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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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NON-INVASIVE QUANTITATIVE CT PERFUSION OF THE LIVER IN AUTOIMMUNE HEPATITIS

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Abstract.

Objective of the study: Computed tomography (CT) perfusion provides a non-invasive approach to assessing hemodynamic alterations in chronic liver diseases. While its usefulness has been demonstrated in viral hepatitis, evidence regarding autoimmune hepatitis (AIH) remains limited. This study aimed to compare CT perfusion parameters - arterial flow (AF), portal flow (PF), and perfusion index (PI) – in patients with AIH – related fibrosis and cirrhosis versus healthy controls (potential liver donors).

Materials and methods: In this single-center prospective study, 21 patients with AIH-related fibrosis and 17 patients with AIH-related cirrhosis were compared with 20 potential living liver donors, i.e. the control group. CT perfusion parameters, including AF, PF and PI were calculated.

Results: Histological staging identified fibrosis stages (F1-F3 stage fibrosis) in 21 patients and cirrhosis (F4) in 17 patients. Inflammatory activity grades ranged from A1 to A4. AF was significantly elevated in both AIH-fibrosis ($p < 0.001$) and AIH-cirrhosis ($p = 0.001$) compared with the control group, but did not differ significantly between fibrosis and cirrhosis ($p = 0.294$). PF was significantly reduced in AIH-fibrosis ($p = 0.001$) and AIH-cirrhosis ($p < 0.001$) compared with controls, with no significant difference between fibrosis and cirrhosis ($p = 0.084$). Both AF and PF demonstrated high sensitivity (95%) in differentiating patients for both AIH-related fibrosis and cirrhosis from the control group.

Conclusion: Increased AF and reduced PF, already evident at the fibrosis stage, may serve as non-invasive markers of AIH-related liver injury severity.

Key words. CT perfusion, autoimmune hepatitis, liver fibrosis.

Introduction.

Chronic liver diseases cover a spectrum of conditions including chronic hepatitis, liver fibrosis and cirrhosis. Liver biopsy is currently considered the gold standard for assessing the extent of fibrosis and cirrhosis [1]. However, it is an invasive and potentially risky procedure associated with pain and, in some cases, life-threatening complications [2]. This has created an urgent need for reliable non-invasive or minimum invasive markers for the diagnosis of chronic liver diseases.

Computed tomography (CT) perfusion has emerged as a promising imaging technique for detecting liver pathological changes before the development of cirrhosis, even at early stages of fibrosis [3]. Thus, CT perfusion parameters enable the assessment of the severity of chronic liver diseases. Previous studies have examined CT perfusion in cases of viral hepatitis B and C, demonstrating its potential advantage in quantifying perfusion changes in fibrosis and cirrhosis [2,4,5]. However, data on autoimmune liver diseases remain scarce.

Autoimmune hepatitis (AIH) is an immune-mediated liver disease with a dynamic and heterogeneous clinical course. Diagnosis of AIH is difficult owing to the lack of specific disease features and it relies on the combination of the following: (1) histological features of hepatitis and (2) laboratory data, including elevated aminotransferases (AST and ALT), autoantibodies (anti-smooth muscle antibodies (ASMA) and/or anti-nuclear antibodies (ANA)), and immunoglobulin G (IgG). AIH can occur in patients of a wide age range, with variable serological markers and a diverse clinical spectrum from asymptomatic to fulminant liver failure [6,7].

In cases of decompensated cirrhosis or acute liver failure, liver transplantation is indicated [8]. Non-invasive imaging techniques are being increasingly used to complement histological examination. Ultrasound elastography is valuable for monitoring disease progression in treated patients with AIH, although liver inflammation may confound liver stiffness measurements, sometimes leading to false-positive results. It has been shown that in patients treated for less than three months, liver stiffness correlates more strongly with histologic grade (inflammatory activity) than with stage (fibrosis). Modern imaging techniques such as elastography, magnetic resonance imaging (MRI) can differentiate cirrhosis or advanced fibrosis from normal liver. However, the accurate staging of early fibrosis remains challenging [9].

Thus, there remains a crucial need for a non-invasive yet reliable method for the assessment of autoimmune liver injury. CT perfusion, which enables quantitative evaluation of hemodynamic changes in hepatic microcirculation, may fill this diagnostic gap. The aim of this study was to compare CT perfusion parameters, including arterial flow (AF), portal flow (PF), and perfusion index (PI), in patients with fibrosis and cirrhosis secondary to AIH with those of a control group (potential liver donors).

Materials and Methods.

This study was approved by the Ethics Committee of the National Scientific Surgery Center named after A.N. Syzganov ((Approval No. 4 (92) dated 10th of November 2023).

Study design and population:

This single-center prospective study was conducted between December 2023 and April 2025 and included 21 patients with AIH-related liver fibrosis and 17 patients with AIH-related liver cirrhosis. The control group consisted of 20 potential related living liver donors.

Inclusion criteria (AIH group): patients of both genders, over

18 years, with serologically, biochemically and histologically confirmed liver fibrosis or cirrhosis secondary to autoimmune hepatitis Type 1 before basis therapy.

