

A NEW PERSPECTIVE ON DIAGNOSIS: THE POTENTIAL OF CT PERFUSION IN CHRONIC LIVER DISEASE (LITERATURE REVIEW)

DOI:10.35805/BSK2024111013

Battalova G.

<https://orcid.org/0000-0003-4261-3537>

Baiguissova D.

<https://orcid.org/0000-0001-5724-7707>

Kalshabay E.

<https://orcid.org/0000-0003-0493-6685>

Mukhamejanova A.

<https://orcid.org/0000-0002-4487-1604>

Mukanova A.

<https://orcid.org/0009-0000-4654-6103>

Nagimova D.

<https://orcid.org/0009-0001-6151-2558>

Kabidenov A.

<https://orcid.org/0000-0001-5038-2033>

Abzhaparova B.

<https://orcid.org/0000-0001-9790-8151>

Baimakhanov B.

<https://orcid.org/0000-0003-0049-5886>

received: 03.09.2024

accepted: 12.09.2024

Author for correspondence:

Baimakhanov B. B.

Doctor of medicine, Professor,
Academician, transplant-surgeon,
chairman of Board of JSC
«National Scientific Center of Surgery
named after A.N. Syzganov»
info@baimakhanov.kz.

Conflict of interest:

The authors declare no potential
conflict of interest requiring disclosure
in this article.

Keywords:

CT perfusion, liver fibrosis,
liver cirrhosis, computed tomography,
liver elastometry.

**Battalova G.¹, Baiguissova D.¹, Kalshabay E.¹,
Mukhamejanova A.¹, Mukanova A.¹, Nagimova D.¹, Kabidenov A.¹,
Abzhaparova B.¹, Baimakhanov B.¹**

¹ JSC Syzganov National Scientific Center of Surgery,
Almaty, Kazakhstan

Abstract: the aim of this study is to analyze the current advances of CT perfusion in the diagnosis of liver disease. Liver fibrosis is a characteristic feature of chronic liver disease and is confirmed by liver biopsy, which is an invasive method. Morphologic parameters of cirrhosis are evaluated by conventional imaging techniques such as ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI). Additional studies of new imaging modalities are needed for earlier diagnosis, surveillance and accurate treatment, CT perfusion has several advantages by examining the arterial and venous blood flow of the liver, which gives a more complete picture of early functional changes in the liver. Despite the advantages of this method, the results of postprocessing in different stages of fibrosis and etiology of its development are not fully understood.

Introduction

The liver has unique blood flow characteristics, with two sets of inflow vessels (hepatic artery and portal artery) and one set of outflow vessels (hepatic veins). Blood flow varies with underlying liver parenchymal injury such as cirrhosis, liver fibrosis, chemotherapy-associated steatohepatitis, and occlusive jaundice. However, the hemodynamics of the diseased liver are complex and not fully understood [1].

Computed tomography (CT) perfusion of liver is a modern imaging technique that allows quantitative assessment of blood flow and contrast agent distribution in the liver. Perfusion imaging allows quantitative determination of physiological parameters of liver microcirculation perfusion at levels signifi-

cantly inferior to the spatial resolution of CT and MR imaging. Due to the peculiarities of the structure and architecture, perfusion imaging in the liver is a more complex task than in other organs. The liver is a mobile organ and is significantly deformed by respiratory movements. In addition, it has a dual vascular supply, and the sinusoidal capillaries in the normal liver are fenestrated [2].

Minimally invasive techniques such as perfusion CT allow for extremely accurate assessment of tissue perfusion. Modern multidetector CT scanners are ideal for measuring perfusion due to their high spatial and temporal resolution [3].

Early diagnosis of liver fibrosis (LF) is key for treatment to halt the progression of cirrhosis and hepatocellular carcinoma. LF is a hallmark of chronic liver

disease and is confirmed by liver biopsy, which is invasive and prone to sampling errors. The morphological parameters of cirrhosis are assessed by conventional imaging techniques such as ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI). New imaging techniques such as magnetic resonance elastography and ultrasound elastography are reliable and informative. Further studies of new imaging techniques such as perfusion CT are needed for earlier diagnosis, follow-up and accurate treatment [4].

The aim of this study is to analyze the current and latest advances in CT perfusion in the diagnosis of liver diseases.

Materials and methods: A comprehensive literature search was performed using PubMed and Google Scholar databases. Key words included CT perfusion, liver fibrosis and cirrhosis, HCC, liver elastometry, liver ultrasound. Articles published between 2001 and 2024 were included. The review included different types of articles including original research, literature and systematic reviews and meta-analysis. Articles were selected based on their examination of the diagnostic method of CT perfusion in liver diseases of various etiologies. Articles were included if they contributed to the understanding of the informativeness of the method, highlighted the latest trends or addressed the gaps in current knowledge.

Methods for the diagnosis of liver diseases

The liver's function depends in part on its blood flow. The portal vein provides about 80% of the hepatic blood flow in the absence of liver disease. However, in cirrhosis, portal perfusion progressively decreases due to increased sinusoidal resistance and the development of spontaneous portosystemic collaterals. With portal vein decompression using operative or interventional portosystemic shunts, hepatic-portal perfusion is further reduced or completely eliminated. Thus, total hepatic blood flow becomes increasingly dependent on hepatic arterial blood flow. Several noninvasive methods have been proposed to quantify hepatic flow in clinical practice. These include imaging techniques based on measurements using Doppler sonogra-

phy, magnetic resonance imaging (MRI), nuclear medicine, or CT. Hepatic flow at the prehepatic level can be measured using Doppler sonography [5]. However, the reproducibility of portal venous flow measurements using Doppler sonography remains controversial, and arterial flow measurements using this method are even more difficult to obtain due to the small diameter of the hepatic artery [5].

