ORIGINAL ARTICLE

CHARACTERIZATION OF STRUCTURAL DISORDERS OF THE LIVER DEPENDING ON THE DURATION OF SUBHEPATIC CHOLESTASIS IN PATIENTS OF DIFFERENT AGE GROUPS

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Oleg Y. Kanikovskyi, Yaroslav V. Karyi, Igor P. Dovgan, Al-Moutasem Bellah M. Al Qatawneh
NATIONAL PIROGOV MEMORIAL MEDICAL UNIVERSITY, VINNYTSIA,UKRAINE

ABSTRACT

The aim: To study structural disorders of the liver depending on the duration of subhepatic cholestasis in patients of different age groups.

Materials and methods: 50 obstructive jaundice patients were subdivided into two groups. Group I (n = 25) consisted of young (18–44-year-old) and middle-aged patients (45–59-year-old), while the Group II (n = 25) included elderly (60–74-year-old) and senile patients (75–90-year-old).

Results: We performed morphological and morphometric studies of 50 liver biopsy specimens taken from patients of different age groups with different duration of obstructive jaundice: less than 7 days, 7-14 days, 14-21 days, 21-28 days, and over 28 days.

Conclusions: In patients of the Groups I and II, pathological hepatic changes in the early stages of mechanical jaundice were manifested in the form of hepatocyte dystrophy and hepatitis development. In the Group I patients, manifestations of steatohepatitis, fibrosis and initial signs of liver cirrhosis were noted in the late stages of subhepatic cholestasis. In addition to the above-mentioned changes, Group II patients, in the late stages of mechanical jaundice, presented signs of severe fibrosis and well-shaped liver cirrhosis. Taking into account the above morphological changes in the liver with different duration of subhepatic cholestasis, we consider reasonable to decompress bile ducts in patients of older age groups at earlier stages of mechanical jaundice compared to young and middle-aged patients, thus preventing post-decompression liver dysfunction and the subsequent development of biliary cirrhosis.

KEY WORDS: obstructive jaundice, liver biopsy, morphological i morphometric study of the liver

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INTRODUCTION

Among all liver pathologies, obstructive jaundice is the most common one, which, according to the WHO, is observed in 10-15% of the world's population [1, 2]. In case of short-term obstructive jaundice, hepatocytes develop a relative adaptation to cholestasis accompanied by a decreased bile secretion. In case of long-term obstruction of bile ducts, post-decompression liver dysfunction often develops due to failure of adaptation mechanisms [3, 4] despite a complete restoration of bile passage. Therefore, the choice of bile duct decompression technique and timing primarily depends on the duration of obstructive jaundice [5, 6]. Elderly patients demonstrated more pronounced changes in the liver associated with comorbidity [7]. The most reliable method of diagnosing structural changes in the liver is histological examination, which allows to ensure timely and comprehensive treatment [8]. In our opinion, the study of structural disorders of the liver with different duration of obstructive jaundice in patients of different age groups is still a pressing problem.

THE AIM

To study structural disorders of the liver depending on the duration of subhepatic cholestasis in patients of different age groups.

MATERIALS AND METHODS

To achieve the goal, we performed morphological and morphometric studies of 50 liver biopsy specimens taken from patients of different age groups with different duration of subhepatic cholestasis. Biopsy material was collected intraoperatively by microresection of the liver and puncture biopsy. The material was fixed in 10% neutral formalin solution (pH - 7.4) for 48 hours, followed by treatment with alcohol of increasing concentration and poured into paraffin. Resulted paraffin blocks were cut into serial semi-thin 5 μm slides, which were stained with hematoxylin/eosin and Van Gieson`s picrofuchsin in order to determine a degree of fibrotic changes in liver tissue and with Sudan III to detect fatty degeneration of hepatocytes. The microscopic

Table I. The relative volumes of structural components of the liver, Group I (M ± m)

Structural components	Duration of subhepatic cholestasis				
	less than 7 days	7-14 days	14-21 days	21-28 days	over 28 days
Hepatocytes, %	68.34±2.03	65.48±2.08	60.35±2.12	52.45±2.17	43.87±2.19
Bile ducts and cholangioles, %	7.01±1.06	6.7±1.08	6.4±1.05	6.02±1.03	5.86±1.02
Connective tissue, %	4.82±0.87	6.32±1.27	10.46±1.37	16.68±1.43	21.94±1.48
Vasculars, %	24.08±1.74	23.15±1.86	22.14±1.78	21.66±1.76	17.36±1.72
Stromal-parenchymal index	0.34±0.008	0.42±0.03	0.59±0.01	1.68±0.04	2.21±0.06

Table II. The relative volumes of structural components of the liver, Group II (M ± m)

