Shear Wave Elastography of the Spleen for Monitoring Transjugular Intrahepatic Portosystemic Shunt Function

A Pilot Study

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Methods—We measured splenic shear wave velocity (SWV), main portal vein velocity (PVV), and splenic vein velocity (SVV) in 33 patients 1 day before and 3 days to 12 months after TIPS placement. We also measured PVV, SVV, and SWV in 10 of 33 patients with TIPS dysfunction 1 day before and 3 to 6 days after TIPS revision. Analyses included differences in portosystemic pressure gradient (PPG), PVV, SVV, and mean SWV before and after TIPS procedures; comparison of median SWV before and after TIPS procedures; differences in PVV, SVV, and SWV before and at different times up to 12 months after TIPS placement; accuracy of PVV, SVV, and SWV in determining TIPS dysfunction; and correlation between PPG and SWV.

Results—During 12 months of follow-up, 23 of 33 patients had functioning TIPS, and 10 had TIPS dysfunction. The median SWV was significantly different before and after primary TIPS placement (3.60 versus 3.05 m/s; \( P = .005 \)), as well as before and after revision (3.73 versus 3.06 m/s; \( P = .003 \)). The PPG, PVV, and SVV were also significantly different before and after TIPS placement and revision (\( P < .001 \)). The PPG and SWV decreased, whereas PVV and SVV increased, after successful TIPS procedures. A positive correlation was observed between PPG and SWV (\( r = 0.70; P < .001 \)), and a negative correlation was observed between PPG and PVV and SVV (\( r = -0.65; P < .001 \)). The areas under the receiver operating characteristic curve for PVV, SVV, and SWV in determining TIPS dysfunction were 0.82, 0.84, and 0.81, respectively.

Conclusions—Splenic SWV is compatible with splenoportal venous velocity in quantitatively monitoring TIPS function and determining TIPS dysfunction.

Key Words—Doppler sonography; shear wave velocity; spleen stiffness; transjugular intrahepatic portosystemic shunt; ultrasound elastography

The transjugular intrahepatic portosystemic shunt (TIPS) is used for management of refractory acute variceal hemorrhage and intractable ascites in late-stage liver diseases with portal hypertension.\(^1\) In addition to monitoring the clinical status, it is important to monitor TIPS hemodynamic function objectively.\(^2,3\) Although the portosystemic pressure gradient (PPG) and hepatic venous pressure gradient are still considered the reference standards for diagnosis and monitoring of portal hypertension, they...
have limited repeatable value in monitoring TIPS function because of their invasive nature. Therefore, noninvasive techniques are preferred for evaluating TIPS function.

Among noninvasive ultrasound imaging techniques, color Doppler sonography has been used to measure intra-TIPS stent flow velocity and splenoportal venous velocities to directly and indirectly assess TIPS function. The accuracy of splenoportal venous velocities for detecting TIPS dysfunction may diminish by the involvement of splenoportal venous hemodynamics in portal hypertension, since the size and location of portosystemic collateral development differ from patient to patient and can profoundly affect portal venous flow. Although some pitfalls of using portal venous Doppler parameters to assess TIPS function have been reported, Doppler velocities sampled in the splenoportal veins are still considered noninvasive indirect indicators for monitoring the development of TIPS dysfunction.

Ultrasound elastography provides a quantitative means of assessing tissue biomechanical properties (stiffness) that are altered after certain pathologic changes. As reported, spleen stiffness estimated by real-time elastography, FibroScan, and Virtual Touch tissue quantification (VTQ; Siemens Medical Solutions, Mountain View, CA) on acoustic radiation force impulse imaging can be used for diagnosis of liver fibrosis and portal hypertension and for predicting variceal bleeding. The novel ultrasound-based acoustic radiation force impulse imaging directly estimates tissue stiffness by measuring the speed of shear wave propagation through the tissue in the region of interest (eg, the spleen). An acoustic push pulse transmitted by the transducer toward the tissue produces elastic shear waves that propagate perpendicular to the path of the pushing pulse in the tissue. The speed of shear wave propagation (shear wave velocity [SWV], meters per second) is directly related to tissue elasticity and tissue stiffness. The shear wave moves faster if the tissue is stiffer, whereas it moves slower if the tissue is softer.

