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Research Article

PERFORATED DUODENAL EVENTS POST-CPRE WITH VBP STENT WHICH PROCEDURE?

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A B S T R A C T

Introduction: Advances in the study of biliary and pancreatic pathologies (1,2,3,4) obtained with endoscopic retrograde cholangiopancreatography (CPRE) have seen an evolution over the years which, from an exclusive diagnostic method, has been transformed, in therapeutic method . the indications to ERCP have changed and the method, while maintaining a diagnostic role, has taken on a position of Level II, with a clear decrease in its diagnostic indications and a decisive change towards an almost exclusively therapeutic use of footprints (13.14). , however, the complications arising in the execution of the procedure with an incidence varying between 1% and 17% of cases (15,16) are opposed, which cause changes in conduct in the care of the patient, and expose him to additional diagnostic and therapeutic procedures, which prolong the stay. The occurrence, in fact, of an unexpected complication constitutes a factor of strong perturbation, representing a therapeutic act which, by inserting itself in a sudden way, conditions the course of the basic disease, endangering the patient's life. In the present work we will deal with complicative perforative events, which occur in patients undergoing ERCP with biliary stenting,

Materials and Methods: Our case history observed at the Department of Medical Surgical and Specialized Sciences II of the AOU Polyclinic University of Catania consists of 41 duodenal perforations on 1197 cases of ERCP, between January 2015 and December 2018, in patients of the average age of 50 (35-65) years, of which 19 are female and 22 are male. The percentage incidence of the lesion is equal to 3. 4%. the diagnostic procedure adopted after the performative event was in that of a direct abdomen CT and X-ray examination, and MRI colangiography. The clinical picture, in all the examined patients belonging to type I and II, was characterized by a nuanced or silent pain symptomatology in retroperitoneal perforations, and of acute pain, fever and leukocytosis, established in those intra-peritoneal, in which the abdominal distension and parietal defense, up to an acute abnormal abdomen.

Results: In the diagnosis of iatrogenic lesion type I and according to Stapfer, the adopted therapeutic treatment opted for the positioning by endoscopy of the nose-duodenal tube (SND) and of the nose-biliary tube (SNB), in order to obtain useful diversion of duodenal juice and bile and to continue in the toilet of the VBP. In the course of absolute fasting, a pharmacological supportive therapy was established with antibiotics and total parenteral nutrition, and inhibitors of gastric and pancreatic secretion. In the patients who obtained the diagnosis of iatrogenic lesion type II ,III and IV according to Stapfer, the illustrated instrumental findings and the severe clinical picture forced us to desist from any type of conservative treatment and to subject the patient to surgical intervention in ur -genza / emergency, during which, once the mobilization of the duodenum with Kocher maneuver was performed, the solution was continued simply or raffia, in consideration of the timeliness of the intervention that guarantees us the absence and / or the limited " mining "of neighboring fabrics to the small breach

Discussion: The debate on what should be the most appropriate treatment of post-CPRE perforation events and with SE: if an aggressive attitude with immediate recourse to surgery or conservative therapy, in relation to the lacerations of the side wall of the duodenum, we have diversified our therapeutic approach: and we have opted, as expected, for ab initio surgery in the absence of contamination of neighboring tissues. the timeliness of the intervention, has allowed us to guarantee ourselves from the risks of dehiscence, and to resort to a simple raffia of the solution continuously provided for after "kocherization" of the duodenum; departing from what is recommended by the guidelines, with a initially conservative approach. We considered the severity condition of the clinical picture in which the patients were paying for the treatment of perforation; it is the worsening of local conditions, documented by CT and MRI monitoring, which requires surgery. the therapeutic strategy adopted for conservative treatment was due only to the patient's favorable general and local condition. **Conclusion:** the timeliness of the intervention, allows to reduce the risks and the gravity of the clinical picture that acts as a compass on which treatment to opt.