Structural components	Duration of subhepatic cholestasis				
	less than 7 days	7-14 days	14-21 days	21-28 days	over 28 days
Hepatocytes, %	65.45±2.1	59.37±2.13*	52.64±2.17*	48.38±2.2*	39.92±2.24*
Bile ducts and cholangioles, %	6.24±1.02	5.82±1.05	5.24±1.03	5.02±1.02	4.29±1.01*
Connective tissue, %	6.11±0.98	8.75±1.25*	14.12±1.42*	19.47±1.57*	24.62±1.59*
Vasculars, %	21.70±1.64	20.66±1.72	19.82±1.76	16.14±1.73*	12.13±1.73*
Stromal-parenchymal index	0.42±0.01	0.98±0.02*	1.24±0.03*	1.89±0.046*	2.68±0.075*

Note: * – $p < 0.05$ – statistically significant difference in relation to the data of the Group I.

structure of the liver parenchyma was studied using a light microscope OLIMPUS BX41 at 100x, 200x and 400x magnification. Morphometric parameters of structural changes were determined using a computer software (Quick Foto Micro 2.3).

The patients were distributed by age according to WHO recommendations. During the study, 50 patients with obstructive jaundice were assigned to two groups. Group I (n = 25) consisted of young (18–44-year-old) and middle-aged patients (45–59-year-old), while the Group II (n = 25) included elderly (60–74-year-old) and senile patients (75–90-year-old). Each study group was subdivided into five subgroups of patients with different duration of obstructive jaundice: less than 7 days, 7-14 days, 14-21 days, 21-28 days, and over 28 days. Five liver biopsy material units were studied in each subgroup.

The research was conducted in compliance with the major principles of GCP guidelines (1996), Council of Europe Convention on Human Rights and Biomedicine (1997), World Medical Association Declaration of Helsinki on ethical principles for medical research involving human subjects (1964-2000) and Order of Ministry of Health of Ukraine № 281 of November 1, 2000, being approved by the Committee on Bioethics of the National Pirogov Memorial Medical University, Vinnytsia (Minutes No. 30 dated 10.12.2018).

The obtained data were statistically processed using descriptive statistic methods involving Microsoft Office Excel 2010 spreadsheet. As quantitative indicators, we calculated sample mean, standard deviation, and mean error. In case of normal distribution of quantitative indicators, we used Student's t-test for their comparison. The difference between the analyzed indicators was considered statistically significant at a significance level of 0.05 (error probability 5% ($p < 0.05$).

RESULTS

Histological study of liver biopsy slides of Group I patients with a duration of subhepatic cholestasis up to 7 days was characterized by the pronounced plethora of central veins, sinusoidal capillaries, and portal veins, centrilobular cholestasis accompanied by a blockade of stellate reticuloendotheliocytes with bile pigments. The venous lumens were significantly dilatated. Parenchyma was characterized by an unclear division into lobes. Most hepatic tubules had signs of discomplexation. Isolated hepatocytes were imbibed with bile. Some of them were in a state of necrosis; mitotically active binucleated hepatocytes were identified. In some cases, the hepatic cells showed signs of small- and large droplets obesity. Morphologically, relative volume of hepatocytes was 68.34 ± 2.03%. The relative volume of connective tissue was 4.82 ± 0.87%, vascular volume

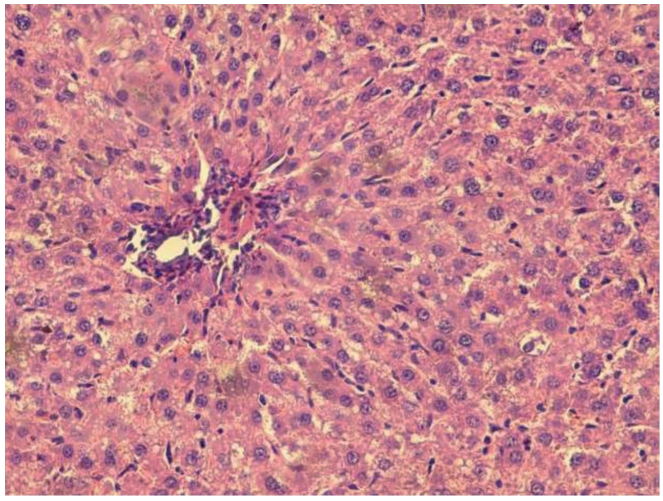

Fig. 1. Group I. Liver tissue subhepatic cholestasis less than 7 days. Hematoxylin-eosin staining, x400