Ultrasound Elastography is the most commonly used instrumental method to date for assessing the effectiveness of antiviral therapy in patients with chronic hepatitis C. A statistically significant decrease in liver tissue stiffness was noted in both patients with fibrosis and patients with cirrhosis [6].

MRI is routinely used to assess cirrhosis and its complications. However, detecting early stages of fibrosis is more challenging and several new MRI techniques have been used for this purpose. Innovative techniques MR elastography: Similar to sonographic transient elastography (TE), MR elastography is based on the fact that the speed and wavelength of a wave propagating in tissue increases as the stiffness of the medium, such as a fibrotic liver, increases. MR elastography requires special software and hardware. A driver device is placed over the patient's right upper abdomen and generates acoustic pressure waves with a frequency of 40-120 Hz. These waves create shear waves in the liver. The images display the propagating mechanical wave and a special algorithm generates a quantitative stiffness map. In several studies, MR elastography has detected progressive liver fibrosis and cirrhosis in patients with chronic hepatitis B. The quantitative assessment significantly correlated with the stage of fibrosis. It has also proven to be an effective tool for differentiating low and high grade cirrhosis [7].

Unlike ultrasound, MR elastography is not affected by the absence of an acoustic window, obesity, or the presence of ascites, and is not operator dependent. MR elastography has been established as a diagnostic tool for progressive fibrosis regardless of age, gender, BMI, inflammation, and the etiology of liver disease. Limitations of MR elastography include its cost and the

fact that it is time consuming. Liver stiffness may also be affected by liver iron overload, steatosis, vascular occlusion, cholestasis, and portal hypertension [8].

Nuclear medicine techniques such as single-photon emission computed tomography and dynamic positron emission tomography have been used to study liver perfusion. These techniques are hampered by their limited spatial resolution. In particular, noninvasive direct measurement of portal vein activity is not possible even with positron emission tomography, which has the best spatial resolution among nuclear medicine techniques [5].

Certain liver perfusion parameters can be determined noninvasively from CT scans in patients with chronic liver disease.

CT scans have shown that liver perfusion, hepatic arterial fractional perfusion, and mean transit time of iodinated contrast are significantly altered in cirrhosis, and that these parameters correlate with the degree of liver dysfunction based on clinical and biological data in chronic liver disease. These findings highlight the importance of perfusion as a marker of liver function [5].

In this regard, CT perfusion plays an important role in the diagnosis and monitoring of chronic liver diseases, due to the ability to quantitatively assess the parameters of the liver blood supply, which allows identifying and monitoring pathological changes at the microcirculatory level.

Evaluation of hemodynamic parameters of the liver

CT perfusion allows measuring important parameters such as:

Blood flow (hepatic blood flow, HBF) is the volume of blood passing through a unit of tissue in a certain period of time. A decrease in HBF may indicate the development of fibrosis or cirrhosis. Blood filling (hepatic blood volume, HBV) is the total volume of blood in the liver tissue. This value also changes with the development of fibrosis and cirrhosis. Plasma transit time (mean transit time, MTT) is the time it takes for blood to pass through the liver tissue; may change with the development of vascular disorders. Permeability (permeability surface area product, PS) is an indicator charac-

terizing the permeability of the vascular wall, which increases with inflammatory processes and tumor changes.

These parameters help to identify even small changes in the structure and function of the liver, which can be early signs of a chronic disease such as fibrosis or cirrhosis.

CT perfusion can be used to assess the stage of liver fibrosis, which is especially important in the absence of available minimally invasive methods. An increase in the density of connective tissue during fibrosis changes the blood flow, which allows the use of perfusion parameters for a qualitative and quantitative assessment of the degree of damage.

In the early stages of fibrosis, blood flow and blood filling can decrease due to the onset of changes in microcirculation. As the disease progresses (transition to cirrhosis), perfusion parameters change significantly, and changes in the vascular pattern of the liver are also observed.

CT perfusion allows for repeated studies and monitoring the dynamics of perfusion changes. This can be useful to assess the effectiveness of therapy aimed at slowing the progression of fibrosis or improving liver function. For example: After antifibrotic therapy, blood flow and blood filling parameters can be expected to improve. If treatment is ineffective, perfusion parameters may continue to deteriorate, indicating the need to adjust therapy.

One of the important consequences of chronic liver disease is the development of portal hypertension. CT perfusion can help determine the degree of blood flow impairment in the portal system, assess changes in arterial and venous blood flow in the liver, and predict the development of complications associated with portal hypertension, such as esophageal and gastric varices.

Chronic liver disease, especially cirrhosis, is a risk factor for the development of hepatocellular carcinoma. CT perfusion allows us to evaluate areas of the liver with increased blood supply, which may indicate the development of HCC, determine the tumor boundaries and the degree of invasion into adjacent vessels. After surgery, chemotherapy or radiotherapy, CT perfusion can be used to monitor the restoration of blood flow

to the liver or, conversely, to detect recurrence of the disease. Perfusion changes can indicate the tumor's response to therapy and predict long-term outcome. Another result of the authors' study was that perfusion changes in chronic liver diseases significantly correlated with the severity of the disease [5].

The study found that portal and general perfusion are prognostically valuable parameters that allow assessing changes in blood flow in liver tissue after antiviral therapy with direct-acting drugs in patients with liver fibrosis and cirrhosis as a result of chronic hepatitis C. An increase in the values of these parameters is most likely associated with a decrease in the severity of portal hypertension signs after completion of specific treatment. Perfusion computed tomography provides an idea of the effect of antiviral therapy on liver tissue hemodynamics, which allows judging the degree of fibrosis regression at each stage of liver disease in the patients examined [9].

Thus, CT perfusion is becoming an important tool in the diagnosis and monitoring of chronic liver diseases, providing physicians with data on hemodynamic changes that cannot be obtained by other imaging methods.

