**Supplemental Table 1.** Area Under the Receiver Operating Characteristics Curves for Transient Elastography and Noninvasive Markers for the Diagnosis of Advanced Fibrosis in Patients with Nonalcoholic Fatty Liver Disease Stratified According to BMI and ALT levels.

|  |  |
| --- | --- |
| **Tools** | **ROC AUC (C.I.)** |
|  |
| **BMI<30 & ALT<=100 (n=472; F3-F4 fibrosis 20.9%)** |
| **Liver Stiffness Measurement** | 0.916 (0.887-0.941) |
| **FIB-4**  | 0.817 (0.766-0.864) |
| **NAFLD Fibrosis Score** | 0.783 (0.726-0.835) |
|  |  |
| **BMI<30 & ALT>100 (n=119; F3-F4 fibrosis 27.7%)** |
| **Liver Stiffness Measurement** | 0.848 (0.775-0.917) |
| **FIB-4**  | 0.756 (0.646-0.85) |
| **NAFLD Fibrosis Score** | 0.75 (0.641-0.855) |
|  |  |
| **BMI>=30 & ALT<=100 (n=295; F3-F4 fibrosis 38.3%)** |
| **Liver Stiffness Measurement** | 0.794 (0.739-0.843) |
| **FIB-4**  | 0.753 (0.694-0.807) |
| **NAFLD Fibrosis Score** | 0.712 (0.652-0.772) |
|  |  |
| **BMI>=30 & ALT>100 (n=82; F3-F4 fibrosis 37.8%)** |
| **Liver Stiffness Measurement** | 0.759 (0.639-0.86) |
| **FIB-4**  | 0.715 (0.598-0.822) |
| **NAFLD Fibrosis Score** | 0.741 (0.617-0.854) |

**Supplemental Table 2.** Accuracy of Fibroscan, FIB-4 and NAFLD Fibrosis Score for the Diagnosis of Severe Fibrosis in Patients with Nonalcoholic Fatty Liver Disease Stratified According to BMI and ALT Levels.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Tools** | **Cut-off** | **Sensitivity (%)** | **Specificity (%)** | **Positive****predicted****value (%)** | **Negative****predicted****value (%)** | **Positive****Likelihood****Ratio** | **Negative****likelihood****ratio** | **Uncertainty****area (%)** | **Accuracy (%)** | **Wrong****classification (%)** | **False****positive (%)** | **False****negative (%)** |
| **BMI<30 & ALT<=100 (n=472; F3-F4 fibrosis 20.9%)** |
| **LSM** | 9,6 | 70.7 (62.1-80.4) | 90.6 (87.8-93.7) | 66.7 (57.4-76.1) | 92.1 (89.4-95.2) | 7.5 (4.2-9.6) | 0.3 (0.2- 0.4) | 11 (8.1-13.8) | 76.9 (73.1-80.9) | 9.7 (6.8-12.3) | 9.4 (6.3-12.2) | 29.3 (19.6-37.9) |
|  | 7,9 | 88.9 (83.1-95.5) | 78.6 (74.5-83) | 52.4 (44.5-59.8) | 96.4 (94.4-98.6) | 4.1 (3.1-4.9) | 0.1 (0.1-0.2) | 21.4 (17-25.5) | 11.1 (4.5-16.9) |
| **FIB-4** | 2,67 | 26.3 (16.7-34.8) | 97.6 (96-99.3) | 74.3 (60.1-90.2) | 83.3 (79.8-86.9) | 10.9 (5.8-27.7) | 0.8 (0.7- 0.9) | 25.8 (22-29.9) | 66.5 (62.1-70.6) | 7.6 (5.1-10) | 2.4 (0.7-4) | 73.7 (65.2-83.3) |
|  | 1,3 | 72.7 (63.6-81.6) | 77.2 (72.9-81.6) | 45.9 (38.2-53.8) | 91.4 (88.3-94.7) | 3.2 (2.3- 3.8) | 0.4 (0.2-0.5) | 22.8 (18.4-27.1) | 27.3 (18.4-36.4) |