Exclusion criteria (AIH group): viral hepatitis, drug-induced hepatitis, other types of autoimmune liver disease (primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), and overlap with AIH syndromes), acute stage of AIH, Wilson's disease, hemochromatosis, non-alcoholic steatohepatitis, focal liver lesions, hepatic vein abnormalities (thrombosis, cavernous transformation), history of splenectomy, dysfunction of vital organs (cardiac, renal, or respiratory failure), and refusal to participate.

Inclusion criteria (control group): potential donors for living donor liver transplantation with clinically and radiologically confirmed healthy livers.

Exclusion criteria (control group): donors with hepatic steatosis >5% confirmed by biopsy, focal liver lesions (cysts or hemangiomas), and refusal to participate.

A flowchart illustrating the patient selection process is presented in Figure 1.

The patients were diagnosed based on laboratory, immunological, serological, diagnostic and clinical data. The severity of AIH-related cirrhosis was assessed utilising the Child-Pugh score. Electronic medical records were reviewed to collect the data on patients' characteristics, including age, sex, body mass index (BMI), laboratory and serological findings.

CT acquisition protocol:

CT perfusion imaging was performed in the cranio-caudal direction using a 160-slice MDCT scanner (Aquilion Prime SP, Canon Medical Systems, Japan). Scan parameters included a tube voltage of 80 kVp, tube current of 30 mAs, gantry rotation time of 0.5 s, and slice thickness of 0.5 mm, with a detector coverage of 8 cm. Patients were instructed to maintain shallow breathing without deep inspiration or breath-holding during image acquisition.

Initially, an unenhanced scan was acquired for anatomical localization of abdominal organs. Intravenous contrast medium was then administered via a 20-G cubital vein catheter using a dual-syringe automated power injector (Ulrich, Germany). A non-ionic iodinated contrast agent (Ultravist 370 mgI/mL; Schering, Berlin, Germany) was injected at a dose of 50 mL; in patients with obesity, the dose was increased to 60 mL. The injection rate was 4.5-5.0 mL/s. The dynamic perfusion scan lasted 92 seconds and consisted of a single pre-contrast acquisition, followed by 20 consecutive scans at 4-second intervals and additional 3 scans at 5-second intervals.

Image post-processing:

Two radiologists with 7 and 12 years of experience in abdominal radiology, respectively, who were blinded to the clinical and histopathological data, independently performed image post-processing. Perfusion analysis was conducted using the dedicated workstation Vitrea (Canon Medical Systems, USA) with the "4D Dual Input Liver" application.

Perfusion values were calculated using a dual-input maximum slope model. Regions of interest (ROIs) were manually placed in the abdominal aorta, portal vein, hepatic parenchyma, and spleen, with a graph generated to produce time-density curves (TDC). For the liver, ROIs were positioned within segments III, IV, VI, VIII, carefully avoiding peripheral areas and large vessels. The ROI size was set to >1.0 cm². Perfusion parameters: arterial flow (AF) ml/min/100 ml, portal flow (PF) ml/min/100 ml and perfusion index (PI; AF/(AF + PF)) % were calculated on perfusion maps (Figure 2).

Ultrasound examination and liver biopsy:

All patients, including those in the control group (potential liver donors), underwent abdominal ultrasound examination (Hitachi, Japan) by a radiologist with 15 years of experience in order to exclude focal liver lesions, hepatic steatosis, and hepatic venous pathology (thrombosis, occlusion, or cavernous transformation).

Subsequently, percutaneous liver biopsy was performed under ultrasound guidance in patients with liver fibrosis and cirrhosis secondary to AIH 10-14 days before CT perfusion. Before the

