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The Effect of Chronic Diffuse Liver Pathology on the Risk of Intra- and Post-Hepatectomy Complications

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ABSTRACT

Improvement of the technical aspects of liver resections reduces the risk of many specific intra- and post-operative complications. However, post-resection liver failure (PRLF) remains a difficult problem that significantly complicates the post-operative period. To assess the effect of chronic diffuse liver pathology on the frequency of complications of liver resections, the control group of 81 patients, operated in the NSCS Department of hepato-and-biliary tract surgery and in the Department of surgery of portal hypertension and pancreatoduodenal zone from 1998 to 2009 was studied. The patients were divided into 2 groups: group A was composed of patients with concomitant diffuse liver disease, namely chronic viral hepatitis and steatosis (53 patients; 65.4%) and group B included 28 patients; 34,6% with no concomitant liver pathology. The PRLF frequency analysis showed that the development of severe complications in the early postoperative period clearly correlated with the presence of diffuse liver disease. In patients with no chronic liver diseases, PRLF occurred in 2 cases (7.1%) after extensive liver resections (2 of 28). In patients with hepatic pathology, PRLF of varying severity developed in 18.9% (10 of 3). After extensive liver resections PRLF developed more than twice as often in the patients with chronic liver disease: 28.6% versus 13.3% (8 of 28 vs. 2 of 13). After segmental resections, PRLF occurred only in patients with chronic pathologies of the liver (8.0%). Concomitant chronic diffuse liver diseases caused a significant decrease in the functional status of hepatocytes, i.e. a decline of hepatic extraction fraction in 17.1% (67.5 ± 2.3% vs. 81.4 ± 1.9%) and an increase in half-life elimination of the radiopharmaceutical drop to 26,5% (37.2 ± 1.7 min vs. 29.4 ± 1.2 m) (P<0.001) in comparison with group B. Thus, hepatectomy in concomitant chronic diffuse liver pathology increases the risk of PRLF associated with reduced functional reserve of hepatocytes and slower compensatory regeneration process.

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INTRODUCTION

Development of new techniques of liver resection widened significantly the opportunities for surgical interventions for primary and secondary focal processes in the liver. The list of indications for liver resection has been increased in the recent decade that led to introduction of one- and two-steps extended resections [1-3]. An increase in quality and volume of surgeries has drawn great attention to various risk factors influencing the outcomes of surgical treatment [4].

Improvement of the technical aspects of liver resection allowed leveling the risk of many specific post-resection complications. However, post-resection liver failure (PRLF) remains to be a difficult challenge up to the present time, in particular, prevention of its development and reduction of severe hepatargia frequency [4-6].

Acute PRLF is one of the most severe complications of expanded liver resection. It may be the cause of 18-75% of lethal outcomes [8]. The main cause seems to be low pre-operative functional liver reserve or insufficient volume of the parenchyma after liver resection [15]. In patients with diffuse or marked dystrophic changes of the parenchyma, insufficient volume of the residual hepatic tissue, and severe concomitant diseases of the cardio-vascular system and respiratory organs, as well as the problem of prevention of acute PRLF are still significant [9].

Liver resection is possible in cirrhosis A by the classification of Child-Pugh, in some observation in cirrhosis B, but it is contraindicated for patients with cirrhosis C [10, 11]. In the randomized study of liver pathology conducted in 2004, the Barcelona Clinic Board developed the classification of hepatocellular cancer (Barcelona - Clinic Liver Cancer staging system) taking into account the tumor process and severity of liver cirrhosis [12]. It should be used when it was impossible to choose an optimal method of treatment for a concrete situation, e.g. liver resection or transplantation, radiofrequency destruction or transarterial chemoembolization or medicinal therapy [8].

The study of many factors rendering direct effects on the PRLF frequency resulted in identification of the criteria divided into factors related to patients' profile, surgical intervention type and postoperative management of patients. High frequency of chronic diffuse pathology of the liver is associated, first of all, with viral hepatitis while the alimentary factor seems to be the regional peculiarity. In viral hepatitis, the risk of development of post-resection complications was caused by the viral activity and progressing cytolisis and liver fibrosis while an increase in the body mass index was concomitant by development of fatty hepatosis which, if prolonged, may lead to functional disorders of hepatocytes with cholestasis and progressing fibrosis.