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (CPRE) has made progress in the study of biliary and pancreatic diseases (1,2,3,4). Over the years it has undergone an evolution which, from an exclusive diagnostic method, has been transformed, in therapeutic (endoscopic sphincterotomy-,choledocal clearance, stent of the main bile duct -VBP. (5,6,7) with an increase in its invasiveness, and sometimes the method presents itself as only an action, of many pancreatic biliary diseases (choledocholithiasis, acute cholangitis, benign VBP stenosis, bilious digestive fistulas, dysfunction of Oddi's sphincter, neoplasm of VBP, acute biliary pancreatitis, chronic pancreatitis and pan-creased carcinoma with concomitant obstructive jaundice) (8,9,10) and as an alternative to traditional surgical techniques. With the advent of noninvasive investigative methods (primarily the biliary-MRI) (11,12,13),

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the scenario of the ERCP is further changed and the method, although maintaining a diagnostic role, has assumed a II level position, with a clear decrease in its indications and decided I turn to an almost exclusively therapeutic use (14.15). , however, the complications arising in the execution of the procedure with an incidence varying between 1% and 17% of the cases (16,17), which cause changes in conduct in the care of the patient, and, expose it to additional diagnostic and therapeutic procedures, which prolong the stay. The occurrence, in fact, of an unexpected complication constitutes a factor of strong perturbation, representing a therapeutic act which, by inserting itself in a sudden way, conditions the course of the basic disease, endangering the patient's life. The possibility of potential iatrogenic damage requires that in the course of CPRE with the affixing of Stents, specific rules of conduct are observed, the failure to comply with which makes it difficult to demonstrate the absence of professional fault profiles. the onset of iatrogenic damage. It is related to the complexity of the intervention even in expert hands and / or to the specific organic state ". in order to avoid dramatic outcomes (mortality is estimated to be between 0.1 and 2%) (18), a weighted and correct conduct is unavoidable: the endoscopist must therefore recognize or at least immediately suspect iatrogenic lesions produced and promptly take, in relation to the gravity of the case, the necessary therapeutic measures. Having available the presidia and the technical-professional requisites, proceed, where possible, own initiative and possibly making use of the collaboration of specialists from other disciplines, or send the management of the case entirely to the latter, providing them the necessary information on the examination carried out while continuing however to remain responsible in the therapeutic initiatives adopted. the mentioned complications are therefore associated to a mortality rate of 16-18% (28), and they have been framed under the nosological profile according to schemes alternative classifications from Howard and Stapfer, Stewart-Way's. CUHK, which have the advantage of distinguishing lesions based on the anatomical site and the causal mechanism of the damage, thus contributing to providing the therapeutic orientations. In the present work we will deal with complicative perforative events, which patients undergoing ERCP needing stents in the bile duct are needed

