Acute biliary pancreatitis: the current role of endoscopic and minimally invasive surgical procedures



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AIM: This review aims to summarize the state of the art in endoscopic and other minimally invasive technique for the treatment of acute biliary pancreatitis. Current indications, advantages or disadvantages for each reported technique and future perspectives are discussed.

BACKGROUND: Acute biliary pancreatitis is one of the most common gastroenterological diseases. Its management range from medical to interventional treatment and involves gastroenterologists, nutritionists, endoscopists, interventional radiologists and surgeons.

Interventional procedures are required in case of local complications, failure of medical treatment and definitive treatment of biliary gallstones. Endoscopic and minimally invasive procedures have progressively gained favor and wide diffusion in treating acute biliary pancreatitis reporting good results in terms of safety and minor morbidity and mortality.

CONCLUSIONS: Endoscopic retrograde cholangiopancreatography is advocated in case of cholangitis and persistent common biliary duct obstruction. Laparoscopic cholecystectomy is considered the definitive treatment for acute biliary pancreatitis. Endoscopic transmural drainage and necrosectomy have gained acceptance and diffusion in treating pancreatic necrosis reporting minor impact on morbidity respect surgery. A surgical approach to pancreatic necrosis progressively shifts towards minimally invasive technique like minimally access retroperitoneal pancreatic necrosectomy, video-assisted retroperitoneal debridement or laparoscopic necrosectomy. Open necrosectomy in necrotizing pancreatitis is reserved to failure of endoscopic or minimally invasive treatment or in case of wide necrotic collections.

KEY WORDS: Acute biliary pancreatitis, Endoscopic retrograde cholangiopancreatography, Laparoscopic cholecystectomy, Pancreatic necrosis

Introduction

Acute Biliary pancreatitis (ABP) represents the most common type of acute pancreatitis (AP) ranging from 40% to 70% of cases ¹. ABP results from the migra-

tion of a gallstone into the common bile duct (CBD) and consequent obstruction of the biliopancreatic junction thus leading to increased pancreatic duct pressure and parenchyma autodigestion followed by local and systemic inflammatory response. ABP severity range from minor self-limiting episodes to life threatening attacks. According to the revised Atlanta classification AP has been classified as mild, moderately severe and severe ². Mild AP accounts for around 80% of cases. Pancreatic parenchyma is affected only by edema without local or systemic complications. Moderately severe AP is characterized by local or systemic complications and transient organ failure (<48 hours), while in severe AP organ failure is persistent ². Pancreatic or peripancreatic necrosis

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Abbreviations

ABP: Acute biliary pancreatitis; ACG: American College of Gastroenterology; AGA: American Gastroenterological Association; AP: Acute pancreatitis; ASGE: American Society of Gastrointestinal Endoscopy; CBD: Common bile duct; DEN: Direct endoscopic necrosectomy. EUS: Endoscopic ultrasonography; ERCP: Endoscopic retrograde cholangiopancreatography; LAMS: Lumen apposing metal stents; LC: Laparoscopic cholecystectomy; MABP: Mild acute biliary pancreatitis; MARPN: Minimally access retroperitoneal pancreatic necrosectomy; MRCP: Magnetic resonance cholangiopancreatography; PD: Pancreatic duct; PST: Papillo-sphincterotomy; RCTs: Randomized controlled trials; SEMS: Self-expandable metal stents; VARD: Video-assisted retroperitoneal debridement

could develop in moderately severe and severe pancreatitis. ABP management varies from conservative to interventional treatment depending on its gravity and complications onset. Endoscopic and minimally invasive procedures have progressively gained favor and wide diffusion in treating ABP etiology and related complications especially pancreatic necrosis reporting good results in terms of safety, morbidity and mortality.

Endoscopic retrograde cholangiopancreatography (ERCP) and laparoscopic cholecystectomy (LC) are the mainstay treatment for gallstones related AP. Several endoscopic and minimally invasive approaches for pancreatic necrosis management have been described. Endoscopic transmural drainage and necrosectomy, minimally access retroperitoneal pancreatic necrosectomy (MARPN), video-assisted retroperitoneal debridement (VARD) and laparoscopic anterior approach are the most popular.

In published literature each of these procedures is widely described. Nevertheless a comprehensive review is quite lacking.

Indications, limitations and literature evidence about each mentioned technique is therefore discussed.