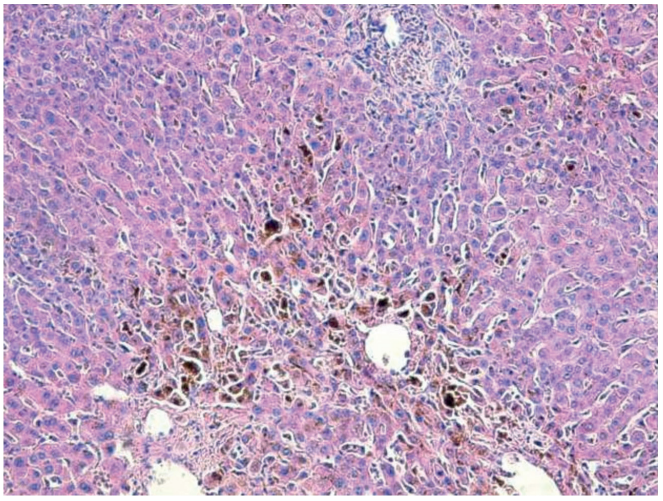

Fig. 2. Group I. Liver tissue with subhepatic cholestasis from 7 to 14 days. Hematoxylin-eosin staining, x200

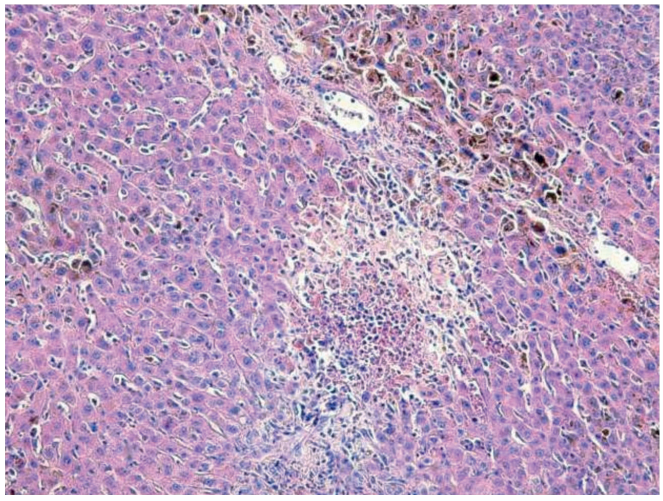

Fig. 3. Group I. Liver tissue with subhepatic cholestasis from 14 to 21 days. Hematoxylin-eosin staining, x200

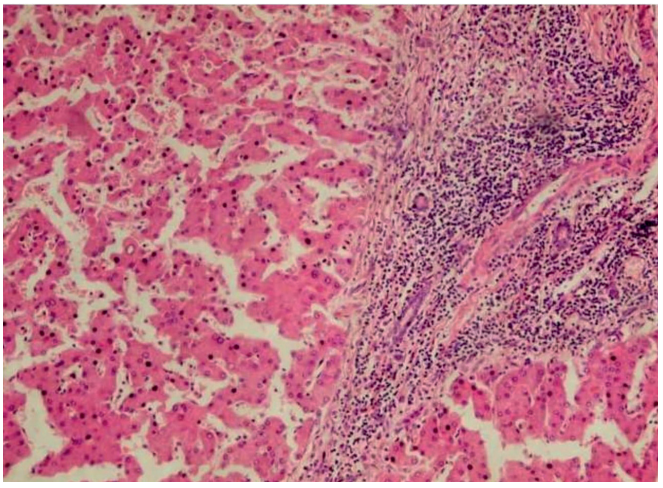

Fig. 4. Group I. Liver tissue with subhepatic cholestasis from 21 to 28 days. Hematoxylin-eosin staining, x200

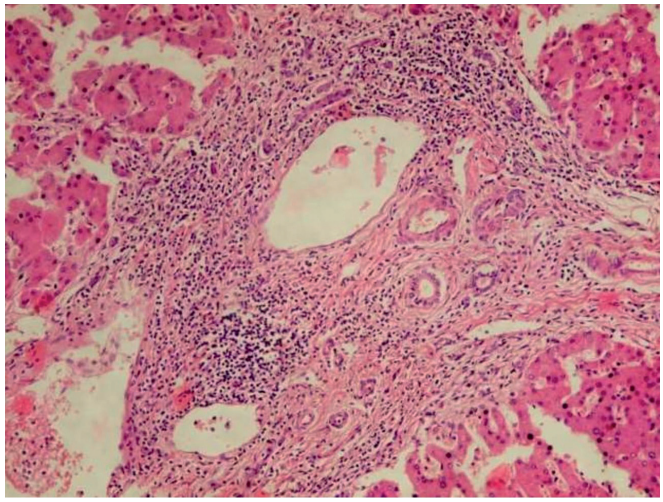

Fig. 5. Group I. Liver tissue with subhepatic cholestasis over 28 days. Hematoxylin-eosin staining, x200

