatic resection[[56](#_ENREF_56)].

Patient complications such as portal cavernoma or cirrhosis are often decisive factors in the election of the endoscopic *vs* the surgical modality. Other factors that may influence this election include the expected patient compliance with endoscopic stent exchanges and, less importantly, the presence or absence of pancreatic calcifications. In a retrospective series of 14 patients, only two patients presented for elective stent exchanges scheduled at 3-month intervals[[57](#_ENREF_57)]. Most patients were admitted with biliary infection due to stent occlusion after the scheduled stent exchange date. Another series that included 29 patients treated with multiple, side-by-side, plastic biliary stents reported the occurrence of at least 20 episodes of cholangitis (in this latter series, stents were exchanged when symptoms of clogging developed). The mean interval between stent exchanges was 6 mo in patients who were alive at the end of follow-up as compared to 22 mo (*P* < 0.05) in the three patients who died during follow-up (two of them from cholangitis)[[58](#_ENREF_58)]. The presence of pancreatic calcifications has been associated with long-term failure of single plastic biliary stenting[[59](#_ENREF_59)] but this factor may be less relevant if simultaneous multiple, side-by-side, plastic stents are used[[60](#_ENREF_60)].

***Endoscopic technique***

**Plastic stents:** If the endoscopic treatment modality is elected, temporary placement of simultaneous multiple, side-by-side, plastic stents is the gold standard amongst the various techniques available. A single nonrandomized series has compared long-term results after temporary placement of single *vs* multiple simultaneous plastic stents; clinical success was reported in 24% *vs* 92% of patients, respectively[[60](#_ENREF_60)].

From a practical point of view, amongst plastic biliary stents, polyethylene models are recommended because they allow obstruction relief more frequently than Teflon models[[61](#_ENREF_61)], and the exchange of plastic stents with an increasing number of stents is usually scheduled at 3-mo intervals for a total stenting duration of 12 mo[[58](#_ENREF_58),[60](#_ENREF_60),[62](#_ENREF_62)]. It has recently been suggested that with multiple, side-by-side, plastic stents, the interval between stent exchanges could be extended[[63](#_ENREF_63)]. However, as mentioned above, special care should be taken regarding the generally poor compliance of patients with alcoholic CP and it is recommended to implement a recall system to care for patients who do not turn up for stent exchanges at scheduled dates.

**Self-expandable metal stents:** “Definitive” insertion of self-expandable metal stents (SEMSs) (*i.e.*, with no intended SEMS removal) for benign biliary strictures has almost been abandoned due to the development of biliary epithelial hyperplasia that leads to late biliary obstruction[[64](#_ENREF_64)]. Recent studies about the endoscopic treatment of CP-related biliary strictures have focused on the temporary placement of covered SEMS with a shift of interest from partially covered to fully covered SEMS designs[[65](#_ENREF_65),[66](#_ENREF_66)]. Spontaneous SEMS migration has been the main drawback with FCSEMS; new stent designs aiming to prevent migration include the adjunction of anchoring fins, the positioning of the stent covering on the internal side of the SEMS and a flared-ends design. Such SEMS remain investigational for the treatment of benign biliary strictures.

If FCSEMS are used to treat benign biliary strictures, a stenting duration >90 days is recommended as this was independently associated with stricture resolution in a multicenter trial that included 133 patients with benign biliary strictures 44 of these being CP-related[[67](#_ENREF_67)]. In this trial, stricture resolution at the time of stent removal was reported in 26 (59%, intention-to-treat analysis) patients with CP. Other studies that included more than 10 patients followed-up for at least one year after FCSEMS removal showed a success rate of approximately 50%: (1) Perri *et al*[[66](#_ENREF_66)] inserted a Niti-S stent with either a straight or a flared-ends design in 17 patients who had previously received a single plastic stent. Two years following FCSEMS removal, 56% of patients had presented no stricture relapse and had normal liver function tests. The flared-ends design partially prevented FCSEMS migration while all straight FCSEMS migrated; and (2) Poley *et al*[[68](#_ENREF_68)] inserted a Hanaro prototype FCSEMS in 13 patients who had previously received a single plastic stent; success was reported in 6 (43%) of them.