ROLE OF ERCP

In the last years indication and timing of endoscopic retrograde cholangiopancreatography (ERCP) in the set-

ting of ABP has been widely debated in literature nevertheless some aspects are still opened.

ERCP is considered a complex endoscopic procedure burdened by risks and possible complications. Adequate training is advocated to maximize success and safety of the procedure. American Society of Gastrointestinal of Gastroenterology Endoscopy/American College (ASGE/ACG) recommended as a quality benchmark an overall success rate in cannulation in ERCP \geq 90% excluding patients with prior abdominal surgery or inadequate sedation ³. Technical success of ERCP is expected to be \geq 85% in other related procedures like stones extraction and stent placement. Complications related to therapeutic ERCP ranges from 7% to 10% and mortality from 0.2% to 2.2% of cases ^{4,5}. Post ERCP pancreatitis, perforation and bleeding from the papilla are well described complications after ERCP in order of 3.47%, 1.34% and 0.60% respectively 6. ASGE/ACG recommended as a quality indicator of the procedure a post ERCP pancreatitis, perforation and post-sphinc-terotomy bleeding rate of 1% to 7%, < 1% and 2% respectively³.

When ERCP is performed particular attention should be reserved to possible risk factors for complications. Difficult or incomplete CBD cannulation and suspected malignancy are recognized as possible predisposing factors for complications, while age is considered as an independent factor 7 .

Urgent ERCP (within 24-48 hours) with papillo-sphincterotomy (PST) is a validated indication for ABP and concomitant acute cholangitis ⁸⁻¹¹. Diagnosis of cholangitis could be quite challenging in course of ABP because signs of inflammation and biliary obstruction are frequently observed ¹². Data from a large multicentric database showed higher probability of unfavorable progression of ABP in case of unsuccessful ERCP and bile duct clearance. In this condition ERCP should be performed by skilled endoscopists in order to obtain high success rate of bile duct clearance ¹¹.

Even in biliary pancreatitis associated to CBD obstruction ERCP with PST and stone extraction is recommended to be performed in a short period of time ^{8,13-16}.

Most stones could pass spontaneously through the papilla into the duodenum. For this reason, performing an early ERCP only on the basis of biochemical signs of the presence of CBD stones in patients with ABP may be insufficient ¹⁷.

Endoscopic ultrasonography (EUS) and magnetic resonance cholangiopancreatography (MRCP) are considered very accurate tools for detection of CBD stones ^{18,19} and suggested to be performed before ERCP in case of ABP without sign of cholangitis ²⁰. These diagnostic exams reach a very high sensitivity and specificity in detecting choledocholithiasis. Therefore, they are very useful in avoiding unnecessary ERCP in case of absence of CBD stones ^{11,12}.

The choice between MRCP or EUS depends on several

factors firstly local expertise and availability ²¹. EUS application is reported to be able to spare ERCP almost in two thirds of cases ²². Anderloni et al considered EUS as the first choice in approaching ABP due to its ready availability, accuracy, safety and cost effectiveness in detecting biliary obstructions. For these reasons they advocate management of CBD stones in a combined simultaneous two step endoscopic session ²³. Limits related to EUS are long learning curve and results that are dependent on the operator. Moreover, this tool is not widely available in clinical practice.

MRCP is a non-invasive imaging exam able to detect CBD stones. It is a more objective exam than EUS and could also clearly reveals other bilio-pancreatic pathologies and anatomic variants ²⁴. MRCP is comparable to EUS in terms of sensitivity, specificity and accuracy in CBD stones detection although it seems to have less sensitivity in less than 6 mm CBD stones ²⁵.

In case of mild or severe ABP without signs of cholangitis or CBD obstruction, the indication and timing of ERCP are still debated ^{11,23}. In this setting the American Gastroenterological Association (AGA) and American Society for Gastrointestinal Endoscopy (ASGE) recommend against the routine use of urgent ERCP 13,26. AGA guidelines analyze 8 randomized controlled trials addressing the role of urgent ERCP in the management of patients with acute gallstone pancreatitis. Compared to conservative management, urgent ERCP had no impact on critical outcomes, such as mortality and multiple organ failures, and on important outcomes, such as single organ failures, infected pancreatic and peripancreatic necrosis, and total rates of necrotizing pancreatitis ²⁷. On the other hand, two recent metanalyses of randomized controlled trials demonstrated a significant decrease in complications, hospital stay and cost in patients with ABP and no signs of cholangitis who underwent early ERCP (within 72 h) compared to conservative treatment ^{28,29}.