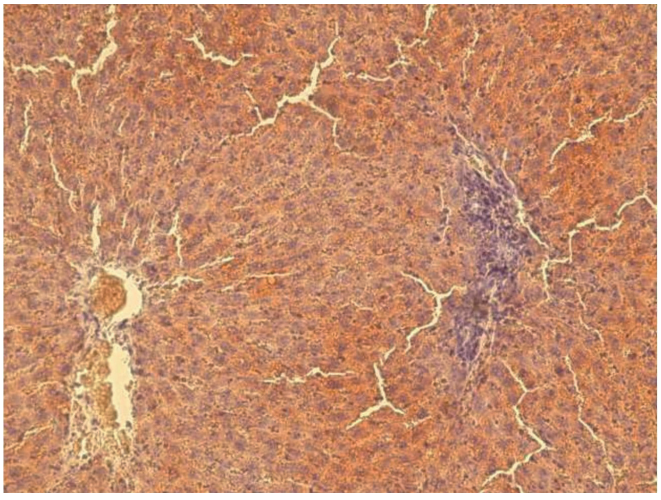

Fig. 6. Group II. Liver tissue with subhepatic cholestasis less then 7 days. Sudan III staining, x400

- 24.08 ± 1.74%, the stromal-parenchymal index - 0.34 ± 0.008. The relative volume of bile ducts and cholangioles was 7.01 ± 1.06% (Table I). These changes were associated with dilatation, edema, and dissection of portal tracts. No fibrous changes of the liver parenchyma were determined in this period (Fig. 1).

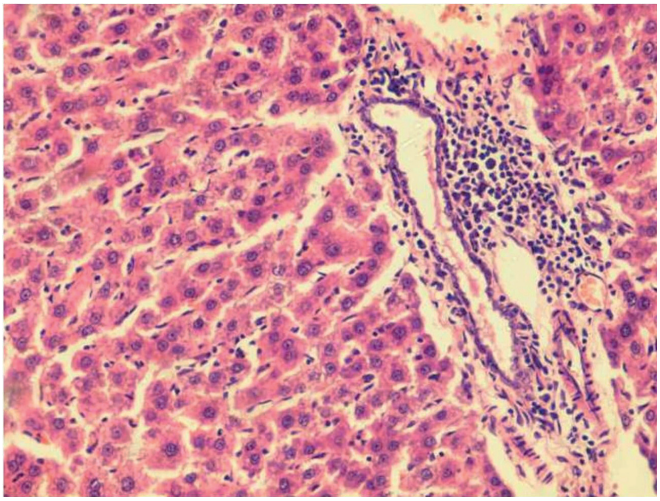

Fig. 7. Group II. Liver tissue with subhepatic cholestasis from 7 to 14 days. Sudan III staining, x400

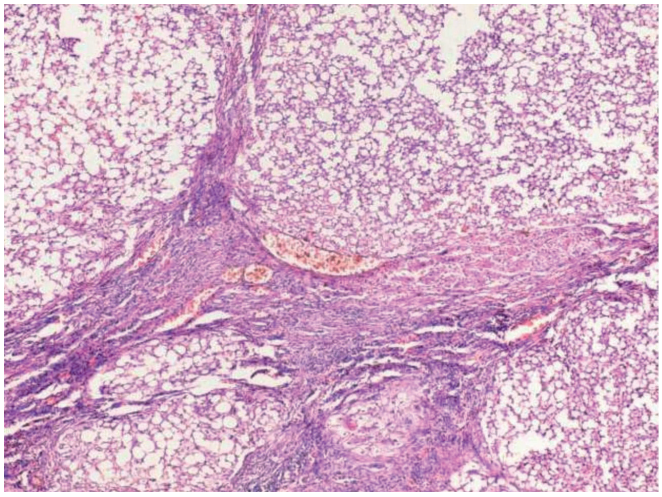

Fig. 9. Group II. Liver tissue with subhepatic cholestasis from 21 to 28 days and over 28 days. Hematoxylin-eosin staining, x100

Histological examination of liver tissue taken from Group I patients with obstructive jaundice lasting from 7 to 14 days also demonstrated the expressed venous plethora and even more pronounced centrilobular cholestasis accompanied by a blockade of stellate reticuloendotheliocytes with bile pigments. Most hepatocytes were imbibed with bile. Some of them were in a state of necrosis; pseudoglandular structures around bile thrombi were observed. In this period, a proliferation of active fibroblasts around the bile duct dilatations was observed. Sclerotic changes around the vessels were insignificant and manifested as a weak growth of soft fibrous tissue around some central veins. Morphologically, relative volume of hepatocytes was 65.48 ± 2.08%. The relative volume of connective tissue was 6.32 ± 1.27%, vascular volume - 23.15 ± 1.86%, stromal-parenchymal index - 0.42 ± 0.03. The relative volume of bile ducts and cholangioles was 6.7 ± 1.08% (Table I). In some cases, an inflammatory cell