Previously, we used VTQ to assess changes in spleen stiffness before and shortly after TIPS placement. Our preliminary results showed a high correlation between portosystemic pressure measured by PPG and spleen stiffness as assessed by VTQ. The spleen was stiffer when PPG was higher before TIPS placement, whereas the spleen became softer when PPG decreased early (3–9 days) after TIPS placement. The aim of this pilot study was to validate the utility of splenic SWV as a noninvasive quantitative marker not only for assessing the success of TIPS procedures but also for long-term monitoring of TIPS function after TIPS placement. The diagnostic performance of splenic SWV for determining TIPS dysfunction was compared with PPG and conventional Doppler splenoportal venous flow measurements.

Materials and Methods

Patients

The Institutional Review Board approved this study, and written informed consent was obtained from all patients. From February 2012 to May 2014, we initially recruited 36 patients with portal hypertension who had a history of hepatitis B cirrhosis diagnosed by previous liver biopsy. All 36 patients also had a history of esophageal varices diagnosed by gastroesophageal endoscopy.

Patients who provided written informed consent, underwent splenic SWV, PVV, and SVV measurements before and after TIPS placement and TIPS revision, and completed follow-up SWV, PVV, and SVV measurements up to 12 months after TIPS placement or until development of TIPS dysfunction were included in the study. Patients who did not provide informed consent were not enrolled in the study. Patients were also excluded if follow-up SWV measurements after TIPS placement were discontinued for any reason (eg, death) before completion of 12 months of follow-up.

Transjugular Intrahepatic Portosystemic Shunt, Percutaneous Transhepatic Varix Embolization, and PPG Measurement

Transjugular intrahepatic portosystemic shunt placement was performed in the interventional division of the Department of Radiology. The patient was in the supine position. An appropriate covered stent (Fluency Plus FVL08080; Angiomed GmbH & Co, Medizintechnik KG, Karlsruhe, Germany) was selected for the TIPS based on the size of the liver, distance between the main portal vein and right hepatic vein, diameter of main portal vein, severity of portal hypertension, and clinical status of the patient (ie, amount of ascites and cardiac function). The PPG was measured during the TIPS procedure. A good hemodynamic response was defined as a reduction of PPG either to less than 12 mm Hg or at least 20% from the baseline value. In addition to TIPS placement, percutaneous transhepatic varix embolization was performed with spring coils (IMWCE-35-5-5 and MWCE-35-14-6 Nester; Cook Medical, Bloomington, IN) to embolize portosystemic collateral varices.
PPG was again measured during TIPS revision. The type of TIPS revision was determined by the site and severity of TIPS dysfunction. The initial TIPS placement, percutaneous transhepatic varix embolization, and TIPS revision were performed by a board-certified interventional radiologist with 10 years of experience in interventional procedures.

**Elastography and Splenoportal Vein Doppler Sonography**

Splenic elastography was performed with a 4C-1 curved linear array transducer (Acuson S2000; Siemens Medical Solutions) and with VTQ software installed on the ultrasound scanner. The patient was placed in the right lateral decubitus position to measure spleen stiffness through an intercostal approach. The left arm of the patient was placed overhead to extend intercostal space. The SWV was sampled in the splenic parenchyma at a depth of 2 cm from the splenic capsule in a region free of visible vessels (Figure 1, C and D). We measured the SWV during patient holding at the end of expiration. The size of the region of interest for measuring SWV was 10 × 5 mm. We measured the splenic SWV 3 times at each portion of the spleen (cranial, middle, and caudal), for a total of 9 SWV measurements. A measurement was repeated if X.XX appeared, indicating an invalid value in the VTQ system, until 9 successful SWV measurements were obtained. In addition to measuring mean SWV, we also used the interquartile range (IQR), which is also called the “middle 50,” as a measure of the statistical dispersion (being equal to the difference between the upper and lower quartiles) to assess the quality of the data. Valid SWV measurements were defined as an IQR-to-median value ratio of less than 30% and a success rate

Figure 1. A and B. Splenoportograms from a 47-year-old patient undergoing TIPS revision 12 months after TIPS placement and coil embolization of varices (yellow arrows). No contrast medium filling in the TIPS (A, white arrow) indicates shunt occlusion. After successful TIPS revision by relining with a covered stent, the contrast medium flows through the TIPS stent (B, white arrow). Portosystemic gradient pressures measured 29 and 15 mm Hg before and after TIPS revision, respectively. C and D. Shear wave elastograms of the spleen obtained with VTQ from the same patient. Shear wave velocities of the spleen measured 3.57 m/s 1 day before TIPS revision and 2.95 m/s 4 days after revision and were significantly different (P < .001).
(ratio of the number of successful acquisitions divided by the total number of acquisitions) of 60% or greater. An unsuccessful measurement was excluded from further analysis.22,23

The main portal vein velocity (PVV) and splenic vein velocity (SVV) were measured at the hepatic hilus (Figure 2) and splenic hilus (Figure 3), respectively. Doppler settings, including Doppler angle correction (the sound beam should be as parallel to the flow direction as possible, at least <60°), sample gate (3 mm), pulse repetition frequency, scale, and Doppler gain, were adjusted according to the depth of the portal and splenic veins and venous flow status. The maximum PVV and SVV were measured 3 times. The mean PVV and SVV were the averages of 3 PVV and 3 SVV measurements, respectively.

The PVV, SVV, and SWV were measured 1 day before TIPS placement and then 3 to 6 days and 3, 6, and 12 months after TIPS placement. The PVV, SVV, and SWV were also measured 1 day before and 3 to 6 days after TIPS revision. We did not perform SWV or splenoportal vein velocity measurements within the first 3 days after TIPS placement because the patient could not tolerate the scanning. Liver stiffness measurement by VTQ before and after TIPS placement was conducted in our previous studies17,18 and was not the topic of this report.

Transjugular intrahepatic portosystemic shunt dysfunction was diagnosed by color Doppler sonography. The criteria for TIPS dysfunction on color Doppler sonography included the following: (1) direct indicators, including lack of blood flow within the TIPS stent on color or spectral Doppler sonography, decompressed flow velocity (<60 cm/s), or elevated maximum flow velocity (>200 m/s) in the TIPS stent; and (2) indirect indicators, including low PVV (<20 cm/s) in the main portal vein and change in flow direction from hepatofugal to hepatopetal in the left portal vein, right portal vein, or both. In addition, the main clinical manifestations of TIPS dysfunction are an increase or the presence of ascites and recurrent variceal bleeding.4–7

For evaluating the reproducibility and reliability of splenic SWV for estimating spleen stiffness by VTQ, 2 observers independently measured the SWV in 10 patients for testing interobserver variation, and a single observer measured the SWV twice in 10 patients for testing inroobserver variation. Two ultrasound physicians with 5 and 10 years of experience, respectively, in abdominal ultrasound and each with 4 years of experience in performing VTQ scanned the 36 cases, and they were blinded to PPG measurements. However, they were aware of the patients with a history of cirrhosis.

**Statistical Analyses**

The quantitative variables, including PPG, PVV, SVV, and splenic SWV, were expressed as mean ± standard deviation. The SWV data were also analyzed by median, IQR, and IQR/median. The Wilcoxon signed rank test was used to compare the median SWV before and after TIPS procedures. A paired t test was applied to test the differences in PPG, PVV, SVV, and mean SWV before and after primary TIPS placement and before and after TIPS revision. After validating the data with the Mauchly sphericity test, repeated-measures analysis of variance was used to examine the differences in PVV, SVV, and SWV before and 3 to 6 days and 3, 6, and 12 months after TIPS placement. The Pearson correlation coefficient was used to assess the association between PPG and SWV and between PPG and splenoportal venous velocity. A column chart was used to compare the SWV values before and after primary TIPS placement and revision. Scatterplots were used to display the differences in follow-up SVV and SWV between func-

**Figure 2.** Doppler angle-corrected (29°) PVV in the main portal vein at the hepatic hilus after TIPS revision.

**Figure 3.** Doppler angle-corrected (35°) SVV at the spleen hilus after TIPS revision.
tioning and dysfunctioning TIPS. The accuracy of PVV, SVV, and SWV for determining TIPS dysfunction was examined by receiver operating characteristic curve analysis. The difference in the area under the receiver operating characteristic curve (AUROC) was then tested by the method of Hanley and McNeil. Interobserver and intraobserver variation was tested by the Pearson correlation coefficient. P < .05 was considered statistically significant. The statistical analyses were performed with SPSS version 22.0 software (IBM Corporation, Armonk, NY).

Results

The initial recruitment included 36 patients with TIPS placement (28 men and 8 women; age range, 28–75 years; mean age, 45 years). Three patients were excluded because of discontinuation of follow-up sonography after TIPS placement. Two of 3 patients died of hepatic encephalopathy, and 1 patient died of variceal rebleeding less than 12 months after TIPS placement. Finally, 33 patients were enrolled in the study. Nine valid splenic SWV measurements were obtained from all patients. Spleen stiffness measurements with valid technical parameters (success rate ≥60% [total number of SWV measurements <15] and IQR <30%) by VTQ were obtained in all patients. The common reason for repeating SWV measurements was poor patient cooperation during SWV measurement with the breath-holding maneuver.

The PPG decreased in all 33 cases with primary TIPS placement. There were statistically significant differences in PPG, PVV, SVV, and mean splenic SWV (all P < .05), as well as median SWV (P = .005) before and after primary TIPS placement (Tables 1 and 2).

During up to 12 months of follow-up after TIPS placement, 23 of 33 patients (70%) had functioning TIPS, and 10 (30%) developed TIPS dysfunction (Figure 1A). In addition to low PVV (<20 cm/s) in the main portal vein, other sonographic and clinical manifestations in the 10 cases with TIPS dysfunction were as follows: (1) change in Doppler flow direction from hepatofugal to hepatopetal in the left portal vein (9 of 10 [90%]); (2) recurrent variceal bleeding (10 of 10 [100%]); and (3) increase in ascites (7 of 10 [70%]). The 10 patients with TIPS dysfunction were treated with angioplasty, bare metal stenting, relining with a covered stent (n = 7; Figure 1B), and parallel TIPS stent placement (n = 3) 1 to 4 months after their primary TIPS placement. The PPG and SWV (Figure 1, C and D) were remarkably decreased, whereas PVV and SVV increased, after TIPS revision in all 10 cases. Statistically significant differences in PPG, PVV, SVV, and mean SWV (all P < .0001), as well as median SWV (P = .003; Table 2) were observed before and after TIPS revision.

A positive correlation was found between PPG and splenic SWV (r = 0.70; P < .001). A negative correlation was found between PPG and PVV and SVV (r = –0.65; P < .001).

### Table 1. Portosystemic Pressure Gradient, Splenic SWV, and Splenoportal Venous Flow Before and After TIPS Procedures

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Primary TIPS (n = 33)</th>
<th>After Primary TIPS (n = 33)</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPG, mm Hg</td>
<td>27.16 ± 3.18</td>
<td>19.09 ± 4.43</td>
<td>6.62</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>SWV, m/s</td>
<td>3.64 ± 0.23</td>
<td>3.18 ± 0.21</td>
<td>4.58</td>
<td>.0002</td>
</tr>
<tr>
<td>SVV, cm/s</td>
<td>18.47 ± 2.29</td>
<td>29.29 ± 2.21</td>
<td>–23.6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>PVV, cm/s</td>
<td>16.52 ± 3.41</td>
<td>28.37 ± 4.0</td>
<td>–23.6</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

### Table 2. Median and IQR of Splenic SWV in 10 Cases Before and After TIPS Procedures

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Primary TIPS</th>
<th>After Primary TIPS</th>
<th>Before TIPS Revision</th>
<th>After TIPS Revision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>3.60</td>
<td>3.05</td>
<td>3.73</td>
<td>3.06</td>
</tr>
<tr>
<td>IQR</td>
<td>0.39 (3.45–3.84)</td>
<td>0.26 (2.93–3.19)</td>
<td>0.38 (3.61–4.03)</td>
<td>0.25 (2.95–3.2)</td>
</tr>
<tr>
<td>IQR/median</td>
<td>0.11</td>
<td>0.09</td>
<td>0.10</td>
<td>0.08</td>
</tr>
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</table>

*The Wilcoxon signed rank test was used to examine the difference in median SWV before and after primary TIPS placement and before and after TIPS revision.*
P < .001). The AUROC values for PVV, SVV, and SWV in determining TIPS dysfunction were 0.82, 0.84, and 0.81, respectively (Table 3). There were no significant differences in AUROC values between PVV and SVV, SVV and SWV, or PVV and SWV as tested by the method of Hanley and McNeil.24 Diagnostic performance parameters for PVV, SVV, and SWV in determining TIPS dysfunction are listed in Table 3. The Pearson correlation coefficients were r = 0.86 and r = 0.94 for interobserver and intraobserver variation, respectively.

Discussion

Our results indicate that spleen stiffness estimated by splenic SWV seems to be feasible for monitoring TIPS function (Figure 4). Given the high frequency of asymptomatic TIPS failure, an accurate screening test is needed to confirm shunt patency and identify shunt dysfunction. A noninvasive means of follow-up would minimize both patient morbidity and costs.1

To date, there have been a few reports on using ultrasound elastography18,19,25 and magnetic resonance elastography26 to estimate spleen stiffness in a short time after TIPS placement. In this report, we show significant differences in both mean and median splenic SWV values not only before and after primary TIPS placement but also before and after successful TIPS revision, which again demonstrate that spleen stiffness as measured by SWV has a close relationship with portal vein pressure. When portal vein pressure is higher, the spleen is stiffer, and SWV increases, whereas when portal vein pressure is lower, the spleen becomes softer, and SWV decreases.17 The explanation for this result would be that portal hypertension would initially and directly induce hypersplenism, with associated histologic changes in the spleen. Portal hypertension will evoke hyperplasia among splenic histiocytes, arterial terminal lengthening, and an increased spleen pulp volume in addition to an increase in portal pressure and hyperdynamic circulation.27 This scenario would be the best explanation for a substantial change in spleen stiffness following resolution of portal hypertension after TIPS placement17,18 as well as after liver transplantation.28

To our knowledge, a study assessing the feasibility of using spleen stiffness measured by SWV for monitoring TIPS function up to 12 months after TIPS placement has not been reported previously. After primary TIPS placement and revision, portal vein pressure is decompressed; spleen congestion is reduced; and splenic SWV, which represents spleen stiffness, is gradually decreased. Our data suggest that spleen stiffness starts decreasing 3 to 6 days after TIPS insertion, and the lowest SWV in this study was measured 3 months after TIPS placement (Figure 5). One of 10 patients underwent a full 12 months of follow-up splenic SWV measurements, during which the time when

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SWV, m/s</th>
<th>SVV, cm/s</th>
<th>PVV, cm/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutoff value</td>
<td>3.61</td>
<td>25.4</td>
<td>18.9</td>
</tr>
<tr>
<td>AUROC</td>
<td>0.81</td>
<td>0.84</td>
<td>0.82</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.92</td>
<td>0.91</td>
<td>0.90</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.66</td>
<td>0.68</td>
<td>0.73</td>
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There were no significant differences in AUROC values between SWV and SVV, SWV and PVV, or SVV and PVV (P > .05).
SWV started to increase was 6 months after TIPS placement, and the time when clinically indicated TIPS dysfunction (eg, increase in ascites) developed, which required TIPS revision, was in 12 months after placement. It seemed that an increase in SWV preceded the clinical presentation of TIPS dysfunction. Conversely, the SWV in 23 cases with normal TIPS function seemed to be stable at all times up to 12 months of follow-up sonography (Figure 5). Our results suggest that splenic SWV can be used to quantitatively assess spleen stiffness as an indicator of TIPS function. Therefore, splenic SWV can be considered an important predictor of the development of TIPS dysfunction.

In addition, a negative correlation between PPG and PVV and SVV indicates that a decrease in spleen stiffness is associated with an improvement in splenoporal venous drainage into the systemic circulation through the TIPS. We observed an increase in both PVV and SVV starting 3 to 6 days after primary TIPS and percutaneous transhepatic varix embolization, as well as after TIPS revision (Table 1). The changing trend of PVV and SVV values seemed to be similar to splenic SWV measurement during 12 months of TIPS function follow-up. Both PVV and SVV were stable in 23 cases with functioning TIPS, whereas they were substantially decreased in the 1 case with TIPS dysfunction (Figure 6).

All PVV, SVV, and SWV values had good predictive ability for determining TIPS dysfunction (Figure 7 and Table 3). There were no significant differences in the AUROC values for determining TIPS dysfunction between PVV and SVV, PVV and SWV, or SVV and SWV, suggesting that splenic SWV is compatible with conventional splenoporal venous Doppler velocities for monitoring TIPS function. Importantly, we found good interobserver reproducibility (r = 0.86) and intraobserver repeatability (r = 0.94) in spleen stiffness estimation with VTQ in this study.

Limitations of this study included a relatively small sample size in the population with TIPS dysfunction and the absence of splenic SWV measurements in the immediate post-TIPS placement period. In addition, the 3-month interval in the SWV follow-up schedule seemed not to be short enough to detect possible subclinical TIPS dysfunction because 9 cases developed clinical TIPS dysfunction, and Doppler sonography confirmed dysfunction before approaching the date of the scheduled follow-up SWV measurement after TIPS placement. Furthermore, we obtained 9 splenic SWV measurements in our study, whereas 10 SWV measurements in the liver are currently recommended. The recommended protocol of 10 SWV measurements for assessing tissue stiffness is taken into consideration for standardization of abdominal organ (eg, spleen) stiffness assessments in future studies. Finally, we are not able to test whether the same splenic SWV could be measured by using ultrasound scanners designed by different manufactures. Therefore, further studies of spleen stiffness in large populations with TIPS dysfunction with long-term follow-up after TIPS procedures are encouraged.

In conclusion, spleen stiffness measured by SWV is compatible with Doppler splenoporal venous parameters for monitoring TIPS function. Splenic SWV can be used as an alternative quantitative marker for determining TIPS dysfunction.

**Figure 6** Mean splenic SVV measurements before and at different times after TIPS placement in 23 patients with functioning TIPS and 1 patient with TIPS dysfunction diagnosed 12 months after primary TIPS placement. One can clearly note that the SVV seems to be stable in the 23 functioning TIPS, whereas it decreases in the dysfunctional TIPS. The same trend was also observed in PVV measurements during 12 months of follow-up.

**Figure 7** Areas under the receiver operating characteristic curve for testing the diagnostic performance of Doppler PVV, SVV, and splenic SWV in determining TIPS dysfunction. There were no significant differences in AUROC values between PVV and SVV, PVV and SWV, or SVV and SWV (P > 0.05).
References