Conducting CT perfusion:

Basic principles of CT perfusion: Perfusion is the transfer of blood to a unit volume of tissue per unit time, and usually refers to blood transport at the capillary level. CT perfusion is based on the increase and subsequent decrease in the concentration of contrast agent in tissues as a function of time. Since tissue attenuation, measured by CT and expressed in Hounsfield units, is directly proportional to the high concentration of contrast agent in the tissue, CT allows the assessment of tissue perfusion [10].

CT perfusion analysis is based on several fundamental requirements. One of them is sequential CT scanning of the same volume over time, performed before, during and after intravenous contrast administration to track temporal changes in CT attenuation in the tissue volume of interest. Tissue enhancement measured after contrast administration can be divided into two phases depending on the distribution of the contrast agent in the intravascular or extravascular-ex-

tracellular (terstitial) compartment.

In the first phase, enhancement occurs mainly due to the contrast agent in the intravascular space. Later, in the second phase, tissue enhancement occurs as the contrast agent moves from the intravascular to the extravascular extracellular space across the capillary membrane. Thus, in the first phase, enhancement is largely determined by blood flow, while in the second phase, enhancement is dependent on blood volume and capillary permeability to contrast agent [11].

The amount of contrast agent present in the volume of interest reflects the sum of the amount of contrast agent in the blood vessels and the amount of contrast agent that has passed into the interstitial space by passive diffusion. Another requirement for CT perfusion analysis is the selection of a vessel (usually an artery) supplying the tissue of interest to obtain an intensity-time curve (arterial input function) by placing a region of interest (ROI) within the lumen of the vessel. Unlike other organs where the ROI is usually placed only in the artery, in liver CT perfusion the ROI should be placed in both the artery and the portal vein because the liver has a dual blood supply, from the hepatic artery and the portal vein. A third requirement for CT perfusion analysis is the use of kinetic models to calculate the various perfusion parameters in the tissues being analyzed. For liver CT perfusion, one of three methods can be used, including the model-free maximum slope method, the compartment model-based method, and the distributed parameter model-based method, or a combination of them [10].

A typical CT perfusion protocol consists of a pre-contrast image acquisition and subsequent dynamic acquisitions, performed sequentially after intravenous administration of iodinated CT contrast. The pre-contrast CT scans can serve as a localizer to select the anatomical scanning range for the subsequent dynamic scan. In the case of liver imaging, the scanning range should ideally include the main portal vein so that time-intensity curves of both the abdominal aorta and portal vein can be calculated [12].

Contrast agents should be adminis-

tered in small amounts at high flow rates to obtain a short and well-terminated bolus. The iodine concentration of the contrast agents should be at least 300 mg iodine per milliliter, and the total iodine dose administered should be approximately 12-18 g. It is recommended to administer a contrast bolus of 30-60 mL of iodinated contrast agent followed by a 50 mL flush of normal saline at an infusion rate of 4 mL/sec or higher through an 18-20 gauge antecubital intravenous cannula. The amount of contrast agent should be adjusted depending on the concentration of the contrast agent. Contrast agents with high iodine concentrations (> 350 mg iodine per milliliter) are generally recommended to obtain a higher contrast-to-noise ratio [10].

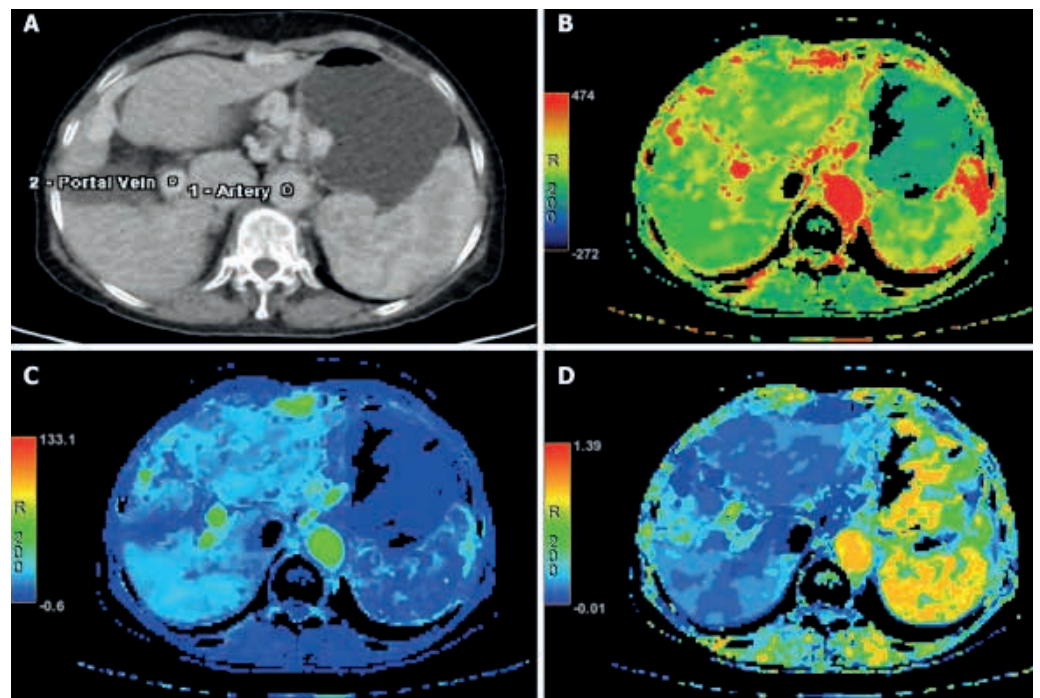
After acquisition of CT data, various CT perfusion parameters can be cal-

culated using either a model-free or a model-based approach, with the former being easier to implement. Regardless of the algorithm used, several image processing steps are required to calculate CT perfusion parameters. Image processing includes motion correction or image alignment, selection of arterial (and/or portal) input features, definition of ROIs, and voxel-wise calculation of perfusion parameters. Perfusion analysis of the liver is calculated differently from that of other organs because the liver has a dual blood supply, the hepatic artery and the portal vein. Therefore, the effective intensity-time curve obtained from liver tissue is the result of superposition of the arterial and venous components [10,13]

Post-processing of CT perfusion of the liver is shown in the figure1 [14].

