A Newly Developed Shear Wave Elastography Modality: With a Unique Reliability Index

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Key Words
Net amount of effective shear wave velocity · Reliability index · Shear wave measurement · Shear wave imaging · Shear wave elastography

Abstract
Objective: The aim of this study was to prospectively assess the usefulness of the reliability index, namely the percentage of the net amount of effective shear wave velocity (VsN).

Methods: One hundred and sixty-eight patients with chronic liver disease, who underwent ultrasound elastography, were consecutively enrolled. Shear wave measurement (SWM), FibroScan, virtual touch quantification, and shear wave elastography were performed for all patients, and the variations in the measurement results were compared with VsN. The absolute average value of the difference between SWM_Vs and Vs measured using other elastography devices is termed |ΔVs|. VsN was classified into three groups: ≥50, <50, and 0 (failure measurement). In these groups, there was a significant difference in abdominal circumference, body mass index, the distance between the ultrasound probe surface and the liver, and |ΔVs|. When the distance between the ultrasound probe surface and the liver was >2 cm, VsN tended to be significantly lower (p < 0.001).

Results: When VsN was <50, |ΔVs| became high, and there was variation in the results between each device.

Conclusions: The results of this study show that VsN is a useful value to decide whether Vs is appropriate or not.

Introduction
A variety of ultrasound elastography devices are currently available. They have been reported to be useful in the decision of the clinical treatment of hepatic disease, or in the diagnosis of noninvasive liver fibrosis [1–5]. Using elastography, it is also possible to noninvasively predict hepatocarcinogenesis [6, 7]. As a result of performing follow-up on high-risk groups using this modality, it can be expected that hepatic cancer will be detected at an early stage. Consequently, curative treatments such as resection [8–10], locoregional therapy [11, 12], and transplantation [13–15] are possible.

Ultrasound elastography can be classified by measuring physical quantity and excitation [16, 17]. In point shear wave elastography, generally only one shear wave
velocity (Vs) is measured within the region of interest (ROI), which is presumed to be homogeneous (typically \( \sim 1 \text{ cm}^2 \)) [17]. Therefore, it may be difficult to determine whether the measurements obtained using shear wave imaging are valid. Several examination conditions influence Vs: breath holding and the body movement of subjects; holding the hands of examiners, and other conditions. Furthermore, in performing elastography, it is important to avoid the vessels, multiple reflections, attenuation shortage, and other factors. Even when considering interquartile range (IQR) or standard deviation (SD), it is unclear whether a high level of IQR or SD has been influenced by measurement errors or the state of the liver. Therefore, deciding whether Vs is correct or not is too difficult. Thus, there is a need for a new method to achieve accurate examination.

Shear wave measurement (SWM; Hitachi Aloka Medical Ltd., Tokyo, Japan) is one of the shear wave imaging modalities currently under development. The SWM device has a unique reliability index: the percentage of the net amount of effective shear wave velocity (VsN) is used to determine whether or not the Vs value is reliable. This device can be applied to measure a plurality of points in one measurement, and it calculates the Vs value using only appropriate waves. The VsN shows which percentage of the measurement value is used in the calculation of Vs. In other words, the higher the VsN, the more stable the measurement.

In the present study, we investigated the performance of VsN in determining whether or not Vs is appropriate, using different shear wave imaging devices, namely the FibroScan (FS), virtual touch quantification (VTQ), and shear wave elastography (SWE) devices.

**Patients and Methods**

**Patients**

This was a cross-sectional study performed at Kinki University Hospital (Osakasayama, Japan). From July 2014 to March 2015, consecutive patients with chronic liver disease, who underwent ultrasound elastography, were enrolled. The study protocol conformed to the requirements listed in the Declaration of Helsinki and was approved by the Local Ethics Committee. Informed consent regarding participation in the study was obtained from each patient.

**Clinical and Laboratory Assessments**

Clinical data were collected at the time of elastography. Relevant clinical data recorded were age, sex, weight, height, abdominal circumference, and cause of chronic liver disease. The body mass index (BMI) was calculated as weight (in kg) divided by height (in m) squared.

