Original article

doi:10.5633/amm.2025.0301

Preoperative and Postoperative Liver Function Analysis After Liver Resection

Marko Gmijović[1], Zoran Damnjanović[2], Aleksandar Kamenov[3], Vladimir Stojiljković[3], Milica Bjelaković[4], Marko Stojanović[4], Tamara Jovanović[5], Novica Bojanić[6], Jelena Živadinović[7], Vladan Cvetanović[7], Dimitrije Djordjević[8]

[1]Department of Endocrine Surgery, University Clinical Center Niš, Faculty of Medicine, University of Niš, Serbia
[2]Department of Vascular Surgery, University Clinical Center Niš, Faculty of Medicine, University of Niš, Serbia
[3]Department of Cardiovascular Surgery, University Clinical Center Niš, Faculty of Medicine, University of Niš, Serbia
[4]Department of Gastroenterology and Hepatology, University Clinical Center Niš, Faculty of Medicine, University of Niš, Serbia
[5]Institute for Public Health Niš, Serbia
[6]Faculty of Medicine, University of Niš, Serbia
[7]Department of Anesthesiology and Resuscitation, University Clinical Center Niš, Faculty of Medicine, University of Niš, Serbia
[8]University Clinical Center of Niš, Clinic of Plastic and reconstructive surgery, Niš, Serbia

Contact: Marko Gmijović

48 dr Zorana Djindjića Blvd., 18000 Niš, Serbia
Email: dr.gmija@gmail.com

Preoperative diagnostics and preparation of patients undergoing liver resection procedures are crucial for the outcome of surgical treatment.

The study included 30 patients who underwent hepatectomy due to primary or secondary tumor changes. Preoperative and postoperative liver parenchyma status was monitored based on the determination of biochemical liver function parameters (alkaline phosphatase, AST, ALT, γGT, bilirubin - T.Bil and D.Bil, LDH, albumin) and metabolic syndrome parameters (glucose, urea, creatinine, blood pressure).

The values of AST and ALT differed statistically significantly between pre- and postoperative

measurements (p<0.001 for both genders). The values of D-Bil were statistically significantly higher after surgery compared to the preoperative period (p=0.017). LDH values were statistically significantly higher after surgery compared to the preoperative period (p<0.001). Albumin values were statistically significantly lower after surgery compared to the preoperative period (p<0.001). Analyses performed on the fifth postoperative day indicate that liver function improves compared to preoperative measurements.

The study provided insights into the characteristics of liver tissue damage after hepatectomy based on liver function monitoring parameters. Surgical stress, anesthetics, bleeding, ischemia-reperfusion injury, and subtle mechanisms of oxidative stress and apoptosis lead to transient liver damage, while regeneration starting on the fifth postoperative day shows a positive trend.

Keywords: liver surgery, liver resections, liver function.

Preoperativna i postoperativna analiza funkcije jetre nakon resekcije jetre

Marko Gmijović[1], Zoran Damnjanović[2], Aleksandar Kamenov[3], Vladimir Stojiljković[3], Milica Bjelaković[4], Marko Stojanović[4], Tamara Jovanović[5], Bojanić Novica[6], Živadinović Jelena[7], Vladan Cvetanović[7], Dimitrije Đorđević[8]

[1]Klinika za endokrinu hirurgiju, Univerzitetski klinički centar Niš, Medicinski fakultet Univerziteta u Nišu, Srbija

[2]Klinika za vaskularnu hirurgiju, Univerzitetski klinički centar Niš, Medicinski fakultet Univerziteta u Nišu, Srbija

[3]Klinika za kardio hirurgiju, Univerzitetski klinički centar Niš, Medicinski fakultet Univerziteta u Nišu, Srbija

[4]Klinika za gastroenterologiju i hepatologiju, Univerzitetski klinički centar Niš, Medicinski fakultet Univerziteta u Nišu, Srbija

[5]Institut za javno zdravlje Niš, Srbija

[6]Medicinski Fakultet Univerziteta u Nišu, Srbija

[7]Klinika za anesteziologiju i reanimatologiju, Univerzitetski klinički centar Niš, Medicinski fakultet Univerziteta u Nišu, Srbija

Kontakt: Marko Gmijović

Bul. dr Zorana Đinđića 48, 18000 Niš, Srbija

E-mail: dr.gmija@gmail.com

Hirurzi koji se bave hirurgijom jetre ističu važnost temeljne preoperativne procene funkcionalnosti jetre i njenih rezervi, kako bi se što više smanjio hirurški rizik, naročito kod bolesnika sa cirozom jetre, žuticom ili onih koji su na dugotrajnoj hemoterapiji.

