

# A MODERN APPROACH TO THE CHOICE OF ENDOBILIARY REPLACEMENT TIME IN PATIENTS WITH OBSTRUCTIVE JAUNDICE OF CANCEROUS GENESIS

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© **B.Kh. Kalakhanova**, Postgraduate, the Department of Surgery<sup>1</sup>;  
**G.M. Chechenin**, PhD, Associate Professor, the Department of Surgery<sup>1</sup>; Surgeon, 50<sup>th</sup> Department of Surgery (Department of Hepatic and Pancreatic Surgery)<sup>2</sup>;  
**S.S. Lebedev**, PhD, Associate Professor, the Department of Surgery<sup>1</sup>; Surgeon, 50<sup>th</sup> Department of Surgery (Department of Hepatic and Pancreatic Surgery)<sup>2</sup>;  
**Y.V. Barinov**, PhD, Associate Professor, the Department of Surgery<sup>1</sup>; Surgeon, 50<sup>th</sup> Department of Surgery (Department of Hepatic and Pancreatic Surgery)<sup>2</sup>;  
**A.A. Seregin**, Head of the Department of Interventional Radiological Diagnostic and Treatment Techniques<sup>3</sup>;  
**G.G. Melkonyan**, PhD, Tutor, the Department of Surgery<sup>1</sup>;  
**R.B. Mumladze**, D.Med.Sc., Professor, Head of the Department of Surgery<sup>1</sup>

<sup>1</sup>Russian Medical Academy for Postgraduate Education, Ministry of Health of Russia, Barrikadnaya St., 2/1, Moscow, Russian Federation, 123995;

<sup>2</sup>S.P. Botkin City Clinical Hospital, 2<sup>nd</sup> Botkinsky Proezd, 5, Moscow, Russian Federation, 125284;

<sup>3</sup>Privolzhsky District Medical Center of Federal Medico-Biologic Agency of Russia, Nizhne-Volzhskaya naberezhnaya St., 2, Nizhny Novgorod, Russian Federation, 603005

**The aim of the investigation** was to determine an optimal time of endobiliary stenting in patients with obstructive jaundice syndrome of cancerous genesis on the comparative analysis basis.

**Materials and Methods.** We studied the treatment results of 360 patients with obstructive jaundice syndrome of cancerous genesis using minimally invasive techniques. Mean age was 60.0±8.3 years (from 37 to 84 years). The first stage of treatment was biliary decompression using percutaneous external drainage of ducts, the second — the restoration of biliary duct patency and antegrade bile passage using percutaneous stenting. Group 1 consisted of 150 patients with early stenting, group 2 — 210 patients after delayed stenting of biliary passage.

**Results.** Three groups of complications were found: complications related to the procedure, inflammatory complications, and progressive hepatic failure. In group 1, 23 of 150 patients (15.3%) had complications, in group 2 — 44 of 210 patients (21.9%) ( $p=0.039$ ). Lethality in an early postoperative period in group 1 was 2.6%, in group 2 — 4.8% ( $p=0.038$ ). Group 1 had significant and statistically reliable improvement of some laboratory findings.

**Conclusion.** The most effective and safe technique to help patients with obstructive jaundice of cancerous genesis is an early stenting — within the first three days after external percutaneous biliary drainage.

**Key words:** biliary tract replacement; biliary drainage; obstructive jaundice of cancerous genesis.

Obstructive jaundice syndrome includes a sufficiently large group of diseases, the common feature is the development of obstruction of major biliary passages. The most common cause of these diseases is primary and metastatic hepatobiliary tumors (30.2–67.3% patients) [1–3]. Hypertension in biliary tract, no bile in the intestine result in the development of inflammatory changes of the biliary tract, and bile element flow in blood causes intoxication and the development of severe morphofunctional impairments of hepatic, renal parenchyma, as well as other organs and systems [4, 5]. Under these conditions the most effective and safe way to help patients with obstructive jaundice of cancerous genesis is minimally invasive biliary decompression,

which significantly decreases intoxication and reduces the risk of multiple organ failure [6–8]; external biliary drainage being the most frequently used [9, 10]. However, the technique does not recover normal bile passage and presents a number of predictable complications: the development of acute hepatic failure due to “a rapid decompression syndrome”; dysproteinemia, intestinal endotoxin activation, augmentation of intoxication syndrome due to the lack of bile in the intestinal lumen, and other pathophysiological mechanisms [9, 11, 12]. Biliary replacement (stenting) is an advanced technique to reconstruct bile passage, the question of time yet requires further clarification and verification [13–15]. Some authors suggest carrying out the replacement with

**For contacts:** Kalakhanova Bella Khalitovna, e-mail: rfhkjcy26@mail.ru

bile duct drainage as a single-stage operation, while the others — as a delayed procedure, not until 4–5 days after obstruction jaundice arresting [14–16].

