THE PATIENTS WITH POSTOPERATIVE BILIARY STRICTURES: EVALUATION OF THE SURGICAL MANAGEMENT AND REMOTE OUTCOMES

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ABSTRACT

Objectives. Surgical management of patients with benign biliary strictures and biliary lesions is a current issue for discussion and raises many scientific research directions. The purpose of this study was to systematize our experience in the treatment of benign biliary strictures, analyzing both immediate and remote complex results.

Material and methods. Between 1989-2015 years, there were 203 hospitalized patients with benign biliary strictures in Surgery Department no. 2 of Public Institution, State Medical and Pharmaceutical University (PI SMPhU) "Nicolae Testemitanu". The study is conducted as part of postdoctoral research; thesis/dissertation title is Clinical-functional efficiency of modern surgical treatment of benig biliary strictures according to immediate and remote clinical results and was approved by the Science Council of PI SMPhU "Nicolae Testemițanu" and Ethical Committee (EC) of Ministry of Health (MoH). Clinical evaluation included several consecutive steps: 1) setting the etiopathogenic diagnosis; 2) pre-operatory decompression of the biliary tree; 3) reconstructive surgical act. In the case of biliary strictures, after the initial assessment, bilio digestive derivations were performed according to the level of the obstacle, preferring the bilio-jejunal on isolated loop en Y a la Roux.

Conclusions. The iatrogenic stricture of bile duct has a complicated evolution, with many surgeries, requiring many hospitalizations. It should be endeavored to detect them in a timely manner and to prevent septic complications. In the first phase biliary tree decompression will be used, and after decreasing the inflammatory process biliary-digestive reconstruction will be performed. These patients require a complex remote monitoring and analysis of health status.

Key words: biliary strictures; etiopathogenic diagnosis; hepaticojejunostomy; reconstructive surgery act

INTRODUCTION

Bile duct lesions that occur most often after a cholecystectomy, present a formidable challenge for surgical services that require a complex approach for optimal management. If the injury is not recognized in time or has been poorly managed, then serious complications can occur, such as cholangitis, biliary cirrhosis or portal hypertension. These complications involve considerable a cost for treatment, loss of employment and long-term disability [6, 18].

The incidence of biliary injuries during open cholecystectomy is reported to be about 0.1-0.2%. The incidence of biliary injuries during laparoscopic cholecystectomy is certainly greater than the one following open cholecystectomy and according to published data varies between 0.4-0.6% [6, 22]. It is also noteworthy that after laparoscopic cholecystectomy bile injuries are more severe and complex than those encountered during an open cholecystectomy [1, 4, 12].

In order to define the types of biliary lesions (BL) there have been proposed several classifications of BL, but none is universally accepted because each has its own limitations. Among them, a fundamental role is played by Bismuth's classification and Strasberg's classification, which are most commonly used by practitioners. Bismuth's classification addresses the group of patients presenting an established biliary stricture and distributes patients based on the level of damage, which is a determining factor of the evolutionary result [5]. Dr. Sikora amended type III strictures in type IIIa / IIIb, according to Bismuth, depending on the level of confluence of hepatic ducts, being intact or destroyed [20]. Strasberg's classification applies to acute injury with bile leaks, lateral damage and sectioning [21]. A subgroup of transections (type E according to Strasberg) incorporates Bismuth classification. The major disadvantage of these classifications is that some important factors affecting the result are not presented, such as the vascular lesions, time until recognition of the damage, the presence of biliary fistula (internal/external), portal hypertension, liver function, and the presence or absence of previous reparatory operations.

The Hannover classification is the most refined in terms of the combination of classification of Strasberg and Bismuth and is addressed directly to the assessment of biliary-vascular lesions [3]. Hopefully a comprehensive classification system, universally accepted at all levels of surgical services, will be proposed in the near future and will mandatorily include all the relevant parameters that influence long-term outcome [12].

A detailed clinical evaluation and a thorough preoperative preparation are important factors for a successful management of a patient with BL. The ma-

jor preoperative aim is to document the degree of liver dysfunction, to establish the exact level and type of stricture, the presence or absence of biliary infection, and to investigate possible complications such as secondary biliary cirrhosis and portal hypertension or possible biliary fistula. Besides BL diagnosis, it is also equally important to detect the associated medical risk factors, especially liver disease coexistence, electrolyte dysfunction, coagulation, metabolic or in association with infection disorders.