U istraživanju je učestvovalo 30 pacijenata kojima je urađena hepatektomija zbog tumorskih procesa, uključujući metastaze kolorektalnog karcinoma. Parametri su analizirani u dve faze: pre operacije i

postoperativno. Preoperativno i postoperativno praćeno je stanje parenhima jetre na osnovu određivanja biohemijskih parametara funkcije jetre (aktivnost enzima alkalne fosfataze, AST, ALT, γGT, bilirubin - T.Bil i D.Bil, LDH, albumin) i parametara metaboličkog sindroma (glukoza, urea, kreatinin, krvni pritisak).

Istraživanje je omogućilo uvide u karakteristike oštećenja jetrenog tkiva nakon resekcije jetre na osnovu parametra praćenja jetrine funkcije. Na osnovu savremenih metoda obrade podataka i primene odgovarajuće literature, ovi rezultati mogu pomoći u daljem unapređenju terapijskih postupaka i strategija za postoperativnu negu, pružajući korisne smernice za poboljšanje ishoda lečenja.

Ključne reči: hirurgija jetre, resekcije jetre,funkcija jetre

Introduction:

Liver surgeries represent one of the most challenging aspects of abdominal surgery due to the complex anatomy and vital functions of the liver (1-3). Preoperative diagnostics and preparation of patients undergoing liver resection procedures are crucial for the outcome of surgical treatment. Medical history, clinical examination, and imaging diagnostic procedures form the basis for decision-making regarding indications for liver surgery (1,2). Moreover, one of the most important steps in liver surgery is a precise preoperative assessment of current functional capabilities and reserves. In this way, patients with a high surgical risk can be identified, particularly those with liver cirrhosis, jaundice, and those undergoing prolonged chemotherapy (3). Liver resections represent a significant surgical stress for the body, leading to complex physiological and biochemical changes that can compromise liver function. Pathophysiological mechanisms contributing to postoperative liver dysfunction include surgical stress, hemodynamic changes induced by anesthesia, intraoperative blood loss, ischemia-reperfusion syndrome, oxidative stress, and hepatocyte apoptosis (2,4). A vital characteristic of the liver is its ability to regenerate, meaning it can recover from injuries, toxic and ischemic damage, and, most importantly for surgeons, after resection procedures (4). Preoperative preparation and postoperative monitoring of patients after liver resection procedures, in addition to the surgical and anesthesiological parameters monitored during any surgical intervention, also include specific quantitative assessments of the volume of liver tissue remaining after resection, and qualitative evaluation of the functional quality of this residual parenchyma, or its ability to take over further postoperative liver function (5,6). Our research aims to identify liver tissue damage based on laboratory parameters (hepatocyte damage markers, liver excretory function markers - biliary obstruction, liver synthetic function markers, and inflammatory syndrome markers). After reviewing the literature, we formulated the following scientific hypothesis:

To determine the degree of liver tissue damage during the surgical procedure based on functional biochemical tests pre- and postoperatively.

From this hypothesis, the objectives of the study were set:
To determine the preoperative and postoperative functional status of the liver parenchyma based on the measurement of biochemical liver function parameters (alkaline phosphatase activity, AST, ALT, γGT, bilirubin - T.Bil and D.Bil, LDH, albumin) and metabolic syndrome parameters (glucose, urea, creatinine).

Materials and Methods:

A prospective analysis was conducted on 30 patients who underwent liver resection due to a primary neoplastic process or metastases from colorectal cancer. The patients were hospitalized at the Department of Digestive Surgery, University Clinical Center Niš. The following were analyzed for all patients:

Preoperative parameters:

Standard preoperative tests evaluating liver function in the patients included in the study (alkaline phosphatase, AST, ALT, γGT, bilirubin, LDH, albumin), as well as the presence of metabolic syndrome (glucose ≥6.1 mmol/L; urea ≥6.1; creatinine ≥6.1; blood pressure ≥130/85 mm Hg).

Postoperative parameters:

Postoperative liver function and the presence of metabolic stress were monitored by analyzing blood samples from the patients at the Central Laboratory of the University Clinical Center Niš on the first, third, and fifth postoperative days.

Statistical Data Analysis:

Data are presented as means and standard deviations. Comparison of values between the four measurements (preoperative, days I, III, V) was performed using repeated measures analysis of variance (ANOVA). The Bonferroni test was used as a post hoc analysis. Statistical processing was performed using the SPSS 20.0 software package. The null hypothesis was tested with a significance level of $p < 0.05$.