**The aim of the investigation** was to determine an optimal time of endobiliary stenting in patients with obstructive jaundice syndrome of cancerous genesis.

**Materials and Methods.** The study involved 360 patients with hepatobiliary tumors, and advanced obstructive jaundice, among them there were 200 (55.6%) female, and 160 (44.4%) — male patients. Mean age was 60.0±8.3 years (from 37 to 84 years).

All patients underwent clinical instrumental examination including physical examination, ultrasound (Logiq Eq, General Electric, USA), magnetic resonance imaging (Signa Excite HD 1,5T, General Electric) and/or computed tomography (Light Speed, General Electric).

The present retrospective study was approved by the Ethics Committee of Russian Medical Academy for Postgraduate Education and complies with the requirements of Helsinki Declaration (adopted in June, 1964 (Helsinki, Finland) and revised in October, 2000 (Edinburgh, Scotland)). Written informed consent was obtained from all patients.

The diagnosis was verified histologically in all patients. Pancreatic tumor appeared to be the most common cause of obstructive jaundice: in 228 of 360

(63.3%) patients. Hepatic metastases were diagnosed in 54 patients (15%), Klatskin tumor — in 42 (11.7%), major duodenal papilla tumor — in 30 (8.3%), common bile duct tumor — in 6 (1.6%). The disease duration averaged 1.2±0.4 years (from 3 months to 2 years).

Bile decompression using percutaneous external duct drainage was the first stage, the restoration of patency of bile ducts and antegrade bile passage by percutaneous stenting — the second stage. The procedure was performed on a radiological apparatus (OEC 9800 Plus, General Electric, USA). Nitinol expandable stents (Taewoong Medical, South Korea), from 6 to 10 mm in diameter were used.

Depending on the technique used the patients were divided into two groups (divided in accordance with “an envelope” method). Group 1 involved 150 patients who underwent the stenting of bile ducts within the first three days after external cholangiostomy (an early stenting technology) including single-stage drainage and stenting performed in 60 of 150 patients (16.7%). Group 2 consisted of 210 patients who underwent the stenting of bile ducts 7–21 days after external drainage (a delayed stenting).

The most indices of both groups had no significant differences (Table 1) that gives grounds to assess the groups as homogeneous and comparable, and carry out a comparative analysis of treatment results.

Table 1  
Characteristics of the patients in the groups under study

Parameter	Group 1 (n=150)	Group 2 (n=210)	p
Age, years (M±m)	57.4±2.0	58.2±2.0	0.774
Number of male, abs. number/%	68/45.3	92/43.8	0.876
Disease duration, years (M±m)	1.2±0.4	1.2±0.4	0.743
Obstructive jaundice syndrome duration prior to admission, days (M±m)	7.0±1.0	9.0±1.0	0.773
Tumor localization, abs. number/%:			
cancer of the head of the pancreas;	96/64.0	132/62.8	0.867
cancer of major duodenal papilla;	13/8.7	17/8.9	0.934
cancer of common bile duct;	2/1.3	4/1.9	0.975
Klatskin tumor;	17/11.3	25/11.9	0.963
hepatic metastatic lesion	22/14.7	32/15.2	0.745
Blood bilirubin level, μmol/L (M±m)	152.0±5.0	156.0±5.0	0.874
Number of patients (abs. number/%) with blood bilirubin level (μmol/L):			
under 60	6/4.0	11/5.3	0.882
from 60 to 200	47/31.3	64/30.4	0.921
over 200	97/64.7	135/64.3	0.971
Aspartate aminotransferase, U/L (M±m)	95.0±2.0	98.0±2.0	0.768
Alanine aminotransferase, U/L (M±m)	87.0±2.0	89.0±2.0	0.875
Creatinine, μmol/L (M±m)	56.0±1.0	62.0±1.0	0.723
Urea, mmol/L (M±m)	3.7±1.0	4.2±1.0	0.134

**Results and Discussion.** X-ray tube operation time during stenting in groups 1 and 2 was 12.2±6.2 and 15.6±8.0 min, respectively (p=0.871), total operating time — 44.0±10.0 and 47.0±13.2 min, respectively (p=0.873). There were no significant differences in these parameters between the groups.

During the first three days after stenting, group 1 patients on the average had 500±100 ml bile a day (from 100 to 800 ml) discharging by a suction catheter, group 2 patients — 1200±200 ml (from 600 to 3000 ml); p=0.046.

In group 1, 26 patients (17.3%) required oral administration of bile; in group 2 — 78 patients (37.1%). For a number of reasons, 4 patients (2.7%) of group 1 could not take their own bile *per os*, in group 2 — 28 patients (13.3%).

After the procedure, group 1 patients were found to have more rapid decrease of total bilirubin concentration (See the Figure), the differences being statistically insignificant.