FCSEMS currently are the most promising alternative to multiple, side-by-side, plastic biliary stents. Despite their main advantages, *i.e.*, a reduced number of endoscopy procedures and a lower incidence of stent obstruction, FCSEMSs need improvements in their design as well as additional large multicentre trials before they can possibly be recommended as a first-line option for the endoscopic treatment of CP-related biliary strictures.

**OTHER COMPLICATIONS**

Other complications to CP include splenic vein thrombosis, pancreatic adenocarcinoma, pancreatic ascites, and pleural effusion.

Splenic vein thrombosis is present in approximately 12% of patients with CP and it is usually asymptomatic but may cause bleeding in 7% of patients[[69](#_ENREF_69)]. In the case of bleeding, endoscopic variceal obturation using N-butylcyanoacrylate is effective in achieving hemostasis and a splenectomy is an effective way to prevent recurrent bleeding[[70](#_ENREF_70)].

For the treatment of pancreatic adenocarcinoma, the endosonography-guided delivery of various cytotoxic agents is a rapidly evolving field that remains investigational[[71](#_ENREF_71)].

Pancreatic ascites and pleural effusion are rare complications of CP; they may or may not be associated with PPC and they present a high morbidity. The aim of endoscopic therapy in such patients is to insert a stent to bridge the MPD rupture that is responsible for pancreatic juice leakage; high success rates have been reported[[72](#_ENREF_72)].

**CONCLUSION**

Progresses have recently been made in the field of the endoscopic treatment of CP-related complications.

With regard to uncomplicated PPCs, endoscopic drainage has been shown to be feasible in almost all cases and to be superior to surgical drainage. Techniques associated with the best clinical outcome have been identified. With regard to CP-related biliary obstructions, improvements in the design of FCSEMS are challenging the standard technique and have the potential to improve patient acceptability.

**REFERENCES**

1 **Abdallah AA**, Krige JE, Bornman PC. Biliary tract obstruction in chronic pancreatitis. *HPB (Oxford)* 2007; **9**: 421-428 [PMID: 18345288 DOI: 10.1080/13651820701774883]

2 **Andrén-Sandberg A**, Dervenis C. Pancreatic pseudocysts in the 21st century. Part I: classification, pathophysiology, anatomic considerations and treatment. *JOP* 2004; **5**: 8-24 [PMID: 14730118]

3 **Bradley EL**. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992. *Arch Surg* 1993; **128**: 586-590 [PMID: 8489394]

4 **Dumonceau JM**. Endoscopic management of chronic pancreatitis: an evidence-based approach. In: Testoni P, ed. In: Testoni P, Mariani A, Arcidiacono PG. Acute and chronic pancreatitis: new concepts and evidence-based approaches. Milan: Minerva Medica, 2013 (in press)

5 **Tanaka M**, Fernández-del Castillo C, Adsay V, Chari S, Falconi M, Jang JY, Kimura W, Levy P, Pitman MB, Schmidt CM, Shimizu M, Wolfgang CL, Yamaguchi K, Yamao K. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. *Pancreatology* 2012; **12**: 183-197 [PMID: 22687371 DOI: 10.1016/j.pan.2012.04.004]

6 **Talamini G**, Zamboni G, Salvia R, Capelli P, Sartori N, Casetti L, Bovo P, Vaona B, Falconi M, Bassi C, Scarpa A, Vantini I, Pederzoli P. Intraductal papillary mucinous neoplasms and chronic pancreatitis. *Pancreatology* 2006; **6**: 626-634 [PMID: 17135772 DOI: 10.1159/000097605]

7 **Chalian H**, Töre HG, Miller FH, Yaghmai V. CT attenuation of unilocular pancreatic cystic lesions to differentiate pseudocysts from mucin-containing cysts. *JOP* 2011; **12**: 384-388 [PMID: 21737901]

8 **Brugge WR**, Lauwers GY, Sahani D, Fernandez-del Castillo C, Warshaw AL. Cystic neoplasms of the pancreas. *N Engl J Med* 2004; **351**: 1218-1226 [PMID: 15371579 DOI: 10.1056/NEJMra031623]

9 **van der Waaij LA**, van Dullemen HM, Porte RJ. Cyst fluid analysis in the differential diagnosis of pancreatic cystic lesions: a pooled analysis. *Gastrointest Endosc* 2005; **62**: 383-389 [PMID: 16111956]