| **NFS** | 0,676 | 13.1 (5.7-19.7) | 98.9 (98.1-100.1) | 76.5 (58.2-99.6) | 81.1 (77.3-84.8) | 12.3 (4.5-51.6) | 0.9 (0.8-1) | 31.1 (26.7-35.4) | 62.5 (58.1-67.2) | 6.4 (4.2-8.5) | 1.1 (0.3-2.2) | 86.9 (80.3-94.3) |
|  | -1,455 | 73.7 (65.1-83.1) | 75.6 (71.3-80.1) | 44.5 (36.9-52) | 91.6 (88.5-94.9) | 3 (2.3- 3.6) | 0.4 (0.2-0.5) | 24.4 (19.9-28.7) | 26.3 (16.9-34.9) |
|  **BMI<30 & ALT>100 (n=119; F3-F4 fibrosis 27.7%)** |
| **LSM** | 9,6 | 66.7 (50.5-83.3) | 82.6 (75.1-91) | 59.5 (43.9-76.1) | 86.6 (79.5-93.9) | 3.8 (0.6- 0.5) | 0.4 (0.2-0.6) | 10.1 (4.2-15.1) | 69.7 (62.2-78.2) | 18.5 (10.9-25.2) | 17.4 (9-24.9) | 33.3 (16.7-49.5) |
|  | 7,9 | 78.8 (66.3-93.1) | 70.9 (61.9-80.9) | 51 (36.7-64.9) | 89.7 (83.5-97.7) | 2.7 (1.3-3.5) | 0.3 (0.1-0.5) | 29.1 (19.1-38.1) | 21.2 (6.9-33.7) |
| **FIB-4** | 2,67 | 27.3 (11.2-41.6) | 96.5 (92.2- 100) | 75 (50-100) | 77.6 (70.2-85.6) | 7.8 (2.5-29.2) | 0.8 (0.6-0.9) | 26.1 (17.6-33.6) | 61.3 (52.9-70.6) | 12.6 (6.7-17.6) | 3.5 (0-7 .8) | 72.7 (58.4-88.8) |
|  | 1,3 | 63.6 (46.7-80.8) | 74.4 (64.9-84.1) | 48.8 (33.7-63.6) | 84.2 (76.3-92.8) | 2.5 (0.9-3.4) | 0.5 (0.2-0.7) | 25.6 (15.9-35.1) | 36.4 (19.2-53.3) |
| **NFS** | 0,676 | 0 (0-0) | 100 (100-100) | Undefined | 72.3 (64.7-80.7) | Undefined | 1 (1-1) | 23.5 (16-31.1) | 63.9 (55.5-73.1) | 12.6 (6.7-18.5) | 0 (0-0) | 100 (100-100) |
|  | -1,455 | 54.5 (38-70.9) | 88.4 (82.2-96) | 64.3 (47.3-82.1) | 83.5 (76.2-91.5) | 4.7 (2.5-10.7) | 0.5 (0.3-0.7) | 11.6 (4-17.8) | 45.5 (29.1-62) |
| **BMI>=30 & ALT<=100 (n=295; F3-F4 fibrosis 38.3%)** |
| **LSM** | 9,6 | 76.1 (68.4-84.6) | 68.1 (61.4-75.1) | 59.7 (51.8-67.7) | 82.1 (76.4-88.4) | 2.4 (1.7-2.9) | 0.4 (0.2-0.5) | 17.3 (12.9-21.4) | 58.6 (53.2-64.1) | 23.4 (18.6-28.1) | 31.9 (24.9-38.6) | 23.9 (15.4-31.6) |
|  | 7,9 | 90.3 (85.1-96) | 47.8 (40.8-54.6) | 51.8 (44.9-58.8) | 88.8 (82.7-95.3) | 1.7 (1.4-2) | 0.2 (0.1-0.3) | 52.2 (45.4-59.2) | 9.7 (4-14.9) |
| **FIB-4** | 2,67 | 20.4 (12.7-27.7) | 95.6 (92.8-98.6) | 74.2 (59.1-90) | 65.9 (60.2-71.8) | 4.6 (2.4-12.5) | 0.8 (0.8-0.9) | 29.5 (24.4-34.6) | 54.6 (48.8-60.3) | 15.9 (11.5-20) | 4.4 (1.4-7.2) | 79.6 (72.3-87.3) |
|  | 1,3 | 65.5 (57-74.3) | 75.8 (69.4-82.6) | 62.7 (53.9-71.6) | 78 (72-84.4) | 2.7 (1.7-3.4) | 0.5 (0.3-0.6) | 24.2 (17.4-30.6) | 34.5 (25.7-43) |
| **NFS** | 0,676 | 26.5 (17.9-34.5) | 90.7 (86.6-95.4) | 63.8 (49.5-78.6) | 66.5 (60.8-72.5) | 2.8 (0.1-4) | 0.8 (0.7-0.9) | 46.1 (40.3-51.5) | 40.3 (34.6-46.1) | 13.6 (9.8-17.3) | 9.3 (4.6-13.4) | 73.5 (65.5-82.1) |
