Liver fibrosis assessments using FibroScan, Virtual-Touch tissue quantification, the FIB-4 index, and Mac-2 binding protein glycosylation isomer levels compared with pathological findings of liver resection specimens in patients with hepatitis C infection

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Abstract
Background and purpose: Viral infection promotes fibrosis through repeated regeneration of hepatocytes. Evaluation of fibrosis stage is important to monitor progression of liver disease and risk of hepatocellular carcinoma (HCC). While liver biopsy is the gold standard, the method is invasive and faces several limitations. The aim of this study was to determine correlations among METAVIR scores and Fibroscan, Virtual-Touch tissue quantification (VTQ), fibrosis index based on four factors (FIB-4 index), and Mac-2 binding protein glycosylation isomer (M2BPGi) level to examine differences in reliability of non-invasive methods to evaluate fibrosis.

Methods: We used liver resection specimens from patients with hepatitis C virus (HCV). Correlations were assessed between METAVIR scores and each test. Receiver operating characteristic (ROC) curves were generated to determine the sensitivity, specificity, and cut off values of the tests.

Results: Among the four tests, VTQ had the best correlation with the METAVIR score, followed by FibroScan. In ROC curves, the area under the curve (AUC) for diagnosis of fibrosis grade ≥F2 were as follows: 0.94 for FibroScan, 0.89 for VTQ, 0.85 for the FIB-4 index, and 0.77 for M2BPGi level. The respective values for diagnosis of grade ≥F3 were 0.85, 0.84, 0.74, and 0.73, and those for a diagnosis of F4 were 0.91, 0.88, 0.67, and 0.78.

Conclusions: FibroScan and VTQ best reflected the results of hepatic fibrosis diagnosis using liver resection specimens among the four examination methods evaluated.

Background
Chronic hepatitis is a disease state most commonly caused by viral infections, in which hepatocytes exhibit inflammation/necrosis, resulting in fibrosis due to repeated regeneration of hepatocytes. [1, 2] Further progression results in liver cirrhosis and an increased risk of developing hepatocellular carcinoma (HCC). The diagnosis of liver fibrosis is very important for determining treatment, predicting chronic liver disease, and assessing the risk of liver cancer. [3] Pathological evaluation of liver biopsy specimens is the gold standard for diagnosis, but because biopsy is invasive, it is difficult to perform frequently. [4–7] In addition, various problems are associated with biopsy that prevent accurate evaluation, such as sampling difficulty, the small amount of specimen obtained, and the
subjectivity of the pathologist’s evaluation. [8, 9] For this reason, visual evaluation by ultrasonography and measurements of various blood-based parameters have been conducted as noninvasive methods of hepatic fibrosis diagnosis.

Conventionally, noninvasive methods of assessing the liver fibrosis stage include measuring platelet counts, levels of liver fibrosis markers such as hyaluronic acid and type 4 collagen 7S, the aspartate aminotransferase to platelet ratio index, the fibrosis index based on four factors (FIB-4 index), FibroTest, and the serum level of Mac-2 binding protein glycosylation isomer (M2BPGi). [10–14]

In recent years, FibroScan and Virtual-Touch tissue quantification (VTQ) have gained attention due to advances in ultrasonic diagnostic equipment. Many reports have compared the META-analysis of histological data in VIRal hepatitis (METAVIR) scores of those tests with liver biopsy, both of which are reported to be highly reliable. [12, 15–18] As mentioned previously, however, liver biopsy is invasive and faces limitations with respect to sample amount and pathologist subjectivity. No report has so far compared liver resection specimens in combination with VTQ, FIB4-index and M2BPGi, and only a few reports have compared liver resection specimens with FibroScan. [19]

In this study, we used FibroScan and VTQ, which measure liver stiffness via ultrasound, in liver resection specimens from patients with hepatitis C virus (HCV). Correlations were calculated between METAVIR scores and each of these ultrasound tests as well as two hematological marker-based methods: the FIB-4 index and M2BPGi level. ROC curves were generated to determine the sensitivity, specificity, and cutoff values of the tests. From the results, we examined differences in reliability. Inspections were conducted by experienced examiner.

**Methods**

**Patients**

We recruited adult patients with chronic hepatitis C who were indicated for surgery for HCC at our hospital from March 2011 to November 2017. In addition, patients with liver metastasis were recruited as normal controls (n=14: alcohol; every day/by chance/none: 1 / 7 / 6). Ultrasonography and histology revealed no fatty liver.