Objective of the present study was investigating the effect of concomitant chronic diffuse liver pathology to results of resections performed due to benign and malignant liver focal neoplasms.

MATERIAL AND METHODS

To identify indications and modality of liver resection, particularly the extended one, it is necessary to take into consideration all specific factors effecting on the peri-operative period. The control group of 81 patients was analyzed to evaluate the effect of chronic diffuse process in the liver on the frequency of liver resection complications. The patients were operated in the Department of liver and biliary tract surgery and in the Department of portal hypertension and pancreato-duodenal zone surgery of the National Specialized Center for Surgery (Tashkent, Uzbekistan) in 1998 - 2009. The patients were divided into group A composed of patients with concomitant diffuse liver pathology, namely chronic viral hepatitis and fatty hepatosis (53 patients; 65.4%), and group B of 28 patients with no liver pathology.

Among 53 patients with concomitant liver pathology, 31 had viral hepatitis and 22 had fatty hepatosis. In 28 cases (34.6%), extended liver resections were performed; in 25 cases, various variants of segmentectomies (30.9%) were used, in 14 cases of viral hepatitis and 11 – in fatty hepatosis. In the group of patients with no chronic liver pathology, major resections were performed in 18.5% of cases (in 15 of 81), segmentectomy was performed in 16.0% (13 patients).

During examination of the patients in the pre- and postoperative periods, the dynamic monitoring of clinical and biochemical blood indicators was conducted. Radionuclide investigation of the hepatic blood volume was performed on the gamma-camera (FO Gamma LFOV with computer PDP 11/34. USA) using the technique of dynamic and static scintigraphy. Colloid radiopharmaceutical 99mTc-technefit of native production was used as the activity indicator (0.6 MBk/kg of body mass). Deconvolution analysis applied to process the obtained radio-chronograms yielded in identification of two parameters characterizing the functional activity of liver parenchyma:

1. Fr extr - the parameter of the liver extraction fraction (%).
2. T ½ - the period of the radiopharmaceutical half-life elimination (min) characterizing excretive liver function.

The hepatocyte functional activity was evaluated with radioisotope scintigraphy in 34 patients in the pre-operative period and on day 5-7 after extensive liver resection. In 22 cases, the patients had concomitant chronic diffuse liver pathology and 12 patients did not have liver pathology. Findings of clinical examination were processed with the method of variational statistic developed by W.S. Gosset (Student) and R.A. Fisher. The average and standard error (M±m) were calculated. The findings were considered reliable if the level of the significance of the reliability indicator of the difference of average values (P) was no more than 0.05. The statistic processing of the obtained findings and their graphic presentation were performed on the PEVM "Pentium-4" using the standard MS Excel-XP, Statistica 6.0, BIOSTAT.

Ethical approval

The review board and ethics committee of Republican Specialized Center of Surgery named after acad.V.Vakhidov approved the study protocol and gave permission.

RESULTS AND DISCUSSION

The study of PRLF frequency showed that development of this life-threatening complication in the early post-operative period clearly correlated with the presence of diffuse liver pathology. For instance, in group B, PRLF occurred in 2 cases after extensive liver resections, it accounted 7.1% (2 of 28). In group A, the frequency of PRLF of various severities was 18.9% (10 of 53). The total frequency of PRLF development in the groups under study was 14.8% (12 of 81)

It should be noted that severe PRLF in group developed in 9.4% of cases (in 5 patients) in 4 cases it was accompanied by chronic viral hepatitis and in one case by fatty hepatosis. In group B, severe PRLF was diagnosed in one patient (4.5%). Severe PRLF was the consequence of extensive liver resection in all cases. After extensive liver resection PRLF complicated the post-operative period twice more often in chronic liver pathology: 28.6% vs. 13.3% (8 of 28 vs. 2 of 13). In segmental resections, PRLF was found only in group 2 (8.0%).