Results:

Demographic and Clinical Characteristics of the Study Population

The study included 30 patients (16 male and 14 female) (Figure 1). The average age of the study population was 60.03 years (Min 37, Max 77 years).
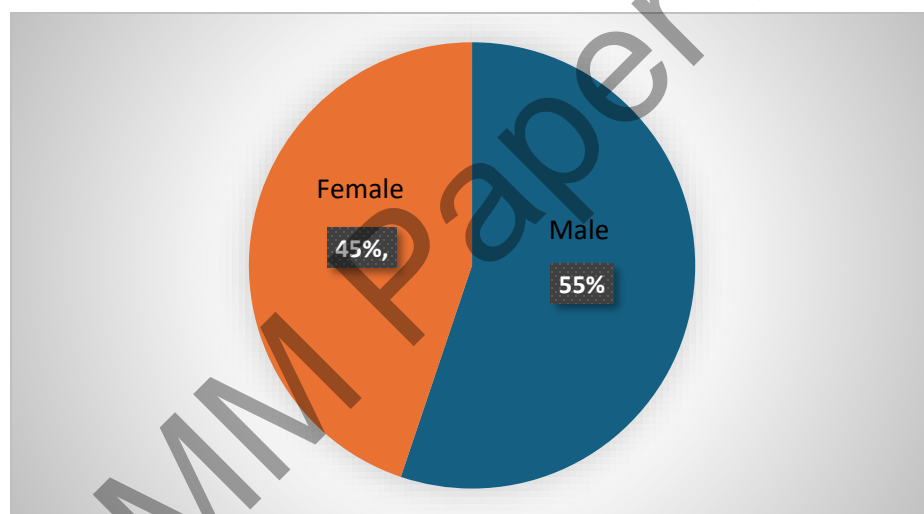

Figure 1. Distribution of the study population by gender.

By type of liver resection, a total of 30 surgeries were performed in this study. Of these, four were hepatectomies, four bisegmentectomies, 11 metastasectomies, and 11 segmentectomies. According to the classification of resections into major and minor types, hepatectomies and bisegmentectomies are categorized as major resections, while segmentectomies and metastasectomies belong to minor resections.

Accordingly, in the analyzed group of patients, a total of 8 major resections (26.7%) and 22 minor resections (73.3%) were performed, with a predominance of less invasive surgical procedures. This

distribution indicates a tendency to preserve functional liver parenchyma while performing oncologically adequate surgeries.
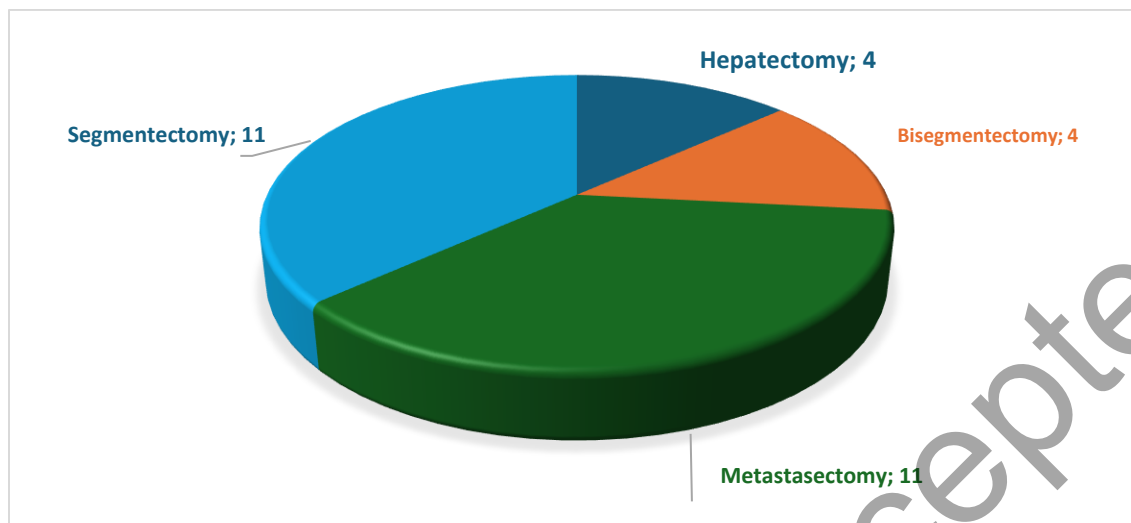

Figure 2. Distribution of surgical procedures by type of resection.