MATERIALS AND METHODS

The analysis of the cases observed at the Department of medical surgical and specialist sciences II of the AOU Polyclinic University of Catania consists of 41 duodenal perforations on 1197 cases of ERCP, between January 2015 and December 2018, in patients of average age of 50 (35-65) years, of which 19 are female and 22 are male. The percentage incidence of the lesion is equal to 3. 4%. the diagnostic procedure after perforation was that of implementing a diagnostic protocol that included a CT examination and the abdominal X-ray with a MR colangio. the indication for the CPRE endoscopy procedure for the 31 cases (75%) was for a choledochic calculosis in the remaining n 10 cases (25%) for the presence of recurrent cholangitis. With stenosis and replacement of stents. For the 17 (41%) patients there was a comorbidity (pulmonary emphysema, ischemic heart disease, arterial hypertension, diabetes mellitus, chronic bronchopathy); In all the patients treated papillation cannulation was difficult. For the 13 cases (31%) with choledolithiasis, after sphincterotomy, there was a partial removal of the calculi with the Dormia basket and therefore a prosthesis was positioned to allow the outflow of the bile without the residual calculi could rebuild the papilla. The lesions found were: for the 15 (36%) cases the perforations concerned the lateral wall in 2 (5%) cases the medial wall of the duodenum; In 13 (31%) cases the perforations were ampullary and in 11 (24.5%) cases the perforations concerned the distal wall of the main bile duct. the injuries were classified according to the Stapfer Classification: n 13 type I cases; n 13 Type II cases and 11 Type III cases. And finally n 4 type IV cases. Immediately after admission, the patients presented the clinical picture, which was distinguished, in relation to the type of membership in type I and II, there was a nuanced or silent pain symptomatology in retroperitoneal perforations, and of acute pain, fever and leukocytosis, confirmed in the intra-peritoneal ones, in which abdominal distension and parietal defense were associated, up to an acute abdomen. In Type III and IV lesions The initial clinical picture was characterized by mild pain in the right side, minimal abdominal tension and blurred signs of sepsis. As the hours passed, there was a dramatic, more intense pain, sometimes subcutaneous emphysema, high fever and rapid deterioration of the general state with evolution towards septic shock accompanied by signs of acute abdomen. Diagnostic imaging (tc rx and cholangio RM) showed a contrast medium (mdc) spreading in the retroperitoneal space, (fig 1) which occurred during the examination, and the presence of free air both in the peritoneal cavity and in the retroperitoneal area, at the posterior mediastinum, around the large vessels and in the pericardial area, with the finding of free air mainly in the periepatic area (Fig. 2).