Therefore, the Dutch Pancreatitis Study Group designed the APEC trial in order to clarify the role of early ERCP with sphincterotomy in patients with predicted severe ABP without cholangitis ³⁰.

232 patients with predicted severe ABP without cholangitis were randomized to early (within 24 hours after presentation at the emergency department) ERCP with PST or conservative treatment. Early ERCP with biliary sphincterotomy did not reduce the primary end point of death or major complications ³¹.

Role of LC

Recurrence of pancreatitis after an ABP episode is reported to occur within the next months in about 30%-50% of patients ^{32,33}.

For this reason, cholecystectomy is suggested even after a mild acute biliary pancreatitis (MABP) attack and it is considered the definitive treatment for ABP as it reduces the recurrence of pancreatitis and other gallstone-related disorders 34,35 .

Current guidelines recommend cholecystectomy during the index admission for patients with MABP ¹³ and delayed cholecystectomy after severe acute biliary pancreatitis ³⁶. The timing of cholecystectomy during the index admission is a matter of study. Early cholecystectomy (within 72 hours after admission) versus delayed cholecystectomy (beyond 72 hours after admission) has been investigated in a lot of randomized controlled trials and metanalyses.

Two most recent metanalyses on randomized controlled trials (RCTs) concluded that early cholecystectomy compared to delayed cholecystectomy following mild gallstone pancreatitis is equally safe and feasible both in complication rate and rate of conversion to open procedure and significantly reduces the recurrence rate of acute pancreatitis or biliary complications ^{37,38}.

In two recent RCTs early cholecystectomy (within 12-72 hours) has been demonstrated to shorten hospital stay, not influence postoperative complications and ERCP rate ^{39,40}. Anyway, these studies have several bias limitations so that widespread adoption of early LC is not recommended.

In case of mild acute pancreatitis, ERCP and PST are recommended in patients unfit for cholecystectomy in order to prevent recurrent attacks ^{14,41,42}.

Recurrent ABP is caused by persistent papillary obstacle potentially leading to chronic pancreatitis. In a retrospective study all patients with recurrent ABP were treated with ERCP and PST leading to no further recurrence of ABP at biochemical or instrumental (US or MRCP) follow up. According to these results the authors considered ERCP and PST as a valid tool for the prevention of recurrent acute biliary pancreatitis ⁴³.

A recent large retrospective study confirms the protective effect of ERCP and PST in patients with MABP who do not undergo cholecystectomy during the index admission. ERCP significantly decreased the rate of all cause and pancreatitis readmissions, also in case of severe pancreatitis. In patients with comorbidities who are not fit for or refuse surgery, ERCP should be strongly considered as an alternative to surgery ⁴⁴.

Despite these benefits in a recent large retrospective study, Garg et al. ⁴⁵ showed the decreased rate of both cholecystectomy and ERCP during the index MABP admission. This decrease could not be explained only by increasing disease severity or comorbidity. These authors advocate further research to understand the implications and reasons underlying this deviation from guidelines.

PANCREATIC NECROSIS MANAGEMENT

Pancreatic or peripancreatic necrosis could develop either in moderately severe or severe pancreatitis. Pancreatic and peripancreatic infected necrosis is amenable to interventional treatment (percutaneous, endoscopic o surgical) during the late phase (> 4 weeks from symptoms onset) or before in case of organized collection causing persistent organ dysfunction, complications or persistent patient's unwellness. Since the traditional open debridement and necrosectomy is burdened by high morbidity and mortality ⁴⁶ several less invasive approaches had been developed during years.

Percutaneous drainage, endoscopic transmural drainage, laparoscopic anterior approaches, MARPN, VARD or step-up approach with percutaneous drainage followed by VARD had been proposed. In fig. 1 we propose an algorithm for pancreatic necrosis management.

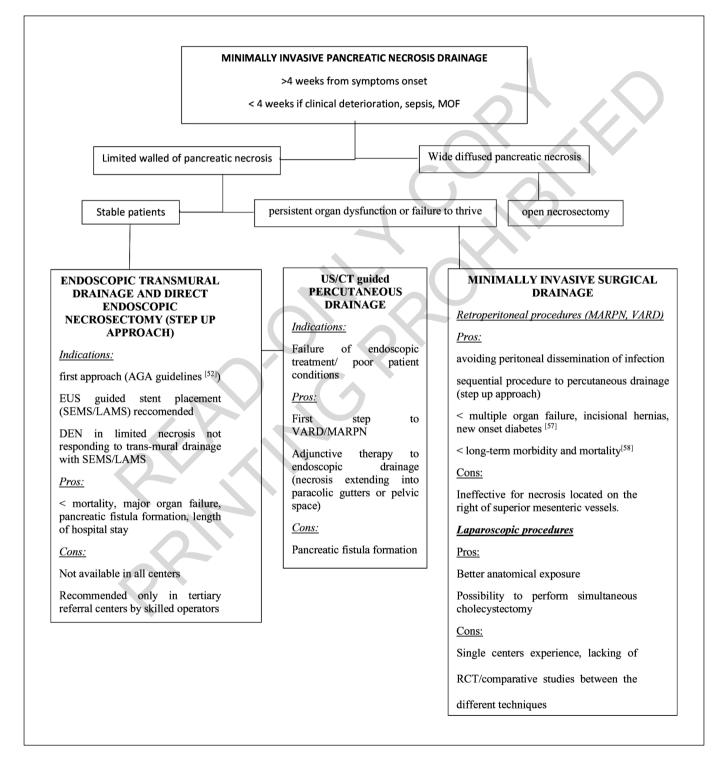


Fig. 1: Algorithm for pancreatic necrosis management.

Role of Percutaneous Drainage

Percutaneous drainage is the first-choice approach for patients with infected pancreatic necrosis considered not amenable to undergone endoscopic drainage due to its unavailability, unsuccess or poor patient conditions. Even in case of infected walled off pancreatic necrosis in the early phase of acute necrotizing pancreatitis (< 2-4 weeks) percutaneous drainage could achieve source infection control if medical therapy is un-effective. It could be either a definitive therapy or adjunctive therapy to endoscopic drainage for necrosis extending into paracolic gutters or pelvic space. Finally positioning a 24 French or larger drainage catheters allows to form a tract for performing a VARD or MARPN.

Role of Endoscopic Transmural Drainage and Necrosectomy

Transmural endoscopic drainage was firstly described in 1996⁴⁷. Through access to gastric or duodenal cavity pancreatic or peripancreatic collection could be drained preferentially by EUS guide.

Plastic stents, self-expandable metal stents (SEMS) or the new lumen apposing metal stents (LAMS) could be placed allowing drainage of necrotic material into the gastric or duodenal cavity. Endoscopic walled off necrosis drainage should be preferred to percutaneous drainage because avoiding risks of pancreato-cutaneous fistula formation.

Endoscopic necrosectomy could be realized after stent placement configuring a step-up approach. Direct endoscopic necrosectomy (DEN) could be realized through endoscope passage into the cavity with debris removal. The 2020 AGA Clinical Practice Update on management of pancreatic necrosis ⁴⁸ suggests the use of endoscopic transmural drainage of walled off necrosis in particular using SEMS or LAMS as the first approach for treatment of limited necrosis. DEN should be reserved to limited necrosis who does not adequately responds to trans-mural drainage with SEMS/LAMS and should be performed only in tertiary referral centers by skilled operators.

Role of Minimally Invasive Surgical Procedures

Surgical intervention for pancreatic necrosis is today reserved to infected pancreatic necrosis or sterile pancreatic necrosis with persistent organ dysfunction or failure to thrive. Procedures should be planned in the late phase (> 4 weeks) of pancreatitis where the systemic inflammatory response has declined reducing morbidity and mortality.

Minimally invasive surgical procedures are preferred to open debridement and necrosectomy when possible given the lower morbidity ⁴⁸. Anyway, open necrosectomy has still a role where endoscopic and minimally invasive techniques are not possible, or unsuccessful due to the large amount and wide distribution of necrosis into the abdomen ⁴⁹. Minimally invasive approaches include MARPN, VARD and laparoscopic transgastric debridement.