The duration of the surgical intervention ranged from 87 minutes to 180 minutes. Seven patients underwent surgery due to a primary liver process, while the remaining 21 patients were operated on due to colorectal cancer metastases. All patients underwent intermittent clamping of the hepatoduodenal ligament (Pringle maneuver) for 15-25 minutes for resection and bleeding control. During the surgical procedure, no blood loss greater than 300 ml was recorded. Five patients received a postoperative transfusion in the form of whole blood (2x350 ml) and fresh frozen plasma (2x220 ml).

The values of AST and ALT differed statistically significantly between preoperative and postoperative measurements (p<0.001 for both genders). D-Bil values were statistically significantly higher after surgery compared to the preoperative period (p=0.017). LDH values were statistically significantly higher after surgery compared to the preoperative period (p<0.001). Albumin values were statistically significantly lower after surgery compared to the preoperative period (p<0.001) (Table 1).
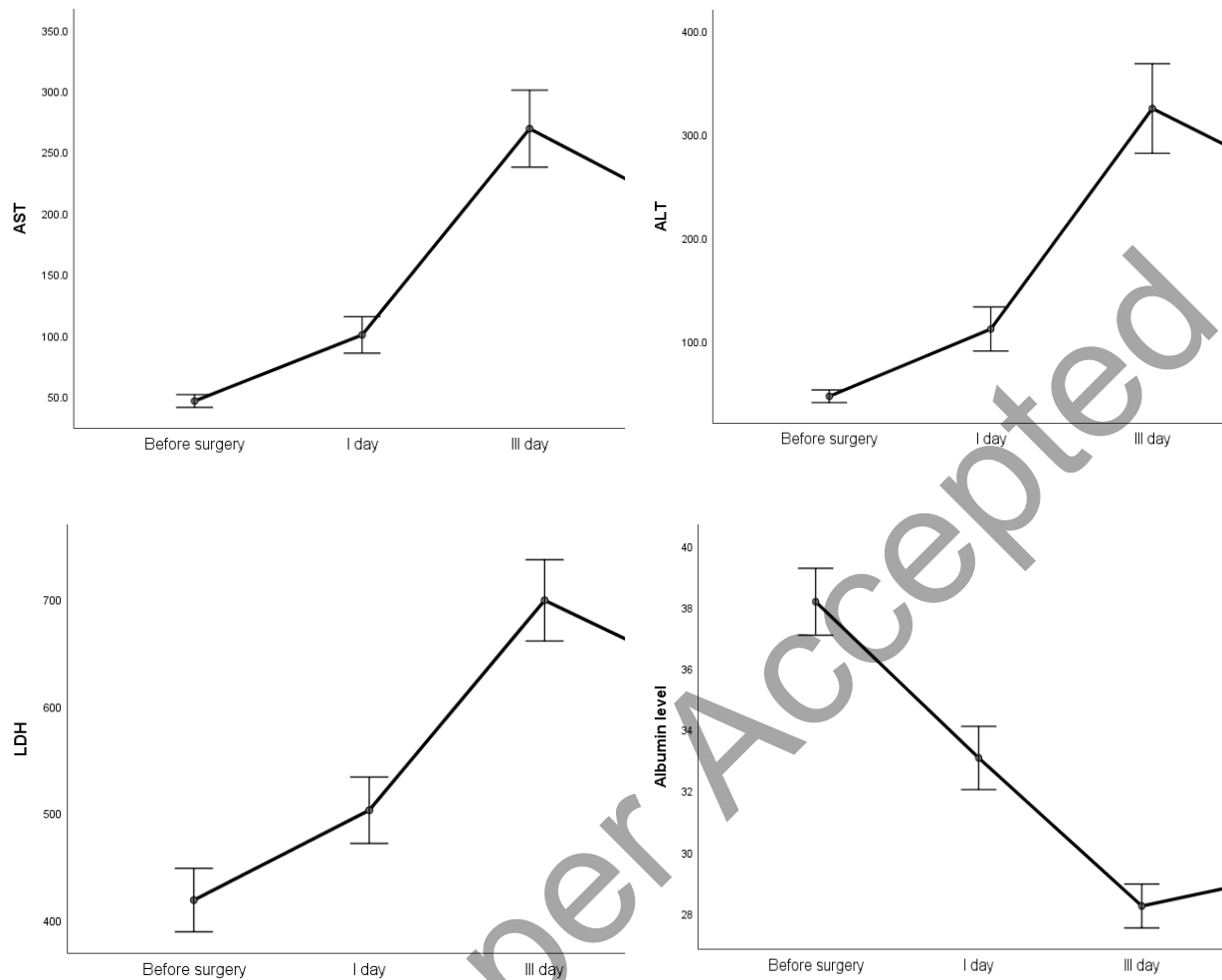
Figure 3. AST, ALT, LDH and albumin levels in follow up period