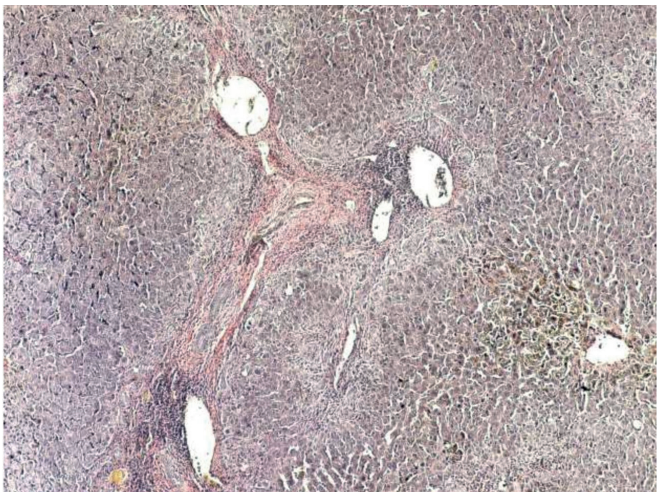

Fig. 8. Group II. Liver tissue with subhepatic cholestasis from 14 to 21 days. Van Gieson`s picrofuchsin staining, x100

infiltrate consisting of mononuclear cells, histiocytes and segmental leukocytes was present (Fig. 2).

Histological examination of liver tissue taken from Group I patients with a subhepatic cholestasis lasting from 14 to 21 days revealed pronounced centrilobular cholestasis associated with the blockade of stellate reticuloendotheliocytes by bile pigments. Pseudoglandular structures around biliary thrombi, growth of fine fibrous tissue around some central veins, and fuchsinophilia of portal tracts were also noted. Morphologically relative volume of hepatocytes was 60.35 ± 2.12%, connective tissue - 10.46 ± 1.37%, vascular volume - 22.14 ± 1.78%, stromal-parenchymal index - 0.59 ± 0.01. The relative volume of bile ducts and cholangioles was 6.4 ± 1.05% (Table I). This period of obstructive jaundice was characterized by presence of inflammatory cell infiltrate from mononuclear cells, segmental leukocytes and histiocytes (Fig. 3).

Morphologically, histological examination of liver biopsy material taken from patients of Group I with obstructive jaundice lasting from 21 to 28 days presented a progression of cellular and portal disorders. Bile discharge and deposition of bile thrombi in the intercellular space took place. Groups of hepatic cells were subject to necrosis and lysis (biliary infarction), associated with reactive inflammation developed in the form of clusters of segmented leukocytes and macrophages. Morphologically, the relative volume of hepatocytes was 52.45 ± 2.17%. Stroma collapse, its fibrosis with moderate infiltration of lymphohistiocytic elements, proliferation of bile ducts was observed. Relative volume of connective tissue was 16.68 ± 1.43%, vascular volume – 21.66 ± 1.76%, stromal-parenchymal index - 1.68 ± 0.04. The bile ducts were dilated, tortuous, their lumen was filled with bile cylinders and bile microliths. Morphologically, relative volume of bile ducts

and cholangioles was 6.02 ± 1.03% (Table I). The largest number of bile cylinders was found in the center of lobules, in liver cells, less often in the cytoplasm of stellate reticuloendotheliocytes. Bile droplets and grains were observed in the cytoplasm (Fig. 4).

Morphologically, the histological examination of liver tissue taken from Group I patients with subhepatic cholestasis lasting more than 28 days showed further progression of parenchymal and portal disorders. These changes contributed to forming fibrous connective tissue septa. Bile passed into the surrounding tissue from damaged bile ducts, forming bile basins with perifocal polymorphic infiltration of inflammatory cells. The spread of fibrosis foci and liver parenchyma necrosis was observed. Morphologically, relative volume of bile ducts and cholangioles was 5.86 ± 1.02%. The relative volume of hepatocytes tended to further decrease and was equal to 43.87 ± 2.19%. An inflammatory granulomatous reaction developed in the portal tracts. The process was also characterized by expressed periductal fibrosis in the form of concentric collagen layers around bile ducts. Relative volume of connective tissue was 21.94 ± 1.48%, vascular volume - 17.36 ± 1.72%, stromal-parenchymal index - 2.21 ± 0.06 (Table I). These changes indicated the development of severe fibrosis and the onset of liver cirrhosis (Fig. 5).