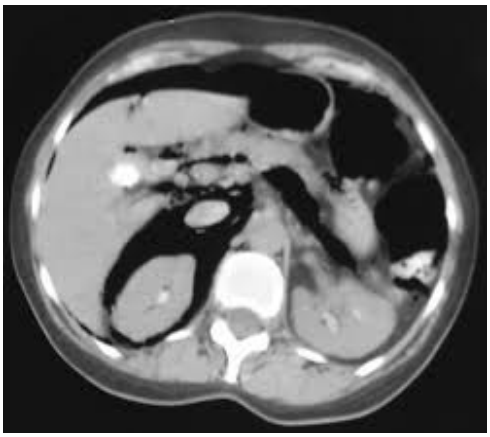

Fig 1 Direct Rx Add duodenal perforation

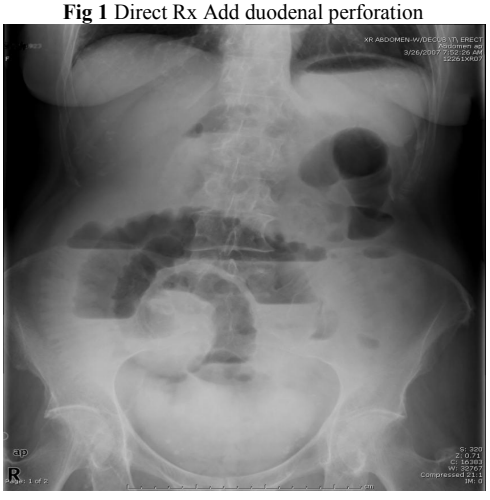

Fig 2 duodenal perforation CT

The therapeutic orientations for each type of iatrogenic lesion were classified according to the stapfer classification and were: Type I (31.5%) Perforation of the lateral or medial wall (in front of the papilla of Vater) of the duodenum. the diagnosis was not formulated during the endoscopic examination as there was no knowledge of spreading the contrast medium introduced into the papilla; the presence of intra- or re-peritoneal air was not easily detectable for the position that the patient, often sedated, who took during the examination; the amount of air, when highlighted, was not related to the extent of the lesion, but also to the site of the intra- or re-peritoneal perforation, to the duration of the procedure and to the volume of air blown. in Type II (31.5%) - ampollar perforation -, by far the most frequent, it was produced during the section of the ampullar sphincter and is, therefore, considered the "true" sphincter-resection perforation; The diagnostic confirmation, was obtained with the evidence of an extravasation in the CT examination whose usefulness allowed the detection of intra- or extra-peritoneal collections, of endopic peritoneal free air and of pneumomediastinum. the perforations in Type III (27%) - concerned the distal tract of the VBP that was determined, from the introduction in the VBP of operative instruments, such as the metallic guide or the Dormia basket, as well as stents. In both typologies the diagnosis was placed together with the endoscopic procedure both for the extravasation of the contrast medium introduced in the VBP and for the appearance of retropneumoperitoneum, whose extent was not correlated with the severity of the perforation, which is usually small; . finally in Type IV (10%) the presence of retro peritoneal air was correlated by the micro perforations of the duodenum due to the high pressure used to keep the duodenal lumen distended. The detection of retro peritoneal air was visualized at the end of the procedure. Therefore, the cardio-circulatory balance was restored, to urgent / emergency surgery. The prognosis, for the site of the lesion and for the "physiological" diagnostic delay, was severe, developing a circumscribed or generalized peritonitis. Surgical treatment was performed in n 13 (31.5%) patients presenting with a diagnosis of choledocholithiasis and a median laparotomy was performed; aspiration of bile and duodenal material in the peritoneal cavity, cholecystectomy and using a needle button introduced into the cystic colangiography is performed. Kocher maneuver and right flexion mobilization of the colon, Suture of the lateral, median and / or posterior breccia and apposition of omentum, choledocotomy, removal of the calculus or calculi, washing of the biliary tract with physiological solution; exploration by means of ogival end probes (Dogliotti probes), Kehr tube apposition. Washing of the subhepatic, retrperitoneal and abdominal cavity. Drainage in tile drainage that drains the retroperitoneum and the subhepatic region and a drainage in the Douglas. Furthermore, a multi-kidney nasogastric tube has been positioned in the antral region. In addition to antibiotic therapy with meropenem (1000mg x 3 times die e.v.) NPT for 20 days, albumin. In n11 (24.5%) patients with cholangitis proceeded to median laparotomy; aspiration of bile and duodenal material in the peritoneal cavity. Kocher maneuver and right flexion mobilization of the colon, Suture of the breccia and apposition of omentum. In 3 patients is performed choledocotomy and duodenotomy, washing of the bile duct with physiological solution; exploration by means of ogival end probes (Dogliotti probes), visualization of the papilla and its opening; apposition of Kehr tube in the choledochus and transverse closure of the duodenotomy. In 4 (9%) cases a hepatic-jejunostomy was performed on a loop defunctionalized to Roux as the common bile duct appeared of reduced caliber. In all, the subhepatic, retrperitoneal and abdominal cavity was washed. Drainage in tile drainage that drains the retroperitoneum and the subhepatic region and a drainage in the Douglas. Furthermore, a multi-kidney nasogastric tube has been positioned in the antral region. In addition to antibiotic therapy with meropenem (1000mg x 3 times die e.v.) NPT for 20 days, albumin.