ANOVA for repeated measurements showed statistically significant changes in the values of the following laboratory parameters during the follow-up period: Alkaline Phosphatase (p=0.001), AST (p=<0.001), ALT (p=<0.001), GGT (p=0.023), T-BIL (p=0.033), D-BIL (p=0.130), LDH (p=<0.001), Albumin (p=<0.001), Glucose (p=0.016), Urea (p=0.001), Creatinine (p=0.004), STA (p=0.324), DTA (p=0.388). The values of Alkaline Phosphatase, AST, ALT, LDH, and Albumin significantly differ between preoperative measurements and measurements on the 1st, 3rd, and 5th days: (p=<0.001, p=0.001, and p=1.000), AST (p=0.005, and p=<0.001), ALT (p=0.021, p=<0.001, and p=<0.001), LDH (p=<0.001, p=<0.001, and p=<0.001), Albumin (p=<0.001, p=<0.001, and p=<0.001). The values of the following parameters change between the preoperative period and the first day: GGT (p=<0.001), T-BIL (p=0.011), Glucose (p=0.043), Urea (p=<0.001), Creatinine (p=0.050).

Table 1. Laboratory parameters during the follow-up period in the studied population.

Tabela 1. Laboratorijski parametri u periodu pracenja u ispitivanoj populaciji.

Parameter	Preoperative	Day I	Day III	Day V	p[1]	p Pre vs I	p Pre vs III	p Pre vs V
Alkaline Phosphatase	119.9±66.15	170.23±89.64	173.4±57.44	123.87±57.69	0.001	<0.001	0.001	1.000
AST	45.96±28.75	100.1±81.87	269.07±172.72	197.23±164.32	<0.001	0.005	<0.001	<0.001
ALT	47.08±33.32	111.93±116.29	324.73±236.74	246.67±177.64	<0.001	0.021	<0.001	<0.001
GGT	44.53±31.835	85.53±56.201	73.6±80.264	70.13±71.345	0.023	<0.001	0.174	0.196
T-BIL	13.53±9.79	18.59±12.43	17.41±8.15	14.82±7.28	0.033	0.011	0.131	1.000
D-BIL	3.93±5.02	6.27±5.63	5.68±4.33	4.68±3.44	0.130			
LDH	418.47±163	502.57±170	699.03±208.51	620.43±204.31	<0.001	<0.001	<0.001	<0.001
Albumin	38.17±5.97	33.07±5.5	28.23±3.92	29.37±3.93	<0.001	<0.001	<0.001	<0.001
Glucose	6.76±3.18	7.65±2.7	6.62±2.87	6.52±2.99	0.016	0.043	1.000	1.000
Urea	6.2±2.21	8.18±2.2	6.41±3.31	6.21±3.07	0.001	<0.001	1.000	1.000
Creatinine	90.02±13.77	105.72±23.37	85.31±18.49	82.97±17.36	0.004	0.050	1.000	0.302
STA	131.07±10.76	174.17±241.17	130.8±12.12	130.67±12.21	0.324			
DTA	80.97±5.288	80.63±5.654	79.53±5.244	79.87±4.925	0.388			

[1] ANOVA for repeated measures, post hoc p-values for pre vs Day 1, vs Day 3, vs Day 5

Discussion

Liver surgery has a relatively short history compared to other areas of surgery, which developed and were widely accepted around the world many decades earlier. Modern liver surgery dates back to the early 1950s, when, thanks to the joint efforts of surgeons and anatomists, the intrahepatic segmental anatomy of the liver was discovered. The full development of this surgical field became possible only in

the last 40 years, thanks to the introduction of modern diagnostic methods, especially ultrasound and computerized tomography (2,8).

Along with the development of diagnostics, surgical techniques, anesthesia, preoperative preparation, and postoperative intensive care and nursing of these patients also evolved. Today, liver surgery is a safe area of surgery, with a relatively low overall mortality rate (below 5%). However, it is still associated with a relatively high risk of complications, which can reach up to 20%. The most dangerous complications are related to the development of postoperative liver failure (up to 5%) (2,3). Many patients with hepatobiliary malignancies require large resectional procedures that leave a smaller portion of healthy tissue. Therefore, adequate preoperative qualitative analysis of liver function, along with quantitative volumetric tests, is crucial for the success of resection procedures.