In this context, our study focuses on what happens after the damage has already been produced and the surgical modality for solving the existing problems [16]. The moment of BL repairs is critical, especially when we realize that the first attempt to repair is the best in terms of long-term outcome. The outcome of main bile duct injury is an increase of diameter, wall thickening, an increase in proliferative connective cells and an increase in elastic fibers. One important relevant aspect is the presence of inflammatory infiltrate in the wall of bile duct wall. In an elective situation, a minimum period of 3 months after the injury and reconstruction is optimal for the resolution of edema and tissue inflammation from the biliary-hepatic region and for a proximal dilatation of the biliary tree [6, 11]. In patients with an total external biliary fistula, the interval from injury to reconstruction can be extended to six months, in order to provide the appropriate surgical management, which will ensure the return of externalized bile in the digestive tract, avoiding electrolyte disturbances and development of acholia [8]. Unjustified haste in trying to solve an injury at an early stage by reconstruction is associated with a high risk of bile leak postoperatively - 30%, forming a distant stricture - 25% and a high mortality - 30%.

The aim of the management of bile stricture is to restore the flow of bile in the gastrointestinal tract through a bypass that prevents reflux cholangitis, biliary sludge duct which is formed due to stasis and the formation of gallstones, re-stricture of the bile duct or chronic progressive liver injury. The surgical reconstruction is superior to other techniques, such as percutaneous or endoscopic (balloon dilation or stenting). Hepaticojejunostomy (HJA) is the gold standard in the treatment of biliary strictures. The key surgical principles associated with a successful reconstruction of biliary stricture are the exposure of healthy, well-vascularized stump bile that drains the entire liver, and preparation of a corresponding segment of intestine (usually a loop Roux-en-Y of jejunum> 80 cm) to make close edges and tension free anastomosis – mucosa to mucosa [13, 15]. Hepp-Couinaud technique for accessing the left hepatic duct under the base of the quadratus lobe enables repair of high lesions, performing a bypass with reliable results. A side-to-side HJA, performed through a longitudinal incision of the left hepatic duct, produces a large anastomosis, minimizes the dissection behind the biliary tract and reduces the risk of excessive devascularization of liver ducts [2, 23].

The data from a few tertiary centers presents the postoperative mortality ranging from 5% to 8%. In the last decade, with perfected surgical techniques and management of biliary strictures addressed, there is a considerable decrease in operative mortality with many consistent series reporting *zero* perioperative deaths [14]. Risk factors adversely affecting the survival rate are: age, repeated reconstructive surgery, significant comorbid medical condition, sepsis, bile, and secondary biliary cirrhosis [9].

Several factors must be considered when discussing the long-term outcomes after reconstruction addressed to biliary strictures. Several tertiary care centers reported a satisfactory result in 80-90% of patients. Important factors, presented at scientific forums, underline that predictors of adverse outcome typically include proximal strictures (Bismuth type 3 and 4), multiple previous attempts of reconstruction, presence of parenchymal liver disease, portal hypertension, difficult biliary anastomosis, biliary sepsis, lack of experience of the surgeon [18, 19].

Psychosocial repercussions of BL are high; most patients are in the most productive years of their lives. When faced with a serious post-operative complication, requiring major surgical reconstruction carried out by several specialists, a program with integrity assessment and rehabilitation is needed, being a major cost to the health system. Despite the excellent results in long-term reconstructive surgery, Quality of life (QoL) is modest and not well documented. Current studies are often incomplete and do not allow these goals to be established on this difficult issue.

MATERIALS AND METHODS

In the present study, 203 patients with iatrogenic biliary lesions secondary to laparoscopic or open cholecystectomy, gastric resections, admitted at the Surgery Clinic no. 2 between the 1989-2015 years, were looked after (fig. 1).

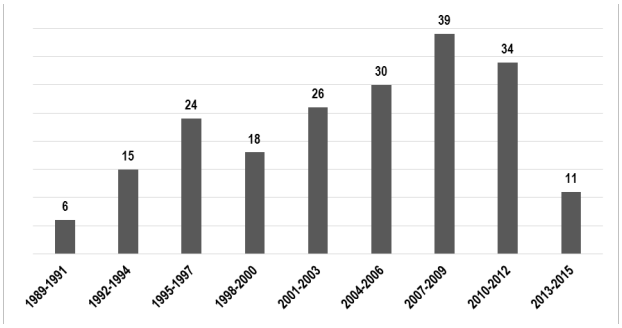

Fig. 1. Distribution of the evaluated cases over the 1989 -2015 years, no. abs.