**Liver Histological Assessment**

Percutaneous ultrasound-guided liver biopsy was performed on the right lobe of the liver using a Tru-Cut semiautomatic 18-gauge needle apparatus (Monopty; CR Bard, Tempe, Ariz., USA) within 2 weeks before or after elastography. The liver biopsy specimens were fixed in formalin, embedded in paraffin, and stained with hematoxylin and eosin and Masson’s trichrome stain. All biopsy specimens were examined by pathologists who were blinded to the patient characteristics. Liver fibrosis was scored using the New Inuyama Classification [18]. The stage of fibrosis was classified from F0 to F4 as follows: F0 = no fibrosis; F1 = fibrosis portal expansion; F2 = bridging fibrosis (portal-portal or portal-central linkage); F3 = bridging fibrosis with lobular distortion (disorganization), and F4 = cirrhosis.
Shear Wave Measurement
SWM was performed using ultrasonography (HI-VISION Ascendus; Hitachi Aloka Medical Ltd.) and the EUP-C715 convex probe (1–5 MHz; Hitachi Aloka Medical Ltd.). Patients were examined in the supine position with the right arm under maximal abduction and instructed to hold their breath in the middle of natural breathing. The examinations were performed on the right lobe of the liver through the intercostal spaces, with the transducer held firmly on the skin. The ROI for the SWM was 1 × 1.5 cm in size and was located approximately 4 cm below the surface of the body. In addition, to obtain accurate values, scanning was performed to avoid large vessels and attenuation by the lung, ribs, and skin. The $V_s$ was measured 5 times, and then the median values were evaluated as the SWM_Vs. Similarly, the median $V_s$N was used for evaluation (fig. 1). The distance between the ultrasound probe surface and the liver was also recorded.

FibroScan
FS was performed using a dedicated liver stiffness measurement device, a FibroScan with the M-probe (Echosens, Paris, France). The posture of the patient was the same as that used for SWM. The procedure was performed on the right lobe of the liver through the intercostal space. Examinations that achieved no successful measurements after at least 10 attempts were deemed ‘failures’. The median liver stiffness value (in kPa) was considered as being representative of the elastic modulus of the liver. As an indicator of variability, the ratio of the IQR of liver stiffness to the median value (IQR/M) was calculated. Examinations with <10 valid measurements or an IQR/M >30% or a success rate <60% were considered potentially ‘unreliable’ [19]. For evaluation, the liver stiffness value was converted to FS_Vs (in kPa) using the relationship $E = 3pV_s^2$ (E = liver stiffness; $p =$ density, which was approximated as 1 g/cm$^3$ in the living human body).

Virtual Touch Quantification
VTQ was performed using an ACUSON S2000 with a convex 4C1 probe (Siemens AG, Munich, Germany). The ROI for VTQ was 1 × 1.5 cm and was located 1–2 cm below the surface of the liver. The $V_s$ was measured 5 times, and then the median value was evaluated as VTQ_Vs.

Shear Wave Elastography
SWE was performed using an Aixplorer with a convex prove SC6-1 (SuperSonic Imagine, Aix-en-Provence, France). The ROI for SWE was located at approximately 4 cm below the surface of the skin. The Q box was set to the site without the influence of multiple reflections in color mapping and the $V_s$ was measured. It was measured 5 times, and then the median values were evaluated as the SWE_Vs.

Statistical Analysis
Descriptive statistics are shown as mean ± SD, median (minimum and maximum), or percentage, as appropriate. Comparisons between the groups were carried out using the Wilcoxon signed-rank test and confirmed using the nonparametric Mann-Whitney U test between groups. Correlation between the data was tested with the nonparametric Spearman rank correlation analysis. The Jonckheere-Terpstra analysis was applied for comparison of the trends in each $V_s$ and liver fibrosis. The Kruskal-Wallis one-way analysis of variance test was used for comparison among multiple groups. Differences were considered statistically significant at p values <0.05. Analysis was performed using SPSS Statistics 20 (IBM, Armonk, N.Y., USA).

Results
Demographics and Baseline Features
A total of 169 patients were assessed using elastography. However, VTQ had broken down at the time of measurement in 1 case, thus 168 cases were enrolled. The clinical characteristics and laboratory data are shown in table 1. Seventy-two patients (42.9%) had...
chronic hepatitis C, 37 (22.0%) chronic hepatitis B, 32 (19.0%) nonalcoholic fatty liver disease, and 6 (3.6%) had alcoholic liver disease. In the remaining 16 patients, autoimmune hepatitis, primary biliary cirrhosis, normal liver with tumor, and other conditions were included. Ninety-one patients (54.2%) were women. The patients’ mean age was 60.6 ± 14.9 years. Their mean height was 160.0 ± 8.5 cm and their mean weight was 60.6 ± 13.4 kg. The mean BMI was 23.1 ± 5.1 and their mean waist circumference was 86.5 ± 11.0 cm. Height and weight were significantly higher in men (p < 0.001); however, a significant difference was not observed regarding abdominal circumference and BMI between men and women.