Precise assessment of liver function and capacity involves the analysis of the following groups of parameters:

1. **General health of the patient**: The first and fundamental assessment is the general health status of the patient. This includes factors such as age, presence of other chronic diseases or comorbidities, and the ability of the patient to tolerate the surgery, which can be classified according to the ASA (American Society of Anesthesiologists physical status classification system) and Apache II (Acute Physiology and Chronic Health Evaluation II) scores (3,9).

2. **Type of planned surgical procedure**: The size and type of liver resection also affect patient preparation. Larger resections may require additional preparation.

3. **Liver volumetry (CT/MRI)**: Volumetry helps in the quantitative assessment of liver parts that will be removed and those that will remain after the surgery. The necessary minimal remaining liver volume after resection (Future Liver Remnant, FLR) should not be less than 30% for a healthy liver, and 40%–50% for a liver affected by cirrhosis, fibrosis, severe steatosis, or damage caused by cytotoxic therapy (6).

4. **Assessment of liver functional capacity**:To assess liver function, biochemical parameters are used (alkaline phosphatase enzyme activity, AST, ALT, γGT, bilirubin - T.Bil and D.Bil, LDH, albumin) and parameters of metabolic syndrome (glucose, urea, creatinine), which, in combination with clinical findings, can be categorized into more precise scores, such as the Child-Pugh, MELD (Model for End-Stage Liver Disease), ALBI score, APRI score, FIB-4 score, and the LIMON score (a non-invasive monitoring system measuring the elimination of indocyanine green ICG) (10).

The Child-Pugh classification is the easiest and most common method for quantitatively determining the degree of liver insufficiency based on basic clinical and biochemical parameters. By combining indicators of liver excretory and synthetic function and the presence of portal hypertension, this scoring system provides an adequate picture of the overall functional state of the liver. It includes 5 elements (serum levels of bilirubin and albumin, presence of ascites and encephalopathy, and prothrombin index), based on which patients are categorized into one of three stages: A, B, and C. Patients in stage A have less than 6 points, in stage B from 6 to 9 points, and in stage C more than 9 points (6,7).

Table 2. Child-Pugh Classification /Modification by J. M. Henderson (1994)/

Points	Bilirubin (µmol/L)	Albumin (g/L)	Prothrombin Index - Quick	Encephalopathy	Ascites
1	< 20	>35	>70%	0	0
2	20-30	28-35	40-70%	I-II degree	Small
3	> 30	<28	<40%	III-IV degree	Large

Patients with Child A liver insufficiency are considered suitable candidates for resection procedures (postoperative mortality risk of only 1-2%), while patients with Child B are only suitable for limited resections (postoperative mortality risk of 10%). In patients with Child C stage, resection is contraindicated (postoperative mortality risk over 50%) (7).

One of the functional tests is the retention of ICG (Indocyanine Green). Based on clinical experience during the 1980s and early 1990s, an ICG-R value below 10% was considered a safety limit for performing larger hepatic resections in cirrhotic patients. However, with advancements in surgical techniques and perioperative care, this upper safety limit was first extended to 14%, and later to 20% for major hepatectomies. The MELD score (Model for End-Stage Liver Disease), based on values of bilirubin, INR, and creatinine, is commonly used to predict three-month mortality in patients with bleeding esophageal varices. Its values range from 6 (for healthy individuals) to 40 (for terminal liver insufficiency). Today, this score is predominantly used to determine priority for liver transplantation, which is carried out within the MELD score range of 10-20 (7).