The mean age of the 203 patients was 49.15 ± 0.94 years, in the range: 21-78 years old, they were 37 (18.2%) men and 166 (81.8%) women. Depending on the symptoms presented and the clinical manifestations of patients with postoperative biliary strictures the following clinical picture is found at the time of admission for reconstructive intervention: presence of biliary colic in 103 (50.7 ± 4.93%) cases;

jaundice in 157 (77.3 ± 3.34%) cases; cutaneous pruritus in 104 (51.2 ± 7.36%) cases; hepatomegaly -32 (15.8 ± 6.45%) cases; fatigue in 140 (69.0 ± 3.91%) cases; presence of external biliary fistula in 137 (67.5 ± 4.01%) cases. Stated symptomatic was directly correlated with the presence of chronic biliary-hepatic suffering, motivated by supported biliary injury and followed by reparative operations or drainage of the biliary tree. The intensity of clinical signs was explained by the degree of drainage of the biliary tree, the amount of bile that got in the digestive tract, the presence of local septic complications, or angiocholitis, the transient or persistent mechanical jaundice, the degree of hepatic failure.

Direct etiologic cause of postoperative biliary strictures in 91 (44.8%) of the cases were the consequences of lesion of the MBD during a traditional cholecystectomy. Usually these are cases of acute cholecystitis or situations with major fibrosis with deformation of the report of the gallbladder and biliary-vascular complex. The major complexity of cases imposed them to be resolved by traditional access, often during night shifts with inadequate anesthesical relaxation, difficult access to subhepatic space, adding a possible inadequate incision by size. In 107 (52.7%) cases the lesion was secondary to laparoscopic cholecystectomy. These situations often are motivated by scleroatrophic cholecystitis, anatomical abnormalities, bleeding during surgery. Clinical experience was 16 (7.88%) cases of lesions, which constituted 0.05% of all clinical cases of cholecystectomy operated during this period. The remaining 187 (92.12%) cases were from other surgical services. Gastric resection for complicated callous ulcers with penetration caused iatrogenic injury just in 5 (2.5%) cases. An important point is that over time from the lesions to its finding in our study was 7.29 ± 0.49 days, which increased the gravity of patients at the stage of drainage of biliary tree and obviously had a major impact on biliary stricture formation. An important criterion in increasing complexity of strictures furtherly developed was that 99 (48.8 ± 5.02%) of patients had two or more drainage operations or plastic MBD at the time of lesion. Any repeated trauma obviously increases the local inflammatory process, grade of fibrous tissue and develops a difficult biliary stump due to the excessive fibroplastic process and changed local anatomy. In the remaining 104 (51.2 ± 4.90%) of cases there is only one intervention, thanks to the presence of partial lesions with retention preservation of MBD path. Timely detection of these patients prevented septic complications and limitation of re-operation just in order to restore MBD on the Kehr or Robson drainage. The presence of small lesions often makes us technically easier to resolve the biliary drainage through minimally invasive endoscopic methods often associated with percutaneous echo-guidance. Endoscopic stenting was possible at 15 (7.39%) patients, which excluded the need for open intervention. As a result, it provides natural bile flow into the duodenum and satisfactory physiological preparation and qualitative precondition for reconstructive interventions.

We also conducted a comparative study of diagnostic imaging methods, which allowed us comparative evaluation of sensitivity and specificity, negative and positive predictive values for the diagnosis of patients with benign biliary strictures. Imaging examinations (ultrasound, CT, MRCP, ERCP, CPTH and cholangio-fistulography) showed conclusive pictures of the biliary tree, intra- and extrahepatic sectors, the degree of expansion, distal discontinuous extra hepatic bile duct and even invisible in some cases. They were used to discover the level of stricture and state of different sectors of biliary tree, the biliary wall thickness above the obstacle and the presence of endobiliary inclusions. Preoperative visualization of the biliary tree was obtained by cholangio-fistulography in 29 (14.29%) cases, by ERCP in 157 (77.34%) cases and by CPTH in 19 (9.36%) cases.