Table 1.

Perfusion of liver CT scan after data processing. A: ROI is located on the abdominal aorta and portal vein for perfusion calculation; B-D: Perfusion parameters of liver CT scan are calculated automatically, including hepatic artery fraction (B), liver blood flow (C), and liver blood volume (D).



DOI: 10.3748/wjg.v28.i42.6068 Copyright ©The Author(s) 2022.

Results of liver CT perfusion post-processing.

In the study by Vignesh G. et al. [15], CT perfusion values are compared in liver pathologies such as HCC, hemangioma, abscess and simple liver cysts. Perfusion parameters in liver cysts showed no intracystic blood flow (BV), blood flow velocity (BF) and mean transit time (MTT) with increased induced residual fraction time to onset (IRFTO). Perfusion values in hemangioma showed increased in-

tralesional BV, BF and IRFTO with relatively decreased MTT. Perfusion values in HCC showed increased intralesional BV and BF with relatively decreased MTT and IRFTO. Perfusion parameters in liver abscess showed decreased intralesional BV, BF and PS with increased MTT and IRFTO. Of all the parameters evaluated, four parameters, namely BF, BV, MTT and IRFTO, showed statistical significance in differentiating benign and malignant lesions. Of the 36 patients, 18 had malig-

nant lesions and 14 had benign lesions. Since the growth and migration of cancer cells depend on the proliferation of new blood vessels through the process of tumor angiogenesis, tissue perfusion is of critical importance in oncology. Angiogenesis can be quantified to assess tumor growth at an early stage and obtain prognostic, predictive and surrogate power. CT perfusion also allows for the assessment of how chemotherapy and radiotherapy affect tumor vascularization and perfusion [3].

Ronot M. et al. [2] in their study found significant changes in some perfusion parameters in patients with cirrhosis. The study showed an increase in CT perfusion indices of arterial perfusion and a decrease in portal venous perfusion. There was an increase in arterial fraction and mean transit time in cirrhotic liver compared to normal liver. The authors also observed a decrease in portal and total liver perfusion. In addition, they showed that patients with chronic liver disease without cirrhosis also had altered perfusion parameters (including total liver perfusion, arterial fraction, and mean transit time), which were significantly different from those in patients with cirrhosis. Fibrosis was assessed using the METAVIR score, with the final population consisting of patients with stage F1 (mild fibrosis) in 58% of patients, F2 (moderate fibrosis) in 27%, and F3 (intermediate fibrosis) in 15%. There were no patients with F0 (no fibrosis) or F4 (severe fibrosis). Twenty-one patients also had steatosis (fatty liver infiltration), of which seven were mild, six were moderate, and eight were severe. Portal venous perfusion and total liver perfusion were significantly lower in patients with intermediate fibrosis compared with minimal fibrosis. Mean blood transit time was increased in patients with intermediate fibrosis. Arterial perfusion and volume of distribution did not differ significantly between groups. Mean transit time was an independent factor associated with fibrosis. A cutoff value of 13.4 seconds can be used to distinguish between minimal and intermediate fibrosis with a sensitivity of 71% and a specificity of 65%. These data help to better understand how liver characteristics change with fibrosis progression

and can be used to diagnose and monitor liver health in patients.

The study Dushyant V. et al. [16] discusses the use of CT perfusion to assess HCC vascularization and the correlation of CT perfusion parameters with tumor grade and serum markers. The study included 30 patients with unresectable or metastatic HCC. CT perfusion parameters including parenchymal blood flow, blood volume, mean transit time, and permeability surface area product were analyzed and compared among tumors of varying grades with or without portal vein invasion or cirrhosis, and with different extrahepatic metastases. The results showed a significant difference in CT perfusion parameters between primary HCC and liver parenchyma, with well-differentiated HCC demonstrating significantly higher perfusion values than other grades. There was no significant difference in tumor perfusion between the presence or absence of portal vein invasion or cirrhosis, and lymph node metastases had lower perfusion values compared with other extrahepatic metastases. In addition, the study found no significant correlation between CT perfusion parameters and serum markers.

Stashuk G. [9] in their study examined 61 patients with liver fibrosis and cirrhosis as a result of chronic viral hepatitis C, of which 26 patients underwent antiviral therapy (AVT) with the achievement of a sustained virological response (SVR) 24 weeks after the end of treatment. All patients underwent CT perfusion of the liver on a 256-slice Philips ICT computed tomography scanner (Netherlands). The parameters of arterial, portal, general perfusion and liver perfusion index were determined in each patient in segments III, VII and VIII of the liver using the linear regression method. The authors found that the use of direct-acting antivirals (DAAs) in patients with chronic hepatitis C virus infection provides a sustained virological response (SVR) in more than 90% of patients. Such therapy reduces the hepatic venous pressure gradient and promotes fibrosis regression. Elastography was used to assess the effectiveness of DAAs: in a 2020 study, a decrease in liver tissue stiffness was recorded 12 weeks after therapy in both

patients with fibrosis and cirrhosis, except for those with ascites.

After DAA, patients with liver fibrosis showed significant improvement in portal and total perfusion, as well as a decrease in the liver perfusion index, which is associated with a decrease in inflammation and regression of fibrosis. While patients with cirrhosis showed less effectiveness in improving perfusion, especially in severe stages of the disease. Thus, more than 90% of patients achieved a sustained virological response (SVR), indicating high efficacy of therapy against the hepatitis C virus. Patients with compensated cirrhosis show moderate improvements in perfusion, but in patients with decompensated cirrhosis, significant improvements

in blood flow are achieved less often. This confirms that severe stages of cirrhosis complicate the restoration of blood flow and the effectiveness of DAA. As the study showed, liver cirrhosis is an independent factor that limits the effectiveness of antiviral therapy, probably due to the already existing structural changes in the liver. These data highlight that the use of DAAs is preferable in the early stages of fibrosis, when the liver's regenerative capacity has not yet been lost.