10 **Cuoghi A**, Farina A, Z'graggen K, Dumonceau JM, Tomasi A, Hochstrasser DF, Genevay M, Lescuyer P, Frossard JL. Role of proteomics to differentiate between benign and potentially malignant pancreatic cysts. *J Proteome Res* 2011; **10**: 2664-2670 [PMID: 21425880 DOI: 10.1021/pr2000557]

11 **Konda VJ**, Aslanian HR, Wallace MB, Siddiqui UD, Hart J, Waxman I. First assessment of needle-based confocal laser endomicroscopy during EUS-FNA procedures of the pancreas (with videos). *Gastrointest Endosc* 2011; **74**: 1049-1060 [PMID: 21924718 DOI: 10.1016/j.gie.2011.07.018]

12 **Jacobson BC**, Baron TH, Adler DG, Davila RE, Egan J, Hirota WK, Leighton JA, Qureshi W, Rajan E, Zuckerman MJ, Fanelli R, Wheeler-Harbaugh J, Faigel DO. ASGE guideline: The role of endoscopy in the diagnosis and the management of cystic lesions and inflammatory fluid collections of the pancreas. *Gastrointest Endosc* 2005; **61**: 363-370 [PMID: 15758904]

13 **Vitas GJ**, Sarr MG. Selected management of pancreatic pseudocysts: operative versus expectant management. *Surgery* 1992; **111**: 123-130 [PMID: 1736380]

14 **Yeo CJ**, Bastidas JA, Lynch-Nyhan A, Fishman EK, Zinner MJ, Cameron JL. The natural history of pancreatic pseudocysts documented by computed tomography. *Surg Gynecol Obstet* 1990; **170**: 411-417 [PMID: 2326721]

15 **Lerch MM**, Stier A, Wahnschaffe U, Mayerle J. Pancreatic pseudocysts: observation, endoscopic drainage, or resection? *Dtsch Arztebl Int* 2009; **106**: 614-621 [PMID: 19890418 DOI: 10.3238/arztebl.2009.0614]

16 **Gouyon B**, Lévy P, Ruszniewski P, Zins M, Hammel P, Vilgrain V, Sauvanet A, Belghiti J, Bernades P. Predictive factors in the outcome of pseudocysts complicating alcoholic chronic pancreatitis. *Gut* 1997; **41**: 821-825 [PMID: 9462217]

17 **Varadarajulu S**, Bang JY, Sutton BS, Trevino JM, Christein JD, Wilcox CM. Equal Efficacy of Endoscopic and Surgical Cystogastrostomy for Pancreatic Pseudocyst Drainage in a Randomized Trial. *Gastroenterology* 2013; [Epub ahead of print] [PMID: 23732774 DOI: 10.1053/j.gastro.2013.05.046]

18 **Rosso E**, Alexakis N, Ghaneh P, Lombard M, Smart HL, Evans J, Neoptolemos JP. Pancreatic pseudocyst in chronic pancreatitis: endoscopic and surgical treatment. *Dig Surg* 2003; **20**: 397-406 [PMID: 12900529 DOI: 10.1159/000072706]

19 **Cahen D**, Rauws E, Fockens P, Weverling G, Huibregtse K, Bruno M. Endoscopic drainage of pancreatic pseudocysts: long-term outcome and procedural factors associated with safe and successful treatment. *Endoscopy* 2005; **37**: 977-983 [PMID: 16189770 DOI: 10.1055/s-2005-870336]

20 **Hookey LC**, Debroux S, Delhaye M, Arvanitakis M, Le Moine O, Devière J. Endoscopic drainage of pancreatic-fluid collections in 116 patients: a comparison of etiologies, drainage techniques, and outcomes. *Gastrointest Endosc* 2006; **63**: 635-643 [PMID: 16564865 DOI: 10.1016/j.gie.2005.06.028]

21 **Bello B**, Matthews JB. Minimally invasive treatment of pancreatic necrosis. *World J Gastroenterol* 2012; **18**: 6829-6835 [PMID: 23239921 DOI: 10.3748/wjg.v18.i46.6829]

22 **Barthet M**, Lamblin G, Gasmi M, Vitton V, Desjeux A, Grimaud JC. Clinical usefulness of a treatment algorithm for pancreatic pseudocysts. *Gastrointest Endosc* 2008; **67**: 245-252 [PMID: 18226686 DOI: 10.1016/j.gie.2007.06.014]