The parameters of the liver extraction fraction in concomitant chronic diffuse liver pathology in the pre- and post-operative periods are presented in figure 1. Concomitant chronic diffuse liver pathology in patients with focal neoplasms contributes to reliable reduction (P<0.001) of the hepatocyte functional status, that was clearly expressed by the reduction of the liver extraction fraction by 17.1% (67.5±2,3% vs. 81.4±1.9%). This suggests that lower functional reserve of hepatocytes is associated with PRLF high frequency in the patients with concomitant liver pathology in the early post-operative period.

In addition to the fraction of liver extraction we studied half-life elimination period of radiopharmaceutical (RP) from the liver. The presence of concomitant chronic diffuse pathology in the patients with focal neoplasms provides reliable prolongation of the RP half-life elimination period by 29.8% (from 29.4±1.2 min to 42.1±3.6 min) (P<0.001) in comparison with the group with no parechymatous processes.

In group A, on days 5-7 after the surgery, reliable prolongation of the RP half-life elimination period was noted in comparison with the preoperative period (from 37.2±1.7 min to 64.5±4.2 min, respectively; P<0.001). In group B, an increase in this parameter value was noted: from 29.4±1.2 min to 42.1±3.6 min (P<0.001) (Figure 2). The dynamics of the liver function changes in the post-operative period was monitored by biochemical blood tests (total protein, albumin, ALT, AST, bilirubin). In the majority of patients, on day 1 after the surgery, the levels of ALT, AST and total bilirubin in the blood serum increased the number of total protein and, particularly, albumin fraction reduced both in the study group and the controls.

However, reliably (P < 0.05) quicker restoration of the parameters closer to the physiological values was observed in group B (11.3±0.4 days), while the parameters in group A approached the normal value in 16.5±0.7 days (Table 1). Surgical interventions in the patients with diffuse liver changes were always associated with a high risk of complications both in the post-operative period and during the surgery. Profuse, difficult for control intra-operative hemorrhages in these patients present special difficulties for surgeons.

In our research, the intra-operative blood loss during the extensive liver resections was 684±35 ml in the patients with diffuse liver pathology, while in the absence of the concomitant pathology, the total volume of blood loss did not exceed 574±29 ml (P<0.05). In segmentectomies, the volume of the total intra-operative blood loss also reliably increased in group B against group A (529±26 ml vs. 433±16 ml, respectively; P<0.01).

The hepato-duodenal ligament (HDL) had to be clipped for prevention hemorrhage in group D during extensive liver resection in 3 of 15 cases (20.0%), while in less traumatic segmental resections, HDL clipping was made in 2 cases of 13 (15.4%). Among 28 patients with concomitant pathology who had extensive liver resection, HDL clipping was required in 9 cases (32.1%), while in segmental resections, HDL clipping was made in 6 of 25 cases (24.0%).

Some hemodynamic disturbances and severe ischemia of the hepatic tissue occurred during HDL cross-clamping, the risk of postoperative complications increased. In the initially compromised liver parenchyma (cirrhosis, chronic hepatitis, and mechanic jaundice), the resistance to hepatic ischemia reduced, respectively, to occlusion of HDL. However, the increased complexity of the surgery in diffuse liver changes assumes prolongation of the duration of the HDL cross-clamping.

In extensive liver resections in patients with diffuse liver pathology, the duration of the cross-clamping was 34.5±2.1 min, while in group A, it was reliably shorter and on the average lasted 27.9±1.7 min (P<0.05). In less traumatic segmental resections, the total clamping duration in group B was 19.8±1.3 min., while in group 1itreliably increased to 23.1±1.9 min (P<0.05) (Figure 3).