Hayri O. et al. [3] in his work he compares the studies of other authors on changes in CT perfusion parameters in liver cirrhosis (Table 1).

Changes in CT perfusion parameters in liver cirrhosis

Table 1.

Study	Year	Quantity	BF	BV	ALP	PLP	HPI	MTT
Van Beers et al.	2001	34	-	-	-	-	↑	↑
Guan et al.	2005	14 (rats)	↓	↓	-	-	↑	↑
Hashimoto et al.	2006	38	↓	-	-	-	↑	-
Chen et al.	2009	39	-	-	-	-	-	↓
Li et al.	2011	22	↑	↑	↑	↑	-	-
Ippolito et al.	2012	45	-	↑	↑	↓	↑	-
Ma et al.	2013	40 (rats)	↓	↓	↑	↓	↑	↓

Note: ↑ - increase; ↓ - decrease; BF - blood flow; BV - blood volume; ALP - arterial liver perfusion; PLP - portal liver perfusion; HPI - liver perfusion index; MTT - mean transit time.

Liver perfusion was significantly reduced in patients with cirrhosis (67 ± 23 ml min⁻¹ x 100 ml⁻¹ versus 108 ± 34 ml min⁻¹ x 100 ml⁻¹ in the control group ($p = 0.009$) and 98 ± 36 ml min⁻¹ x 100 ml⁻¹ in patients with non-cirrhotic chronic liver disease ($p = 0.003$)). The arterial fraction was significantly increased in patients with cirrhosis ($41 \pm 27\%$ vs. $17 \pm 16\%$ in controls ($p = 0.022$) and $19 \pm 6\%$ in patients with non-cirrhotic chronic liver disease ($p = 0.004$)). The mean transit time was also significantly increased in patients with cirrhosis (51 ± 79 sec vs. 16 ± 5 sec in controls ($p < 0.001$) and 17 ± 8 sec in patients with non-cirrhotic chronic liver disease ($p < 0.001$)). There was no significant difference in the volume of distribution between the groups ($25.5 \pm 4.4\%$ in controls, $24.1 \pm 4.3\%$ in patients with non-cirrhotic chronic liver disease, and $28.9 \pm 8.6\%$ in patients with cirrhosis

($p = 0.22$)). There was no significant difference between the control group and patients with non-cirrhotic liver disease in any parameter [17].

At the diagnosis of cirrhosis, the areas under the ROC curves were 0.81 ± 0.07 for liver perfusion, 0.78 ± 0.08 for arterial fraction and 0.89 ± 0.05 for mean transit time. The areas under the ROC curves did not differ significantly (liver perfusion vs. arterial fraction, $p = 0.69$; liver perfusion vs. mean transit time, $p = 0.14$; arterial fraction vs. mean transit time, $p = 0.13$) (Fig. 4). The best cut-off point for differentiating patients with cirrhosis from patients without cirrhosis was considered to be a mean transit time of 22.6 sec, yielding a sensitivity and specificity of 81%. Increased vascular resistance in cirrhotic liver reduces portal perfusion. The decrease in portal perfusion is buffered by hepatic arteri-

alization, increasing the arterial fraction of liver perfusion. However, the increase in arterial perfusion is often insufficient to maintain total liver perfusion in cirrhosis due to high extrahepatic porto-systemic shunting, which explains why the authors observed a decrease in total liver perfusion. The authors found that perfusion parameters measured by CT tended to be altered in patients

with non-cirrhotic chronic liver disease. Some hemodynamic changes may occur in the liver before the development of cirrhosis. However, the differences between control subjects and patients with non-cirrhotic chronic liver disease did not reach statistically significant levels in the patient group. In contrast, perfusion parameters were significantly altered in cirrhosis (Table 2).

Perfusion parameter	Severity of the disease					r	p
	Norm (n = 6)	Non-cirrhotic liver diseases (n = 16)	Child A (n = 7)	Child B (n = 7)	Child C (n = 4)		
Liver perfusion (ml min ⁻¹ 100 ml ⁻¹)	108 ± 34 (99)	98 ± 36 (95)	70 ± 22 (64)	69 ± 30 (58)	56 ± 13 (54)	-0,55	< 0,001
Arterial fraction (%)	17 ± 16 (16)	19 ± 6 (19)	24 ± 9 (24)	38 ± 20 (41)	75 ± 30 (85)	0,59	< 0,001
Volume of distribution (%)	25,5 ± 4,4 (24,2)	24,1 ± 4,3 (23,5)	23,4 ± 2,1 (23,7)	33,9 ± 8,7 (36,6)	29,4 ± 11,7 (30,6)	0,29	0,07
Mean transit time (sec)	16 ± 5 (16)	17 ± 8 (17)	72 ± 12 ^a (39)	33 ± 9 (33)	45 ± 21 (42)	0,70	< 0,001

Note: Each row shows the correlation (r) and significance (p) between the five disease severity classes and a given perfusion parameter. Data are presented as mean ± standard deviation; median is shown in parentheses. Child A, Child B, and Child C classification refer to the Child-Pugh classification. ^aThe mean transit time in patients with Child A cirrhosis is higher than in Child B patients due to one patient with a high transit time.