Complications after the procedure were diagnosed in 67 of 360 patients (18.6%) — total 77 complications that is comparable with the findings of other authors [8, 10, 14].

The patients were found to have a certain range of complications, which were combined in three groups (Table 2). The first group included complications closely related to the procedures (puncture and catheterization of ducts): right-sided hydrothorax, local bile peritonitis, external bile fistula formation. The second group involved inflammatory complications, the third one — the conditions characterizing the disease course after stenting: the presence or absence of progression of organ and system failure. It should be noted that up to the present day there is no consensus on how to assess the process: as a complication or as a natural course of the disease after the procedure [13, 15]. We incline to the second opinion, since in some cases even after a well-done procedure there can be multiple organ failure progression (in our study, mainly, hepatorenal failure) that may be due to the lack of hepatic tissue reserve for their morphofunctional recovery.

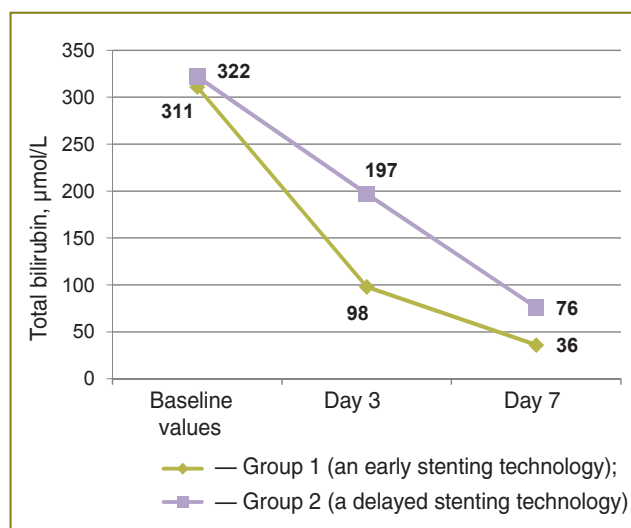
In group 1 (an early stenting technique) the complications were diagnosed in 23 of 150 patients (15.3%), in group 2 (a delayed stenting) — in 44 of 210 patients (21.0%); moreover, 7 patients (16.0% of this group patients) were found to have more than one complication. Thus, there were 54 complications in group 2. The differences between the groups were significant (p=0.039).

Inflammatory complications including purulent ones were most common,

group 1 patients had significantly less complications (p=0.019).

Multiple organ failure progression rate after adequately performed procedure was the same in both groups (p=1.000). It is important to note that only severe patients with a marked original hepatorenal failure had such an outcome: a bilirubin level in blood was over 200 mmol/L, aspartate aminotransferase and alanine aminotransferase levels were higher than the norm by more than 2.0±0.3 times, serum creatinine was higher than the norm by 1.4±0.3 times, urea — by 1.2±0.3 times.

Case fatality within a month in group 1 (4 of 150 patients, 2.6%) was significantly lower (p=0.038) than in group 2 (10 of 210 patients, 4.8%). In all cases the patients' death was caused by progressing multiple organ failure, despite an adequate bile decompression.



Bilirubin level changes after bile duct stenting (mean values) in patients with obstructive jaundice of cancerous genesis

Table 2

The assessment of complications after an early and delayed stenting of bile ducts in the patients under study

Characteristics of complications	The number of complications, abs. number/%		p
	Group 1 (n=150)	Group 2 (n=210)	
Procedure related complications:	5/3.3	13/6.2	0.009
right-sided hydrothorax	4/2.6	5/2.4	0.934
local bile peritonitis	1/0.7	3/1.4	0.039
external biliary fistula	0	5/2.4	<0.001
Inflammatory complications:	8/5.3	27/12.9	0.019
progression and/or the development of purulent cholangitis	5/3.3	13/6.2	0.011
acute pancreatitis	3/2.0	14/6.7	0.008
Progressive hepatic failure	10/6.7	14/6.7	1.000
Total	23/15.3	54/25.7	0.039

Currently, there is no doubt that obstructive jaundice is the severest complication of tumors of hepatopancreatoduodenal area and should be eliminated as soon as detected due to the threat of cholangitis, acute pancreatitis, hepatic failure development [2, 4].

No bile in the jejunum prevents from recovering the balance of its microflora, discontinuing activation of toxins and reducing intoxication, which among other things determines the severity of patients' condition [2, 5]. Taking bile *per os* cannot be considered as physiological: alkaline condition of bile definitely has a negative effect on gastric and esophageal mucosa [5, 8, 13].

External drainage without recovering antegrade bile passage in the small intestine achieves the main purpose of the procedure: bile decompression, though, according to our findings, it does not result in radical improvement of the results — it reduces neither complications, primarily, inflammatory ones, nor lethality.