RESULTS

In the diagnosis of iatrogenic lesion type I according to Stapfer (24.5%) the adopted therapeutic treatment opted for the endoscopic positioning of gastric nose tube (SND) and biliary nose tube tube (SNB), in order to obtain useful diversion of duodenal juice and bile and continue in the toilet of the BVP. In the course of absolute fasting, a pharmacological supportive therapy was established with antibiotics and total parenteral nutrition, and inhibitors of gastric and pancreatic secretion. In the following days, serial radiographic controls document the gradual disappearance - also clinically highlighted - of the air previously detected in the peritoneal cavity, in the retroperitoneal space and in the mediastinum. The benefits obtained and the progressive reduction of bilirubinemia, in the absence of any septic status index (including negative echographic monitoring for perilesional abscess collection), confirm the validity of the therapeutic approach that we implemented, inducing us to continue in the -the same until obtaining the complete resolution of the picture, with the mission of the patients on average on the 14th post-CPRE day. In the iatrogenic type II lesions with important comorbidities, a conservative treatment was started initially (absolute jejunum, SND, antibiotic therapy, NPT), which was ineffective with worsening of the addominal and general conditions of the patient. In particular, CT monitoring of the abdomen, performed after the first 3 days of supportive therapy, detects in the retroperitoneum - in the pancreatic loggia, in the right peri-and para-renal spaces, - a gaseous falcon, in whose context it spreads the administered contrast medium; the investigation also showed the presence of peritoneum bile with sepsis for which a cholecystectomy was performed, a choledocotomy with reclamation of the VBP and positioning of the Kehr tube, a toilet-washing of the peritoneal cable and biliary digestive derivation were subsequently sent in intensive care. in 9% of the cases (4 cases) the patients had an exitus. In patients in whom the clinical picture was severe (type II, III and IV lesions) the latter obliged us to desist from any type of conservative treatment and to subject the patient to urgent / emergency surgery, in In the course of which, in the presence of a limited "counter-mining" of the neighboring tissues associated with the small breach, the postoperative course was free of complications with the almost complete disappearance of air and abscesses - radiographically documented - both of the retropneutology of pneumomediastinum and with the resignation of patients in the twentieth day, after removal of biliary en-doprosthesis and restoration of feeding. ; In the treatment, the large perforation of the loop repair of the duodenum was implemented a couple of days after the sphincterotomy operation. the bilio-digestive anastomosis of derivation of the VB upstream on a jejunal loop excluding the terminal anastomoses of the hepato-choledochus. they prevail, and are considered the most physiological because they observed the function of the

sphincter of Oddi. If the anastomoses is sufficiently large and the jejunal loop is long enough (60-70 cm), there can be no danger of reflux of the digestive fluid. The risk of ulcer exists but is not so important. The Hepp technique represents an unquestionable progress and makes it possible to achieve a wide anastomosis with the restricted biliary tract. With a latio-lateral biliary-jejunal anastomosis so large that it is possible on a healthy bile duct to achieve a mucous-mucous sinking. After the intervention, in addition to clinical examinations, it included: an exploration of cholestasis, liver function and coagulation factors, and repeated blood cultures in the case of cholangitis. This repairing surgery is dominated by the choice of the best biliary anastomosis, to get immediately healing. Depending on the type of lesions and the anatomical variants of the hilarious region, cholangiography allows the identification of the positioning of the anastomoses with greater precision. When the bile duct is thin, the juxuncional Y-loop of Roux is the best intervention to carry out. The loop in fact easily rises to the hilum and is theoretically protected from reflux thanks to its length which can be about 70 cm. The packaging of a Roux loop has nothing difficult to achieve. The blocked extremity has risen to the trans-meso-colic level of the avascular space located in front of the second duodenal potion. The length of the jejunal opening is equivalent to the length of the biliary mouth. The anastomosis is carried out at separate points with a slow resorption wire or with a thin absorbable wire. The points of the back plane have passed to the front; the same actions are repeated for the anterior plan.