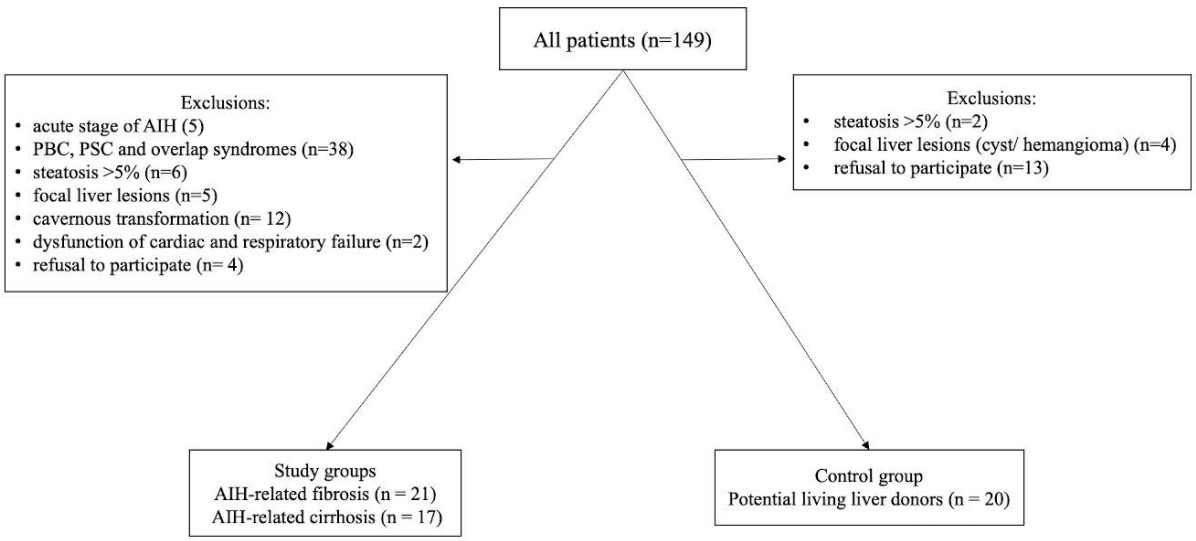

Figure 1. *Flowchart of study exclusion criteria.*

operation, blood routine examination and blood clotting time detection were conducted. Under local anesthesia and after aseptic preparation of the surgical field, a puncture needle was advanced into the peritoneal cavity through the right intercostal space. The passage of the needle through the liver capsule and into the parenchyma (segment VIII) was confirmed by both real-time ultrasound visualization and tactile feedback. Tissue sampling was conducted using an automated biopsy device (Pro-Mag™ Ultra, Canada) equipped with a 16-G × 20 cm needle. A single liver core biopsy specimen was obtained, measuring 19 mm in length.

Histopathologic analysis:

Tissue samples were fixed in 10% neutral buffered formalin. The specimens were then dehydrated using a standard protocol in a closed-system tissue processor (Thermo SCIENTIFIC Excelsior AS, USA) and embedded in paraffin. Paraffin sections 4-5 μm thick were cut on a rotary microtome (Sakura Accu-Cut SRM 200, Japan). For routine examination, the sections were stained with hematoxylin using the automated stainer (Thermo SCIENTIFIC Gemini AS, USA). Histochemical analysis was performed with the following staining methods: Masson's trichrome, Schiff's reagent, Perls' Prussian blue, orcein, and silver impregnation.

Prepared slides were examined under microscopes (ZEISS AXIO Imager Z2, Germany) equipped with an Axiocam 506 color camera and ZEISS ZEN Imaging Software.

The assessment of fibrosis and inflammatory activity was performed using the modified Ishak classification and the Batts-Ludwig system, with correlation to the Meta-analysis of Histological Data in Viral Hepatitis (METAVIR) score.

Statistical analysis:

Descriptive statistics are reported as mean ± standard deviation (SD) for normally distributed variables and as median with interquartile range (IQR) for non-normally distributed variables. The normality of distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests.

Interobserver agreement between the two radiologists was evaluated using the interclass correlation coefficient (ICC), which was calculated on the full dataset with 95% confidence intervals (CI).

Group comparisons of CT perfusion parameters were performed using one-way ANOVA test followed by the post hoc test or the Kruskal-Wallis test.

The diagnostic value of CT perfusion parameters for AIH-fibrosis and AIH-cirrhosis was evaluated using the receiver operating characteristic (ROC) curve analysis, with calculation of the area under the curve (AUC), sensitivity, and specificity.

A p value < 0.05 was considered to indicate statistical significance.

All statistical analyses of the data were performed using IBM SPSS statistics (version 27).

Results.

Biopsy results:

Among AIH-fibrosis patients the stage F1 was observed in 10 patients, F2 in 7 patients, F3 in 4 patients, and F4 (AIH-cirrhosis) in 17 patients. The degree of inflammatory activity was A1 in 12 patients, A2 in 16 patients, A3 in 7 patients, and A4 in 3 patients.

Laboratory data:

Among AIH-cirrhosis patients according to the Child-Pugh score, Class A was identified in 9 patients, Class B in 7 patients, and Class C in 1 patient.

The mean age of patients with fibrosis was 40.8 ± 14.4 years, of those with cirrhosis was 41.2 ± 15.3 years, and of liver donors was 31.9 ± 8.6 years. No statistically significant differences were found between the groups in terms of age ($p = 0.51$) and gender ($p = 0.820$), while the body mass index (BMI) of the donors was significantly lower in comparison with the AIH-fibrosis and AIH-cirrhosis groups ($p = 0.002$). Laboratory tests showed proportionally elevated ALT and AST levels in both AIH-fibrosis and AIH-cirrhosis groups ($p = 0.794$ and $p = 0.055$ respectively). ANA tested positive in 85.7% of patients with AIH-fibrosis, and in 94.1% of patients with AIH-cirrhosis. ASMA tested positive in 76.2% and 88.2% of patients with AIH-fibrosis and AIH-cirrhosis, respectively, while IgG tested positive in 85.7% and 88.2% of patients with AIH-fibrosis and AIH-cirrhosis, respectively (Table 1).

Patients with AIH-fibrosis had a mean BMI of 25.9 ± 4.1, those with AIH-cirrhosis had 25.1 ± 3.3, whereas the control group demonstrated a lower mean BMI of 22.1 ± 3.4. One-way ANOVA confirmed a statistically significant difference in BMI among the groups ($p = 0.002$).

To assess whether differences in BMI between the groups affected perfusion measurements, an ANCOVA was performed with BMI included as a covariate. The analysis demonstrated that BMI had no significant effect on AF ($p = 0.485$) or PF ($p = 0.269$) in patients with both fibrosis and cirrhosis. After BMI adjustment, the differences in AF and PF between groups remained statistically significant, indicating that BMI did not confound the observed perfusion patterns.