MARPN is a multistep technique firstly described in Glasgow and Liverpool around the year 2000 50,51. Necrotic cavity is reached through a left retroperitoneal approach avoiding intraabdominal dissemination of infectious necrotic tissue. Firstly a 12-French catheter over a flexible guidewire is placed into the necrotic area under local anesthetic under CT guidance using a standard Seldinger technique. Then under local anesthesia the guidewire skin entry point is widened and the catheter is removed leaving the guidewire in situ under radiologic control by a C-arm. The catheter is replaced by a plastic sheath, and the tract is serially dilated using a renal dilatation set until a 30-French tract has been obtained. Finally, through a rigid nephroscope connected to a video-screen necrotic-areas are visualized and necrotic tissues are removed by grasps. A suction-irrigation system is placed for continuous lavage of the cavity. Multiple procedures are needed to obtain necrotic tissue debridement, collapse of the cavity and granulation tissue growing.

VARD is a technique realized through a small left flank subcostal incision and direct necrosis removal. Then a laparoscope is inserted in the retroperitoneal space to reach the deeper necrotic tissue.

Videoscopic necrosectomy is then accomplished by laparoscopic instruments ⁵². Drains positioning and cavity lavage is also possible. VARD could be considered a minimally invasive evolution of the traditional trans-lumbar approach with 20 cm incision.

VARD could also be realized after failure of percutaneous drainage. In this sequential technique called "stepup approach" a videoscopic necrosectomy through the drainage tract is accomplished by laparoscopic instruments.

VARD is a good option for center located pancreatic necrosis that extends into the left paracolic gutters but could be ineffective for necrosis located on the right of superior mesenteric vessels.

The milestone for this technique is the PANTER trial which demonstrated no difference in mortality respect open approach but less multiple organ failure, incisional hernias and new onset diabetes ⁵³. Moreover, long-term morbidity and mortality were inferior in the stepup approach ⁵⁴. Laparoscopic pancreatic necrosectomy was firstly described by Gagner in 1996 ⁵⁵ and comprehended trans-gastric, trans-gastrocolic and trans-mesocolic necrosectomy. Laparoscopic necrosectomy is reported to give a better exposure of the lesser sac, left paracolic gutter and head of the pancreas, apparently overcoming the main limitation of the retroperitoneal approach in not debriding the necrotic tissue completely, with better identification of the anatomy ⁵⁶. It may also provide better access to fluid collections not amenable to endoscopic approach. These may facilitate a more thorough debridement of the necrotic cavity ⁵⁷. Some case series had been reported in literature suggesting that laparoscopic approach is safe because join the benefits of minimally invasive surgery and reduce incidence of major complications and mortality ^{58,59}. The trans-gastric laparoscopic approach is accomplished through 2-3 ports placement, anterior gastric wall opening and creation of a wide cyst-gastrostomy left open to allow drainage of the necrotic cavity.

A nasogastric tube could be also left in situ for postoperative lavage. It provides debridement in a single operation and, when feasible, can reduce the morbidity associated with traditional open necrosectomy and avoid the limitations of other minimally invasive approaches ⁶⁰. According to these principles some authors have recently reported an endoscopy-assisted single trans-gastric trocar laparoscopic pseudocysto-gastrostomy in 3 patients affected by large pseudocysts ⁶¹. A large communication between the stomach and the pseudocyst cavity allows an easy and complete one stage debridement inside the pseudocyst. This procedure is accomplished under endoscopic guidance using conventional laparoscopic instruments.

The avoidance of repeated necrotic debridement which is usually necessary after endoscopic treatment due to the small size of endoscopic forceps could make this look like a promising technique. Another advantage of laparoscopic techniques is the possibility to perform a simultaneous cholecystectomy. The main limitation in validating laparoscopic approach is the lacking of comparative studies between the different techniques or randomized controlled trials.

Discussion

ABP is a complex pathology that often requires an interventional approach. Main indication for interventional treatments in ABP regards gallstones etiology and related complications like cholangitis, CBD obstruction and pancreatic necrosis. During years endoscopic and minimally invasive surgical procedures have developed reducing morbidity and mortality related to the severity of the pathology and traditional open approach.

ERCP, LC and other minimally invasive or endoscopic techniques have been extensively analyzed individually. Nevertheless they are rarely discussed all together in a comprehensive review.

The best therapeutic approach for pancreatic necrosis management is still debated.