23 **Binmoeller KF**, Seifert H, Walter A, Soehendra N. Transpapillary and transmural drainage of pancreatic pseudocysts. *Gastrointest Endosc* 1995; **42**: 219-224 [PMID: 7498686]

24 **Panamonta N**, Ngamruengphong S, Kijsirichareanchai K, Nugent K, Rakvit A. Endoscopic ultrasound-guided versus conventional transmural techniques have comparable treatment outcomes in draining pancreatic pseudocysts. *Eur J Gastroenterol Hepatol* 2012; **24**: 1355-1362 [DOI: 10.1097/MEG.0b013e32835871eb]

25 **Binmoeller KF**, Weilert F, Shah JN, Bhat YM, Kane S. Endosonography-guided transmural drainage of pancreatic pseudocysts using an exchange-free access device: initial clinical experience. *Surg Endosc* 2013; **27**: 1835-1839 [DOI: 10.1007/s00464-012-2682-9]

26 **Beckingham IJ**, Krige JE, Bornman PC, Terblanche J. Endoscopic management of pancreatic pseudocysts. *Br J Surg* 1997; **84**: 1638-1645 [PMID: 9448608]

27 **Cahen D**, Rauws E, Fockens P, Weverling G, Huibregtse K, Bruno M. Endoscopic drainage of pancreatic pseudocysts: long-term outcome and procedural factors associated with safe and successful treatment. *Endoscopy* 2005; **37**: 977-983 [PMID: 16189770 DOI: 10.1055/s-2005-870336]

28 **Arvanitakis M**, Delhaye M, Bali MA, Matos C, De Maertelaer V, Le Moine O, Devière J. Pancreatic-fluid collections: a randomized controlled trial regarding stent removal after endoscopic transmural drainage. *Gastrointest Endosc* 2007; **65**: 609-619 [PMID: 17324413 DOI: 10.1016/j.gie.2006.06.083]

29 **Nguyen-Tang T**, Dumonceau JM. Endoscopic treatment in chronic pancreatitis, timing, duration and type of intervention. *Best Pract Res Clin Gastroenterol* 2010; **24**: 281-298 [PMID: 20510829 DOI: 10.1016/j.bpg.2010.03.002]

30 **Banerjee S**, Shen B, Baron TH, Nelson DB, Anderson MA, Cash BD, Dominitz JA, Gan SI, Harrison ME, Ikenberry SO, Jagannath SB, Lichtenstein D, Fanelli RD, Lee K, van Guilder T, Stewart LE. Antibiotic prophylaxis for GI endoscopy. *Gastrointest Endosc* 2008; **67**: 791-798 [PMID: 18374919 DOI: 10.1016/j.gie.2008.02.068]

31 **Izbicki JR**, Yekebas EF, Strate T, Eisenberger CF, Hosch SB, Steffani K, Knoefel WT. Extrahepatic portal hypertension in chronic pancreatitis: an old problem revisited. *Ann Surg* 2002; **236**: 82-89 [PMID: 12131089]

32 **Sriram PV**, Kaffes AJ, Rao GV, Reddy DN. Endoscopic ultrasound-guided drainage of pancreatic pseudocysts complicated by portal hypertension or by intervening vessels. *Endoscopy* 2005; **37**: 231-235 [PMID: 15731938 DOI: 10.1055/s-2005-860997]

33 **Andrén-Sandberg A**, Dervenis C. Pancreatic pseudocysts in the 21st century. Part II: natural history. *JOP* 2004; **5**: 64-70 [PMID: 15007187]

34 **Varadarajulu S**, Bang JY, Phadnis MA, Christein JD, Wilcox CM. Endoscopic transmural drainage of peripancreatic fluid collections: outcomes and predictors of treatment success in 211 consecutive patients. *J Gastrointest Surg* 2011; **15**: 2080-2088 [PMID: 21786063 DOI: 10.1007/s11605-011-1621-8]

35 **Fabbri C**, Luigiano C, Cennamo V, Polifemo A, Barresi L, Jovine E, Traina M, Imperio N, Tarantino I. Endoscopic ultrasound-guided transmural drainage of infected pancreatic fluid collections with placement of covered self-expanding metal stents: a case series. *Endoscopy* 2012; **44**: 429-433 [DOI: 10.1055/s-0031-1291624]