**Liver stiffness measurements**
Liver stiffness was measured using FibroScan and VTQ. Blood parameter was FIB-4 index and the level of M2BPGi. FibroScan measurements should be repeated at least 10 times to obtain a median value and interquartile range. If the rate of successful measurements among the total measurements is <60% or the interquartile range/median value is >0.3, the measurements are considered low quality and should not be used in clinical decision making. [20] VTQ was performed using the ACUSON S2000 ultrasound system (Siemens Medical Solutions Inc., CA, USA). Five VTQ measurements were obtained to calculate the average value. FibroScan and VTQ were performed in the intercostal space with the patient lying in the dorsal decubitus position with the right upper limb raised, and liver stiffness measurements were obtained from the right lobe of the liver. Fibroscan and VTQ were measured by the same examiner. The M2BPGi level and FIB-4 index were measured in blood samples obtained before surgery. Two ultrasound elastography and blood examinations were performed within 1 month before surgery. HCV was determined by blood test.

**Histological analysis**

Liver specimens were obtained by resection of non-tumor tissues, at a site away from the tumor. Because, non-tumor tissue just near the tumor is largely compressed and not accurately examined. Sites near the tumor could not be evaluated, because tumor tissue is broken down by thermocoagulation during liver resection. In addition, specimens obtained from sites near the resected margins or liver surface cannot be evaluated accurately and thus were not included in the study.

The liver resection specimens were fixed in formalin and embedded in paraffin. The sections were subjected to hematoxylin–eosin and azan staining. All surgical specimens were analyzed independently by two experienced pathologists who were blinded to the clinical data. In the case of a discrepancy between the pathologists, the histological grade of each specimen was determined by consensus between them. Fibrosis was graded according to the METAVIR scoring system as follows: F0, no fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis with rare septa; F3, numerous septa without cirrhosis; and F4, cirrhosis. [21]

SPSS software version 18 (SPSS, Chicago, IL, USA) was used for all statistical analyses. P-values less
than 0.05 were considered statistically significant.

Results

Study population

A total of 108 patients were included in the current study (80 males, 28 females; mean age, 69.0 (21-87) years). The METAVIR fibrosis grade according to FibroScan was F1, F2, F3, and F4 in 2, 36, 39, and 17 of the 94 patients, respectively. The HCC patients mean (range) FIB-4 index was 4.27 (0.3-13.7), and the mean (range) M2BPGi level was 2.79 (0.29-8.75). Among the 108 total subjects, a sustained virological response (SVR) was seen in 74 patients, and failure to achieve sustained virological response (non-SVR) was observed in 20 patients (Table 1). SVR status was determined by blood test before surgery. Details on non-SVR are shown in Table 2 (Table 2).

Box plots of Fibroscan, VTQ, Fib4-index and M2BPGi

The box plots of the METAVIR scores with respect to each method are shown in Figure 1 (Figure 1). According to Spearman's rank correlation analysis, positive correlations between each method and the METAVIR fibrosis stage were observed (FibroScan: \( r=0.61, p\leq0.001 \) (Figure 1a); VTQ: \( r=0.64, p\leq0.001 \) (Figure 1b); FIB-4 index: \( r=0.40, p\leq0.001 \) (Figure 1c); and M2BPGi: \( r=0.32, p=0.01 \) (Figure 1d)). The median METAVIR scores for each method were as follows: FibroScan, F0: 3.9, F1: 7.6, F2: 8.8, F3: 13.1, F4: 22.8; VTQ, F0: 1.03, F1: 1.22, F2: 1.38, F3: 1.88, F4: 2.42; FIB-4 index, F0: 1.27, F1: 3.60, F2: 2.78, F3: 4.20, F4: 4.04; M2BPGi, F0: 0.55, F1: 1.40, F2: 1.71, F3: 2.37, F4: 3.60. Among the four methods, VTQ had the best correlation with the METAVIR score (\( r=0.64, p<0.001 \)), followed by FibroScan (\( r=0.61, p\leq0.001 \)). The results for the non-SVR group are shown in Figure 2 (Figure 2). According to Spearman's rank correlation analysis, positive correlations between each method and the METAVIR fibrosis stage were observed (FibroScan: \( r=0.65, p\leq0.001 \) (Figure 2a); VTQ: \( r=0.70, p\leq0.001 \) (Figure 2b); FIB-4 index: \( r=0.44, p\leq0.001 \) (Figure 2c); and M2BPGi: \( r=0.31, p=0.01 \) (Figure 2d)). The median METAVIR scores for each method were as follows: FibroScan, F0: 3.9, F1: 9.6, F2: 8.9, F3: 13.6, F4: 22.0; VTQ, F0: 1.03, F1: 1.25, F2: 1.40, F3: 1.89, F4: 2.39; FIB-4 index, F0: 1.27, F1: 5.99, F2: 4.18, F3: 4.88, F4: 6.05; M2BPGi, F0: 0.55, F1: 1.50, F2: 1.90, F3: 2.37, F4: 3.53.