Table 2. Correlations between liver disease severity and perfusion parameters

The table above demonstrates significant changes in liver perfusion and arterial fraction, indicating deterioration of liver blood supply with disease progression. Thus, until now, CT perfusion of the liver has not been a diagnostic method of choice for liver diseases and has been used for scientific purposes to study changes in its blood flow. However, CT perfusion measures parameters such as blood flow, blood filling and mean transit time, which gives a more complete picture of early functional changes in the liver. This can be especially useful for the early detection of microcirculation disorders that are difficult to detect using traditional CT or MRI. Most of the available scientific studies are aimed at studying changes in the perfusion of

liver lesions, in particular, changes in blood flow in HCC and in dynamics, after its treatment. Also, the results of CT perfusion of the liver in cirrhosis have been obtained, proving hemodynamic changes with its progression. To date, there are a limited number of studies devoted to CT perfusion of the liver in its fibrotic changes and different stages. Ronot M. et al.; Stashuk G. et al. [2,9] in their studies obtained correlated data on hemodynamic changes in the liver with fibrosis of 1, 2 and 3 degrees in the outcome of viral hepatitis C. The development of liver fibrosis with different etiologies and stages of the disease remains incompletely studied and relevant, since obtaining data on early changes in liver perfusion will allow timely treatment

and delay the development of decompensated liver cirrhosis [18].

What's known: CT perfusion has long been utilized as a valuable imaging tool in oncology to evaluate tumor vascularity, detect angiogenesis, and monitor responses to therapies. In the context of liver pathology, previous research has shown its capability to distinguish between benign and malignant lesions by analyzing perfusion parameters such as blood flow (BF), blood volume (BV), and mean transit time (MTT). Studies have indicated that these parameters often vary significantly in conditions like hepatocellular carcinoma (HCC), cirrhosis, and fibrosis, providing insight into how perfusion changes reflect disease severity and progression.

What's new: Recent studies expand the application of CT perfusion in liver disease, emphasizing its potential to non-invasively monitor chronic liver conditions beyond oncology. Findings show that perfusion metrics can differentiate stages of fibrosis and cirrhosis, detect early hemodynamic changes, and assess liver health more precisely. Furthermore, the studies highlight the promising role of CT perfusion in evaluating the effectiveness of antiviral therapies, such as direct-acting antivirals (DAAs) for hepatitis C, by demonstrating perfusion improvements correlated with fibrosis regression. However, they also note challenges related to standardizing CT perfusion protocols, which could affect its broader clinical adoption.

Limitations: CT perfusion methodology and parameters may vary depending on the equipment and protocols used. The lack of standard values and interpretation methods limits the reproducibility of results and makes it difficult to compare data between different studies, which reduces the clinical applicability of the method for monitoring chronic liver diseases.

Conclusion

The reviewed studies underscore the value of CT perfusion in assessing liver pathology, especially in differentiating between benign and malignant lesions and tracking liver disease progression, including cirrhosis and fibrosis. Perfusion parameters like blood flow (BF), blood volume (BV), mean transit time (MTT), and induced residual fraction time to onset (IRFTO) show significant promise as biomarkers, offering insights into vascular changes associated with liver diseases. Particularly in oncology, perfusion CT enables early detection of tumor angiogenesis, monitoring of therapeutic effects, and prediction of patient outcomes. Additionally, in patients with chronic liver diseases, changes in CT perfusion parameters correlate with the severity of fibrosis and cirrhosis, highlighting the potential for CT perfusion to be a useful, non-invasive tool for monitoring disease progression. Despite this promise, standardization of CT perfusion techniques remains a challenge, limiting its broad clinical adoption. Nonetheless, as techniques advance and protocols are refined, CT perfusion could become a vital imaging tool in diagnosing and managing chronic liver diseases and hepatic malignancies.

Authors' Contributions: Conceived and designed the study: D.Z.; Collected the data: B.G., K.Ye., M.A., N.D.; Contributed data or analysis tools: K.A., M.A.; Performed the analysis: D.Z., B.G.; Written the paper: D.B., B.G., K.Ye., M.A., N.D.; authors have approved the final version of the article.

Conflict of interest: The authors declare no conflict of interest.

Funding: The study was conducted under grant funding AP23488602 of the scientific and technical project "CT perfusion in the diagnosis of chronic liver disease" for 2024-2026.

References

1. Yamazaki S., Takayama T., Mitsuka Y., et al. Predictive value of perfusion CT for blood loss in liver resection. *Biosci Trends*. 2020;14(5):384-389. doi:10.5582/BST.2020.03303
2. Ronot M., Leparq B., Van Beers B., Vilgrain V. CT and MR perfusion techniques to assess diffuse liver disease. *Abdom Radiol (NY)*. 2020;45(11):3496-3506. doi:10.1007/S00261-019-02338-Z
3. Oğul H., Kantarci M., Genç B., et al. Perfusion CT imaging of the liver: review of clinical applications. *Diagn*