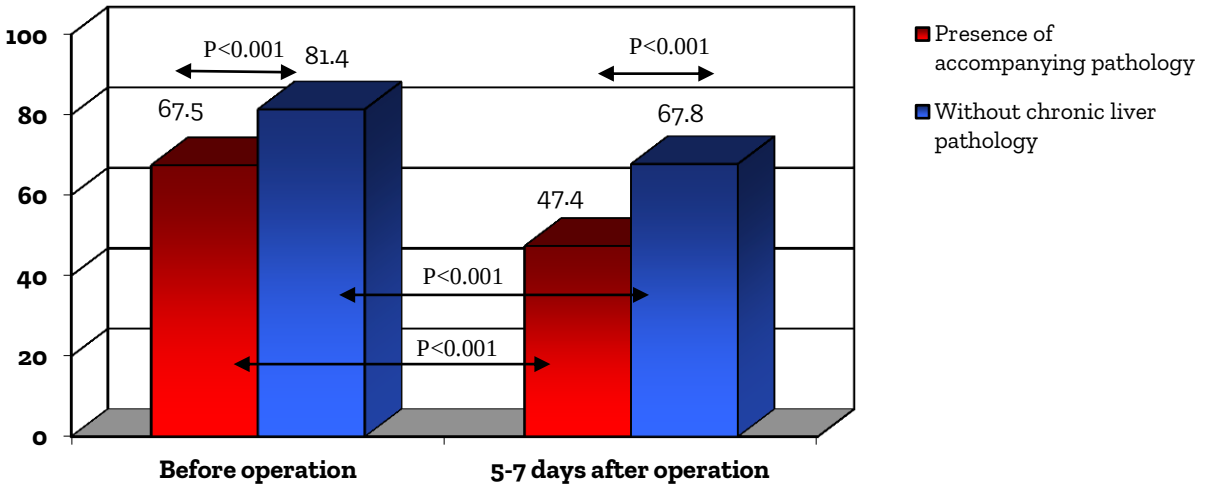

Figure 1. Evaluation of hepatocyte functional activity. Fraction of liver extraction (%) in concomitant chronic diffuse liver pathology before and after resection.

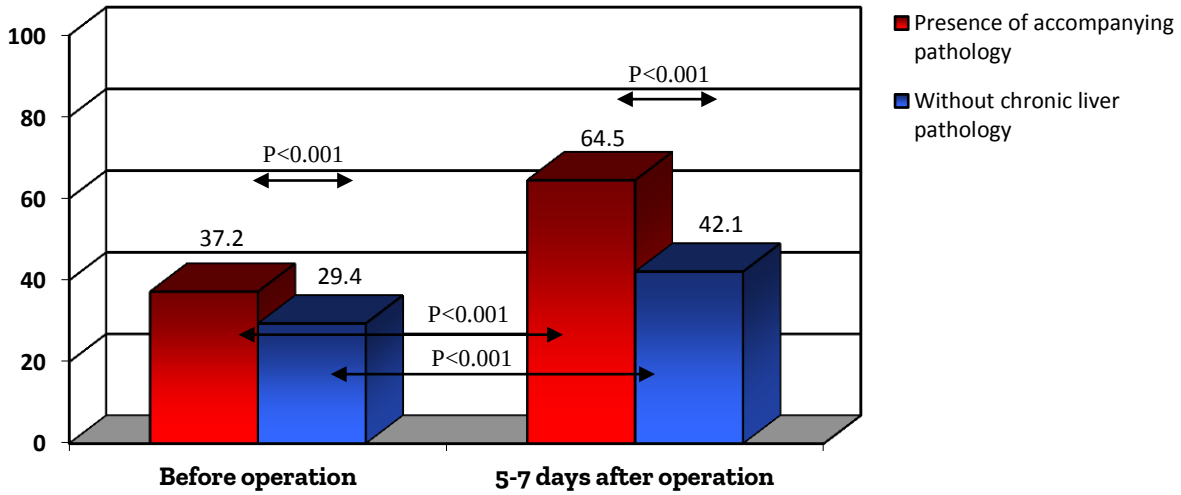

Figure 2. Evaluation of the functional activity of hepatocytes. RP half-life elimination period (min) in concomitant chronic diffuse liver pathology before and after liver resection.