ROC analysis of Fibroscan, VTQ, Fib4-index and M2BPGi
The sensitivity, specificity and cut-off values were compared among the four diagnostic methods. The ROC curves for each method are shown in Figure 3 (Figure 3). The areas under the ROC curve (AUC) for a diagnosis of fibrosis grade F2 or greater were as follows: 0.94 for FibroScan, 0.89 for VTQ, 0.85 for the FIB-4 index, and 0.77 for the M2BPGi level (Figure 3a). The respective values for a diagnosis of grade F3 or greater were 0.85, 0.84, 0.74, and 0.73 (Figure 3b), and those for a diagnosis of F4 were 0.91, 0.88, 0.67, and 0.78 (Figure 3c). The results of the non-SVR group are shown in Figure 4 (Figure 4). The AUC for a diagnosis of fibrosis grade F2 or greater were as follows: 0.95 for FibroScan, 0.93 for VTQ, 0.87 for the FIB-4 index, and 0.81 for the M2BPGi level (Figure 4a). The respective values for a diagnosis of grade F3 or greater were 0.85, 0.83, 0.67, and 0.67 (Figure 4b), and those for a diagnosis of F4 were 0.89, 0.86, 0.65, and 0.76 (Figure 4c).

The cutoff values for each test for a diagnosis of grade F2 or greater were as follows: FibroScan, 6.2; VTQ, 1.27; FIB-4 index, 1.74; M2BPGi, 1.40. The respective values for a diagnosis of F3 or greater were 8.9, 1.46, 2.91, and 1.76, and those for a diagnosis of F4 were 15.0, 3.25, and 2.70.

(Table 3) The results of the non-SVR group were as follows: FibroScan, 5.6; VTQ, 1.26; FIB-4 index, 1.74; M2BPGi, 1.63. The respective values for a diagnosis of F3 or greater were 9.8, 1.78, 3.20, and 2.15, and those for a diagnosis of F4 were 16.0, 1.94, 4.56, and 2.70. The cutoff value was taken as the maximum value of [sensitivity + specificity - 1] (Table 4).

Discussion
Many reports have compared the METAVIR scores of those tests with liver biopsy, both of which are reported to be highly reliable. [12, 15-18] As mentioned previously, however, there are cases in which liver biopsy cannot provide accurate or objective results. Only a few reports have compared liver resection specimens with FibroScan, VTQ and M2BPGi. [19, 25] In this study, we compared four different methods used to evaluate liver resection specimens: FibroScan, VTQ, the FIB-4 index, and the M2BPGi level. In the comparisons of METAVIR scores with each examination method, the correlation coefficients between the METAVIR score and FibroScan and between METAVIR and VTQ were very similar, and these two methods seemed to predict the degree of hepatic fibrosis better than the other two methods. In the ROC curve analyses, both FibroScan and VTQ exhibited AUC...
values greater than 0.8 for each METAVIR fibrosis grade, indicating a better sensitivity and specificity. These results suggest that FibroScan and VTQ results reflect the hepatic fibrosis grade in liver resection specimens.