Histological examination of liver biopsy slides taken from Group II patients with obstructive jaundice lasting less than 7 days revealed a noted granular and small vacuolar dystrophy of hepatocytes. The latter was determined in centrilobular located hepatocytes. Also, we observed a discomplexation of hepatic tubules, foci of collapsed hepatic tissue with significant dilatation of sinusoidal spaces, proliferation and activation of stellar reticuloendothelial cells. Another characteristic feature was a combination of hydropic and fatty liver dystrophy. The latter was small droplets and focal one. Heteromorphism of hepatocytes, nuclear polymorphism, polychromia, and manifestation of apoptosis in some cells also were observed. Morphologically, relative volume of hepatocytes was 65.45 ± 2.1%. The relative volume of connective tissue was 6.11 ± 0.98%, vascular volume - 21.70 ± 1.64%, stromal-parenchymal index - 0.42 ± 0.01. These values did not statistically significantly exceed the corresponding values shown of the study Group I with a duration of obstructive jaundice less than 7 days ($p > 0.05$). Morphologically, the relative volume of bile ducts and cholangioles was 6.24 ± 1.02% (Table II), which also did not statistically significantly differ from the corresponding readings of the study Group I ($p > 0.05$) (Fig. 6).

Group II patients with a duration of subhepatic cholestasis from 7 to 14 days was pronounced changes of alternative, inflammatory and reparative-sclerotic nature in the structural components of the liver. The phenomena of intracellular and intraductal cholestasis were building up in all parts of lobules with the formation of bile clots in dilated bile ducts. Signs of cholangitis persisted, but lymphocytes and histiocytes began to dominate in the inflammatory infiltration material, and the concentration of polymorphonuclear leukocytes decreased (signs of chronic inflammatory process). We detected numerous small hepatocyte necrosis foci with infiltration of collapsed stroma by neutrophils, lymphocytes and histiocytes. Most hepatocytes had signs of protein and fatty degeneration. Inflammatory infiltrate cells were represented by lymphocytes detected in both portal tracts and sinusoids in the form of lymphocyte chains. In addition, sclerotic changes were detected in central veins and vessels of portal zones. Portal areas presented a build-up of periductal fibrosis, lymphohistiocytic infiltration, a significant number of fibroblasts, and formation of thin connective tissue septa in some cases, which wedged in the interparticle stroma and parenchyma. Morphologically, relative volume of bile ducts and cholangioles was 5.82 ± 1.05% and vascular volume - 20.66 ± 1.72%. These indicators did not significantly exceed the corresponding readings of the study Group I with a duration of subhepatic cholestasis from 7 to 14 days ($p > 0.05$). Morphologically, the relative volume of hepatocytes was 59.37 ± 2.13%, connective tissue - 8.75 ± 1.25%, and stromal-parenchymal index - 0.98 ± 0.02 (Table II), which statistically significantly exceeded the corresponding figure of the study Group I ($p < 0.05$) (Fig. 7).

Histological examination of liver tissue taken from patients of the Group II with obstructive jaundice lasting from 14 to 21 days revealed more pronounced changes of inflammatory and reparative-sclerotic nature in all structural components of the liver, accompanied by signs of widespread intracellular and intraductal cholestasis with the formation of bile clots. The most pronounced changes manifested in the central parts of the lobules, accompanied by an outflow of bile beyond the limits and the formation of bile basins, which led to the emergence of large focal necrosis of the parenchyma. Almost all cases associated with hepatocytes in the state of hydropic dystrophy, which were located mainly in the central parts of liver lobules, less often in the peripheral ones. Adipose hepatosis was also noted. Hepatocytes had different degrees of fatty degeneration, manifested within the range of small- to large-droplet steatosis. As a rule, small lipid droplets were found in the cytoplasm of centrilobular hepatocytes. Heteromorphism of hepatocytes, nuclear polymorphism, polychromia, and manifestation of apoptosis were also

observed. The pronounced dystrophic changes in liver tissue associated with a progression of periportal and centrolobular perivenular fibrosis, as well as pericellular sclerosis sites. In some cases, we detected the cirrhosis signs presented as thin fibrous septa wedged in liver lobules, central veins connected with the vessels of the portal tract, associated with the emergence of small false lobules consisting of proliferating hepatocytes in the condition of fatty and protein dystrophy, and the absence of radial orientation of hepatic cords. Fibrous septa and stroma of dilated sclerosed portal tracts had signs of focal inflammatory infiltration, consisting mainly of lymphocytes and macrophages. Morphologically, relative volume of bile ducts and cholangioles was 5.24 ± 1.03, vascular volume - 19.82 ± 1.76%, which did not statistically significantly differ from the corresponding readings of the study Group I with a duration of obstructive jaundice from 14 to 21 days ($p > 0.05$). Relative volume of hepatocytes was 52.64 ± 2.17%, connective tissue - 14.12 ± 1.42%. These readings statistically significantly exceeded the corresponding figures of the study Group I ($p < 0.05$). Stromal-parenchymal index was 1.24 ± 0.03 (Table II), which was also statistically significantly higher than the figures of the study Group I with a duration of subhepatic cholestasis from 14 to 21 days ($p < 0.05$) (Fig. 8).