The performed imaging examination allowed to systematize the level of strictures. So in our study, 6 (3.0%) patients were reported as type I, 92 (45.3%) type II, 90 (44.3%) as a type III, 15 (7.4%)- type IV and type V - 0 (Table 2). Bile duct dilation above stricture was more than 1.5 cm at 77 (37.93%) patients, from 1.5 to 2.0 cm at 102 (50.25%) patients, and more 2.0 cm at 7 patients. This moment was of great importance to the formation of biliodigestive anastomosis. Biliodigestive derivations are essential to rebuilding the biliary tree and restoring properly the biliodigestive flow. Any reconstruction of biliary channel, in our experience, fulfilled the following requirements: a) excision of fibrous tissue from proximal biliary channel; b) formation of a wide anastomosis; c) presence of an intact mucous membrane without any inflammatory processes at 3600 of the anastomosis line; d) good vascularization on suture line; e) lack of tension on the anastomosis line. Currently achieving biliary-digestive derivations using Roux loop has become a recognized standard in biliary strictures surgery. But notable advances were recorded in terms of forming the hepaticojejunoanas-tomosis. Technological development of applying this anastomosis was directly related to evolution in processing the biliary stump and suture material. In current practice, anastomosis is performed with ordinary sutures, which are passed through all layers. We allow as PDS suture material, Vicril 4 / 0-5 / 0. We focus on a good hermeticism, applying sutures with 2-3 mm step. On posterior lip the nodes are applied facing the lumen, and on the anterior - the outside. Suture line is reinforced with sero-serous sutures up to 5 in number, only when needed. For strictures type I and II according to Bismuth, an end-to-side choledocojejunostomy using hepatic duct and Roux loop is already a recognized norm. It was carried out in 86 (42.4 ± 5.33%) cases of our study sample. We accept as PDS suture material, Vicril 3 / 0-4 / 0. In this situation, usually we have a

pretty "long" stump, which adjusts well to the intestinal mucosa. The surgeon had extra-tissue for maneuvers when preparing the common hepatic stump allowing to apply sutures only on healthy tissue.

In case of Bismuth type III strictures hepaticojejunostomy was faced with a small biliary stump, it requires continuing the incision longitudinally on the left channel, after the preparing it from the hepatic hilum. In our experience, we had special cases, with intrahepatic anatomical positioning situation without adequate exteriorization in hilum which did not assure us an anastomosis mouth of proper dimensions. We resorted to mobilizing right hepatic duct and extending the incision longitudinally. Just this way we could ensure a broad and functional anastomosis. We accepted tas PDS suture material, Vicril 5/0-6/0. Usually these high derivations require mandatory drainage of anastomosis mouth. The drainage was performed according to the Veolker procedure, separately for each biliary channel and for 2-3 months. Hepaticojejunostomy was carried out in 102 (50.2 ± 4.95%) cases, there were long incisions on both channels liver in 47 of them (23.15%).

For strictures of type IV, when liver channels junction is completely destroyed, leaving two separate channels in the wound would bring up technical difficulties for reconstructive surgery. Intraoperatively liver channels will be released of parenchyma and fibrous tissue. The essential element that must guide surgery is resection till healthy tissue. They conducted separate anastomoses with each bile duct with Roux loop using 5/0 ordinary resorbable suture in single plan under surgical optical control in 15 (7.4 ± 6.99%) cases. We had situations when the right hepatic duct was very short and we had to section and anastomosis separately paramedian right and lateral right channels. Anastomoses were finished with separate drainage of both channels according to Veolker procedure for a period of 6 months. The anastomosed loop required mandatorily serosa-muscle sutures with liver capsule with non-resorbable material, which excluded traction at the anastomosis level postoperatively.

RESULTS

The postoperative evolution was favorable; the length of hospitalization was 11.97 ± 0.16 days, with amplitude from 8.00 - to 20.00 days. Postoperative mortality was absent at the stage of reconstructive operations. Immediate postoperative complications after surgical reconstruction operations were recorded in 69 (34.0 ± 5.70%) cases. Most feared postoperative complication was the postoperative abscess, found at 1 (11.74 ± 1.4%) patient. The situation was resolved by echo-guided percutaneous drainage with no need to solve classically. Transitory bile leak during first 72 hours after surgery was most frequent, evaluated at 24 (34.8 ± 9.93%) patients, did not require additional interventions, being clarified with the rehabilitation of intestinal passage after surgery. Wound infection was recorded at 15 (21.7 ± 11.01%) patients and was resolved by conservative aseptic dressings. Alarming postoperative complications were partial anastomosis dehiscence established in 12 (17.4 ± 11.43%) cases. These cases were resolved conservatively, due to intraoperative drainage with anastomosis drainage system both posteriorly and anteriorly together with transanastomotic drainage after Veolker. Postoperative bleeding complications were encountered in version of wound hematoma - 9 (13.0 ± 11.89%) cases, recreation resolved by the cutting of infection through widened dressings with anesthetically potentiation. Postoperative pulmonary complications were recorded in 7 (10.1 ± 12.30%) cases, mostly pneumonia or bronchopneumonia due to prolonged intubation. The serious consequences of biliary infection were scored in episodes of cholangitis at 1 (11.74 ± 1.4%) patient. Clinic situation was solved through targeted antibacterial and infusion therapy. The statistical correlation of clinical status, biochemical indices, level of stricture with postoperative morbidity showed that they influenced the arousal of complications ($p = 0.01$).

Remote surveillance on average was 29.89 ± 0.48 months, with amplitude range from 2.00 to 68.00 months. Excellent or good results were obtained at 134 (66.01%) patients, while 69 (33.99%) remaining patients showed reasonable or weak results. To assess quality of life in remote postoperative stage with a periodicity of 3 and then every 6 months postoperatively was used the assessment system represented by J. Terblanche. We mention four fundamental groups for evaluation scale. All results were measured with a digital database. In this assessment, we noticed that the best evolution in terms of indicators of inquiry have been established for the group I, evaluated in 123 (60.6 ± 4.41%) cases with a truthfulness of $p_{1,2}<0.001$; $t = 5.38$. These patients demonstrated a sustainable recovery and a lack of complaints from the hepatobiliary system, with a full reinstatement in social activity. Group II cumulated satisfactory results observed in 39 (19.2 ± 6.31%) cases with a truthfulness of $p_{2,3}> 0.05$; $t = 1.10$. All patients were in good state of health, only episodically had clinical transient signs of a chronic liver and biliopathy. The last did not have any serious impact. These states were corrected by diet, hepatoprotective therapy, which were received episodically in the hospital. Group III represented patients who presented complaints at the time of the tests exam and hepatobiliary function disorders. These patients were registered in 18 (8.9 ± 6.91%) observations and truthfulness of $p_{3,4}> 0.05$; $t = 0.25$. All of them required episodically surgical hospitalization with hepatoprotective infusion treatment under multidisciplinary control, which included hepatobiliary surgeon, hepatologist, gastroenterolo-gist, endoscopist. Making treatments allowed health compensation and avoidance of hepatobiliary suf-

fering progression. An unfortunate impact was that the vast majority of them have changed their profile and social activity regime. Group IV accounted patients with recurrent biliary stricture and essential disturbance of hepatobiliary function on reflux angiocholitis background or of severe cholestatic hepatitis. These situations we noticed at 23 (11.3 ± 6.75%) patients with a truthfulness of $p_{1,4}$ <0.001; t = 6.12. In all 23 cases were found strictures of hepaticojejunoanastomosis, we performed plastic surgery of hepaticojejunoanastomosis with plastic elements of Heineke-Mikulicz type. Intervention aimed to liquidate the stricture and anastomotic restoration within the present tissues on anastomosis line. All cases had an intraoperative fibroplastic process on hepatojejunostomy level while the bile duct was not directly involved, presenting normal tissue. This moment was decisive in omitting the need to restore the anastomosis and achieve only a plasty of anastomosis mouth using 5/0 PDS atraumatic suture only in single plane and separate drainage of both liver channels. Drains were maintained for up to six months, having a housing role in order to stabilize the formation of the anastomosis mouth. The achieved postoperative results were very good. It's worth noticing that the issue of HJA strictures or anastomosis restricture require further study and has a major scientific actuality. Thus are analyzed and studied effects of complications on patient including its implications and their resounding on quality of life, disease progression and prognosis as well the impact on remote survival.

ISCUSSIONS

Iatrogenic strictures of main biliary ducts are characterized by a high degree of severity, with the tendency to a more proximal location, more frequently found in recent years. Most restorative and temporary drainage interventions on biliary ducts require a new biliary-digestive intervention [6, 7].

In surgery for benign biliary strictures, reconstruction of biliary system through HJA has become a standard procedure. The anastomosis is performed through modern suture in a single layer mucosa-to-mucosa using a jejunal arm Roux-en-Y. It was proved to be safe and feasible, even in high reconstructions simultaneously applying on several bile ducts [6, 8, 15].

When Performing HJA, different types of suture of bile stump are applied to the intestine. Particularly important is the distance of suture application, the depth and the type of the suture. In current practice, anastomosis is performed with ordinary sutures that are passed through all layers. PDS suture material, Vycril 4/0-5/0 are accepted. We focus on a good eremitism, using sutures with a 2-3 mm step. The posterior lip is performed with the nodes in the lumen, and the anterior one with the nodes outside. Suture line is strengthened with up to 5 anterior sero-serous sutures only when necessary [17].

Regardless of biliary stump level, the precise mucosa-to-mucosa suture in a single plan of discontinued sutures and the placement of transanastomotic drainage tubes ensured a sufficient anastomosis with bile flow or remote strictures. It is quite important during high anastomosis, on the hilum level to drain each bile duct separately. Long-term outcome for these cases was reported as being comparable to low hepatico-jejuno-anastomosis [10, 23].

Hepp-Couinaud technique relies on left extrahepatic hepatic duct. Fascia incision concentrated around the hepatic artery, portal vein and represents the "hilarium plaque", which allows easy exposure of the extrahepatic left hepatic duct. Left hepatic duct is an excellent choice for repairing proximal strictures, because it is located under 4th segment and makes an optimal access to the stoma. In addition, it has a rich blood supply that is not affected by iatrogenic lesions, unlike the fragile blood supply of the common hepatic duct.

Remote results of HJA on Roux- en-Y loop are reported as very good by the majority of publications in the field, with excellent results in 85% of cases.

At least 5 years after the reconstruction are considered an optimal period of postoperative evaluation of the results. A series of studies underlines that two thirds of complications occur within 2 years, 80% within 5 years, while 20% of failures may occur 5 years after the operation. According to Leslie H. Blumgart, 40% of re-strictures were identified after more than five years since the reconstructive surgery. Therefore, monitoring during the first five years or more is necessary in evaluating the results. In choosing the critical length of time, the professionals should consider comparing the results from different series of treatments.

Large international experience in studying the quality of life (QoL) presents promising opportunities of this method for all branches of clinical medicine and can be used with traditional indicators for monitoring the effectiveness of surgical treatment. There is currently no data on the level of disability and postoperative rehabilitation after reconstructive surgery. Therefore, we consider it important to study the future quality of life of patients with iatrogenic lesions and scar biliary strictures. The effectiveness of bilio-digestive anastomoses should be evaluated in the immediate postoperative period and in time. Research of QoL can help solving the problem of patients' rehabilitation and their return to normal life.

CONCLUSIONS

The diagnosis and management of benign biliary strictures remain a challenge. Given the risks of septic biliary complications, the costs and the high associated morbidity due to repeated surgeries, an accurate diagnosis is crucial. A detailed medical his-

tory and a multidisciplinary approach to guide the treatment goals, is important in ensuring a satisfactory lasting outcome after surgery.

Factors such as the detailed knowledge of the patient's medical history or embracing a multidiscipli-nary approach in managing treatment objectives have important contribution to a satisfactory and lasting outcome.

The definitive goal of surgical management is to restore bile flow in the proximal gastrointestinal tract that prevents any reflux cholangitis, re-strictures of the biliary tree and chronic hepatobiliary pain.

The reconstructive surgical act addressed to iatrogenic biliary strictures is directly related to the localization. Choosing the appropriate reconstructive surgical method to address iatrogenic biliary strictures depends on their localization. For type I strictures, an end-to-side choledochojejunostomy with a Roux-en-Y excluded loop is optimal. For the type II, the solution consists of a choledochojejunostomy with a Roux-en-Y single loop, and case of a high upper extension of the stricture, we proceeded to hepaticojejunostomy with a Roux-en-Y excluded loop.

For type III stenosis, an end-to-side hepaticojejunostomy with a Roux-en-Y excluded loop and transanastomotic drainage of the right and left hepatic ducts is applied. For type IV, a double hepaticojejunostomy with a Roux-en-Y excluded loop and mandatory transanastomotic drainage of both ducts is preferred.

A unified method for remote assessment of patients with postoperative biliary stricture would make possible a good estimation of the occurring complications and quality of life (QoL). Curently, it is important to know and evaluate the impact of biliary strictures and reconstructive operations on the patient's health and rehabilitation based on biomedical, physiological and socio-economic indices. Study of QoL, among the multitude of factors related to health, would allow a deeper analysis of multifactorial components of human health according to WHO criteria, namely the medical-physiological, psychological and social problems of the patient.

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