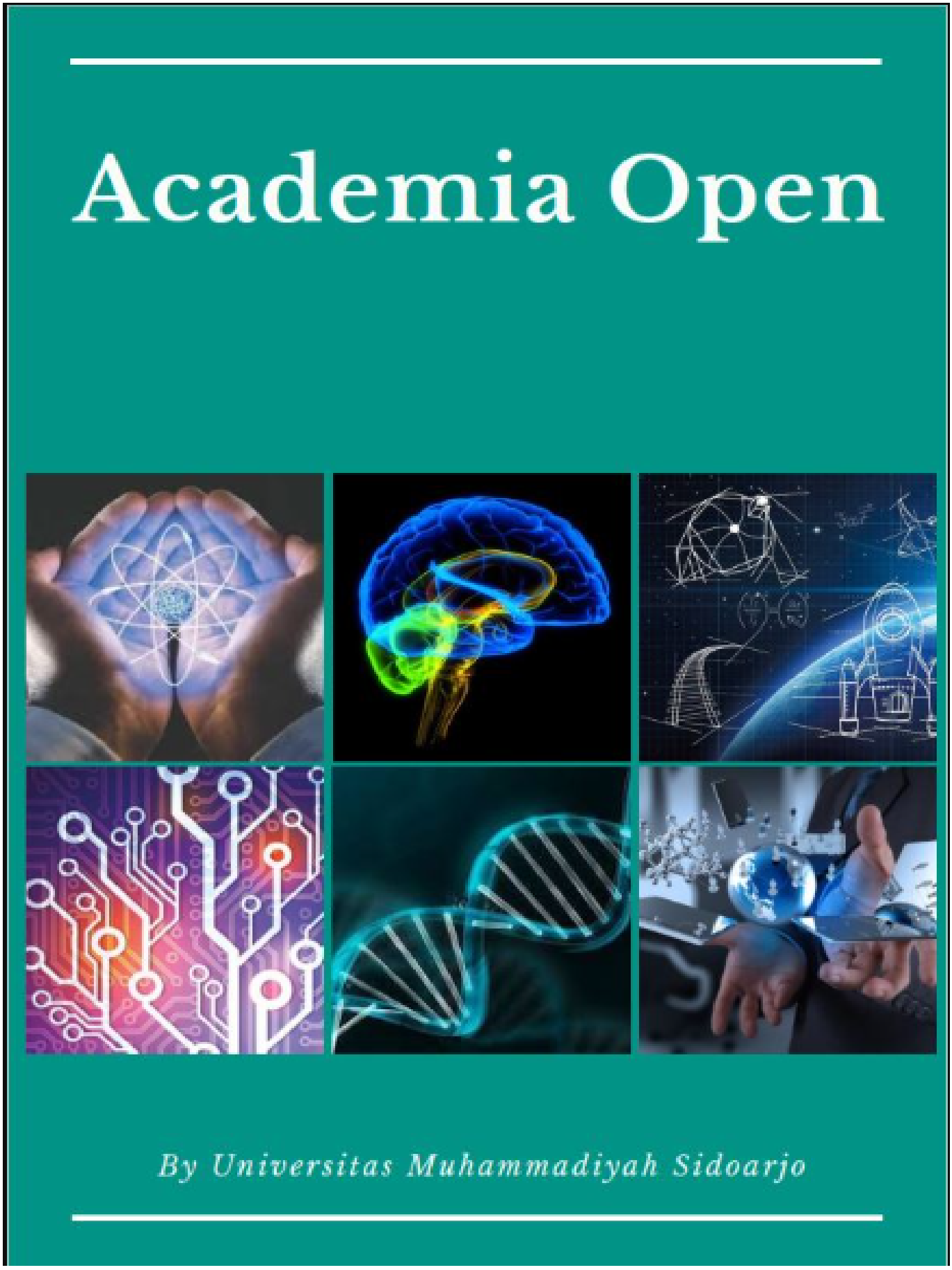
Academia Open

Vol. 11 No. 1 (2026): June
DOI: 10.21070/acopen.11.2026.13122



ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Academia Open

Vol. 11 No. 1 (2026): June
DOI: 10.21070/acopen.11.2026.13122

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ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