Ragazzo et al. compared FibroScan, VTQ, the enhanced liver fibrosis test, the aspartate aminotransferase to platelet ratio index, and the FIB-4 index with biopsy results for evaluation of fibrosis. [12] In our study, FibroScan demonstrated an AUC of 0.94 for a diagnosis of fibrosis grade F2 or greater, 0.85 for grade F3 or greater, and 0.91 for grade F4, and these values were very similar to those reported by Ragazzo et al. [12] The respective AUC values using VTQ were 0.89, 0.84, and 0.88, which were somewhat lower than those reported by Ragazzo et al. [12] Vallet-Pichard et al. compared the FIB-4 index and M2BPGi level with METAVIR scores, respectively. [10, 13] Our comparison of the FIB-4 index with the METAVIR score revealed an AUC of 0.85 for diagnosing fibrosis of grade F2 or higher, 0.74 for grade F3 or higher, and 0.67 for F4, and these results were lower than those of Vallet-Pichard et al. Using the M2BPGi level to diagnose fibrosis, the AUC was found to be 0.77 for fibrosis grade F2 or higher, 0.73 for F3 or higher, and 0.78 for F4, and these values were also lower than those reported by Vallet-Pichard et al. [10, 13]

Nagata et al reported that M2BPGi levels are significantly decreased regardless of degree of fibrosis in patients with SVR who achieved viral elimination. [22] In addition, Bachofner et al reported that FIB-4 index levels are also decreased in patients with SVR after treatment. [23] In this study, the AUC of FIB-4 index and M2BPGi appeared to be low, which seemed to be due to the inclusion of SVR cases. In consideration of these effects, we conducted a similar study on non-SVR cases. Although the values differed, the advantage of FibroScan and VTQ did not change.

To summarize the comparisons between our results and those of past reports, the diagnosis of hepatic fibrosis using ultrasound has a slightly different value in VTQ, but no significant difference in the AUC was observed. However, when using blood-based parameters (i.e., the FIB-4 index and M2BPGi level) to diagnose fibrosis, the AUCs were lower in this study than in previous reports. The presence of HCC, HCV infection, inflammation, and differences by gender may have influenced the results. Sato et al reported differences in blood test data depending on the presence of HCC. It has
been reported that M2BPGi (≥ 2.8 COI) tends to increase as HCC develops, and the FIB-4 index (≥ 3.7) is high when HCC is present. [24]

Compared with blood-based parameters, the AUC associated with ultrasound-based parameters were higher than those associated with blood-based parameters in almost all previous reports. Regarding these differences, ultrasonic parameters can be used to evaluate the liver specifically, while blood-based parameters such as the FIB-4 index and M2BPGi level, are influenced by factors outside of the liver. As noted above, the FIB-4 index and M2BPGi level yielded relatively poor results in comparison with previous studies. [10–13] According to the ROC analyses, the sensitivity and specificity of the FIB-4 index and M2BPGi level for diagnosing fibrosis decreased as liver fibrosis progressed. However, the detection of fibrosis using blood-based parameters was equivalent to that using FibroScan and VTQ for mild fibrosis grades.

There are several limitations in this study. The number of patients included in the study was modest, and the study population was restricted to HCC patients; blood-based parameters, in particular, may be altered by the presence of HCC, which might affect the accuracy of the results. Future studies including patients who underwent liver transplantation and other patient groups are necessary. In addition, there were 32 cases where the measurement site and resected specimen differed. Because there is the possibility of measurement error resulting from this, it would be preferable to make the excision site and the measurement part identical. There was also some discrepancy in the results of two ultrasonic elastographies. Although it is reasonable that the presence of HCC and gender-related differences might affect the results, these effects could not be investigated in this study.

In conclusion, FibroScan and VTQ were most strongly correlated with the diagnosis of hepatic fibrosis using liver resection specimens among the four examination methods evaluated.

**Abbreviations**

HCC: hepatocellular carcinoma, VTQ: Virtual-Touch tissue quantification, FIB-4 index: fibrosis index based on four factors, M2BPGi: Mac-2 binding protein glycosylation isomer, HCV: hepatitis C virus, ROC: Receiver operating characteristic, AUC: the area under the curve

**Declarations**
**Ethical approval and consent to participate**

The study was carried out in accordance with the ethical guidelines of the Declaration of Helsinki and approved by the ethics and research committees of Hiroshima University Hospital (Hiroshima, Japan: no. E-946). Informed consent was obtained from each patient in writing.

**Availability of data and materials**

The data used to support the findings of this study are included within the article.

**Consent for publication**

Not applicable

**Competing interests**

Kazuaki Chayama has received honoraria from Bristol-Myers Squibb and MSD K.K. and research funding from Dainippon Sumitomo Pharma and AbbVie. Michio Imamura has received research funding from Bristol-Myers Squibb.

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**Authors' Contributions**

NU took the lead in drafting the manuscript. HA, TN, EM, MT, AH, MI, MY, KC viewed the literature and critically reviewed the manuscript. TK provided supervision, participated in the literature review and in drafting the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Clinical and biological characteristics of patients.

|                          | HCC (n=94)          | Liver metastasis (n=14) |
|--------------------------|---------------------|-------------------------|
| Age, Years               | 69 (65-87)          | 60 (21-85)              |
| Gender (male/female)     | 70 / 24             | 10 / 4                  |
| Plt (×10³/µl)            | 14.2 (3.1-34.6)     | 27.8 ( 81-195 )         |
| BMI                      | 21.5(18.5-33.5)     | 21.7(19.0-27.5)         |
| Alb (g/dl)               | 4.1 (2.8-5.1)       | 4.4 (3.4-4.8)           |
| T-Bil (mg/dl)            | 0.7 (0.3-2.9)       | 0.8 ( 0.5-2.1 )         |
| AST (U/L)                | 36.5 (13-114)       | 19 ( 14-62 )            |
| ALT (U/L)                | 30.9 (9-114)        | 16 ( 10-61 )            |
| M2BPGi                   | 2.79 (0.29-8.75)    | 0.55 ( 0.29-3.89 )      |
| FIB-4 index              | 4.27 (0.3-13.7)     | 2.14 ( 0.34-1.42 )      |
| SVR/nonSVR               | 20 / 74             | —                       |
| Fibrosis (F:0-1/2/3/4)   | ( 2 / 36 / 39 / 17 )| —                       |
| Inflammation (A:0/1/2/3) | ( 0/17/60/17 )      | ( 14/0/0/0 )            |
| Fibroscan(kPa)           | 13.9 (2.5-46.4)     | 5.1 ( 2.5-8.3)          |
| VTQ(m/s)                 | 1.79 (0.89-3.45)    | 1.23 ( 0.96-1.47 )      |
| HCC Stage( I/II/III )    | ( 48/35/11 )        | —                       |

Plt: platelet count, Alb: albumin, BMI: Body Mass Index, T-Bil: total bilirubin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, M2BPGi: Mac-2 binding protein glycosylation isomer, SVR: sustained viral response, VTQ: Virtual-Touch tissue quantification, HCC: hepatocellular
Table 2. Clinical and biological characteristics of the non-SVR group.

|                          | Non SVR               |
|--------------------------|-----------------------|
| Age, Years               | 69 (21-85)            |
| Gender (male/female)     | 56 / 18               |
| Plt (×10^3/μl)           | 14.2 (3.1-31.0)       |
| BMI                      | 21.5 (18.5-33.5)      |
| Alb (g/dl)               | 4.1 (2.8-5.1)         |
| T-Bil (mg/dl)            | 0.7 (0.3-2.9)         |
| AST (U/L)                | 36.5 (14-114)         |
| ALT (U/L)                | 30.9 (9-114)          |
| M2BPGi (COI)             | 2.79 (0.29-8.75)      |
| FIB-4 index              | 4.27 (0.34-13.7)      |
| Fibrosis (F:1/2/3/4)     | ( 1 / 24 / 33 / 16)   |
| Inflammation (A:0/1/2/3) | ( 0/12/50/12 )        |
| Fibroscan(kPa)           | 13.9 (2.5-46.4)       |
| VTQ(m/s)                 | 1.69 (0.95-3.28)      |
| HCC Stage( I/II/III )    | ( 30/25/9 )           |

SVR: sustained viral response, Plt: platelet count, BMI: Body Mass Index, Alb: albumin, T-Bil: total bilirubin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, M2BPGi: Mac-2 binding protein glycosylation isomer, VTQ: Virtual-Touch tissue quantification, HCC: hepatocellular carcinoma.