36 **Itoi T**, Binmoeller KF, Shah J, Sofuni A, Itokawa F, Kurihara T, Tsuchiya T, Ishii K, Tsuji S, Ikeuchi N, Moriyasu F. Clinical evaluation of a novel lumen-apposing metal stent for endosonography-guided pancreatic pseudocyst and gallbladder drainage (with videos). *Gastrointest Endos*c 2012; **75**: 870-876 [DOI: 10.1016/j.gie.2011.10.020]

37 **Polkowski M**, Larghi A, Weynand B, Boustière C, Giovannini M, Pujol B, Dumonceau JM. Learning, techniques, and complications of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline. *Endoscopy* 2012; **44**: 190-206 [PMID: 22180307 DOI: 10.1055/s-0031-1291543]

38 **Trevino JM**, Tamhane A, Varadarajulu S. Successful stenting in ductal disruption favorably impacts treatment outcomes in patients undergoing transmural drainage of peripancreatic fluid collections. *J Gastroenterol Hepatol* 2010; **25**: 526-531 [PMID: 20074158 DOI: 10.1111/j.1440-1746.2009.06109.x]

39 **Dumonceau JM**, Macias Gomez C, Casco C, Genevay M, Marcolongo M, Bongiovanni M, Morel P, Majno P, Hadengue A. Grasp or brush for biliary sampling at endoscopic retrograde cholangiography? A blinded randomized controlled trial. *Am J Gastroenterol* 2008; **103**: 333-340 [PMID: 17900324 DOI: 10.1111/j.1572-0241.2007.01543.x]

40 **Arvanitakis M**, Van Laethem JL, Parma J, De Maertelaer V, Delhaye M, Devière J. Predictive factors for pancreatic cancer in patients with chronic pancreatitis in association with K-ras gene mutation. *Endoscopy* 2004; **36**: 535-542 [PMID: 15202051 DOI: 10.1055/s-2004-814401]

41 **Varadarajulu S**, Tamhane A, Eloubeidi MA. Yield of EUS-guided FNA of pancreatic masses in the presence or the absence of chronic pancreatitis. *Gastrointest Endosc* 2005; **62**: 728-36; quiz 751, 753 [PMID: 16246688 DOI: 10.1016/j.gie.2005.06.051]

42 **Ardengh JC**, Lopes CV, Campos AD, Pereira de Lima LF, Venco F, Módena JL. Endoscopic ultrasound and fine needle aspiration in chronic pancreatitis: differential diagnosis between pseudotumoral masses and pancreatic cancer. *JOP* 2007; **8**: 413-421 [PMID: 17625292]

43 **Davids PH**, Tanka AK, Rauws EA, van Gulik TM, van Leeuwen DJ, de Wit LT, Verbeek PC, Huibregtse K, van der Heyde MN, Tytgat GN. Benign biliary strictures. Surgery or endoscopy? *Ann Surg* 1993; **217**: 237-243 [PMID: 8452402]

44 **Fritscher-Ravens A**, Brand L, Knöfel WT, Bobrowski C, Topalidis T, Thonke F, de Werth A, Soehendra N. Comparison of endoscopic ultrasound-guided fine needle aspiration for focal pancreatic lesions in patients with normal parenchyma and chronic pancreatitis. *Am J Gastroenterol* 2002; **97**: 2768-2775 [PMID: 12425546 DOI: 10.1111/j.1572-0241.2002.07020.x]

45 **Krishna NB**, Mehra M, Reddy AV, Agarwal B. EUS/EUS-FNA for suspected pancreatic cancer: influence of chronic pancreatitis and clinical presentation with or without obstructive jaundice on performance characteristics. *Gastrointest Endosc* 2009; **70**: 70-79 [PMID: 19249774 DOI: 10.1016/j.gie.2008.10.030]

46 **Dumonceau JM**, Koessler T, van Hooft JE, Fockens P. Endoscopic ultrasonography-guided fine needle aspiration: Relatively low sensitivity in the endosonographer population. *World J Gastroenterol* 2012; **18**: 2357-2363 [PMID: 22654426 DOI: 10.3748/wjg.v18.i19.2357]

47 **Rösch T**, Hofrichter K, Frimberger E, Meining A, Born P, Weigert N, Allescher HD, Classen M, Barbur M, Schenck U, Werner M. ERCP or EUS for tissue diagnosis of biliary strictures? A prospective comparative study. *Gastrointest Endosc* 2004; **60**: 390-396 [PMID: 15332029]