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DOI: 10.21070/acopen.11.2026.13122

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DOI: 10.21070/acopen.11.2026.13122

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Academia Open

Vol. 11 No. 1 (2026): June
DOI: 10.21070/acopen.11.2026.13122

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ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

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Quantitative Characterization of Liver Safety in Surgical Diseases and Postoperative Course: Karakterisasi Kuantitatif Keamanan Hati pada Penyakit Bedah dan Perjalanan Pascaoperasi

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Abstract

General Background: Accurate assessment of liver functional reserve remains critical in surgical practice, as hepatic dysfunction substantially elevates postoperative morbidity and mortality risks. **Specific Background:** Conventional biochemical markers (ALT, AST, bilirubin) predominantly reflect cytolysis and cholestasis but fail to evaluate hepatocellular energetic status or regenerative capacity. **Knowledge Gap:** Current diagnostic approaches lack objective quantitative indicators that directly measure mitochondrial function and viable hepatocyte populations in surgical patients. **Aims:** This study evaluated a novel prognostic coefficient based on the ratio of cytochrome C to TMPD oxidase mitochondrial activities for quantifying liver parenchymal preservation in patients with hepatobiliary surgical diseases. **Results:** Analysis of 24 patients demonstrated strong inverse correlation between coefficient values and viable hepatocyte percentages. Coefficients of 2.5-3.5 units indicated favorable prognosis, 5-7 units signaled elevated complication risk, while values ≥8 units predicted unfavorable outcomes, irrespective of standard biochemical parameters. **Novelty:** Unlike traditional markers, this coefficient directly reflects mitochondrial respiratory chain integrity and hepatocellular viability through objective biochemical measurements. **Implications:** The proposed coefficient serves as an integrated quantitative marker of hepatic functional reserve, enabling improved surgical risk stratification and outcome prediction in hepatobiliary surgery.

Highlight :

- The cytochrome C to TMPD oxidase ratio correlates better with hepatocyte viability than standard biochemical markers in both experimental and clinical contexts.
- Coefficient values predict postoperative outcomes: 2.5-3.5 units indicate favorable prognosis, 5-7 units suggest complications, and ≥8 units correlate with mortality.
- Mitochondrial dysfunction demonstrates universal quantifiable patterns across different etiologies, showing consistent relationships between the coefficient and hepatocyte viability.

Keywords :Liver Functional Reserve, Mitochondrial Dysfunction, Cytochrome C Oxidase, Hepatocyte

Academia Open

Vol. 11 No. 1 (2026): June
DOI: 10.21070/acopen.11.2026.13122

Viability, Postoperative Prognosis

Published date: 2025-12-16

ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

Academia Open

Vol. 11 No. 1 (2026): June
DOI: 10.21070/acopen.11.2026.13122

STUDY OF THE POSSIBILITY OF A QUANTITATIVE CHARACTERIZATION OF THE SAFETY OF THE LIVER IN SURGICAL DISEASES OF THE ORGAN AND THE COURSE OF THE POSTOPERATIVE PERIOD .

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Abstract. This experimental and clinical study is aimed at the quantitative assessment of liver parenchyma preservation in surgical diseases of the liver and hepatobiliary system. A comparative analysis of conventional biochemical and morphological methods with a proposed coefficient based on the ratio of cytochrome C and TMPD oxidase mitochondrial activities was performed. A strong correlation between the coefficient and hepatocyte viability was demonstrated, reflecting hepatic functional reserve. The method showed high prognostic value for predicting postoperative outcomes. The obtained results suggest that the proposed coefficient may serve as an objective marker of liver functional capacity in surgical practice.

Keywords: liver, hepatic functional reserve, mitochondria, cytochrome C, TMPD oxidase, postoperative outcomes.