- Interv Radiol. 2014;20(5):379-389. doi:10.5152/DIR.2014.13396
4. Virarkar M., Morani A., Taggart M., Bhosale P. Liver Fibrosis Assessment. *Semin Ultrasound CT MR*. 2021;42(4):381-389. doi:10.1053/J.SULT.2021.03.003
 5. Van Beers BE., Leconte I., Materne R., Smith A., Jamart J., Horsmans Y. Hepatic perfusion parameters in chronic liver disease: dynamic CT measurements correlated with disease severity. *AJR Am J Roentgenol*. 2001;176(3):667-673. doi:10.2214/AJR.176.3.1760667
 6. Yaraş S., Sezgin O., Üçbilek E., Özdoğan O., Altıntaş E. Significant decrease in liver stiffness detected by two dimensional shear-wave elastography after treatment with direct-acting antiviral agents in patients with chronic Hepatitis C. *Turk J Gastroenterol*. 2020;31(2):142-147. doi:10.5152/TJG.2020.19418
 7. Lurie Y., Webb M., Cytter-Kuint R., Shteingart S., Lederkremer GZ. Non-invasive diagnosis of liver fibrosis and cirrhosis. *World J Gastroenterol*. 2015;21(41):11567-11583. doi:10.3748/WJG.V21.I41.11567
 8. Singh S., Venkatesh S., Wang Z., et al. Diagnostic performance of magnetic resonance elastography in staging liver fibrosis: a systematic review and meta-analysis of individual participant data. *Clin Gastroenterol Hepatol*. 2015;13(3):440-451.e6. doi:10.1016/J.CGH.2014.09.046
 9. Stashuk G., Moysyuk Y., Smirnova D., Sumtsova O V. КТ-перфузия печени как неинвазивный метод оценки гемодинамики печеночной паренхимы у пациентов с фиброзом и циррозом в исходе хронического вирусного гепатита С. *Вестник рентгенологии и радиологии*. 2022;102(6):359-368. doi:10.20862/0042-4676-2021-102-6-359-368
 10. Kim SH., Kamaya A, Willmann JK. CT perfusion of the liver: principles and applications in oncology. *Radiology*. 2014;272(2):322-344. doi:10.1148/RADIOL.14130091
 11. Sahani D. Perfusion CT: An Overview Of Technique And Clinical Applications. Published online 2010.
 12. Miles K. Perfusion CT for the assessment of tumour vascularity: which protocol? *Br J Radiol*. 2003;76 Spec No 1(SPEC. ISS. 1). doi:10.1259/BJR/18486642
 13. Cressoni M., Cozzi A, Schiaffino S, et al. Computation of contrast-enhanced perfusion using only two CT scan phases: a proof-of-concept study on abdominal organs. *Eur Radiol Exp*. 2022;6(1). doi:10.1186/S41747-022-00292-Y
 14. Wang L., Zhang Y., Wu Y., et al. Computed tomography perfusion in liver and spleen for hepatitis B virus-related portal hypertension: A correlation study with hepatic venous pressure gradient. *World J Gastroenterol*. 2022;28(42):6068-6077. doi:10.3748/WJG.V28.I42.6068
 15. Gadupudi V., Ramachandran R., Pulivadula M., et al. The Role of Computed Tomography Perfusion in Various Focal Liver Lesions. *Cureus*. 2022;14(12). doi:10.7759/CUREUS.32420
 16. Sahani V., Holalkere N., Mueller P., Zhu A. Advanced hepatocellular carcinoma: CT perfusion of liver and tumor tissue--initial experience. *Radiology*. 2007;243(3):736-743. doi:10.1148/RADIOL.2433052020
 17. Ippolito D., Sironi S., Pozzi M., et al. Perfusion CT in cirrhotic patients with early stage hepatocellular carcinoma: Assessment of tumor-related vascularization. *Eur J Radiol*. 2010;73(1):148-152. doi:10.1016/j.ejrad.2008.10.014
 18. Breguet R., Ronot M., Goossens N., et al. Liver volume is a prognostic indicator for clinical outcome of patients with alcoholic hepatitis. *Abdominal Radiology*. 2017;42(2):460-467. doi:10.1007/s00261-016-0892-7

ФОТИАДИ ЮРИЙ КУЗЬМИЧ



Фотиади Юрий Кузьмич родился в 1949 году в городе Белореченске Краснодарского края, Российской Федерация, по национальности – грек. Образование высшее - в 1966 году поступил в Актюбинский государственный медицинский институт, в 1973 году успешно окончил указанное учебное заведение по специальности «Лечебное дело» и получил квалификацию «Врач».

Трудовую деятельность начал врачом скорой помощи Кызылординской городской больницы в 1973 году, в феврале 1976 года стал хирургом городской больницы №1, с марта 1980 года — хирургом Кызылординской городской больницы, с 1996 по 2017 год — заведующий хирургическим отделением, с 2017 года – врач хирург, с 2019 года – работает врачом хирургом-консультантом.

За годы работы молодым специалистом Ю. К. Фотиади был главным врачом городской больницы был Омаров Ернияз Омарулы, а Оразов Капланбек Баликбайулы – заведующим хирургическим отделением. При поддержке этих квалифицированных руководителей Юрий Кузьмич познал все тайны и направления медицинской сферы. Врач, подготовленный этими людьми, несомненно, будет лучшим в области медицины. Однако, не ограничиваясь

этим, благодаря своей любознательности, в ходе совершенствования своих знаний, он постоянно повышал их в странах дальнего и ближнего зарубежья, в частности: в Москве, России, в городах Казани, Республика Татарстан, в городе Уфе, Башкортостан, в городе Харькове, Украина, осваивая современные инновации в области хирургии своего времени и помогая больным вставать на ноги.

Юрий Кузьмич честно и достойно выполнял свои служебные обязанности и первым в больнице применил современный диагностический и лечебный метод лапароскопии, позволяющий выполнять ваготомические операции при лечении язв желудка и двенадцатиперстной кишки, выявлять заболевания органов грудной и брюшной полости, органов с помощью специального оптического инструмента, и в то же время он реализовал методы Линтона при выполнении операций при патологиях вертикальных границ и выполнении операций на синих венах ног, а также не уставал руководить и обучать молодых хирургов.

Высококласный хирург-консультант, квалифицированный врач, человек, заслуживший искреннюю благодарность среди народа. Юрий Кузьмич – один из врачей, перенесших в ходе оказания медицинской помощи множество серьезных операций, и, благодаря своему мастерству, помог многим пациентом. У него также сильно развита интуиция, благодаря чему и своему опыту, он точно ставил диагноз пациента, используя свою мастерство для выполнения сложных видов операций и в общей сложности принял участие в около 10 000 операциях.

По его показаниям, поставленные им диагнозы каждый раз подтверждались. Это конечно приходит с накопленным опытом, благодаря долгой и упорной работе.

Квалифицированный врач Юрий Кузьмич известен в народе как «Врач с золотыми руками».