The surgery itself causes varying degrees of liver damage. The pathophysiological mechanisms contributing to postoperative liver dysfunction include surgical stress, hemodynamic changes induced by anesthesia, intraoperative blood loss, ischemia-reperfusion syndrome, oxidative stress, and apoptosis of hepatocytes (8). Surgical stress triggers activation of the hypothalamic-pituitary-adrenal axis, resulting in increased secretion of cortisol and catecholamines. This response contributes to a systemic inflammatory response with enhanced release of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP). These changes can further worsen hepatocellular dysfunction and contribute to postoperative complications. The pharmacodynamic effects of anesthetics significantly affect hepatic perfusion. Volatile anesthetics, such as isoflurane and sevoflurane, can reduce blood flow through the liver, while intravenous anesthetics, such as propofol and remifentanil, can lead to systemic hypotension, further compromising hepatocyte oxygenation (8-11). Intraoperative bleeding can result in hypovolemia and compromised liver perfusion, increasing the risk of ischemia-reperfusion injury. Clamping of the vascular inflow vessels – the Pringle maneuver – can further worsen liver function. Additionally, massive blood transfusions can lead to the development of disseminated intravascular coagulation (DIC) and microthrombosis in intrahepatic sinusoids, further impairing liver function (12-14). The ischemia-reperfusion syndrome arises from temporary interruption of blood flow through the liver during vascular manipulation. The ischemic phase leads to a reduction in aerobic metabolism and the accumulation of lactate in hepatocytes, while reperfusion induces a sudden increase in reactive oxygen species (ROS), which cause oxidative damage to cell membranes, proteins, and mitochondrial DNA (15,16). Oxidative stress caused by increased ROS production, including superoxide and hydroxyl radicals, triggers lipid peroxidation and hepatocyte damage. The depletion of antioxidant mechanisms, including superoxide dismutase (SOD), catalase, and glutathione, further contributes to cytotoxicity and liver dysfunction. Apoptotic processes in hepatocytes are initiated by the

activation of the mitochondrial (intrinsic) and receptor-mediated (extrinsic) pathways of cell death, thereby increasing the risk of postoperative insufficiency (2,9,10).

Postoperative recovery of liver function begins on the third postoperative day and typically normalizes by the tenth day following surgery. Balzan and colleagues demonstrated the significance of the "50-50 criteria," which are based on a combination of elevated serum bilirubin levels (greater than 50 μmol/l or 2.9 mg/dl) and a reduced prothrombin index (less than 50 percent) on the fifth postoperative day (12,17). This study included 30 patients, 16 men and 14 women, with an average age of 60 years. Data analysis did not reveal a significant correlation between postoperative liver function parameters and demographic characteristics such as gender and age.

The biochemical parameter analysis in our study showed significant changes in liver function following resection. Specifically, AST and ALT values increased significantly after surgery compared to the preoperative period (p<0.001), indicating hepatocyte damage due to the surgical intervention. Additionally, there was a significant increase in direct bilirubin (D-Bil) (p=0.017) and lactate dehydrogenase (LDH) (p<0.001), which may suggest liver dysfunction and potential hemolysis. In contrast, albumin levels were significantly lower postoperatively (p<0.001), which may reflect decreased synthetic liver function or increased protein catabolism during the postoperative period. The increase in direct bilirubin (p=0.017) may indicate temporary bile duct obstruction or hepatocellular dysfunction.

Increased plasma levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) following liver resection represent significant clinical indicators used to assess liver function and postoperative recovery. These changes in enzyme levels may result from various factors, including the type of resection, the amount of blood loss, the duration of surgery, as well as individual patient characteristics (18). Different types of liver resections have different effects on AST and ALT levels. Research shows that larger resections, such as hemihepatectomy or total hepatectomy, lead to a more significant increase in these enzymes due to greater trauma and hepatocyte damage. Authors noted that transaminase levels peaked within the first 24 hours after surgery and gradually returned to normal over the next five days. Elevated AST and ALT levels were associated with longer surgery duration and larger resections, suggesting that greater surgical trauma leads to more extensive liver tissue damage (19).

These findings are consistent with previous research. Studies show that liver resection often leads to a transient increase in aminotransferases and bilirubin, while decreased albumin levels may be a result of surgical stress and reduced liver reserve function. The increase in LDH further confirms postoperative stress and possible liver cell damage. Monitoring these parameters is crucial for the early detection of complications and optimal management of postoperative recovery in patients (12,18)

Conclusion

Standard liver function tests remain essential for assessing its functional state and regenerative capacity. In our study, significant changes were identified in biochemical parameters before and after surgery. Surgical stress, anesthetics, bleeding, and ischemia-reperfusion injuries through subtle mechanisms of oxidative stress and apoptosis lead to transient liver damage, while regeneration, starting on the fifth postoperative day, shows a positive trend. The combination of standard biochemical tests with dynamic liver function tests and volumetric studies can be highly useful in distinguishing patients at high risk of complications in liver surgery. In any case, this area of research requires further clinical investigations.

References:

1. Elias D, Lasser P, Rougier P, Ducreux M, Bognel C, Roche A: Frequency, technical aspects, results, and indications of major hepatectomy after prolonged intra-arterial hepatic chemotherapy for initially unresectable hepatic tumors. J Am Coll Surg 1995;180:213–219.

2. Stojanovic M, Jeremic M, Radojkovic M, Jeremic-Savic L. Liver surgery. In: Jeremic M (Ed). Textbook of abdominal surgery (in Serbian). Niš: Medical faculty University of Niš;2009:1988-996.