48 **Kahl S**, Zimmermann S, Genz I, Glasbrenner B, Pross M, Schulz HU, Mc Namara D, Schmidt U, Malfertheiner P. Risk factors for failure of endoscopic stenting of biliary strictures in chronic pancreatitis: a prospective follow-up study. *Am J Gastroenterol* 2003; **98**: 2448-2453 [PMID: 14638347]

49 **Polkowski M**, Larghi A, Weynand B, Boustière C, Giovannini M, Pujol B, Dumonceau JM. Learning, techniques, and complications of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline. *Endoscopy* 2012; **44**: 190-206 [PMID: 22180307 DOI: 10.1055/s-0031-1291543]

50 **Dumonceau JM**. Sampling at ERCP for cyto- and histopathologicical examination. *Gastrointest Endosc Clin N Am* 2012; **22**: 461-477 [PMID: 22748243 DOI: 10.1016/j.giec.2012.05.006]

51 **Draganov P**, Hoffman B, Marsh W, Cotton P, Cunningham J. Long-term outcome in patients with benign biliary strictures treated endoscopically with multiple stents. *Gastrointest Endosc* 2002; **55**: 680-686 [PMID: 11979250]

52 **Lawrence C**, Romagnuolo J, Payne KM, Hawes RH, Cotton PB. Low symptomatic premature stent occlusion of multiple plastic stents for benign biliary strictures: comparing standard and prolonged stent change intervals. *Gastrointest Endosc* 2010; **72**: 558-563 [PMID: 20638060 DOI: 10.1016/j.gie.2010.05.029]

53 **Dumonceau JM**, Delhaye M, Tringali A, Dominguez-Munoz JE, Poley JW, Arvanitaki M, Costamagna G, Costea F, Devière J, Eisendrath P, Lakhtakia S, Reddy N, Fockens P, Ponchon T, Bruno M. Endoscopic treatment of chronic pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 2012; **44**: 784-800 [PMID: 22752888 DOI: 10.1055/s-0032-1309840]

54 **Davids PH**, Tanka AK, Rauws EA, van Gulik TM, van Leeuwen DJ, de Wit LT, Verbeek PC, Huibregtse K, van der Heyde MN, Tytgat GN. Benign biliary strictures. Surgery or endoscopy? *Ann Surg* 1993; **217**: 237-243 [PMID: 8452402]

55 **Tocchi A**, Mazzoni G, Liotta G, Costa G, Lepre L, Miccini M, De Masi E, Lamazza MA, Fiori E. Management of benign biliary strictures: biliary enteric anastomosis vs endoscopic stenting. *Arch Surg* 2000; **135**: 153-157 [PMID: 10668872]

56 **Regimbeau JM**, Fuks D, Bartoli E, Fumery M, Hanes A, Yzet T, Delcenserie R. A comparative study of surgery and endoscopy for the treatment of bile duct stricture in patients with chronic pancreatitis. *Surg Endosc* 2012; **26**: 2902-2908 [DOI: 10.1007/s00464-012-2283-7]

57 **Kiehne K**, Fölsch UR, Nitsche R. High complication rate of bile duct stents in patients with chronic alcoholic pancreatitis due to noncompliance. *Endoscopy* 2000; **32**: 377-380 [PMID: 10817175]

58 **Pozsár J**, Sahin P, László F, Forró G, Topa L. Medium-term results of endoscopic treatment of common bile duct strictures in chronic calcifying pancreatitis with increasing numbers of stents. *J Clin Gastroenterol* 2004; **38**: 118-123 [PMID: 14745285]

59 **Kahl S**, Zimmermann S, Genz I, Glasbrenner B, Pross M, Schulz HU, Mc Namara D, Schmidt U, Malfertheiner P. Risk factors for failure of endoscopic stenting of biliary strictures in chronic pancreatitis: a prospective follow-up study. *Am J Gastroenterol* 2003; **98**: 2448-2453 [PMID: 14638347]

60 **Catalano MF**, Linder JD, George S, Alcocer E, Geenen JE. Treatment of symptomatic distal common bile duct stenosis secondary to chronic pancreatitis: comparison of single vs. multiple simultaneous stents. *Gastrointest Endosc* 2004; **60**: 945-952 [PMID: 15605010]

61 **Dumonceau JM**, Heresbach D, Devière J, Costamagna G, Beilenhoff U, Riphaus A. Biliary stents: models and methods for endoscopic stenting. *Endoscopy* 2011; **43**: 617-626 [PMID: 21614754 DOI: 10.1055/s-0030-1256315]