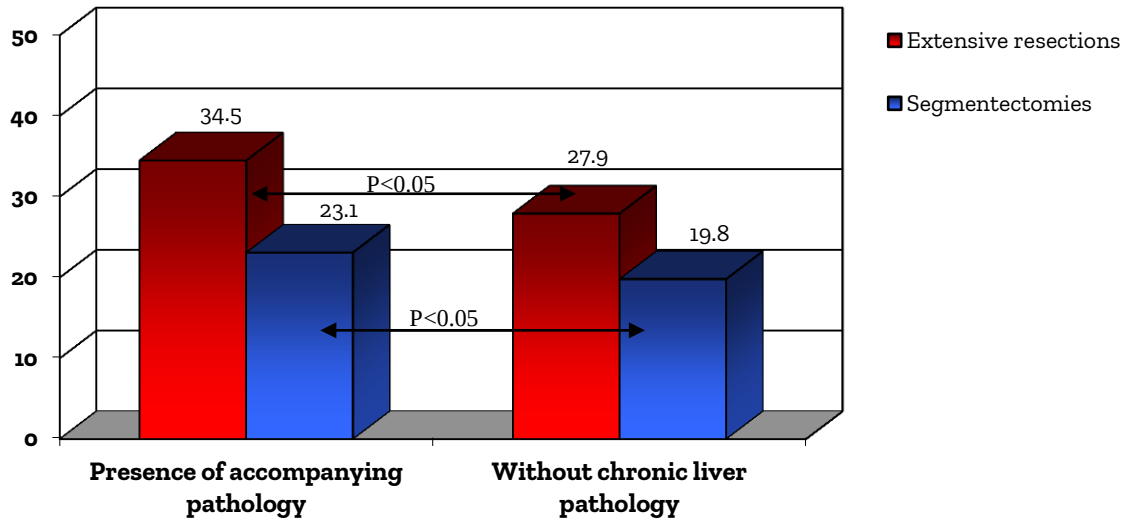

Figure 3. Duration (min) of HDL clamping

Table 1. Dynamics of biochemical characteristics

Parameter	Concomitant liver pathology			No chronic liver pathology		
	Day 1	Day 5	Day 7	Day 1	Day 5	Day 7
Total bilirubin, µmol/l	42.8±2.9	39.0±2.5*	31.2±2.2*	35.6±2.1	29.9±2.4	24.6±1.9
Plasma protein, g/l	47.9±1.9	49.1±1.7*	53.5±1.8*	49.2±2.2	53.7± 1.2	59.1±1.6
Albumin, g/l	26.5±0.8	28.4±1.0	30.1±1.1*	27.9±0.6	30.6±0.8	34.3±0.7
ALT, µmol/l	221.2±16.6*	197.7±3,2*	142.7±13,1*	175.6±11.8	159.2±11.8	101.4±0.5
AST, µmol/l	185.3±11.6*	149.2±11.4*	102.9 ± 10.2*	150.5±9.6	113.8±11.0	74.3±8.6
Parameters normalization	16.5±0.7 days*			11.3±0.4 days		

* reliability of differences in the groups of comparison (P<0.05)

Taking into account the surgical technique complexity, presence of multiple aggravating factors in concomitant diffuse liver pathology, the surgery duration in this group of patients was reliably longer (on average 282±16 min), and in group B the surgery lasted on average 228±14 min (P<0.05). The segmental resections lasted 186±13 min against 140±11min in the controls (P<0.01).

Specific complications developed in the early post-operative periods in the groups under study in 30.9% of cases (25/81 patients). It should be noted that 19 of these 25 cases were the patients with concomitant diffuse liver pathology. These complications included: postoperative liver failure, intraperitoneal hemorrhages from the liver resection surface, bile secretion from the liver resection surface, ascitis, subdiaphragm abscess, acute coronary circulation disorders, and pleuropneumonia.