За свой многолетний и честный труд он получил множество наград, в 2018 году награжден медалью «Золотой доктор». В 2023 году награжден «Знаком отличия» Министерства здравоохранения Республики Казахстан. Консультант-хирург доктор Фотиади Юрий Кузьмич – врач, который не устает обучать и направлять идущих за ним молодых специалистов, давать советы и оказывать медицинскую помощь. Человек, пользующийся уважением среди коллег и благодарностью от пациентов.



Хирургическая служба Республики Казахстан понесла невосполнимую утрату. С глубоким сожалением сообщаем об уходе из жизни выдающегося хирурга и учёного, одного из основоположников хирургии печени, желчных путей и поджелудочной железы Казахстана, основателя большой хирургической школы, председателя Казахстанского общества хирургов, Лауреата Государственной премии Республики Казахстан, доктора медицинских наук, профессора СЕЙСЕМБАЕВА МАНАСА АХМЕТЖАРОВИЧА.

Манас Ахметжарович Сейсембаев родился 2 июня 1950 года в городе Караганда. После окончания средней школы поступил на лечебный факультет Семипалатинского государственного медицинского института, который окончил в 1973 г. С 1974 г. по 1977 г. работал врачом-хирургом, затем заведующим отделением Большеарымской районной больницы Восточно-Казахстанской области. В 1977–1978 гг. М.А. Сейсембаев работал хирургом в отделении экстренной хирургии Центральной городской клинической больницы г. Алматы. В 1978 г. перешел на должность заведующего хирургическим отделением Республиканского клинического госпиталя инвалидов Отечественной войны (г. Алматы). С 1980 г.

по 1991 г. – научный сотрудник, а затем старший научный сотрудник отделения хирургии печени, желчевыводящих путей и поджелудочной железы НИИ клинической и экспериментальной хирургии им. А.Н. Сызганова (г. Алматы). В 1988 г. защитил кандидатскую диссертацию «Выбор рациональной хирургической тактики при стойкой механической желтухе». С 1991 г. по 1998 г. – заведующий отделом торакоабдоминальной хирургии того же учреждения. В 1995 г. защитил докторскую диссертацию «Диагностика и хирургическое лечение постхолецистэктомических заболеваний».

В 1988 г. Манас Ахметжарович избран членом-корреспондентом Национальной академии наук РК. В 1997 г. М.А. Сейсембаеву присвоено ученое звание профессора медицины. В 1998–2001 гг. являлся заведующим отделением хирургии печени, желчевыводящих путей и поджелудочной железы, с 2001 г. по 2003 г. – директор Научного центра хирургии им. А.Н. Сызганова. В 2003–2008 гг. – начальник Республиканского клинического госпиталя инвалидов Отечественной войны г. Алматы. С 2008 по 2010 г. вновь заведовал отделением хирургии печени, желчевыводящих путей и поджелудочной железы Национального научного центра. С 2010 г. по 2011 г. М. А. Сейсембаев назначен генеральным директором АО «ННЦХ им. А.Н. Сызганова», а в 2011 г. Манас Ахметжарович избран председателем совета директоров АО «ННЦХ им. А.Н. Сызганова».

С его именем связаны все основные достижения ННЦХ им. А.Н. Сызганова в области хирургии печени, желчных путей и поджелудочной железы. Являясь соратником и учеником М.А. Алиева, Манас Ахметжарович Сейсембаев с первых лет работы отделения руководил экспериментальными и клиническими исследованиями по проблемам лечения желчно-каменной болезни и его осложнений, ятрогенных повреждений желчных путей, постхолецистэктомическим синдромом, очаговых и диффузных заболеваний

печени и поджелудочной железы. Под руководством М.А. Сейсембаева изучались и разрабатывались способы малоинвазивных и пункционных способов лечения, реконструктивных и восстановительных операций на желчных путях.

Большая исследовательская работа была проведена по изучению способов лечения осложненного и неосложненного эхинококкоза печени. Центр проводил исследования по использованию различных способов обработки остаточных полостей с использованием лазера, электрических, плазменных и криогенных технологий, были разработаны и усовершенствованы методы их проведения.

Под руководством и непосредственном участии М.А. Сейсембаева, Центр одним из первых в Казахстане начал исследования по проблемам лечения циррозов печени у взрослых и детей.

Большой объем исследований был посвящен изучению и внедрению резекционных и реконструктивно-пластических операций при заболеваниях поджелудочной железы, начиная с использования малоинвазивных способов и до объемных реконструктивно-восстановительных вмешательств.

Под руководством М.А. Сейсембаева Центр активно внедрял лапароскопические технологии в гепатопанкреатобилиарную хирургию.

М.А. Сейсембаев активно проводил организаторскую работу, в течение многих лет руководил Обществом хирургов г. Алматы и Алматинской области. В 2015 г. избран Президентом Республиканского общественного объединения «Казахстанское общество хирургов».

Научно-практическую деятельность совмещал с педагогической деятельностью, в качестве профессора хирургических кафедр медицинских университетов, читал лекции и проводил семинары.

Автор более 350 научных работ, в том числе около 160 научных статей, опубликованных в ведущих научных журналах Казахстана и России, 9 монографий и методических руководств, 70 авторских свидетельств на изобретение (положительных патентов на изобретения РК). Под руководством профессора М.А. Сейсембаева защищено 7 докторских и 15 кандидатских диссертаций.

За вклад в развитие здравоохранения и трудовые заслуги М.А. Сейсембаев награжден Почетной грамотой Президента Республики Казахстан (1995 г.), нагрудным знаком «Отличник здравоохранения РК» (2006 г.), орденом им. Н.И. Пирогова (2011 г.), «Золотой медалью» Казахстанской ассоциации эндоскопических хирургов (2013 г.), медалью «Еңбек ардагері» (2017 г.).