Inter-observer agreement:

For the assessment of inter-observer fluctuation, two radiologists (Radiologist 1 and Radiologist 2) independently calculated CT perfusion parameters AF and PF. The ICC was high for the CT perfusion parameter AF: 0.885, 95% CI (0.790-0.939), as well as for PF: ICC 0.730, 95% CI (0.476-0.861) in AIH-fibrosis and AIH-cirrhosis patients. In the control group (liver donors), ICC values were also high: AF: 0.885, 95% CI (0.790-0.939) and PF: ICC 0.722, 95% CI (0.299-0.890). Subsequently, the mean values of AF and PF were used for further analysis.

CT perfusion parameters:

The Kruskal-Wallis test and one-way ANOVA test have revealed a statistically significant increase in AF values in AIH-fibrosis ($p < 0.001$) and AIH-cirrhosis ($p = 0.001$) patients compared to those in the control group. However, no statistically significant difference was found between AF values in AIH-fibrosis patients with AIH-cirrhosis ($p = 0.294$) patients.

The CT perfusion parameter PF was significantly decreased in AIH-fibrosis patients ($p = 0.001$) and AIH-cirrhosis patients ($p < 0.001$) compared to PF values in the control group, whereas no statistically significant difference was found between PF

values in patients with AIH-fibrosis and AIH-cirrhosis (p = 0.084) patients (Table 2 and Figure 3).

For each parameter and each disease subgroup, the area under the ROC curve (AUC) with 95% confidence intervals (CI), optimal cut-off values, as well as sensitivity and specificity are provided (Figure 4).

AF demonstrated high sensitivity (95%) for both AIH-fibrosis and AIH-cirrhosis, with specificity values of 71% and 70% respectively. PF also showed high sensitivity (95%), with specificity of 60% for AIH-fibrosis and 76% for AIH-cirrhosis. Detailed data are presented in Table 3.

Discussion.

The liver possesses unique hemodynamic characteristics, with two inflow pathways (via hepatic artery and portal vein) and a single outflow (via hepatic veins). The magnitude of hepatic blood flow changes depending on the background parenchymal injury, such as fibrosis or cirrhosis [10]. In cirrhosis, caused by damage to hepatic sinusoids and lobular structure, portal venous inflow encounters increased resistance. As the portal pressure rises, the overall hepatic blood supply decreases. Compensatory hepatic arterial perfusion may increase. However, portal venous inflow accounts for approximately three-quarters of total hepatic blood supply. Therefore, the compensatory increase in arterial perfusion cannot fully restore the substantial reduction in portal venous flow. This so-called “buffer response” is insufficient to maintain adequate hepatic perfusion [11,12].

Previous studies have shown that abnormal liver perfusion represents a key pathophysiological alteration in cirrhosis [13]. Wang et al. [14] reported that arterial enhancement fraction (AEF) values were higher in patients with advanced cirrhosis compared with those with milder cases. This suggests that

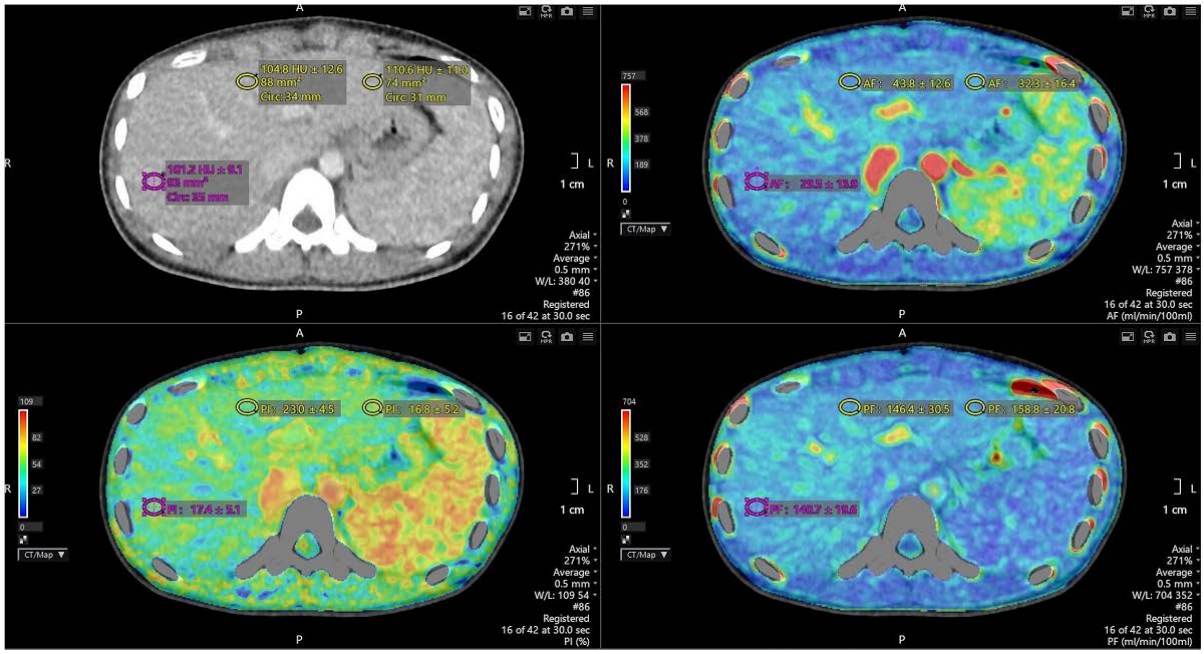

Figure 2. *Perfusion maps: arterial flow (AF) – right top, portal flow (PF) – right bottom, perfusion index (PI) – left bottom.*

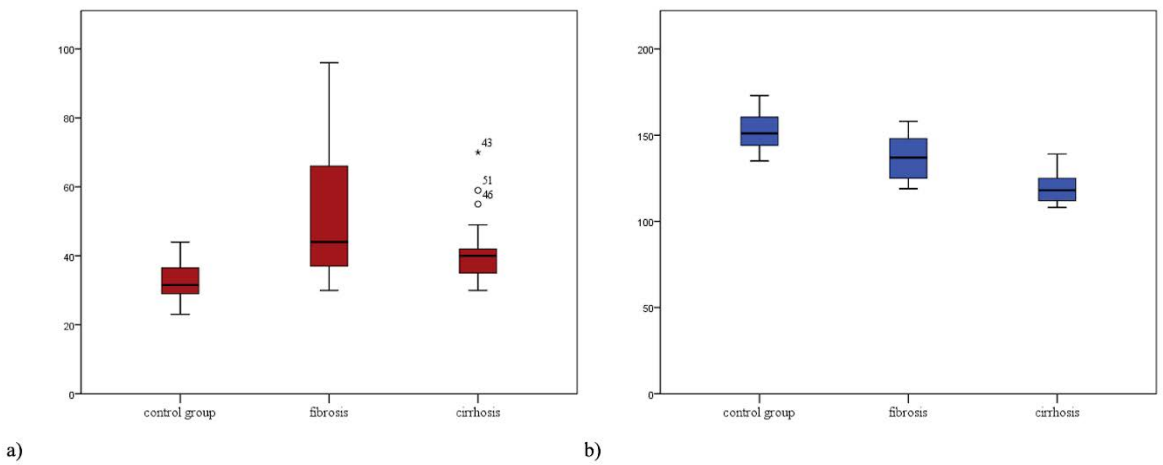

Figure 3. *Boxplot illustrating a) AF values in the control, AIH-fibrosis and AIH-cirrhosis groups and b) PF values in the control, AIH-fibrosis and AIH-cirrhosis groups.*

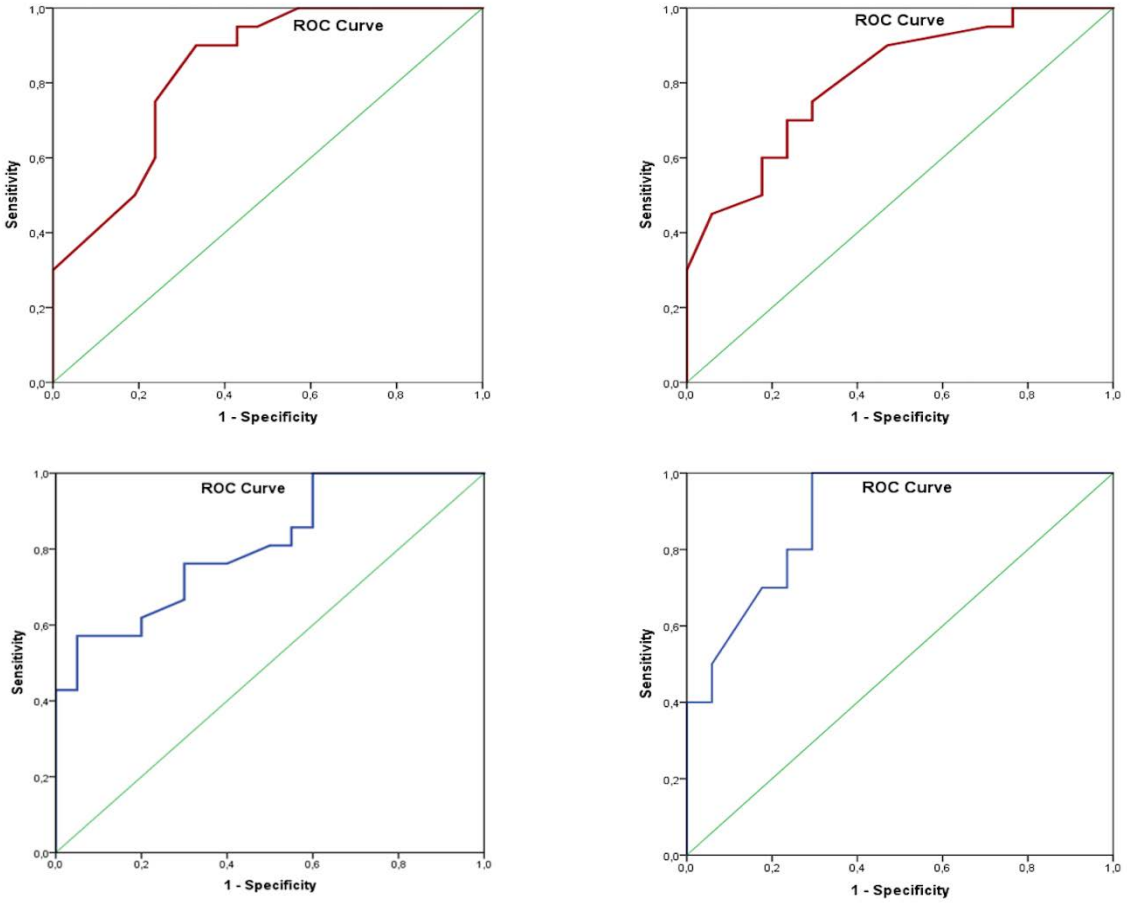

Figure 4. *Receiver operating characteristic curve to differentiate AF parameter for AIH-fibrosis (left top) and AIH-cirrhosis (right top) with control group, and PF parameter for AIH-fibrosis (left bottom) and AIH-cirrhosis (left bottom) with control group.*

Table 1. *Baseline characteristics of study groups.*

Parameters	AIH-fibrosis	AIH- cirrhosis	Control	p- value
Age (years)	40.8±14.4	41.2±15.3	31.9±8.6	0.510
BMI (kg/m^2)	25.9±4.1	25.1±3.3	22.1±3.4	0.002
Gender (male:female)	3:18	4:13	9:11	0.820
ALT (U/L)	92.2±10.5	87.8±8.2	N/A	0.794
AST (U/L)	83.4±8.2	70.1±6.6	N/A	0.055
ANA positive (%)	85.7	94.1	N/A	0.317
ASMA positive (%)	76.2	88.2	N/A	0.414
IgG positive (%)	85.7	88.2	N/A	0.564

AIH: Autoimmune Hepatitis; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; ANA: Antinuclear Antibodies; ASMA: Anti-Smooth Muscle Antibodies; BMI: Body Mass Index. Data are Presented as Mean ± Standard Deviation.

arterial perfusion parameters may be associated with the degree of hepatic dysfunction. Mild hepatic impairment is mainly characterized by hepatocyte degeneration, necrosis, and limited fibrotic proliferation, whereas in moderate and severe cirrhosis extensive collagen deposition occurs, with fibrous septa connecting portal tracts and central veins. Regenerative nodules can compress peripheral hepatic and portal veins, leading to stenosis or even occlusion, thereby increasing vascular resistance and causing abnormal portal and arterial perfusion [15,16].

CT perfusion allows for the detection of both regional and global perfusion changes, and it is an effective method for assessing the hemodynamic characteristics of various diseases. Among currently available imaging methods, CT perfusion is considered to be minimally invasive, and it provides highly reliable quantitative evaluation of abdominal organ perfusion and focal lesions [17]. The advantages of CT perfusion include wide availability, relatively low cost, and feasibility for integration into routine CT protocols [11]. The main drawback remains radiation exposure, although modern protocols using

Table 2. *CT perfusion parameters in patients with AIH-fibrosis, AIH-cirrhosis, and in normal liver parenchyma of living donors.*

CT perfusion parameters	AIH-fibrosis (n=21)	AIH-cirrhosis (n=17)	Control (n=20)	Intergroup differences
AF (ml/100 ml/min)				Fibrosis > Control group ($p < 0.001$)
median	43.00	40.00	32.10	Cirrhosis > Control group
25th percentile	34.00	34.00	29.00	($p = 0.001$)
75th percentile	66.00	45.50	37.00	Fibrosis > Cirrhosis ($p = 0.294$)
PF (ml/100 ml/min)				Control group > Fibrosis ($p = 0.001$)
median	138.00	128.50	154.00	Control group > Cirrhosis ($p < 0.001$)
25th percentile	125.50	116.25	146.50	Cirrhosis < Fibrosis
75th percentile	151.50	146.00	164.00	($p = 0.084$)
PI (%)				Fibrosis > Control group ($p < 0.001$)
median	23.55	23.92	21.45	Cirrhosis > Control group ($p < 0.001$)
25th percentile	19.98	23.30	17.32	Cirrhosis > Fibrosis
75th percentile	28.34	28.96	26.53	($p = 0.642$)

AIH: Autoimmune Hepatitis; AF: Arterial Flow; PF: Portal Flow; PI: Perfusion Index.

Table 3. *Differential values of AF and PF parameters for AIH-fibrosis and AIH-cirrhosis.*

Parameter/group	AUC	95% CI	Cut-off value	Sensitivity (%)	Specificity (%)
AF/fibrosis	0.833	0.710-0.956	43.50	95	71
AF/cirrhosis	0.809	0.671-0.946	43.00	95	70
PF/fibrosis	0.810	0.680-0.939	156.50	95	60
PF/cirrhosis	0.888	0.782-0.994	137.01	95	76

AF: Arterial Flow; AIH: Autoimmune Hepatitis; AUC: Area Under the Curve; CI: Confidence Intervals; PF: Portal Flow.

reduced tube voltage and current significantly reduce the dose. In our study, perfusion CT was performed at 80 kVp and 30 mAs. Despite the implementation of dose-reduction protocols, CT perfusion should be reserved for selected clinical indications. It may still offer diagnostic advantages in specific scenarios where elastography is insufficient or cannot be performed. These situations include: inability to obtain reliable liver stiffness measurements due to obesity, ascites, or narrow intercostal spaces; the need to assess hepatic perfusion during acute exacerbations of autoimmune hepatitis.

Most previous CT perfusion studies had focused on hepatocellular carcinoma and its treatment response, hepatic metastases, pre- and post-transplant hemodynamics, as well as diffuse liver diseases in viral hepatitis B and C [3,14,18-20]. Studies on viral hepatitis have consistently demonstrated a gradual reduction in total liver perfusion (TLP) and portal fraction (PF), with compensatory increases in arterial fraction (AF) [9,21].

Guan et al. [5] in animal models of chronic liver disease, demonstrated that PF decreases with progressive fibrosis, accompanied by sinusoidal capillarization, collagen deposition, and gradual reductions in blood flow (BF), blood volume (BV), and mean transit time (MTT). Hashimoto et al. [1] also reported reductions in hepatic blood flow in advanced chronic liver disease, with higher HPI values in patients with cirrhosis (Child B-C) compared with healthy individuals [3].

The inflammatory pattern in AIH differs fundamentally from viral hepatitis. While viral hepatitis predominantly affects lobular and sinusoidal zones, AIH is characterized by portal and periportal inflammation, massive plasma cell infiltration, and interface hepatitis with hepatocyte necrosis. This localization may contribute to earlier impairment of portal blood flow compared with that in viral hepatitis. Under conditions of periportal inflammation and fibrosis, characteristic of AIH, earlier and more pronounced increases in AF and PI may be observed. Damage to the portal system and collagen thickening of the portal tracts increase vascular resistance and stimulate compensatory arterial inflow [22-24].

In our study, quantitative CT perfusion parameters were assessed in patients with fibrosis and cirrhosis secondary to AIH and compared with a control group of potential living liver donors. In AIH patients, AF and PI values were significantly higher, while PF was significantly lower compared with those in controls. No statistically significant differences in AF, PF, and PI were found between the fibrosis and cirrhosis subgroups. A probable explanation lies in the dominant effect of inflammatory activity, a characteristic feature of autoimmune hepatitis, on liver microcirculation. Inflammatory hyperemia can affect perfusion parameters, especially AF, thereby masking perfusion differences due solely to the fibrosis stage. In our study, 10 patients (26.3%) exhibited high inflammatory activity (activity stage 3 and 4). Nishie et al. [25] investigated CT perfusion parameters in acute hepatitis, including patients with autoimmune hepatitis. The authors demonstrated a characteristic increase in AF and PI in patients with acute hepatitis compared to the control group.

Van Beers et al. [26] demonstrated that in patients with cirrhosis and chronic liver disease TLP decreases, while HPI and MTT increase. The most informative criterion for differentiating cirrhosis from non-cirrhotic liver disease was an MTT cutoff that provided 81% sensitivity and 81% specificity. In our study, the best cutoff values for differentiating AIH

patients with fibrosis and cirrhosis from controls were AF and PF, with a sensitivity of 95%.

Bretas et al. [11] demonstrated high reproducibility of measurements, with ICC values ranging from 0.82 to 0.86 for arterial and portal perfusion. In our study, two radiologists with different levels of abdominal imaging experience performed independent post-processing, achieving good ICC values for AF (0.885) and PF (0.730).

Furthermore, in our study, we observed cases of seronegative AIH-fibrosis and AIH-cirrhosis. According to the European Association for the Study of the Liver (EASL), most patients diagnosed with AIH (85%-95%) exhibit elevated IgG levels [27]. In our study, IgG was elevated in 85.7% and 88.2% of patients with AIH-fibrosis and AIH-cirrhosis, respectively. Komori et al. [8] reported that in the Japanese population with acute AIH, antinuclear antibody (ANA) was negative in 27% of cases, while more than 50% of patients demonstrated normal IgG levels.

In our study, we did not include patients with acute-onset AIH without histological evidence of fibrosis or cirrhosis. However, in patients with AIH-fibrosis and AIH-cirrhosis, the histological assessment demonstrated high inflammatory activity (A3 in 7 patients, A4 in 3 patients). Clinically acute presentation, including elevated transaminases, was observed in 9 patients (23.7%).

Additionally, in our study population, the BMI of patients with fibrosis and cirrhosis was higher compared with the control group's. The control (donor) group was younger (mean age 31.9 years) with healthy livers and had no evidence of hepatic steatosis. Additional statistical testing demonstrated that BMI did not influence perfusion parameters AF and PF. Furthermore, the intergroup differences in perfusion persisted after adjustment for BMI. Therefore, the observed alterations in hepatic perfusion are likely related to AIH-associated hemodynamic changes rather than differences in body habitus.

Limitations.

First, the small number of patients and uneven distribution have limited this study which may have influenced the reliability of the results. Second, no comparative analysis of CT perfusion parameters between different stages of fibrosis and cirrhosis was performed.

Future studies should include larger cohorts of patients with acute AIH without fibrosis (F0) as well as AIH patients with fibrosis. The analyses should take into account not only the fibrosis stage but also the activity stage, considering the peculiarities of AIH pathogenesis, particularly inflammatory activity, for its early detection.

Given the relatively small sample size (~20 subjects per group), ROC curve estimates may be overly optimistic, with wide confidence intervals reflecting model instability. Therefore, ROC performance should be interpreted with caution.

Conclusion.

The findings of this study suggest that a pronounced increase in AF and a decrease in PF at the stages of AIH-related fibrosis and cirrhosis, may help detect and monitor liver damage compared with healthy livers.

Author contributions.

Zh. Zh: Supervision. **G. B.** and **Ye. K.:** Writing – original draft. **B. B.:** Review & editing. **D.B.:** Data collection.

Conflict of interest.

The authors declare that there is no conflict of interest.

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REFERENCES

1. Hashimoto K, Murakami T, Dono K, et al. Assessment of the severity of liver disease and fibrotic change: The usefulness of hepatic CT perfusion imaging. Oncol Rep. 2006;16:677-683.
2. Ronot M, Asselah T, Paradis V, et al. Liver fibrosis in chronic hepatitis C virus infection: differentiating minimal from intermediate fibrosis with perfusion CT. Radiology. 2010;256:135-142.
3. Zhong L, Wang WJ, Xu JR. Clinical application of hepatic CT perfusion. World Journal of Gastroenterology: WJG. 2009;15:907.
4. Li Y, Pan Q, Zhao H. Investigation of the values of CT perfusion imaging and ultrasound elastography in the diagnosis of liver fibrosis. Exp Ther Med. 2018;16:896-900.
5. Guan S, Zhao WD, Zhou KR, et al. CT perfusion at early stage of hepatic diffuse disease. World Journal of Gastroenterology: WJG. 2005;11:3465.
6. Rahim M, Miquel R, Heneghan M. Approach to the patient with acute severe autoimmune hepatitis. JHEP Reports. 2020;2.
7. Muratori L, Lohse A, Lenzi M. Diagnosis and management of autoimmune hepatitis. BMJ. 2023:380.
8. Komori A. Recent updates on the management of autoimmune hepatitis. Clin Mol Hepatol. 2020;27:58-69.
9. Wang L, Fan J, Ding X, et al. Assessment of liver fibrosis in the early stages with perfusion CT. Int J Clin Exp Med. 2015;8:15276.
10. Yamazaki S, Takayama T, Mitsuka Y, et al. Predictive value of perfusion CT for blood loss in liver resection. Biosci Trends. 2020;14:384-389.
11. Bretas E, Torres U, Torres L, et al. Is liver perfusion CT reproducible? A study on intra- and interobserver agreement of normal hepatic haemodynamic parameters obtained with two different software packages. Br J Radiol. 2017;90:20170214.
12. Zussman B, Boghosian G, Gorniak R, et al. The relative effect of vendor variability in CT perfusion results: a method comparison study. AJR Am J Roentgenol. 2011;197:468-473.
13. Ripoll C, Groszmann R, Garcia-Tsao G, et al. Hepatic Venous Pressure Gradient Predicts Clinical Decompensation in Patients with Compensated Cirrhosis. Gastroenterology. 2007;133:481-488.
14. Wang N, Sun Z. Clinical value of AEF in the post-processing technique of liver perfusion-like phase III enhanced CT scan in evaluating the degree of liver function impairment in patients with Hepatitis-B cirrhosis. Pak J Med Sci. 2022;38:1899.
15. Van Der Vorst J, Van Dam R, Van Stiphout R, et al. Virtual

liver resection and volumetric analysis of the future liver remnant using open-source image processing software. World J Surg. 2010;34:2426-2433.
16. Preibsch H, Spira D, Thaiss W, et al. Impact of transjugular intrahepatic portosystemic shunt implantation on liver perfusion measured by volume perfusion CT. Acta Radiol. 2017;58:1167-1173.
17. Kanda T, Yoshikawa T, Ohno Y, et al. Perfusion measurement of the whole upper abdomen of patients with and without liver diseases: Initial experience with 320-detector row CT. Eur J Radiol. 2012;81:2470-2475.
18. Oğul H, Kantarci M, Genç B, et al. Perfusion CT imaging of the liver: review of clinical applications. Diagn Interv Radiol. 2014;20:379-389.
19. Garbino N, Brancato V, Salvatore M, et al. A Systematic Review on the Role of the Perfusion Computed Tomography in Abdominal Cancer. Dose Response. 2021;19.
20. Zhuang Z, Qian L, Wang B, et al. Computed tomography perfusion in living donor liver transplantation: an initial study of normal hemodynamic changes in liver grafts. Clin Transplant. 2009;23:692-699.
21. Ronot M, Leporq B, Van Beers B, et al. CT and MR perfusion techniques to assess diffuse liver disease. Abdom Radiol (NY). 2020;45:3496-3506.
22. Manns M, Lohse A, Vergani D. Autoimmune hepatitis - Update 2015. J Hepatol. 2015;62:S100-S111.
23. Liberal R, Grant C, Mieli-Vergani G, et al. Autoimmune hepatitis: A comprehensive review. J Autoimmun. 2013;41:126-139.
24. Czaja A. Diagnosis and Management of Autoimmune Hepatitis: Current Status and Future Directions. Gut Liver. 2016;10:177-203.
25. Nishie A, Ushijima Y, Takayama Y, et al. Hemodynamic Alteration in the Liver in Acute Hepatitis: A Quantitative Evaluation Using Computed Tomographic Perfusion. In Vivo. 2021;35:3537-3545.
26. Van Beers B, Leconte I, Materne R, et al. Hepatic perfusion parameters in chronic liver disease: dynamic CT measurements correlated with disease severity. AJR Am J Roentgenol. 2001;176:667-673.
27. Dalekos G, Gatselis N, Drenth J, et al. EASL Clinical Practice Guidelines on the management of autoimmune hepatitis. J Hepatol. 2025;83:453-501.