Quantification of Portal Vein Vascularization Using an Automated Post-Processing Video Analysis Tool

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ABSTRACT

Purpose Blood flow dynamics represent a diagnostic criterion for many diseases. However, no established reference standard is available. In clinical practice, ultrasound pulsed-wave Doppler (PW-Doppler) is frequently used to assess visceral blood flow, despite its well-known limitations. A quantitative analysis of conventional color Doppler patterns can be performed using an innovative ultrasound-based algorithm (pixel flow analysis, PFA). This tool already shows promising results in obstetrics, but the technique has not yet been evaluated for portal venous blood flow assessment.

Methods This prospective exploratory research study evaluated the applicability of PFA in the portal venous system. Measurements of portal venous flow using PFA and PW-Doppler were compared in healthy volunteers (n = 20) and in patients with hepatic steatosis (n = 10) and liver cirrhosis (n = 10).

Results In healthy volunteers (60 % female, mean age 23 years, BMI 21.5 kg/m^2 [20.4–23.8]), PFA and PW-Doppler showed a strong positive correlation in fasting conditions (r = 0.69; 95 % CI 0.36–0.87), recording a median blood flow of 834 ml/min (624–1066) and 718 ml/min (620–811), respectively. PFA was also applicable in patients with chronic liver diseases (55 % female, age 65 years (55–72); BMI 27.8 kg/m^2 (25.4–30.8)), but the correlation between PFA and PW-Doppler was poor (r = − 0.09) in the subgroup with steatosis. A better correlation (r = 0.61) was observed in patients with liver cirrhosis.

Conclusion PFA and PW-Doppler assessment of portal venous vascularization showed high agreement in healthy volunteers and patients with liver cirrhosis. Therefore, PFA represents a possible alternative to conventional PW-Doppler sonography for visceral blood flow diagnostics and merits further evaluation.

Introduction

The precise quantification of intravascular blood flow is of interest for many clinical specialties. In visceral medicine, the evaluation of portal venous blood flow dynamics is important for the prediction of complications in patients with chronic liver diseases, such as variceal bleeding [1]. Therefore, an accurate quantification of portal vein vascularization seems crucial for accurate risk stratification and treatment [2]. Another important application for the assessment of liver vascularization comprises follow-up examinations after liver transplantation [3].

* VB and MH contributed equally to this work.

However, precise noninvasive measurements of visceral blood flow volume are difficult to perform, and therefore little is known regarding the diagnostic value of blood flow changes, for example, as a screening tool for hepatic complications. Current methods for direct blood flow evaluation rely on invasive techniques, which are potentially harmful and thus remain restricted to special indications [4]. Indirect quantification of portal blood flow volume based on hepatic clearance of D-sorbitol has shown promising results [5, 6] but requires elaborate methods that are not widely available. More recently, the combination of xenon gas inhalation with computed tomography (CT) imaging has been proposed for the quantification and visualization of blood flow [7], with promising pilot study results in patients with chronic liver disease [8–10]. Cinephase-contrast magnetic resonance (MR) velocity mapping may also quantify blood flow dynamics [11, 12]. However, CT and MR methods are neither standardized nor established, and they involve considerable resources. Hence, there is a need for easy-to-apply noninvasive methods for visceral blood flow quantification. Ultrasound techniques are predestined for this purpose.

The "traditional standard" pulsed-wave-Doppler (PW-Doppler) is widely implemented in common ultrasound devices [13] and calculates blood flow velocity based on ultrasound frequency modulation by moving reflectors (e. g., erythrocytes) [14, 15]. However, PW-Doppler accuracy is limited by rough mathematical and biological assumptions, that is, extrapolation of the average velocity in a laminar flow profile [16]. Beyond conventional PW-Doppler, there are further ultrasound-based methods for noninvasive blood flow quantification e. g., vector flow imaging. This method is an angle-independent technology for vector velocity estimation [17]. Brandt et al. were able to show that this method could be more precise in blood flow measurements in the portal vein compared to standard PW-Doppler [18], but the vector flow imaging method is not widely implemented in common ultrasound devices yet and also doesn't consider the total cross-sectional area of the vessel.