Relevance. Assessment of liver functional status remains one of the most complex and pressing tasks in modern surgery. The liver performs key metabolic, detoxification, and synthetic functions, and a reduction in its functional reserve significantly increases the risk of postoperative complications and mortality [2,6,8]. This issue is particularly relevant in patients with hepatobiliary diseases accompanied by chronic inflammation, cholestasis, ischemia, and fibrotic changes. Evaluation of liver function is essential for diagnosing diseases, assessing the severity of liver damage, determining prognosis, understanding the compensatory capacity of liver functions, and monitoring treatment efficacy [1,3,5].

Despite the widespread use of standard biochemical indicators of liver function (ALT, AST, bilirubin, sedimentation tests), their diagnostic and prognostic value remains limited. These indicators typically reflect the degree of cytolysis or bile flow disturbances but do not allow an objective assessment of the hepatocytes' energetic status or their regenerative potential [4,7,15]. In clinical practice, this limitation complicates the prediction of postoperative outcomes, especially in patients with borderline liver functional reserve. Assessment of liver functional reserve thus represents a challenging clinical task [5].

In recent years, increasing attention has been paid to mitochondrial dysfunction as a central element in the pathogenesis of liver failure. According to Sun et al. (2022) [14], mitochondrial damage leads to ATP deficiency, increased oxidative stress, and activation of hepatocyte apoptosis, which clinically manifests as progressive liver failure. The findings of the present study regarding the increase in the coefficient associated with a decrease in the percentage of viable hepatocytes fully align with these pathogenetic mechanisms. In this context, the search for quantitative indicators reflecting the state of the liver mitochondrial apparatus is a promising direction in surgical hepatology.

Materials and Methods. From the 24 patients we examined, 8 were in the surgical department with diagnoses of cholelithiasis, cirrhosis, and mechanical jaundice. The liver study results, obtained during surgery, showed that depending on the duration of the disease, the length of obstruction of the common bile duct, stenosis of the Vater's papilla, and comorbid conditions, the cytochrome C TMFD oxidase activity ratio ranged from 5 to 7 units. In patients with peptic ulcer disease of the duodenum and uncomplicated cholecystitis, the ratio ranged from 2.5 to 3.4 units. These patients underwent surgery, and the postoperative course was smooth.

The liver of the patients was examined in a cold room after intraoperative biopsy. The liver was quickly washed, and a homogenate was prepared in a medium consisting of 0.25 sucrose, $2x10^{-4}$ M EDTA (ethylene diamine tetraacetic acid), and 0.01 M tris-HCl buffer with pH 7.4, in a tissue-to-medium ratio of 1:2. Polarographic analysis was conducted using a standard Clark-type platinum electrode on an LP-7 polarograph [10].

In the polarographic cuvette (volume 1.1 ml), a homogenate was sequentially added, calculated at 1–2 mg of protein, sodium ascorbate at a final concentration of 2 mM, TMFD-[11] (tetramethylene para-phenylene diamine) at 1 µM, and cytochrome C-[12] at 1 µM. The rate of respiration was expressed in nmol O_2/min/mg of protein. The prognostic coefficient (PC) was calculated using the formula: PC = Cytochrome C – Ascorbate Na / TMFD – Ascorbate Na.

The xenogeneic hepatocyte suspension was obtained using the combined Berry-Friend method, modified by A.I. Archakov [13]. The degree of morphological preservation of the obtained hepatocytes was assessed by light and phase-contrast microscopy, with prior staining using the vital dye – 0.2% trypan blue. The digital data were processed using the method of variation statistics.

Results and Discussion. Interesting data were obtained from our clinical material. In patients with various surgical diseases, as well as liver and biliary tract disorders, liver biopsies were performed. The biopsy samples were analyzed using the same methods as in the experiments conducted on laboratory animals. Table 1 presents the values of the prognostic coefficient and the percentage of viable hepatocytes.

Table 1 .

Values of the Prognostic Coefficient and Percentage of Viable Hepatocytes in Animals with Various Models of

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Hepatocellular Injury and in Patients with Hepatobiliary Diseases

№№	Experimental Data (Rats and Dogs)	Clinical Material

ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo