Published in final edited form as:

J Magn Reson Imaging. 2014 April ; 39(4): 819–826. doi:10.1002/jmri.24233.

Effect of Temporal Resolution on 4D Flow MRI in the Portal Circulation

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Abstract

Purpose—To demonstrate the use of temporal averaging with radial 4D flow MRI to reduce scan time for quantification and visualization of flow in the portal circulation. This study compared phase-contrast MR angiography, 3D flow visualization, and flow quantification of portal venous hemodynamics of time-averaged vs. time-resolved reconstructions.

Materials and Methods—Time-resolved 3D radial (“4D”) phase contrast data were acquired from 44 subjects (15 volunteers, 29 cirrhosis patients) at 3T. Images were reconstructed as a fully-sampled time-resolved reconstruction and multiple time-averaged reconstructions using a variable number of acquired projections to simulate different scan times. Images from each reconstruction were evaluated to compare the quality of anatomical and hemodynamic visualization.

Results—Time-averaged reconstructions outperformed time-resolved reconstructions for flow quantification ($3.9 \pm 3.1\%$ error vs. $5.2 \pm 4.4\%$ error), average streamline length ($47 \pm 7\text{mm}$ vs. $34 \pm 15\text{mm}$), and visualization quality (average grading = 3.7 ± 0.5 vs. 2.2 ± 0.9). In addition, excellent visualization quality was achieved using less acquired projections.

Discussion—Reductions in scan time can be achieved through time-averaging while still providing excellent visualization and quantification in the portal circulation. Scan time reduction of up to 70-80% was possible for high quality assessment, translating into a reduction in scan time from 10-12 minutes to approximately 3-4 minutes.

Keywords

hemodynamics; flow-sensitive 4D MR; velocity mapping; portal venous flow; portal hypertension; diffuse liver disease

INTRODUCTION

Cirrhosis is the end stage of chronic liver damage resulting from viral hepatitis, chronic alcohol abuse, and nonalcoholic fatty liver disease, among other causes (1,2). Importantly, there are tremendous alterations in the hemodynamics of the cirrhotic liver. Increases in both

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Financial disclosures: The University of Wisconsin Departments of Radiology and Medical Physics receive research support from GE Healthcare.

sinusoidal resistance and portal venous blood inflow lead to altered levels of circulating vasoconstrictors and vasodilators (3). As a consequence of this hyperdynamic compensatory response, portal hypertension (PHTN) can develop. PHTN is a major complication of cirrhosis and can lead to portosystemic collaterals (Figure 1), ascites, hepatorenal syndrome, portal venous thrombosis (Figure 2), and splenomegaly (4). The presence of gastroesophageal varices is an important predictor of mortality and decompensation of cirrhosis(5). A comprehensive diagnostic approach that assesses detailed hemodynamic and morphologic information with complete upper abdominal vascular coverage in a single examination would be highly desirable to further our understanding and serve as a non-invasive biomarker of disease progression and therapeutic monitoring.

Portal hypertension is defined by a hepatic venous pressure gradient (HVPG) greater than 5mmHg. HVPG is most commonly assessed by measuring a wedged hepatic venous pressure (WHVP) (6) and is the best validated biomarker for indicating the severity of PHTN. HVPG provides important prognostic information, as an HVPG of 10mmHg or greater increases the risk for variceal development (7), and clinical decompensation (8). Furthermore, an HVPG of 12 mmHg or greater correlates to increased risk of bleeding and mortality (9,10). Unfortunately, HVPG measurement is an invasive study and is not in widespread use (11). In addition, the HVPG incompletely characterizes the hemodynamics of the liver. Specifically, no information on portal blood flow and its distribution within varices can be determined by the HVPG.

In cirrhotic patients, increased portal blood flow is the primary determinant of portal hypertension and most therapies aim to reduce splanchnic flow (eg. non-selective beta-blockers) or redirect portal flow away from the liver via a transjugular intrahepatic portosystemic shunt (4). Direct measurement of flow with the portal circulation, including varices, may be valuable as a surrogate biomarker of HVPG for providing risk stratification and treatment monitoring.

Current non-invasive evaluation of blood flow in the portal venous circulation is achieved with methods including Doppler ultrasound and 2D phase contrast MR imaging. These approaches are widely used and well validated for measuring velocities and flow (12-14) direction, however, are challenging to utilize in the portal vasculature. Doppler ultrasound often incompletely or inaccurately characterizes hemodynamics due to limited acoustic windows compounded by overlying gas-filled bowels(15), inability to measure flow directly, intraobserver variability (16,17), and difficulty to visualize complex and variable anatomy seen in pathological conditions (15). 2D phase contrast MRI resolves many issues with access and quantification, but detailed planning is required to prescribe planes to measure flow in all vessels of interest.

Studies using time-resolved 3D MRI velocity mapping ('4D Flow MRI' or '4D PC-MRI') have shown promise as a comprehensive tool for anatomic and hemodynamic assessment of portal hypertension (18,19). This method can quantify and visualize complex flow characteristics and anatomy allowing retrospective measurement of flow in any vessel of interest.

Recently, 4D flow sequences with highly undersampled 3D radial trajectories (PC-VIPR) have been developed (20,21) that achieves high spatial and temporal resolution in relatively short scan times (10-12 min). Recent studies demonstrated the potential of radial 4D flow MRI for qualitative(22) and quantitative(23) evaluation of portal venous hemodynamics in patients with portal hypertension. While clinically feasible, these scans still add considerable time to the MRI exam and additional reductions in scan time would be highly desirable.

For most 4D flow MRI applications, relatively high temporal resolution (40-80 ms/frame) is needed to resolve pulsatile flow. However, except for patients with congestive heart failure(24), there is low pulsatility within the portal circulation in healthy volunteers and is further decreased in chronic liver disease (25). The lack of pulsatility in the portal circulation may offer an excellent opportunity to reduce scan times and/or increase signal-to-noise ratio through temporal averaging if the primary flow parameter of interest is portal venous flow.

The purpose of this study was to compare time-resolved vs. time-averaged 4D flow MRI for quantification of blood flow in the portal vein, in order to reduce scan time and/or improve SNR performance. A comprehensive comparison was achieved to evaluate the quality of flow quantification, blood flow visualization, and anatomical depiction.

MATERIALS AND METHODS

Human Subjects

Forty-four subjects (29 male, 15 female; 47.8 ± 14.0 years, 84.3 ± 17.4 kg) were included in this HIPPA-compliant and IRB-approved study. Subjects included 15 normal volunteers and 29 patients with cirrhosis identified by clinical history. Written informed consent was obtained from all participants before inclusion. Scanning of patients was performed at the conclusion of clinically indicated abdominal MRI exams, while normal volunteers were imaged as part of a dedicated abdominal research MRI exam.

MR Imaging

All imaging was performed on a 3.0T clinical scanner (Discovery MR 750, GE Healthcare, Waukesha, WI) using a 32-channel phased array body coil (Torso Array Coil, Neocoil, Pewaukee, WI). A balanced 5-point velocity encoded PC-VIPR sequence (20,21,26) was used to provide an acquisition with full upper abdominal coverage, high spatial and temporal resolution, and increased velocity sensitivity in relatively short scan times. Specific imaging parameters included: dual echo acquisition, 24cm axial excitation, $BW = \pm 125$ kHz, with 24,000 projections, axial slab excitation, acquired spatial resolution = $1.25 \times 1.25 \times 1.25$ mm³, $TR/TE = 6.1-7.8/2.1-3.2$ ms (first echo), flip angle = $8-16^\circ$ and $V_{enc} = 60$ cm/s. An adaptive respiratory gating scheme (27) using respiratory bellows and a 50% acceptance window resulted in scan times of approximately 10–12 min depending on the respiratory rate of the subject. ECG trigger locations were stored during the acquisition and later utilized for retrospective cardiac gating. All imaging was performed 10-15 minutes after administration of 0.1 mmol/kg of gadobenate dimeglumine (Multihance, Bracco Diagnostics, Princeton, NJ) in patients and after injection of 0.03mmol/kg of gadofosveset trisodium (Ablavar, Lantheus Medical Imaging, N. Billerica, MA) in the volunteers.

Reconstruction and Post-processing

Image reconstruction was performed with optimized gridding routines (28) utilizing low resolution images for coil combination (29). PC-VIPR images were reconstructed as a time-resolved series with 14 interpolated time frames per R-R cycle using temporal filtering similar to a radial version of view sharing (30). In this study, 3D radial was collected without respect to the ECG waveform or heartbeat. Subsequently, data was retrospectively sorted into cardiac phases. This produces some level of randomness in each cardiac phase. To discard data, we subsampled this data in a pseudo-random fashion again without respect to the cardiac cycle. The combination of these two sampling, creates a highly aperiodic sampling pattern along the cardiac cycle. This was done to minimize errors from periodic subsampling with the Cardiac cycle and from gross changes in flow over the course of the scan.

In addition, time-averaged reconstructions were performed utilizing retrospective subsampling of the data to utilize 100%, 50%, 33%, 25%, 20%, 10%, and 5% of the acquired projections. Image acquisition and post-processing schemes incorporated automatic correction for Maxwell terms (31) and eddy currents (32). PC angiograms for all datasets were generated using complex difference processing and vasculature was segmented (MIMICS, Materialise, Ann Arbor, MI, USA). Qualitative and quantitative hemodynamic assessment was then accomplished on a dedicated post-processing workstation using flow visualization software (EnSight, CEI Inc., Apex, NC, USA) to compare anatomic and hemodynamic visualization, and blood flow quantification for each PC-VIPR data set.

Angiography

Angiographic assessment was performed to determine the diagnostic quality of different scan times. Axial complex difference images were evaluated between images reconstructed using 100%, 33%, and 10% of the acquired data. The three different reconstructions were qualitatively graded in a consensus reading by two experienced radiologists, each with 11 and 12 years of experience in cardiovascular imaging, based upon background noise and blurring of the vessel edge (table 1). It is important to note that time-resolved reconstructions typically use time-averaged reconstructions for its angiogram. Therefore, the time-averaged reconstruction using 100% of the projections is identical to the time-resolved reconstruction in these comparisons regarding angiography quality.

Flow Visualization

Flow visualization quality was assessed by two methods. First, a quantitative measurement of average streamline length was made to determine the quality of a 3D velocity vector field. Using the EnSight software, assessment of streamline length was performed by emitting 100 streamlines from a double-oblique emitter plane placed in the proximal portal vein and the average length of the streamline through a segmented volume was calculated. Streamline termination will occur with the following conditions: the streamlines encounter the boundary of a segmented vessel, the velocity approaches 0, or a streamline intersects itself (33). In data sets with high SNR and minimal artifacts, streamlines will persist for longer lengths before termination. This comparison was performed for the time-resolved and all time-averaged reconstructions.

Second, qualitative grading of the flow visualization was assessed in a consensus reading by the same two experienced radiologists (Table 2). The goal of this grading was to evaluate the quality of streamline visualization of blood flow on a 4 point scale (4 = excellent, 0 = poor). It is based on both the ability to depict anatomy and flow direction and the degree of noise in streamline path and/or velocity distribution. This type of visualization is clinically relevant as it is able to determine abnormal flow patterns and directionality seen in pathological conditions such as portal hypertension. This comparison was performed using the time-resolved reconstruction and the time-averaged reconstructions that used 100%, 33%, and 10% of the acquired projections.

Flow Quantification

Accuracy of flow quantification was evaluated using indirect validation methods. Unfortunately, there was no reference standard available for measuring the true flow within the abdominal vasculature, which would have required the use of invasive flow probes. Therefore, principles of flow consistency were relied upon to validate quantitative flow measurements from this study. Flow consistency is based on mass conservation, where the sum of input and output flow at a confluence of vessels is zero. We also indirectly evaluated the quantitative flow measurements by testing the variability of estimated flow from the different reconstructions. Differences in two flow results must be due to error associated

related to the sampling pattern or that introduced from the reconstruction algorithm, and not from variability in the underlying physiology since the identical data were used.

To assess flow consistency, the sum of flow measured in the superior mesenteric vein (SMV) and splenic (SV) vein was compared to the flow in the main portal vein (PV) (Figure 3). Percentage error was then calculated as: $(PV - SMV + SV)/PV$. Average flow rates were measured with user-defined regions of interest (ROI's) placed in double-oblique planes perpendicular to the centerline of each vessel. All flow measurements were made in all data sets (time-averaged and time-resolved) using the identical ROI and double-oblique plane. Use of the identical ROI was possible since the same underlying data was used for all reconstructions. This ensured that any differences in the estimated flow were related to the sampling and reconstruction, and not due to transient changes in the underlying physiology.

Pulsatility Index

In order to verify that flow in the portal circulation is non-pulsatile, a pulsatility index of the mean velocity V' in the main portal vein was calculated $PI = V'_{\max} - V'_{\min} / V'_{\text{mean}}$ [6]. The velocity measurements were made from the user-defined ROI's of the portal vein using the time-resolved reconstruction.

RESULTS

Acquisition of radial 4D flow MRI and subsequent reconstruction and evaluation was successful in all 44 subjects. Results are summarized in table 3 and images representing the visualization of anatomy and flow are shown in Figure 4.

Angiography

Based on the radiologist review, background noise (mean $\pm$ STD: 1.98 $\pm$ 0.15, median: 2) and vessel blurring (3.98 $\pm$ 0.15, 4) was minimal in the complex difference reconstruction using 100% of the acquired projections. In the reconstruction using 33% of the acquired projections, background noise (1.34 $\pm$ 0.61, 1) and blurring (3.11 $\pm$ 0.75, 3) became more apparent, although anatomical visualization was still considered to be high-quality. In that data that used 10% of the projections, substantial noise and background made many of these anatomic reconstructions non-diagnostic. Figure 4 shows a representative example of complex difference angiograms that show increasing noise and blurring as less data is used in the image reconstruction.

Flow Visualization

Streamline length was greatest in the fully sampled data sets (46.9 $\pm$ 7.4 mm). As the amount of undersampling increased, streamline length decreased as expected although adequate visualization length was still achievable in the reconstructions with increased undersampling. The streamline length of the fully sampled time-averaged reconstruction was also longer on average than the fully sampled time-resolved reconstruction (34.0 $\pm$ 15.2 mm).

The consensus reading of visualization quality by the radiologists reinforces that high visualization quality is achievable with shorter scan times. The scores for the 100%, 33%, and 10% time-averaged reconstructions were 3.7 $\pm$ 0.5, 2.7 $\pm$ 0.6, and 1.5 $\pm$ 0.6, respectively. The score for the time-resolved reconstruction was 2.2 $\pm$ 0.9. These results show that visualization was better in the fully-sampled time-averaged in comparison to time-resolved reconstruction, and that the visualization quality became worse when less projections were included in the reconstruction.

Flow Quantification

Mean portal vein flow rates were higher in the cirrhosis patients (23.7 ± 11.4 ml/s) in comparison to volunteers (16.3 ± 5.0 ml/s) using the fully sampled data sets. Consistency of flow measurements using conservation of mass was better in the time-averaged data ($3.9 \pm 3.1\%$) than the time-resolved data ($5.2 \pm 4.4\%$) using the fully sampled data sets. As the degree of undersampling increased, the degree of error in flow measurements expectedly increased. Mean flow values of the portal vein show good precision with scan times 25% or greater of the original acquisition. As undersampling increased further, flow quantification underestimated the flow in the portal vein. Complete results are summarized in Table 3. Bland-Altman plots are shown in Figure 5 comparing the different reconstruction methods.

Pulsatility Index

The pulsatility index was both low in the normal volunteers (0.34 ± 0.19) and the cirrhosis patients (0.24 ± 0.09).

DISCUSSION

In this study, we have demonstrated the feasibility of using time-averaged reconstruction with radial 4D-Flow MRI, to achieve comprehensive anatomic assessment and focused hemodynamic assessment in the portal vein in considerably shorter scan times than time-resolved acquisitions. Through retrospective undersampling we have shown that scan time reduction of up to 50-75% should be possible for high-quality assessment of non-pulsatile portal venous flow, where time-resolved hemodynamics may not be necessary. This would translate into a reduction in scan time from 10-12 minutes to approximately 3-4 minutes in duration.

When directly comparing a time-resolved versus a time-averaged approach using 100% of the acquired projections, the time-averaged reconstruction provided better results. This was demonstrated by a lower percentage error in flow quantification in patients (3.9% vs. 5.2%), longer streamline lengths (34mm vs 47mm), and higher visualization quality grading based on subjective radiologist evaluation (3.7 vs. 2.2). These results suggest immediate benefits when visualizing and quantifying 4D flow in the portal venous vasculature, as assessment of time-averaged flow conditions provide the best evaluation.

The comparisons between different time-averaged reconstructions show that significant scan time reductions can be made while still acquiring a quality 4D flow examination of the portal venous circulation. Although higher levels of undersampling negatively impacted blood flow quantification and visualization results, it was the angiographic reconstruction that suffered the most from higher levels of undersampling and is the main limiting factor that determined the degree of possible scan time reduction. In our comparisons, the time-averaged reconstruction using 33% of the data still provided high-quality results. We therefore suggest that a scan time reduction to this degree is beneficial when the primary goal is to visualize portal venous flow.

While we have shown that time-averaging is beneficial to quantify blood flow in non-pulsatile conditions such as in the portal vein, the effect on quantification of arterial and venous flow warrants further investigation. It is obvious that employing a time-averaged technique for visualizing blood flow in these systems would result in an inability to *visualize* pulsatile arterial or hepatic venous flow. However, the effect of time-averaging on *quantifying* blood flow is undetermined.

In this study, we utilized a radial acquisition scheme and it is unclear whether these results will translate into Cartesian based approaches. In the radial acquisition scheme, the central

region of k-space is averaged across the cardiac cycle and many heartbeats. Subsequently, the signal in the time-averaged radial reconstruction will better represent the average flow than an ungated Cartesian approach. While the pulsation in the portal vein may not be substantial, further investigation is warranted to investigate time averaged acquisition and reconstructions with Cartesian sampling.

There are some limitations of this study. One limitation in the study design is that the different data was reconstructed retrospectively rather than acquired prospectively. Ultimately, direct comparison of prospectively acquired data sets will be needed to demonstrate the utility of scan time reduction through temporal averaging. However, retrospective reconstruction of the same underlying data is also a strength, since it entirely avoids the confounding effects of any variability due to transient changes in the hemodynamics of the subject. Retrospective reconstruction also facilitates perfect co-registration of cutplanes and ROIs used for flow measurements

Another limitation in the study design is the challenge for comparing flow visualization between time-resolved and time-averaged reconstructions. In our qualitative and quantitative comparison we used streamlines, which depict the instantaneous tangent of the direction of a virtual particle. Pathlines, however, are typically used to visualize data with time-varying velocity components seen in time-resolved reconstructions. In conditions of steady, non-pulsatile flow, streamlines and pathlines are equivalent. Streamlines were used for both time-resolved and time-averaged reconstructions, to allow for similar comparisons and avoid measurement errors that would be due to differences in visualization technique.

In conclusion, we have demonstrated the use of time-averaged radial 4D MRI flow imaging as a mean to shortening scan times when quantification of flow in the portal circulation is needed. Using time averaging, scan time reductions up to 50-75% should be possible. Future work will examine the use of scan time reduction through temporal averaging using prospective acquisition and also what effect temporal averaging has on quantification of pulsatile flow.

Acknowledgments

The authors gratefully acknowledge support from NIH (R01 DK083380, R01 DK088925, R01 HL072260 and RC1 EB010384), and from GE Healthcare.

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Figure 1.

This blood flow visualization demonstrates the clinical utility of 4D flow MRI in evaluating portal hypertension and its associated variceal shunt development. For improved flow visualization, the arterial blood flow was segmented and removed from this image. Streamlines and arrow heads were created to visualize time-averaged flow patterns within the portal venous circulation (red arrows), the vena cava drainage (white arrows), and a splenorenal shunt (yellow arrows) connecting the two. Flow is visualized in the portal (PV), superior mesenteric (SMV), and splenic (SV) veins, as well as a splenorenal shunt (SRS) that directly empties into the left renal vein (LRV).

Figure 2.

This 4D MRI flow visualization of the portal hemodynamics in a patient with suspected portal vein thrombosis confirms not only a lack of flow in the portal vein but also abnormal flow directions in additional vessels. Time-averaged arterial (red/yellow) and portal venous (blue/green, red arrows) flow was visualized. Venous drainage is not included to improve image appreciation. Flow in the splenic vein (SV) drained directly into the superior mesenteric vein (SMV), which demonstrated hepatofugal flow away from the liver. In addition, there was reversed flow in the left portal vein (LPV), draining into the right portal vein (RPV).

Figure 3.