Acute liver failure observed in 12 cases (14.8%) appeared to be the most common and critically difficult complication. In 10 of 12 cases, this complication developed in group B and only in 2 cases (7.1%) in group A. The intraperitoneal hemorrhages occurred in 3 cases: 2 patients (3.8%) with concomitant liver pathology and 1 patient (2%) without any concomitant liver pathology. Secretion bile from the liver resection surface complicated the post-operative period in group A with concomitant pathology in 2 cases (3.8%), while in group B it occurred in one case (3.6%). PRLF complicated with postoperative ascitis was observed in 2 cases in group A and in 1 patient from group B (3.8% vs. 3.6, respectively). The subdiaphragm abscess revealed in one patient in group A (1.9%) was treated with percutaneous puncture-drainage. Pleuropneumonia in early post-operative period was diagnosed in 2 patients (2.5%): one case in group A, and one case in group B. The acute disorder of coronary circulation was observed in one case (19%) in the patients with concomitant liver pathology. The overall mortality in the groups under study accounted for 4.9% (4 of 81 cases). In 3 cases death was caused by PRLF (3.7%) and in one case it was due to massive intraperitoneal hemorrhage (1.2%). In group A, three patients died (5.7%): 2 of them had progressing PRLF; one patienthad intraperitoneal hemorrhage. In group B, one patient died of PRLF (3.6%).

CONCLUSION

1. Resection of liver in patients with chronic diffuse liver pathology increased the risk of PRLF development due to reduction of functional reserve of hepatocytes and slower compensatory process of regeneration.

2. The risk of post-resection liver failure in patients with concomitant chronic diffuse liver pathology increased from 7.1% to 18.9%, and extensive resection increased the risk to 28.6% in the structure of which the severe functional insufficiency of hepatocytes with possible prognosis of lethal outcome to 60%.

3. In the patients with focal process in the liver, concomitant chronic diffuse liver pathology provides reliable reduction of the hepatocyte functional status that reflects a decrease in liver extraction fraction by 17.1% (67.5±2.3% against 81.4±1.9%) and an increase in the half-life elimination of the radiopharmaceutical by 26.5% (37.2± 1.7 min vs. 29.4± 1.2 min) (P<0.001) in comparison with the group without parenchymatous processes.

4. According to scintigraphy, the liver resection induced reduction of hepatocyte functional activity reflected by a decrease in the fraction of liver extraction by 16.7% (from 81.4±1.9% to 67.8±3.4%) and increase in half-life elimination of the radiopharmaceutical by 29.8% (from 29.4% 1.2 min to 42.1±3.6 min) (P<0.001). In its turn, in concomitant chronic diffuse liver pathology, these parameters achieved 43.2% (from 67.5±2.3% to 47.4±4.5%) and 73.4% (from 37.2±1.7 min to 64.5±4.2 min) (P<0.001), respectively.

5. In early post-resection period, the functional insufficiency of the residual hepatocyte volume was reliably higher in the group with concomitant chronic diffuse liver pathology, that results in prolongation of the period of compensatory regeneration with normalization of the main biochemical blood parameters, on the average, on day 16.5±0.7 vs.day11.3±0.4 in the group with no concomitant liver diseases.

6. Chronic diffuse process in the liver contributed to an increase in the risk of intra-operative blood loss in segmental ($P<0.01$) and extensive ($P<0.05$) resections with an increase in the period of vascular isolation by Pringle's method from 19.8±1.3 min to 23.1±1.9 min and from 27.9±1.7 min to 34.5±2.1 min, respectively ($P<0.05$), as well as surgery duration from 140±11 to 186±13 min ($P<0.01$) and from 228±14 min to 282± 16 min ($P<0.05$).

7. The risk of development of complications after resection performed to patients with concomitant chronic diffuse process in the liver rises from 21.4% to 35.8% increasing mortality rate from 3.6% to 5.7% and average duration of the hospital stay from 23.7±0.9 to 28.7±1.0 days ($P<0.001$).

DECLARATIONS

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Authors' Contributions
All authors contributed equally to this work.

Competing interests
The authors declare that they have no competing interests.

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