In a multicenter superiority randomized controlled tri-

al endoscopic step-up approach group results in low rate of pancreatic fistula and minor length of hospital stay respect the surgical step-up approach group ⁶².

A recent metanalysis analyzed six studies (2 RCT and 4 observational studies) including 641 patients with walled off pancreatic necrosis. 326 patients were treated by endoscopic transmural stenting with small caliber pigtail plastic stents and 315 patients by VARD or laparoscopy. Patients treated with endoscopic drainage reported lower mortality, lower major organ failure, lower pancreatic fistula formation and length of hospital stay ⁶³.

A more recent single center trial from USA enrolled 66 patients that were randomized to minimally invasive surgery (laparoscopy or VARD) or endoscopic step-up approach using LAMS. A lower incidence of major complications or death during 6 months follow up in patients undergone endoscopic step-up approach respect minimally invasive surgery is reported. Endoscopic group had lower incidence of enteral and pancreato-cutaneous fistula formation. Lower costs and better quality of life were retrieved in the endoscopic group ⁶⁴. The same results were demonstrated in a latest metanalysis comparing minimally invasive surgery, open necrosectomy and endoscopic step-up approach. In endoscopic step-up approach group incidence of pancreato-cutaneous fistula, enterocutaneous fistula, intra-abdominal bleeding, endocrine pancreatic insufficiency and patient's hospital stay are significantly reduced⁶⁵.

Conclusions

ERCP has an established role as an early procedure in treating ABP associated to acute cholangitis and CBD obstruction. The decision to perform it depends on a reliable diagnosis by EUS or MRCP. Its success depends on the presence of skilled endoscopists preventing further complications leading to unfavorable progression of the disease.

LC provides a definitive treatment of gallstones preventing further pancreatitis attack and other gallstonerelated disorders. Index admission cholecystectomy in MABP is a clearly established procedure although it's early adoption could not be considered a gold standard yet due to the lack of solid data.

In case of infected pancreatic necrosis recent evidences of literature seem to dictate endoscopic step-up approach as the first line therapy.

Given the high complexity related to endoscopic procedures and the lack of definitive data about endoscopic step-up approach we believe these treatments should be undertaken only in specialized tertiary care center with adequate volume caseload and expertise.

Multicenter randomized clinical trials are advocated in order to validate the endoscopic approach as the best one.

Riassunto

SCOPO: Questo articolo descrive lo stato dell'arte delle tecniche endoscopiche e chirurgiche mini-invasive per il trattamento della pancreatite acuta biliare. Le indicazioni, i vantaggi e gli svantaggi di ciascuna tecnica descritta sono discusse unitamente alle prospettive future relative al loro impiego.

PREMESSE: La pancreatite acuta biliare è una delle malattie gastroenterologiche più comuni. Il suo trattamento spazia dall'ambito medico a quello interventistico coinvolgendo nella sua gestione diversi specialisti tra cui gastroenterologi, nutrizionisti, endoscopisti, radiologi interventisti e chirurghi.

L'approccio interventistico è utilizzato in caso di fallimento della terapia medica, per il trattamento delle complicanze locali o come terapia definitive in caso di etiologia litiasica biliare.

Nel corso degli anni le procedure endoscopiche e chirurgiche mini-invasive si sono progressivamente affermate grazie ai buoni risultati ottenuti in termini di sicurezza, minor morbilità e mortalità per il paziente.

CONCLUSIONI: La colangiopancreatografia retrograda endoscopica è consigliata in caso di colangite e ostruzione persistente del dotto biliare comune. La colecistectomia laparoscopica è considerata il trattamento definitivo per la calcolosi biliare condizionante pancreatite acuta.

In caso di necrosi e raccolte pancreatiche o peripancreatiche il drenaggio endoscopico transgastrico e la necrosectomia endoscopica si stanno affermando rispetto alle tecniche chirurgiche tradizionali grazie ad un minor impatto sulla morbilità.

In caso di trattamento chirurgico della necrosi pancreatica le tecniche mini-invasive quali la necrosectomia retroperitoneale, il debridement retroperitoneale videoassistito o la necrosectomia laparoscopica costituiscono una via preferenziale.

La necrosectomia a cielo aperto mantiene un proprio ruolo in caso di fallimento del trattamento endoscopico/mini invasivo o in presenza di estese raccolte necrotiche.

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