The lack of a clinical "gold standard" for visceral blood flow quantification underlines the need for further research. A new ultrasound-based approach focuses on the advanced processing of color Doppler signals, which visualize blood flow velocity coded by different color shades [19]. A pixel-based analysis provides blood flow information over the total vessel cross-sectional area within a defined period of time. PixelFlux (Chameleon-Software, Münster, Germany) is a commercially available tool for color Doppler ultrasound flow analysis, which automatically quantifies intravascular blood flow during a complete heart cycle [20]. ▶ **Fig. 1a/b** demonstrates the principle of this pixel flow analysis (PFA) tool compared to the established PW-Doppler. PFA has already been evaluated for placenta vascularization, umbilical cord flow during pregnancy, and in an experimental setting to detect ischemic lesions in testicular torsion in rats, with promising results [20–23]. Furthermore, a phantom study showed a good correlation of the actual flow recorded with PFA using a plastic tube with a predefined flow volume [22]. However, its applicability and diagnostic value for examinations in an abdominal setting have not yet been described. Therefore, this study compared PFA using PixelFlux with PW-Doppler-based quantification of portal venous blood flow in healthy volunteers and in patients with chronic liver diseases.

Patients and Methods

Study design

The study was designed as exploratory research focusing on the applicability of PFA in the portal venous system and evaluating its correlation with the established PW-Doppler in a cohort of healthy volunteers. We also studied the ability of PFA to characterize portal venous flow modulation after physiological stimuli, i. e., food ingestion. To investigate the potential diagnostic role of PFA, we further characterized the portal venous flow in patients with hepatic steatosis and in patients with liver cirrhosis:

i) Steatosis is frequently associated with obesity. Both conditions attenuate ultrasound signal intensity and may stress the applicability of PFA.
ii) Liver cirrhosis is associated with altered hepatic vascularization and portal hypertension. Affected patients may serve as models of pathological portal venous flow.

Ethical statement

The study was performed in accordance with the guidelines for good clinical practice (E6/R1) and the ethical guidelines of the Helsinki Declaration. The study was approved by the local ethics committee (University of Leipzig, registration number 035/17-ek with amendment) and registered in the German Clinical Trials Register (DRKS00012281). Informed written consent was obtained from all patients and healthy volunteers.

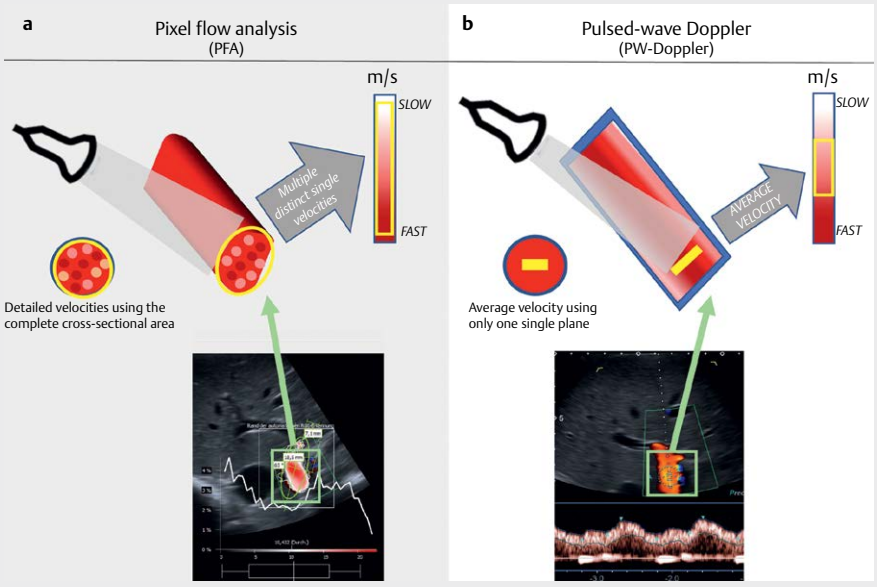
Study cohort

This monocentric prospective cross-sectional study recruited healthy adult volunteers with normal body weight (BMI 18–25 kg/m^2) at a university medical center in Leipzig, Germany . Liver disease was ruled out by laboratory assessments (liver enzymes), abdominal ultrasound, liver stiffness measurements (LSM < 7.0 kPa) [24], and assessment of liver steatosis using a controlled attenuation parameter (CAP < 248 dB/m) [25, 26].

The study cohort comprised subsequent patients who presented for routine ultrasound examinations with

i) non-alcoholic fatty liver disease (NAFLD) and diabetes mellitus type 2 without evidence of advanced fibrosis, defined by CAP > 279 dB/m and LSM < 7.0 kPa and
ii) patients with a history of NASH and advanced, but compensated liver cirrhosis, defined by LSM > 13.2 kPa [27].

Ten patients were recruited for each subgroup. Patients were thoroughly characterized by laboratory assessment of alanine and aspartate aminotransferases (ALT and AST) and gamma-glutamyl-transferase (GGT), as well as anthropometric measures (weight, height, calculation of body mass index (BMI) and conventional ultrasound of the liver and portal venous system, including spleen size measurement). Patients with severe obesity (defined by BMI > 35 kg/m^2) were not included. Further exclusion criteria consisted of the presence of acute hepatitis (ALT or AST > 5 times the upper normal level), inapplicability of vibration-controlled transient elastography, liver transplantation or major liver surgery, pregnancy or lactation, and malignant diseases with restricted life expectancy.



▶ **Fig. 1** Principles of blood flow measurements. **a**) Pixel flow analysis (PFA) is a post-processing tool that evaluates the blood flow velocities of each individual pixel in color Doppler visualization, with respect to the total cross-sectional area of the vessel using an ellipsoid plane. **b**) Pulsed-wave Doppler (PW-Doppler) uses the mean vessel velocity and only considers a single plane. The blood flow is calculated using the manually measured diameter of the vessel.

Conventional ultrasound examination and liver elastography

All examinations were performed on the same day by certified examiners (MH, VB) in a standardized procedure after overnight fasting. All examinations were conducted in a supine position with the patient's right arm elevated behind their head to widen the intercostal spaces. A high-end ultrasound device (Toshiba Aplio 500, software version AB_V7.00 * R003, Canon Medical Systems, Tustin, USA) equipped with a curved array probe (6C1 PVT-375 BT 3.5 MHz) was used. Biliary obstruction, liver congestion due to right heart failure, the presence of ascites, and focal liver lesions were ruled out in all participants.

Noninvasive estimation of liver fibrosis and steatosis was conducted using vibration-controlled transient elastography (VCTE, Echosens, Paris, France). The appropriate probe (M or XL-probe, 3.5/2.5 MHz, respectively) was defined by the skin-to-liver-capsule distance (SCD) (M-probe ≤ 25 mm; XL-probe > 25 mm) [28].

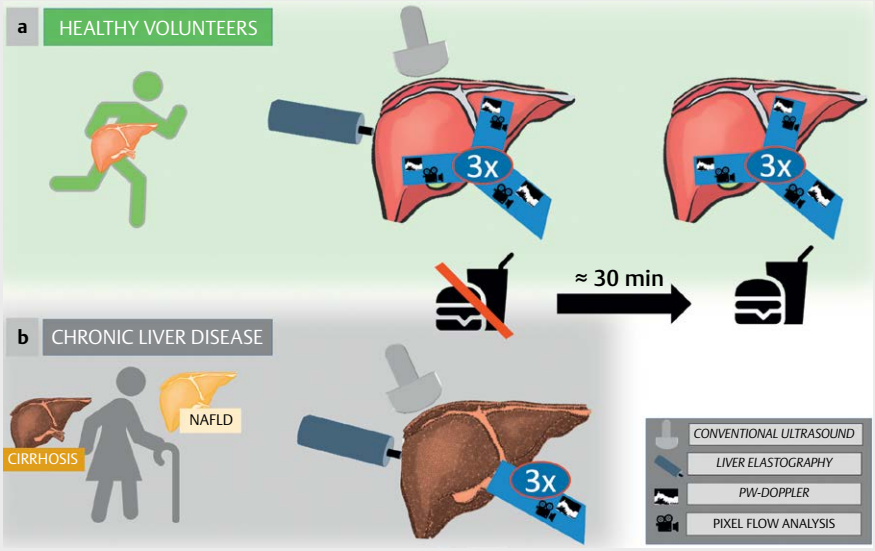
Pulsed-wave Doppler (PW-Doppler)

PW-Doppler of the portal vein was performed by putting the transducer on an intercostal space on the right liver lobe. The angle of the ultrasound waves with respect to the blood flow was reduced as far as possible, ideally no more than 20 °, and a maximum angle of 60 ° was accepted. The focus was adjusted to the measurement area, and the B-mode gain was set as low as possible (see ▶ **Fig. 1b**). Color Doppler was activated using a standardized software pre-set (color map 2). Pulse repetition frequency (PRF) and color gain were adapted to avoid aliasing and blooming artifacts [19]. The PW-Doppler sampling gate was positioned in the vessel's axis and the gate width was adjusted to two-thirds of the vessel's diameter to avoid wall artifacts. The cross-sectional area of the vessel was manually determined by referring to the B-mode image to avoid overestimation. The blood flow volume was then directly calculated using the formula incorporated into the ultrasound device [20].

Automated pixel flow analysis tool (PFA)

PFA is a post-processing tool for analyzing color Doppler patterns from recorded ultrasound video loops. The software analyzes blood flow in the total cross-sectional area of the vessel. Therefore, the transducer had to be tilted slightly to visualize the portal vein in an ellipsoid shape (see ▶ **Fig. 1a**). PFA analyses were performed immediately after PW-Doppler assessment, applying the same color Doppler and fundamental ultrasound parameters. Three consecutive color Doppler cine loops encompassing at least one full heart cycle were recorded and stored in Digital Imaging and Communications in Medicine (DICOM) format.

Post-processing: The video loops were analyzed using commercially available PixelFlux software (Chameleon-Software, Münster, Germany). The distinct technical backgrounds of the analyses are described elsewhere [29]. In brief, the software algorithm automatically detects the region of interest (ROI) and the spatial angle. Each pixel and its specific color hue represent a distinct velocity, which is determined based on the spatial angle. The following parameters were computed for each single frame of the video within the ROI: the mean velocity (V), which corresponds to the summed up velocities based on the individual color hue of the pixels, and the mean perfused area (A), which is given by the number of pixels inside the ROI [29]. All specific velocities are combined, and the total flow volume is calculated using the area of all pixels during a full heart cycle [20]. The software automatically recognizes the beginning and the end of a heart cycle inside the video regarding pulsa-



▶ **Fig. 2** Protocol for blood flow analyses and overview of all study investigations. In the cohort of healthy volunteers (**a**), the blood flow measurements were performed in the main portal trunk and both subsequent branches before and after food ingestion using both pixel flow analysis (PFA) and pulsed-wave Doppler (PW-Doppler). In patients with chronic liver disease (**b**), the blood flow analysis was restricted to the portal vein trunk in fasting conditions. All study participants underwent liver elastography and conventional ultrasound for study inclusion.

tile blood flow. The post-processing procedure analyzing the video loops with PFA took less than 5 minutes.

Protocol for portal venous flow assessment

In the cohort of healthy volunteers, blood flow measurements were performed in the portal vein trunk and both subsequent main branches using both PFA and PW-Doppler, as described earlier (▶ **Fig. 2a**). The total branch blood flow (the sum of both branches) was compared to the flow in the trunk. All measurements were performed three times, and the mean value was used for further analyses. The measurements were repeated 30 min. after ingestion of a standardized meal (400 ml high-caloric commercial chocolate drink) to evaluate portal venous flow modulation after physiological stimuli. In the patient cohort, the blood flow measurements were restricted to the trunk of the portal vein in fasting conditions (▶ **Fig. 2b**). An overview of all investigations including liver elastography and conventional ultrasound is summarized in ▶ **Fig. 2**.

Statistical analysis

Statistical analyses were performed using GraphPad Prism (Version 9, San Diego, California) and Microsoft Excel 365. Mean values and standard deviations are denoted by X ± Y, median values, and interquartile ranges by X [Y, Z], and numbers (%). Paired t-tests were used for comparison analysis of PW-Doppler and PFA, and unpaired t-tests were applied to test the baseline characteristics of significance. A p-value < 0.05 was considered significant. For correlation analysis, Pearson's r (two-tailed) was applied. Bland–Altman analysis was used to eliminate methodical measuring faults. The coefficient of variation was analyzed to evaluate the deviation of the obtained measured values.

Results

Study population

The study included 20 healthy volunteers without chronic liver diseases (60 % female, median age 23 years [IQR 22–26], BMI 21.5 kg/m² [IQR 20.4–23.8]) and 20 prospective patients with chronic liver diseases (n = 10 with hepatic steatosis and n = 10 with liver cirrhosis) (55 % female, age 65 years [55–72], BMI 27.8 kg/m² [25.4–30.8]). The detailed characteristics of the study population are presented in ▶ **Tab. 1**.

I. Analysis of healthy volunteers

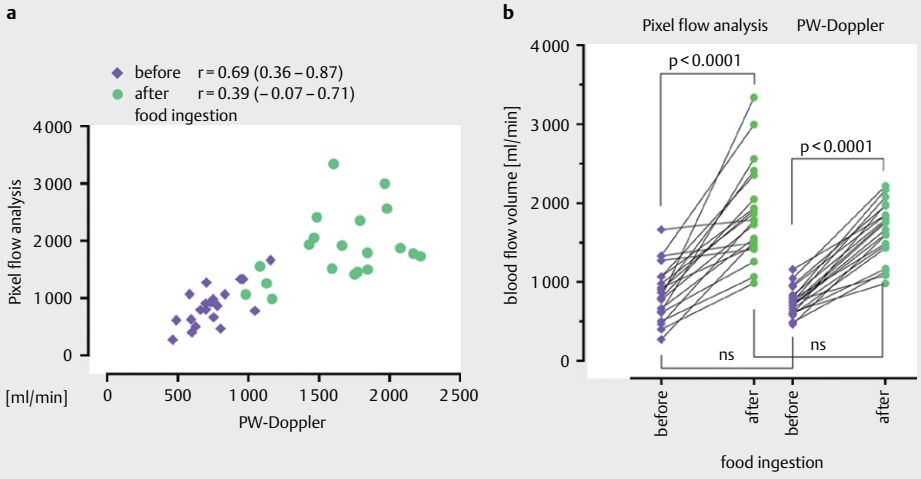
Applicability and correlation of automated pixel flow analysis and pulsed-wave Doppler In the cohort of healthy volunteers, all PFA (n = 360/360) and PW-Doppler measurements (n = 360/360) were applicable. The median angle between the blood flow in the trunk of the portal vein and the transmitted ultrasound waves was 4 ° [2–8]. The angle was 30.0 ° for the left branch of the portal vein (15–40) and 9.5 ° for the right branch (4–16).

PFA and PW-Doppler in healthy volunteers in fasting conditions showed a strong positive correlation (r = 0.689; 95 % CI 0.36–0.87). After food ingestion, the correlation between PFA and PW-Doppler decreased significantly (r = 0.386; 95 % CI −0.068–0.708; p = 0.0008) (▶ **Fig. 3a**).

Regarding median blood flow of the portal vein, no significant difference between measurements in healthy volunteers was observed using either PFA or PW-Doppler (before food ingestion p = 0.05 (mean of differences 122 [95 % CI −1.2–245.7]; after food ingestion p = 0.10 (mean of differences 222 [95 % CI −47.4–491.8]) (▶ **Fig. 3b** and ▶ **Tab. 2**). The mean individual differences between

▶ **Tab. 1** Baseline characteristics. Values are median [interquartile range] or numbers (%). NAFLD = non-alcoholic fatty liver disease; BMI = body mass index; AST = aspartate aminotransferase; ULN = upper limit of normal; CAP = controlled attenuation parameter; LSM = liver stiffness measurement. * portal vein trunk before food ingestion

	Healthy volunteers	NAFLD	Cirrhosis
Number	20	10	10
Female	12 (60 %)	6 (60 %)	5 (50 %)
Age (years)	23 [22–26]	57.5 [54–69.8]	67 [60.8–73]
BMI (kg/m²)	21.5 [20.4–23.8]	30.3 [25.9–30.9]	26.5 [24.6–29.5]
<25	20 (100 %)	1 (10 %)	4 (40 %)
25–30	0 (0 %)	3 (30 %)	4 (40 %)
>30	0 (0 %)	6 (60 %)	2 (20 %)
Body surface (m²)	1.81 [1.71–1.9]	1.87 [1.81–1.95]	1.81 [1.71–1.94]
AST (µkat/l)	0.4 [0.37–0.43]	0.51 [0.44–0.56]	0.64 [0.48–0.77]
>ULN	0 (0 %)	1 (10 %)	2 (20 %)
Peak velocity (cm/s) *	22.3 [17.0–32.8]	19.9 [19.5–21.9]	18.4 [16.0–20.8]
CAP (dB/m)	195 [176.3–219.3]	316.5 [298.3–339.5]	255.5 [252.5–336]
LSM (kPa)	4.6 [3.8–5.2]	4.7 [4.1–5.8]	17.4 [13.6–20]
Spleen size (mm)	108.5 [98.3–115.3]	100.5 [93.3–108.8]	135 [114.5–145.8]



▶ **Fig. 3** Comparison of blood flow analysis in the portal vein in healthy volunteers using both pixel flow analysis (PFA) and pulsed-wave Doppler (PW-Doppler). Panel a shows the Pearson correlation of both applied methods before and after food ingestion. Panel b illustrates the blood flow alterations after food ingestion for both measurements with PFA and PW-Doppler in the portal vein. Entries are in ml/min.

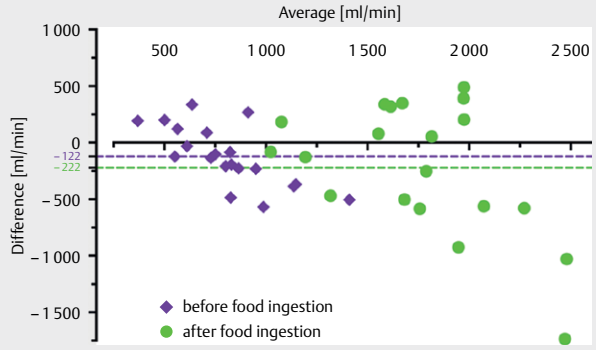
PFA and PW-Doppler were 23 % before and 10 % after food ingestion. Both methods verified a significant increase in blood flow after high caloric meal ingestion with a median rise of 923 [578–1293] ml/min for PFA and 931 [699–1069] ml/min applying PW-Doppler.

For further validation of these results, blood flow measurements were performed in the portal vein trunk and its subsequent intrahepatic branches. The integrity of the total blood flow was defined as the relation of the blood volume in the main trunk and both subsequent branches (▶ **Tab. 2**). For PFA, the blood volume in the branches was slightly underestimated compared to the blood volume in the trunk, whereas PW-Doppler showed a moderate overestimation.

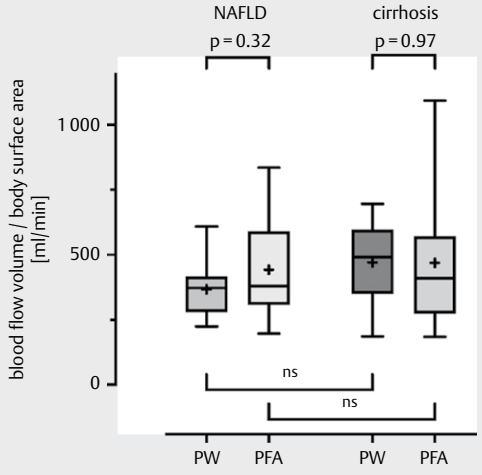
Agreement between pulsed-wave Doppler and pixel flow analysis using the Bland–Altman plot. There was good agreement between the two blood flow measurement methods in the healthy volunteers. ▶ **Fig. 4** shows a Bland–Altman plot illustrating the measurement results in the portal vein trunk. No relevant systematic measuring errors could be identified, and only one outlier in the PFA method was detected. Before and after physiological stimuli with standardized food ingestion, PFA leads to an overestimation, with a mean difference of 122 ml/min between PFA and PW-Doppler (before food ingestion) and 222 ml/min (after food ingestion).

▶ **Tab. 2** Blood flow analysis in healthy volunteers before and after food ingestion. Values are the median [IQR]. Volume in ml/min. Alteration after food ingestion: median blood flow change after standardized food intake; ratio PFA/PW: comparison of the two applied methods calculating the median blood flow in the portal vein trunk presented as a ratio; integrity of blood flow: comparison of total blood flow in the portal vein trunk compared to the sum of the right and left main branches. PW-Doppler = pulsed-wave Doppler; PV = portal vein; PFA = pixel flow analysis

	Before food ingestion		After food ingestion	
	Pixel flow analysis	PW-Doppler	Pixel flow analysis	PW-Doppler
Portal vein (trunk)	834 [624–1066]	718 [620–811]	1783 [1486–2125]	1708 [1457–1875]
Right branch	463 [247–652]	541 [472–680]	820 [608–1081]	1132 [944–1244]
Left branch	206 [161–303]	306 [231–381]	499 [401–611]	627 [477–814]
Alteration after food ingestion (after/before)			2.2 [1.9–2.6]	2.3 [2–2.5]
Ratio of PFA and PW-Doppler	1.2 [0.9–1.3]		1.1 [0.8–1.4]	
Integrity of blood flow (right + left branch)/trunk	0.8 [0.6–1.4]	1.2 [1.1–1.3]	0.7 [0.5–1]	1.1 [1–1.2]



▶ **Fig. 4** Bland–Altman plots for inter-method agreement of pixel flow analysis (PFA) and pulsed-wave Doppler (PW-Doppler) in healthy volunteers before (purple) and after (green) food ingestion.



▶ **Fig. 5** Blood flow in the portal vein trunk in patients with chronic liver diseases in fasting conditions. The blood flow is adapted to the total surface area of the patients. PW = pulsed-wave Doppler; PFA = pixel flow analysis. NAFLD non-alcoholic fatty liver disease.

Variance of repeated measured values depending on the applied method. The coefficient of variation (CoV) was determined for the three repeated measured values of both PFA and PW-Doppler for each healthy volunteer, and subsequently, the average CoV was calculated. Applying PFA, a higher deviation of the three consecutively recorded single measurements was observed than when performing PW-Doppler (average CoV of 24.2 % (± 17.4) using PFA and 11.5 (± 6.7) using PW-Doppler).

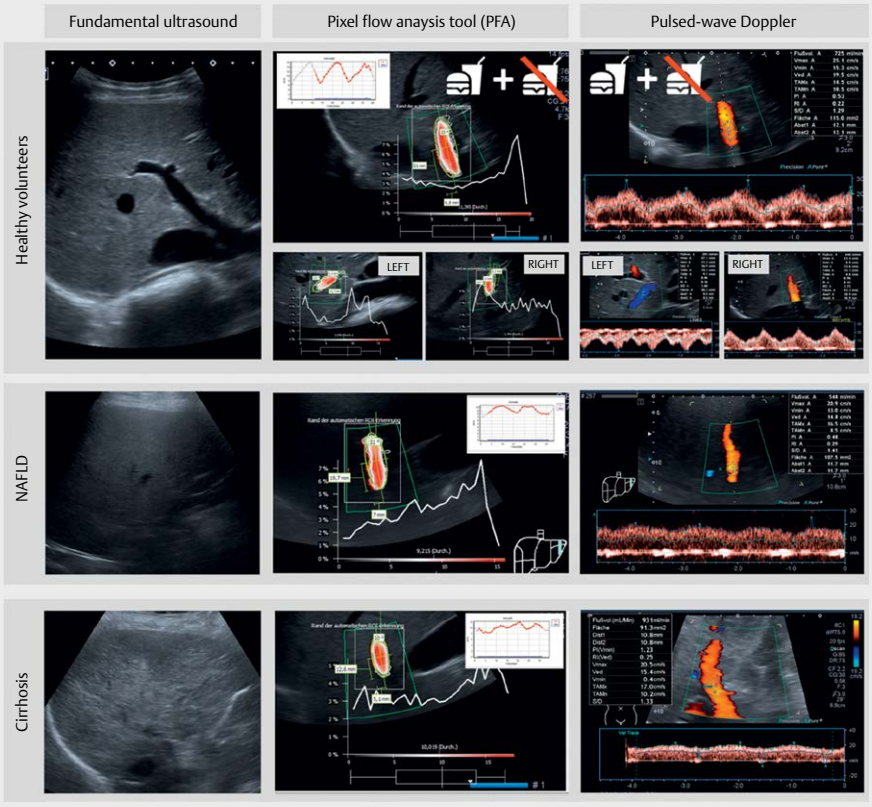
II. Analysis of patient cohort

To investigate the potential diagnostic role of PFA, we characterized portal venous flow in patients with hepatic steatosis and in patients with liver cirrhosis.

Applicability and correlation of automated pixel flow analysis and pulsed-wave Doppler in patients with chronic liver diseases. The blood flow in the portal vein trunk of 10 patients with NAFLD was analyzed after overnight fasting. All measurements (n = 30 PFA and n = 30 PW-Doppler) were successfully performed. The median angle alpha was 5.5 [1.5–7] degrees when performing PW-Doppler in the trunk of the portal vein. CAP measurements indicated a high degree of intrahepatic steatosis (317 [298–340] dB/m; all > 280 dB/m). In this cohort, the correlation between PFA and PW-Doppler was poor (r = – 0.09, 95 % CI – 0.68–0.57)).

Regarding the patients (n = 10) with advanced but compensated liver cirrhosis, all measurements (n = 30 PFA and n = 30 PW-Doppler) were also applicable (median angle alpha of 14 [6–32] degrees). The PFA and PW-Doppler showed good correlation (r = 0.61, 95 % CI – 0.03–0.89).

NAFLD patients had a blood flow of 739 ml/min [615–845] (PFA) and 663 ml/min [611–746] (PW-Doppler). The blood flow for the patients with cirrhosis was 789 ml/min [547–1015] with PFA and 885 ml/min [628–1056] with PW-Doppler. No significant difference was observed between PFA and PW-Doppler in the patient subgroups, even when standardized according to body surface area (▶ **Fig. 5**).



▶ **Fig. 6** Examples of performed blood flow measurements for all cohorts showing conventional ultrasound (left), pixel flow analysis (PFA) (middle), and pulsed-wave Doppler (PW-Doppler) (right). In the cohort of healthy volunteers, the blood flow measurements were performed in the main portal trunk and both subsequent branches before and after food ingestion. In patients with chronic liver disease (NAFLD and cirrhosis), the blood flow analysis was restricted to the portal vein trunk in fasting conditions.

▶ **Fig. 6** illustrates an example of the PFA and PW-Doppler measurements in the cohort of healthy volunteers and patients with chronic liver diseases.

Discussion

To date, there is no gold standard technique for the accurate evaluation of visceral blood flow analysis, although vascularization dynamics may provide valuable clinical insight for various diseases. PFA is a relatively new ultrasound-based approach that may potentially overcome the limitations of the "traditional" standard PW-Doppler [20, 22, 29–31]. PFA provides a deep spatiotemporal analysis of blood flow by pixel tracking throughout a complete heart cycle [22], which facilitates the detection of asymmetric flow distribution, changing vessel diameters, and alternating flow velocities [20]. The advantages of post-processing analysis tools are a highly standardized procedure which embraces the entire cross-sectional area of the vessel with respect to the different velocities that occur in a laminar flow. The flow measurement comprises a total heart cycle. Because the PFA procedure detects the region of interest (vessel) and spatial angle in an automated manner, only a standardized video loop including the cross-sectional area of the target vessel is required for automated analysis of the blood flow volume. This avoids a manual and thus error-prone correction of the adjusted angle using PW-Doppler.

The aim of this study was to acquire pilot data on the applicability of the PFA method in an abdominal setting, with a comparison to PW-Doppler sonography. The results show that PFA is applicable in a wide spectrum of individuals comprising healthy lean volunteers as well as patients with obesity and NAFLD and/or liver cirrhosis. Furthermore, the study identified a strong correlation between PFA and PW-Doppler in measuring the estimated blood flow in the portal vein without significant systematic measuring errors. The validation of both methods using the summation of blood flow (portal vein trunk vs. both subsequent branches) showed satisfactory results for both methods but also indicated a systematic difference between both algorithms. PFA also identified increasing hepatic vascularization after physiological stimuli [14, 15] with results comparable to PW-Doppler measurements. The greater variance of the PFA method regarding individual measurements per participant, as well as the overall results, is another relevant finding that may point to a lower measurement precision but may also reflect a more accurate depiction of the individual biological conditions.

To investigate the potential role of PFA as a diagnostic measurement tool, we characterized portal venous flow in patients with hepatic steatosis and in patients with compensated liver cirrhosis.

Steatosis and obesity are common limitations of ultrasound diagnostics, given that they impair signal propagation in the liver due to (a) limited access through narrow intercostal spaces, (b) attenuation of the ultrasound waves by lipid droplets in the hepatocytes, and (c) a high penetration depth in obese patients. As expected, these patient-related properties affected both PFA and PW-Doppler, which may explain the poor correlation in the patient sample with fatty liver disease. Novel high-performance ultrasound transducers for deep abdominal examinations may reduce such limitations in the future [32].

In patients with liver cirrhosis, the applicability of both methods was good, resulting in a strong correlation comparable to the results of healthy volunteers. There were no significant differences between PFA and PW-Doppler or between the patient groups. Explanations remain highly speculative at this stage, but normal blood flow may still reflect fully compensated liver disease. Another reason could be that despite the highly standardized examination conditions, the influence of portal vein vascularization varies and the range of a "standard value" of the peak velocity is huge [33, 34].

In summary, the results of this first exploratory assessment of PFA in an abdominal setting prove the method's applicability and capacity to describe portal venous blood flow dynamics in the trunk as well as the intrahepatic branches. Comprehensible limitations of the study design include the limited number of individuals in each subgroup, no data on the impact of inter-observer variability, and the aforementioned lack of an established noninvasive "gold standard" for visceral blood flow measurement. However, any invasive measurements are not feasible or ethically justifiable at this stage and will also not be suitable for future clinical studies that include healthy controls and patients with simple hepatic steatosis. Therefore, further evaluation of PFA-based portal venous diagnostics should include patients with advanced liver disease and portal hypertension. In such cases, a significant modulation of portal venous flow can be expected, and clinically indicated invasive measures, such as hepatic venous pressure gradient, may serve as a reference. Further invasive studies in animal models or technical phantoms can help improve PFA applicability in tissues with high ultrasound signal attenuation and support the identification of whether PFA precision exceeds PW-Doppler-based measurements. PFA provides standardized data from brief freehand video loops which may be useful in a variety of clinical scenarios beyond portal-venous assessment, e. g., application in peripheral artery disease, hemodynamic measurements including analysis of peak and diastolic flow.

In conclusion, we present the first data of ultrasound-based pixel flow analysis of the portal venous systems as a feasible alternative to conventional PW-Doppler sonography. PFA applicability and results from standard indications are promising but require further validation.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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