Comparison of Vs and Pathological Diagnosis

Ninety-three patients underwent percutaneous ultrasound-guided liver biopsy. As the stage of fibrosis progressed, a significant increasing trend was seen for the SWE_Vs, FS_Vs, VTQ_Vs, and SWE_Vs (p < 0.001, 0.001, 0.001, 0.001, respectively; Jonckheere-Terpstra analysis; data not shown).
Vs Measured Using SWE, FS, VTQ, and SWE
SWM_Vs ranged from 0.85 to 2.85 m/s, and the median value of SWM_Vs was 1.48 m/s. FS_Vs ranged from 0.95 to 5.00 m/s, and the median value of FS_Vs was 1.37 m/s. VTQ_Vs ranged from 0.74 to 4.48 m/s, and the median value of VTQ_Vs was 1.17 m/s. SWE_Vs ranged from 1.08 to 3.86 m/s, and the median value of SWE_Vs was 1.44 m/s. A significant high correlation was observed between SWM_Vs and FS_Vs (r = 0.832; p < 0.001), between SWM_Vs and VTQ_Vs (r = 0.765; p < 0.001), and between SWM_Vs and SWE_Vs (r = 0.901; p < 0.001; fig. 2).

Reliability Rate for Each Shear Wave Imaging Device
SWM could be calculated in 164/168 (97.6%) patients. A reliable rate of FS_Vs, i.e. a frequency validity ≥60% and IQR/M <30%, was only achieved in 146/168 (86.9%) patients. An unreliable rate of measurement was found in
11/168 (6.5%) patients. In 11 (6.5%) patients, FS_VS could not be measured at all. When body weight, abdominal circumference, or BMI was high, a significant valid measurement of FS was difficult to obtain (data not shown). VTO_VS could be measured in all patients. SWE could be measured in 167/168 (99.4%) patients. An unmeasurable case involved a highly obese woman: the distance from the body surface to the liver surface was 29.4 mm, and her BMI was 34.5. Only the SWM and VTQ could be obtained in her case.

Relationship between the Discrepancy in the Vs and VsN
To examine the extent of the discrepancy between SWM and other elastography modalities, the absolute average value of the difference between SWM_Vs and Vs measured using other elastography devices was calculated by |[(SWM_VS – VTQ_VS) + (SWM_Vs – FS_Vs) + (SWM_Vs – SWE_Vs)]/3|, and was termed |ΔVs|. When VsN was <50, |ΔVs| tended to be significantly higher (p < 0.001; fig. 3, 4). VsN was classified into three groups: ≥50, <50, and 0 (failure measurement). In these groups, there was a significant difference in abdominal circumference, BMI, the distance between the ultrasound probe surface and the liver, and |ΔVs| (table 3). When the distance between the ultrasound probe surface and the liver was >2 cm, VsN tended to be significantly lower (p < 0.001; fig. 5).

Discussion
Each shear wave imaging modality was found to be able to achieve significant correlated measurements, even though the principles of their measurement were somewhat different. The slight differences in Vs seemed to be affected by the differences in shear wave frequency, shear wave intensity, and so on.

However, the success rate of the measurement differed substantially with each elastography. VTO measurement was possible in all cases. On the other hand, Vs could not be measured in some cases with other elastography. Measuring Vs with SWM tended to be difficult in obese patients with a high BMI or a large abdominal circumference. Because the distance between the ultrasound probe surface and the liver was large in these cases, it is likely to lead to insufficient attenuation. It may also weaken the generation of shear wave or the sensing pulse of shear wave.

When VsN was <50, |ΔVs| tended to be significantly high. This means that the discrepancy of measurements is high, and the validity of the Vs value is not high in this condition. In SWM, VsN tended to be <50 when the distance between the ultrasound probe surface and the liver was ≥2 cm. However, there were obese cases in whom Vs could be measured, and there were nonobese cases in whom Vs could not be measured. Therefore, VsN is very useful to determine whether or not the Vs value is correct in SWM.

The results of this study show that VsN is a useful value for deciding whether or not the Vs value is appropriate.

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Disclosure Statement
The authors declare that they have no conflicts of interest.

References
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