62 **Draganov P**, Hoffman B, Marsh W, Cotton P, Cunningham J. Long-term outcome in patients with benign biliary strictures treated endoscopically with multiple stents. *Gastrointest Endosc* 2002; **55**: 680-686 [PMID: 11979250]

63 **Lawrence C**, Romagnuolo J, Payne KM, Hawes RH, Cotton PB. Low symptomatic premature stent occlusion of multiple plastic stents for benign biliary strictures: comparing standard and prolonged stent change intervals. *Gastrointest Endosc* 2010; **72**: 558-563 [PMID: 20638060 DOI: 10.1016/j.gie.2010.05.029]

64 **Dumonceau JM**, Tringali A, Blero D, Devière J, Laugiers R, Heresbach D, Costamagna G. Biliary stenting: indications, choice of stents and results: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. *Endoscopy* 2012; **44**: 277-298 [PMID: 22297801 DOI: 10.1055/s-0031-1291633]

65 **Behm B**, Brock A, Clarke BW, Ellen K, Northup PG, Dumonceau JM, Kahaleh M. Partially covered self-expandable metallic stents for benign biliary strictures due to chronic pancreatitis. *Endoscopy* 2009; **41**: 547-551 [PMID: 19533560 DOI: 10.1055/s-0029-1214708]

66 **Perri V**, Boskoski I, Tringali A, Familiari P, Mutignani M, Marmo R, Costamagna G. Fully covered self-expandable metal stents in biliary strictures caused by chronic pancreatitis not responding to plastic stenting: a prospective study with 2 years of follow-up. *Gastrointest Endosc* 2012; **75**: 1271-1277 [DOI: 10.1016/j.gie.2012.02.002]

67 **Kahaleh M**, Brijbassie A, Sethi A, Degaetani M, Poneros JM, Loren DE, Kowalski TE, Sejpal DV, Patel S, Rosenkranz L, McNamara KN, Raijman I, Talreja JP, Gaidhane M, Sauer BG, Stevens PD. Multicenter Trial Evaluating the Use of Covered Self-expanding Metal Stents in Benign Biliary Strictures: Time to Revisit Our Therapeutic Options? *J Clin Gastroenterol* 2013; [Epub ahead of print] [PMID: 23442836 DOI: 10.1097/MCG.0b013e31827fd311]

68 **Poley JW**, Cahen DL, Metselaar HJ, van Buuren HR, Kazemier G, van Eijck CHJ, Haringsma J, Kuipers EJ, Bruno MJ. A prospective group sequential study evaluating a new type of fully covered self-expandable metal stent for the treatment of benign biliary strictures (with video). *Gastrointest Endosc* 2012; **75**: 783-789 [DOI: 10.1016/j.gie.2011.10.022]

69 **Butler JR**, Eckert GJ, Zyromski NJ, Leonardi MJ, Lillemoe KD, Howard TJ. Natural history of pancreatitis-induced splenic vein thrombosis: a systematic review and meta-analysis of its incidence and rate of gastrointestinal bleeding. *HPB* 2011; **13**: 839-845 [DOI: 10.1111/j.1477-2574.2011.00375.x]

70 **Kang EJ**, Jeong SW, Jang JY, Cho JY, Lee SH, Kim HG, Kim SG, Kim YS, Cheon YK, Cho YD, Kim HS, Kim BS. Long-term result of endoscopic Histoacryl (N-butyl-2-cyanoacrylate) injection for treatment of gastric varices. *World J Gastroenterol* 2011; **17**: 1494-1500 [PMID: 21472110 DOI: 10.3748/wjg.v17.i11.1494]

71 **Carrara S**, Petrone MC, Testoni PA, Arcidiacono PG. Tumors and new endoscopic ultrasound-guided therapies. *World J Gastrointest Endosc* 2013; **5**: 141-147 [PMID: 23596535 DOI: 10.4253/wjge.v5.i4.141]

72 **Pai CG**, Suvarna D, Bhat G. Endoscopic treatment as first-line therapy for pancreatic ascites and pleural effusion. *J Gastroenterol Hepatol* 2009; **24**: 1198-1202 [PMID: 19486258 DOI: 10.1111/j.1440-1746.2009.05796.x]

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