DISCUSSION

The debate on what should be the most appropriate treatment of post-CPRE perforation events and with SE: if an aggressive attitude with immediate recourse to surgery or conservative therapy (21, 22, 23,) is still the subject of controversies that arise above all from the heterogeneity of these lesions (intra- or extra-peritoneal site and more or less early diagnosis) and the absence in the literature of case studies with significant volumes (24, 25, 26,27). In the past, it was common practice to treat these perforation complications with surgery, sometimes excessive in the case of small and small lesions and with significant consequences, especially in patients who are often elderly and unstable (28,29,30,31); currently, the surgical indications have been sharply reduced, also in relation to the revaluation of the attendance experiences [Taylor-nasal gastric tube in aspiration according to Taylor. From the literature data it emerges that over 80% of all CPRE and SE perforations reach healing with conservative treatment (32.33,34). However, it should be remembered that, even today, immediate reparative surgery continues to be rational both for the impossibility of recognizing the perforations contained in a benign course and for the high rate of operative mortality in the event of diagnostic-therapeutic delay or injury extended, cause of sepsis. There is no agreement among the various authors on what are the predictive factors of the failure of medical treatment and of the indication to the surgical approach (35,36,37). Some AA believe that the presence of signs of acute abdomen, which correlate well with gross perforations with the rapid development of suppurative processes within-and retro-peritoneal to which we share the thought; it is not, however, not to underestimate the opinion of those who, on the other hand, do not consider these findings useful for the timely recognition of the severity of the picture, as they are often late or absent in the most common retroperitoneal extrinsic lesions (38,39,40 , 41) although with the new diagnostics by Imaging it is possible to obtain an evaluation of the perforation from the first hours. With regard to conservative treatment (42,43,44,45), endoscopic management is to be preferred where possible, whose objective is to obtain an adequate duodenum gastric decompression by means of an en-noble stent or an SNB on aspiration outflow / drainage of biliary duodenum pancreatic fluids, so as to favor a spontaneous healing of the iatrogenic lesion (46,47,48,49). it is also to be recognized, moreover, the efficacy of interventional radiology methods, such as percutaneous drainage. Therapeutic success is in fact conditioned not only by early diagnosis, but also by the differentiation of the lesions based on the anatomical site and the causal mechanism, factors that are intrinsically linked. For type I and II lesions, considering the characteristics of the duodenal lesion and the related clinical picture, therapy is rarely effective. conservative and urgent surgical intervention is required. In the rare case of early diagnosis, the surgical suture of the duodenal breach - exceptionally endoscopic with the addition of endo-clips (50.51,52,53) - represents the treatment of choice. On the other hand, if there is a large tear, with evident infection of the neighboring tissues due to untimely diagnosis, therapeutic choices are imposed which arise from the awareness of an easy evolution towards the dehiscence of simple repair by direct suture. Therapeutic addresses derive from the surgical experiences of the duodenum biliary -pancreatic district and those of urgent surgery for duodenum-pancreatic traumas (54,55.56). From the first we deduce the indication to transform, by gastric diversion, a high-flow lateral duodenal fistula into a low-flow terminal, whose prognosis is certainly better, with a reduction in mortality from 40 to 14%. From traumatic oncologic surgery, duodenal traumas, instead, the efficacy of the duodenal exclusion or "diverticulization" (antrectomy with gastro-jejunostomy; biliary-duodenal drainage / decompression using Kehr tube; duodenostomy on Petzer probe is evident which offers certain advantages over other surgical approaches in urgency. The simple duodenal suture, whether or not reinforced with the addition of a jejunal or omentum loop, is burdened by prohibitive dehiscence percentages, which can be prevented for the aforementioned local regional septic phenomena; a duo-denocephalopancreatectomy is, on the other hand, decidedly oversized, also due to the high risk of serious morbidity and mortality, inherent in the same procedure. In types III and IV therapy, medical / endoscopic treatment can be established immediately - at the end and / or during the procedure and is followed by a close clinical, laboratory and radiological monitoring, in order to identify as early as possible non-reponder subjects, who develop infected collections, sepsis and severe impairment of the general conditions. Specifically, therapeutic strategies for perforations are affected by the variability of the clinical picture . In patients, not frankly septic, with mild lumbar pain and minimal (or absent) contrast media extravasation, a conservative therapeutic approach is justified. A non-negligible percentage of the patients treated in this way develops, however, often in an insidious way, a persistent septic state which, as from radiological investigations, can involve more or less extensively the retro-duodenal space along the psoas muscle (evidence of small gas bubbles) . In these patients, as well as in those who present, on the contrary, from the onset a severe sepsis rapidly evolving towards the full-blown shock, the