Consistency of blood flow quantification was assessed by using a conservation of mass technique, where the sum of input and output flow values at a confluence is expected to be zero. This method was accomplished by placing user defined double-oblique planes and ROIs within each vessel measuring flow rates in the superior mesenteric (SMV), splenic (SV) and portal (PV) veins. Percentage error was then calculated as: $(PV - SMV + SV)/PV$.

Figure 4.

The quality of angiography and flow visualization was assessed in data sets using time-resolved reconstructions and time-averaged reconstructions using 100%, 33%, and 10% of acquired projections. Axial complex difference (CD) images and maximum intensity projections (MIP) demonstrate the angiographic depiction of different scan times. Average streamline lengths and a streamline visualization grading were used to quantitatively and qualitatively assess the quality of each data set, respectively.

Figure 5.

Bland-Altman plots show the agreement between the different reconstruction methods. The time-averaged reconstruction using 100% of projections (TA100%) is used as the reference standard and is compared in (A) against the time-resolved reconstruction (TR), (B) the time-averaged reconstruction using 33% of projections (TA33%), and (C) the time-averaged reconstruction using 10% of projections (TA10%).

Table 1

Scoring guidelines used for consensus reading of angiographic quality.

Category	Description	Score
Background	<i>Substantial background, interferes with diagnosis.</i>	0
	<i>Moderate background, does not interfere with diagnosis.</i>	1
	<i>No substantial noise.</i>	2
Blurring/edge sharpness	<i>Severe blurring. Vessel dropouts. Non-diagnostic.</i>	0
	<i>Moderate to severe blurring. Loss of diagnostic accuracy.</i>	1
	<i>Moderate blurring. Does not interfere with diagnosis.</i>	2
	<i>Minimal blurring.</i>	3
	<i>No evident blurring.</i>	4

Table 2

Scoring guidelines used for consensus reading of visualization quality.

Description	Score
<i>Poor streamline visualization. Substantial degradation of streamline quality, limiting depiction of anatomy and flow direction. Nondiagnostic.</i>	0
<i>Fair streamline visualization. Significant noise in streamline path and velocity distribution but still diagnostic for anatomy and flow direction.</i>	1
<i>Moderate streamline visualization. Depicts anatomy and flow direction with moderate noise in streamline path and/or velocity distribution.</i>	2
<i>Good streamline visualization. Depicts anatomy and flow direction with small degree of noise in streamline path and/or velocity distribution.</i>	3
<i>Excellent streamline visualization. Depicts anatomy and flow direction with negligible or no noise in streamline path or velocity distribution</i>	4

Table 3

Anatomic and flow visualization comparison between the time-resolved and time-averaged reconstructions

Comparison Method	Time-resolved	100%	50%	33%	Time Averaged 25%	20%	10%	5%
Angiography Score								
Background	2.0 ± .2	2.0 ± .2		1.3 ± 0.6			0.4 ± 0.5	
Blurring	4.0 ± .2	4.0 ± .2	X	3.1 ± 0.8	X	X	1.3 ± 1.0	X
Streamline Length (mm)								
	34.0±15.2	46.9±7.4	43.0±7.0	39.3±6.2	38.0±6.8	38.0±12.5	33.4±13.3	28.5±15.3
Visualization grading								
	2.2 ± 0.9	3.7 ± 0.5	X	2.7 ± 0.6	X	X	1.5 ± 0.6	X
Conservation of Mass								
Volunteers	5.5±3.9%	4.8±2.5%	5.1±3.3%	5.0±4.4%	6.2±4.3%	4.6±5.9%	6.9±5.7%	7.1±7.2%
Cirrhosis patients	5.1±4.6%	3.4±3.3%	3.6±3.3%	4.2±4.3%	5.0±4.9%	5.1±4.5%	7.0±8.4%	6.7±8.5%
PV flow (ml/s)								
Volunteers	15.5 ± 4.5	16.3 ± 5.1	16.3 ± 5.0	15.9 ± 4.6	16.3 ± 5.3	15.1 ± 3.9	14.0 ± 3.2	10.6 ± 3.9
Cirrhosis patients	22.3 ± 10.1	23.7 ± 11.4	23.6 ± 11.5	22.7 ± 10.9	23.4 ± 12.5	22.1 ± 10.6	19.0 ± 9.1	14.9 ± 6.8

Abbreviations: X = assessment was not performed. PV = portal vein. SMV = superior mesenteric vein. SV = splenic vein.