Table 3. Sensitivity, specificity, and diagnostic accuracy of cut-off and Area under the curve values for evaluating liver stiffness in patients with liver tumors and hepatitis C viral infection.
|     | Sensitivity % | Specificity % | AUC  | PPV  | NPV  |
|-----|--------------|---------------|------|------|------|
|     | F0-1VS F2-4  |               |      |      |      |
| Fibroscan | 93%          | 82%           | 0.94 | 93%  | 81%  |
| VTQ  | 82%          | 88%           | 0.89 | 98%  | 88%  |
| FIB-4 index | 91%       | 69%           | 0.85 | 95%  | 63%  |
| M2BPGi | 70%          | 63%           | 0.77 | 83%  | 81%  |
|     | F0-2VS F3-4  |               |      |      |      |
| Fibroscan | 91%          | 72%           | 0.85 | 88%  | 71%  |
| VTQ  | 87%          | 82%           | 0.84 | 88%  | 71%  |
| FIB-4 index | 78%       | 62%           | 0.74 | 79%  | 62%  |
| M2BPGi | 70%          | 62%           | 0.73 | 70%  | 69%  |
|     | F0-3 VS F4   |               |      |      |      |
| Fibroscan | 94%          | 80%           | 0.91 | 79%  | 79%  |
| VTQ  | 94%          | 75%           | 0.88 | 75%  | 75%  |
| FIB-4 index | 67%       | 57%           | 0.67 | 55%  | 55%  |
| M2BPGi | 76%          | 69%           | 0.78 | 74%  | 74%  |

VTQ: Virtual-Touch tissue quantification, M2BPGi: Mac-2 binding protein glycosylation isomer, AUC: area under the curve, PPV: positive predictive value, NPV: negative predictive value.

Table 4. Sensitivity, specificity, and diagnostic accuracy of cut-off and AUC values for evaluating liver stiffness in non-SVR patients with liver tumors and hepatitis C viral infection.

Figures
|                  | Sensitivity% | Specificity% | AUC  | PPV  | NPV  |
|------------------|--------------|--------------|------|------|------|
| **F0-1 VS F2-4** | Fibroscan    | 95%          | 86%  | 0.95 | 90%  | 73%  |
|                  | VTQ          | 87%          | 86%  | 0.93 | 95%  | 54%  |
|                  | FIB-4 index  | 98%          | 72%  | 0.87 | 93%  | 83%  |
|                  | M2BPGi       | 74%          | 71%  | 0.81 | 96%  | 76%  |
| **F0-2 VS F3-4** | Fibroscan    | 88%          | 74%  | 0.85 | 84%  | 83%  |
|                  | VTQ          | 81%          | 81%  | 0.83 | 87%  | 76%  |
|                  | FIB-4 index  | 73%          | 52%  | 0.67 | 69%  | 65%  |
|                  | M2BPGi       | 66%          | 59%  | 0.67 | 70%  | 55%  |
| **F0-3 VS F4**   | Fibroscan    | 83%          | 82%  | 0.89 | 63%  | 97%  |
|                  | VTQ          | 92%          | 70%  | 0.86 | 65%  | 98%  |
|                  | FIB-4 index  | 58%          | 55%  | 0.65 | 67%  | 88%  |
|                  | M2BPGi       | 75%          | 62%  | 0.76 | 66%  | 93%  |
Figure 1. Box plots of the correlations between different diagnostic methods and METAVIR fibrosis stages (F0–F4) in patients with liver tumors and hepatitis C infection. (a) FibroScan, (b) VTQ, (c) FIB-4 index, (d) M2BPGi. METAVIR : META-analysis of histological data in VIRal hepatitis scores VTQ : Virtual-Touch tissue quantification FIB-4 index : fibrosis index based on four factors M2BPGi : Mac-2 binding protein glycosylation isomer level
Box plots of the correlations between different diagnostic methods and METAVIR fibrosis stage (F0–F4) in non-SVR patients with liver tumors and hepatitis C. (a) FibroScan, (b) VTQ, (c) FIB-4 index, (d) M2BPGi. METAVIR: META-analysis of histological data in VIRal hepatitis scores VTQ: Virtual-Touch tissue quantification FIB-4 index: fibrosis index based on four factors M2BPGi: Mac-2 binding protein glycosylation isomer level
Figure 3

ROC analyses of liver stiffness for the diagnosis of various stages of liver fibrosis using liver specimens as the reference. (a) F0–1 versus F2–4, (b) F0–2 versus F3–4, (c) F0–3 versus F4.

ROC curves: Receiver operating characteristic curves
Figure 4

ROC analyses of liver stiffness for the diagnosis of various stages of liver fibrosis in the non-SVR group using liver specimens as the reference. (a) F0–1 versus F2–4, (b) F0–2 versus F3–4, (c) F0–3 versus F4. ROC curves: Receiver operating characteristic curves