surgical option, also in light of the failure of percutaneous drainage maneuvers, becomes mandatory and should be strategically and technically adequate for the extension of the infection usually involving the retro peritoneum . The anterior laparotomic approach is not free from criticism (inadequate to drain large retro-peritoneal collections; dangerous due to the risk of widening the lesion during the Kocher maneuver; potentially contaminating the peritoneal cavity not yet affected), while the direct retro peritoneal approach - posterior laparatomy creates a broad drainage, through short, persistent in time, favorable by gravity and non-contaminating is to be preferred. Moreover the continuous removal of the infected necrotic material, gradually replaced by granulation tissue, allows , a gradual closure by second intention of the laparatomy breach. In the perforations of the distal section of the VBP, in consideration of the tendency to spontaneous closure of the leak, the treatment to be adopted is of a conservative type, provided that the regular flow of the bile downstream of the lesion is guaranteed. The indications for surgery, mostly delayable, are represented by the coexistence of intra-and / or retro-peritoneal collections not otherwise drained, by the presence of residual calculi or by the "entrapment" in the bile street of operative instruments or by the eventuality of failure of conservative therapy (persistence of the "leak" to the injection of contrast medium); in these cases we proceeded to drain the collections and / or reclaim the common bile duct with Kehr tube allocation. In our therapeutic approach, we followed the guidelines set out in the literature, not forgetting to adapt them to the anatomical-clinical peculiarities . , in relation to the lacerations of the side wall of the duodenum, we have diversified our therapeutic approach: and we have opted, as expected, for ab initio surgery in the absence of contamination of neighboring tissues. the timeliness of the intervention, has allowed us to guarantee ourselves from the risks of dehiscence, and to resort to a simple raffia of the solution continuously provided for after "kocherization" of the duodenum; departing from what is recommended by the guidelines, with a initially conservative approach. We considered the severity condition of the clinical picture in which the patients were paying for the treatment of perforation; it is the worsening of local conditions, documented by CT and MRI monitoring, which requires surgery. the therapeutic strategy adopted for conservative treatment was due only to the patient's favorable general and local conditions; the timeliness of the intervention, allowed us to guarantee ourselves from the risks of knowledge, and to resort to a simple raffia of the continuous solution; departing from what is recommended by the guidelines, with a conservative approach. in small lesions. While we have taken as a parameter for the derivative intervention the condition of gravity of the clinical picture in which the patients poured; it is the worsening of the local conditions, documented by the CT monitoring, which requires the surgical intervention

CONCLUSIONS

The technological evolution, which has characterized in recent decades, has not failed to exert its influence in the field of digestive endoscopy which, born exclusively for diagnostic purposes, has become a real therapeutic procedure, guaranteeing resolution, with less invasiveness, of affections that once only bloody intervention could guarantee. But it is also true that the greater field of action of endoscopic procedures has inevitably led to a risk of complications, almost all of which are now predictable but not all preventable, despite the fact that the operators are always in the best practice and in the best diligence of the medical act .The fact that some complications cannot be prevented does not mean that, once they have arisen, they cannot and must not be correctly and completely treated; also because, if the onset of complications does not constitute an error, not noticing the event occurred and not treating it inevitably exposes to professional responsibility. In this context the perforation complications that go to affect the endoscopic treatment of some pathologies of the VBP and, in particular, of those susceptible of being treated with CPRE and with SE are to be framed. their occurrence carries a serious risk to the health and life of the patient. For these reasons, timely re-recognition and prompt medical and / or endoscopic therapy are required where possible or, alternatively, surgical therapy. And this cannot fail to reinforce the need for a constant reciprocal interaction between surgeon and endoscopist, meaning that the former will entrust to the second the patients whose disease can be treated and resolved with less risk through an endoscopic procedure and the latter will entrust to the first those subjects who from his work, although not erroneous, have reported damages that can be resolved exclusively with surgical treatment. the timeliness of the intervention, allows to reduce the risks and the gravity of the clinical picture that acts as a compass on which treatment to opt.

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