Patients of the study Group II with a duration of subhepatic cholestasis from 21 to 28 days and over 28 days, presented large focal necrosis of liver parenchyma and the development of a pronounced periductal sclerotic process. The formation of fibrous septa in combination with nodular regeneration of the parenchyma led to a failure of hepatic histoarchitectonics with subsequent development of the liver cirrhosis. Hepatocytes were in a state of hydropic and fatty dystrophy. The expressed sclerotic processes of the stroma in the form of periportal and centrolobular perivenular fibrosis and pericellular sclerosis were also noted. Cirrhosis of the liver occurred in the vast majority of cases. Patients with obstructive jaundice lasting from 21 to 28 days presented morphologically relative volume of bile ducts and cholangioles equal to 5.02 ± 1.02%, which did not statistically significantly differ from the corresponding figure of the study Group I with a subhepatic cholestasis lasting from 21 to 28 days ($p > 0.05$). Relative volume of hepatocytes was 48.38 ± 2.2%, connective tissue - 19.47 ± 1.57%, and vascular volume - 16.14 ± 1.73%. These indicators statistically significantly exceeded the corresponding readings of the study Group I ($p < 0.05$). Stromal-parenchymal index was equal to 1.89 ± 0.046 (Table II), which was also statistically significantly higher than in the study Group I with a duration of obstructive jaundice from 21 to 28 days ($p < 0.05$). Morphologically, relative volume of bile ducts and cholangioles in patients with a duration of subhepatic cholestasis over 28 days was 4.29 ± 1.01%, which statistically significantly differed from the corresponding figure of the study Group I ($p < 0.05$). Relative volume of hepatocytes was 39.92 ± 2.24%, connective tissue - 24.62 ± 1.59%, vascular volume - 12.13 ± 1.73%, stromal-parenchymal index - 2.68 ± 0.075 (Table II), which also statistically significantly exceeded the corresponding figures of the study Group I with a duration of subhepatic cholestasis over 28 days ($p < 0.05$). These changes suggest a damage of hepatic histoarchitectonics with the development of severe cirrhosis of the liver (Fig. 9).

DISCUSSION

The comparative study of hepatic morphological changes showed that the severity of structural disorders in patients with subhepatic cholestasis depended primarily on the disease duration. At early stages of mechanical jaundice (first 2 weeks), were morphological changes presented as bilirubinostasis with hepatocytes and canaliculi, and signs of protein and fat dystrophy associated with the development of biliary hepatitis [9-11]. At later stages of subhepatic cholestasis (more than 2 weeks), were the bile duct epithelium proliferation and periportal fibrosis. The mechanical jaundice with the duration more than 1-3 months in addition to dystrophic and necrobiotic changes, there were a pronounced fibrosis of the portal stroma and biliary cirrhosis of the liver [9, 10, 12]. In these studies, structural changes in the liver with different durations of subhepatic cholestasis were studied. However, hepatic morphological changes in mechanical jaundice patients of different age groups were not taken into account.

In the Group I patients at early terms of subhepatic cholestasis (up to 7 days, 7 to 14 days), morphological changes in the liver mainly consisted in:
- intraductal cholestasis;
- moderate polymorphic cellular inflammatory infiltration of the stroma.

At later terms of obstructive jaundice (from 14 to 21 days; from 21 to 28 days), changes in the liver parenchyma in patients of the Group I were associated with the development and progression of:
- intraductal and intracellular cholestasis;
- reactive stromal hepatitis;
- dystrophy of hepatocytes;
- small focal necrosis of the liver parenchyma;
- initial fibrosis.

At the latest terms of subhepatic cholestasis (over 28 days), morphological hepatic changes in the Group I patients consisted in:

- multiple diffuse extra- and intracellular bilirubin deposits;
- severe dystrophy of hepatocytes;
- large focal necrosis of the liver parenchyma;
- development of severe fibrosis and onset of liver cirrhosis.

Patients of the Group II with obstructive jaundice lasting up to 7 days, presented the following changes in the liver:
- intracellular and intraductal cholestasis;
- stromal hepatitis;
- combination of protein and fatty liver dystrophy.

In patients of the Group II with subhepatic cholestasis lasting from 7 to 14 days and from 14 to 21 days, changes were associated with the development and progression of:
- intracellular and intraductal cholestasis associated with the formation of bile clots;
- chronic inflammation;
- severe dystrophy of hepatocytes;
- small and large focal necrosis of the liver parenchyma;
- severe fibrosis and onset of cirrhosis of the liver.