When an early stenting of bile ducts is used in the treatment, in fact, two bile outflow tracts are formed: external (along a suction catheter) and natural, physiological (along the bile ducts reconstructed by a stenting technique) that, according to the findings, results in the more rapid bile decompression providing the evacuation of "inspissated" bile, intoxication reduction, decreased lethality in the immediate postoperative period.

The significance of this technique is also lies in the fact that it provides natural, close to physiological, bile inflow in the intestine that, in its turn, prevents further activation of duodenal microflora breaking a vicious circle of endogenous intoxication support.

An early stenting management can serve both as a final treatment option, and also as a preparation stage of a patient before radical surgery.

**Conclusion.** The most effective and safe technique to help patients with obstructive jaundice of cancerous genesis in an acute period is bile decompression by external percutaneous biliary drainage and an early stenting of bile ducts — within the first three days.

An early stenting technology combined with external drainage provides the recovery of antegrade (natural) bile flow that enables to achieve more rapidly the prime objective — bile decompression, as well as provide physiological inflow of bile in jejunum avoiding inflammatory congestive complications (cholangitis, pancreatitis) including purulent conditions, and significantly reduce endogenous intoxication, and decrease lethality in the immediate postoperative period.

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## References

1. Shevchenko Yu.L., Vetshev P.S., Stoyko Yu.M., et al. Diagnostics and surgical management in obstructive jaundice syndrome. *Annaly hirurgiceskoj gepatologii* 2008; 13(4): 96–105.
2. Lomakin I.A., Ivanov Yu.V., Sazonov D.V., et al. Diagnostics and management of patients with obstructive jaundice. *Klinicheskaya praktika* 2012; 3: 42–50.
3. Greenlee R.T., Hill-Harmon M.B., Murray T., Thun M. Cancer statistics, 2001. *Cancer J Clin* 2001; 51: 15–36.
4. Ribachkov V.V., Dryazhenkov I.G., Kabanov E.N. Causes of endogenous intoxication in purulent cholangitis. *Annaly hirurgiceskoj gepatologii* 2009; 14(2): 28–32.
5. Akhaladze G.G. Purulent cholangitis: problems of pathophysiology and treatment. *Consilium medicum* 2003; 5: 4.
6. Gal'perin E.I., Vetshev P.S. *Rukovodstvo po khirurgii zhelchnykh putey* [Guidelines on biliary tract surgery]. Moscow: Vidar; 2006; 559 p.
7. Prokubovskiy V.I., Kapranov S.A. Transhepatic biliary duct replacement. *Hirurgia* 1990; 1; 18–23.
8. Kim H.J., Lee S.K., Kim M.H., Song M.H., Park D.H., Kim S.Y., et al. Percutaneous transhepatic cholangioscope treatment of patients with benign bilio-enteric anastomotic strictures. *Gastrointest Endosc* 2003; 58(5): 733–738.
9. Vetshev P.S., Stoyko Yu.M., Levchuk A.L., et al. The possibilities of modern diagnostic techniques and validation of management in obstructive jaundice. *Vestnik khirurgicheskoy gastroenterologii* 2008; 2: 24–32.
10. Gusev A.V., Balagurov B.A., Borovkov I.N., et al. Drainage and replacement of biliary ducts in obstructive jaundice. *Vestnik novykh meditsinskiy tekhnologiy* 2008; 15(4): 97–98.
11. Izrailov R.E., Kulezneva Yu.V., Xat'kov I.E., et al. The role of interventional radiology in minimally invasive treatment of patients with tumors of biliopancreatobiliary area. *Diagnosticheskaya intervensionnaya radiologiya* 2011; 5(3): 37–43.
12. Zavrazhnov A.A., Popov A.Yu., Petrovskiy A.N., et al. The significance of minimally invasive bile decompression techniques in the treatment of patients with obstructive jaundice. *Neotlozhnaya meditsinskaya pomoshch'* 2012; 2: 54–58.
13. Kulezneva Yu.V., Izrailov R.E., Kapustin V.I. Management of antegrade biliary decompression in patients with obstructive jaundice of cancerous genesis. *Vestnik Natsional'nogo mediko-khirurgicheskogo tsentra im. N.I. Pirogova* 2010; 5(2): 24–28.
14. Tulin A.I., Zerav S.N., Kupch S.K. Endoscopic and percutaneous transhepatic stenting of bile ducts. *Annaly hirurgiceskoj gepatologii* 2007; 12(1): 53–61.
15. Shapovalyants S.G., Budzinski S.A., Fedorov E.D., et al. Endoscopic management of the bile ducts postoperative scar strictures (20-year experience). *Annaly hirurgiceskoj gepatologii* 2011; 16(2): 10–17.
16. Shevchenko Yu.L., Vetshev P.S., Stoiko Yu.M., Priority trends in the obstructive jaundice patients management. *Annaly hirurgiceskoj gepatologii* 2011; 3: 9–15.