3. Stojanović M, Jeremić M, Bogićević A, Radojković M, Zlatić A, Jeremić Lj, Stanojević G, Nagorni A, Brzački V, Raičević-Sibinović S, Benedeto-Stojanov D, Denčić S, Stamenković S. The influence of new surgical concept on results of liver resection. Acta Fac. Med. Naiss. 2004; 21 (4): 179-84.

4. Joliat GR, Kobayashi K, Hasegawa K, Thomson JE, Padbury R, Scott M, et al. Guidelines for Perioperative Care for Liver Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations 2022. World J Surg. 2023 Jan 30;47(1):11–34.

5. Guglielmi A, Tripepi M, Salmaso L, Fedeli U, Ruzzenente A, Saia M. Trends in hospital volume and operative mortality in hepato-biliary surgery in Veneto region, Italy. Updates Surg. 2023 Oct;75(7):1949–59.

6. Schindl MJ, Redhead DN, Fearon KC, Garden OJ, Wigmore SJ. The value of residual liver volume as a predictor of hepatic dysfunction and infection after major liver resection. Journal of Gastrointestinal Surgery. 2005 Feb;9(2):137-44.

7. Gex L, Bernard C, Spahr L. Child-Pugh, MELD and Maddrey scores. Rev Med Suisse. 2010 Sep 29;6(264):1803–4, 1806–8.

8. *Rahbari NN, Garden OJ, Padbury R, et al. Posthepatectomy liver failure: a definition and grading by the International Study Group of Liver Surgery (ISGLS). Surgery 2011;149:713-24. 10.1016/j.surg.2010.10.001*

9. Van den Broek MA, Olde Damink SW, Dejong CH, Lang H, Malagó M, Jalan R, et al. Liver failure after partial hepatic resection: definition, pathophysiology, risk factors and treatment. Liver Int. 2008;28:767–80.

10. *Reissfelder C, Rahbari NN, Koch M, et al. Postoperative course and clinical significance of biochemical blood tests following hepatic resection. Br J Surg 2011;98:836-44.*

11. *Taub R. Liver regeneration: from myth to mechanism. Nat Rev Mol Cell Biol 2004;5:836-47.*

12. *Balzan S, Belghiti J, Farges O, et al. The "50-50 criteria" on postoperative day 5: an accurate predictor of liver failure and death after hepatectomy. Ann Surg 2005;242:824-8, discussion 8-9.*

13. Choukèr A, Schachtner T, Schauer R, Dugas M, Löhe F, Martignoni A, Pollwein B, Niklas M, Rau HG, Jauch KW, Peter K, Thiel M. Effects of Pringle manoeuvre and ischaemic preconditioning on haemodynamic stability in patients undergoing elective hepatectomy: a randomized trial. Br J Anaesth. 2004 Aug; 93 (2):204-11.

14. Choukér, A., Martignoni, A., Schauer, R.J. *et al.* *α*-Gluthathione S-Transferase as an Early Marker of Hepatic Ischemia/Reperfusion Injury after Liver Resection. *World J. Surg.* 2005;(29): 528–534

15. Chiarla C et al . Plasma bilirubin correlations in non-obstructive cholestasis after partial hepatectomy Clin Chem Lab Med, 2008 (46): 1598-1601.

16. I. Giovannini, C. Chiarla, F. Giuliante, M. Vellone, F. Ardito, G. Sarno, et al. Analysis of the components of hypertransaminasaemia after liver resection. Clin Chem Lab Med, 2007;(45): 357-360.

17. K. Tanaka, H. Shimada, K. Matsuo, M. Ueda, I. Endo, S. Togo.Remnant liver regeneration after two-stage hepatectomy for multiple   bilobar colorectal metastases   Eur J Surg Oncol, 2007; (33): 329-335.

18. C. Reissfelder, N.N. Rahbari, M. Koch, B. Kofler, N. Sutedja, H. Elbers, et al. Postoperative course and clinical significance of biochemical blood tests following hepatic resection Br J Surg. 2011; (98): 836-844.

19. Olthof PB, Huiskens J, Schulte NR, Wicherts DA, Besselink MG, Busch OR, Heger M, van Gulik TM. Postoperative peak transaminases correlate with morbidity and mortality after liver resection. HPB (Oxford). 2016 Nov;18(11):915-921. doi: 10.1016/j.hpb.2016.07.016. Epub 2016 Sep 2. PMID: 27600437; PMCID: PMC5094483.