Patients of the Group II with obstructive jaundice lasting 21 to 28 days and over 28 days presented the following morphological changes in the liver:
- large focal necrosis of the liver parenchyma;
- severe periductal and periportal fibrosis;
- failure of hepatic histoarchitectonics and the development of severe liver cirrhosis.

CONCLUSIONS

1. In patients of the Groups I and II, pathological hepatic changes in the early stages of mechanical jaundice were manifested in the form of hepatocyte dystrophy and hepatitis development.
2. In the Group I patients, manifestations of steatohepatitis, fibrosis and initial signs of liver cirrhosis were noted in the late stages of subhepatic cholestasis. In addition to the above-mentioned changes, Group II patients, in the late stages of mechanical jaundice, presented signs of severe fibrosis and well-shaped liver cirrhosis.
3. Taking into account the above morphological changes in the liver with different duration of subhepatic cholestasis, we consider reasonable to decompress bile ducts in patients of older age groups at earlier stages of mechanical jaundice compared to young and middle-aged patients, thus preventing post-decompression liver dysfunction and the subsequent development of biliary cirrhosis.

REFERENCES

1. Sha J., Dong Y., Niu H. A prospective study of risk factors for in-hospital mortality in patients with malignant obstructive jaundice undergoing percutaneous biliary drainage. Medicine (Baltimore). 2019; 98(15): e15131. doi: 10.1097/MD.0000000000015131.
2. Topal B., Vromman K., Aerts R. et al. Hospital cost categories of one-stage versus two-stage management of common bile duct stones. Surg Endosc. 2010; 24(2): 413-416. doi: 10.1007/s00464-009-0594-0.
3. Celotti A., Solaini L., Montori G. et al. Preoperative biliary drainage in hilar cholangiocarcinoma: Systematic review and meta-analysis. Eur J Surg Oncol. 2017; 43(9): 1628-1635. doi: 10.1016/j.ejso.2017.04.001.
4. Liu C., Lu J.W., Du Z.Q. et al. Association of Preoperative Biliary Drainage with Postoperative Morbidity after Pancreaticoduodenectomy. Gastroenterol Res Pract. 2015; 2015: 796893. doi: 10.1155/2015/796893.
5. Kanikovskyi O.Y., Karyi Y.V., Babiichuk Y.V. et al. Comparative assessment of bile duct decompression methods in patients with obstructive jaundice of non-tumor genesis. Wiad Lek. 2019; 72(7): 1247-1252.
6. Nychytaylo M.Y., Dziubanovskyi O.I. Comparison of dynamics of cytolytic and cholestatic indicators and the tempo of the biliary decompression after one-step laparoscopic and open operation interventions of patients with choledocholithiasis complicated with obstructive jaundice. Hospital Surg. 2017; 1: 8-16.
7. Costi R., Mazzeo A., Tartamella F. et al. Cholecystocholedocholithiasis: a case-control study comparing the short- and longterm outcomes for a "laparoscopy-first" attitude with the outcome for sequential treatment (systematic endoscopic sphincterotomy followed by laparoscopic cholecystectomy. Surg Endosc. 2010; 24(1): 51-62.
8. Campion J.P., Fremond B., Guillouzo A. Hepatocytes isoles et suppleance hepatigue. Gastroenterol Clin Boil. 2014; 18(1): 53-56.
9. Mavdzhudov M.M. Diagnostics and surgical treatment of major duodenal papilla benign stenosis. A dissertation of a candidate of medical sciences: 14.00.27 (Dushanbe). 2009, 155p.
10. Ratchyk V.M. Diagnostics and surgical treatment of subhepatic cholestasis of benign genesis at complication development stages (clinical-experimental research). A dissertation of a doctor of medical sciences: 14.01.03 (Dnipropetrovsk). 2009, 351p.
11. Amosova E.N., Lyikovskiy O.I., Sidorova N.N. et al. Microcirculatory changes in patients with chronic diseases of the biliary tract. Lek Sprava. 1999; 1: 51-54.
12. Ponsky J., Heniford B., Gersin K. Choledocholithiasis: evolving intraoperative strategies. Amer Surg. 2000; 66(3): 262-268.

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ORCID and contributionship:
Oleg Y. Kanikovskyi: 0000-0002-9302-8760 [A, E, F]
Yaroslav V. Karyi: 0000-0003-1578-9019 [A-D]
Igor P. Dovgan: 0000-0001-9049-6553 [C, E]
Al-Moutasem Bellah M. Al Qatawneh: 0000-0002-7318-5347 [E]

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CORRESPONDING AUTHOR

Yaroslav V. Karyi
National Pirogov Memorial Medical University
56 Pirogov St., 21018 Vinnytsya, Ukraine
tel. +380677429457
e-mail: yaroslavkaryi@gmail.com

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