|  | -1,455 | 79.6 (72.3-87.3) | 48.9 (41.7-56.2) | 49.2 (41.9-56.8) | 79.5 (71.9-86.9) | 1.6 (1.3-1.8) | 0.4 (0.2-0.6) | 51.1 (43.8-58.3) | 20.4 (12.7-27.7) |
| **BMI>=30 & ALT>100 (n=82; F3-F4 fibrosis 37.8%)** |
| **LSM** | 9,6 | 71 (56.2-88.6) | 64.7 (51.9-78.4) | 55 (40-70.5) | 78.6 (66.9-92.1) | 2 (0.7-2.7) | 0.5 (0.1-0.7) | 24.4 (14.6-34.1) | 50 (39-61) | 25.6 (15.9-34.1) | 35.3 (21.6-48.1) | 29 (11.4-43.8) |
|  | 7,9 | 90.3 (78.6-100) | 37.3 (23.5-49.5) | 46.7 (33.7-59.5) | 86.4 (70.8-100) | 1.4 (1- 1.8) | 0.3 (0-0.6) | 62.7 (50.5-76.5) | 9.7 (0-21.4) |
| **FIB-4** | 2,67 | 12.9 (3.2-26.1) | 92.2 (84- 98.3) | 50 (14.3-87.5) | 63.5 (52.4-75) | 1.7 (0.3-7.3) | 1 (0.8-1.1) | 30.5 (20.7-40.2) | 51.2 (40.2-62.2) | 18.3 (9.8-25.6) | 7.8 (1.7-16) | 87.1 (73.9-96.8) |
|  | 1,3 | 64.5 (47.8-82.6) | 74.5 (63.3-86.7) | 60.6 (44.7-78.4) | 77.6 (66.2-89.2) | 2.5 (0.4-3.5) | 0.5 (0.2-0.7) | 25.5 (13.3-36.7) | 35.5 (17.4-52.2) |
| **NFS** | 0,676 | 6.5 (0-16.7) | 98 (93.5-100) | 66.7 (0-100) | 63.3 (52.8-74.6) | 3.3 (0-8.2) | 1 (0.9- 1.1) | 45.1 (34.1-56.1) | 45.1 (34.1-56.1) | 9.8 (2.4-15.9) | 2 (0-6.5) | 93.5 (83.3-100) |
|  | -1,455 | 77.4 (63.7-93.3) | 68.6 (56.4-81.2) | 60 (45-76.8) | 83.3 (72.9-94.9) | 2.5 (0.7-3.3) | 0.3 (0.1-0.5) | 31.4 (18.8-43.6) | 22.6 (6.7-36.3) |

**Supplemental Table 3.** Accuracy of Fibroscan by M and XL Probes According to BMI.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Tools** | **Cut-off** | **Sensitivity (%)** | **Specificity (%)** | **Positive****predicted****value (%)** | **Negative****predicted****value (%)** | **Positive****likelihood****ratio** | **Negative****likelihood****ratio** | **Uncertainty****area (%)** | **Accuracy (%)** | **Wrong classification (%)** | **False positive (%)** | **False negative (%)** |
| **Entire cohort (n=244; F3-F4 fibrosis 40.1%)** |
| **LSM XL probe** | **9,3** | 58.2 (48.3 – 67.8) | 86.3 (81 – 91.8) | 74 (64.7 – 84.8) | 75.4 (69 – 82.1) | 4.2 (1.6 – 5.6) | 0.5 (0.4 – 0.6) | 34.8 (28.7 – 40.6) | 53.3 (47.1 – 59.8) | 11.5 (7.4 – 15.2) | 13.7 (8.2 – 19) | 41.8 (32.2 – 51.7) |
|  | **5,7** | 91.8 (86.6 – 97.5) | 50 (42.1 – 58.2) | 55.2 (47.5 – 62.7) | 90.1 (83.9 – 97.1) | 1.8 (1.5 – 2.1) | 0.2 (0.0 – 0.3) |  |  |  | 50 (41.8 – 57.9) | 8.2 (2.5 – 13.4) |
| **LSM M probe** | **9,6** | 78.6 (70.6 – 86.8) | 71.9 (65.2 – 79.7) | 65.3 (57.1 – 74.1) | 83.3 (76.9 – 89.6) | 2.8 (1.8 – 3.5) | 0.3 (0.2 – 0.4) | 14.8 (10.2 – 19.3) | 63.1 (57.4 – 69.3) | 20.5 (15.2 – 25.4) | 28.1 (20.3 – 34.8) | 21.4 (13.2 – 29.4) |
|  | **7,9** | 90.8 (85.5 – 96.8) | 52.7 (44.4 – 61) | 56.3 (48.2 – 64.3) | 89.5 (83.4 – 96.5) | 1.9 (1.5 – 2.2) | 0.2 (0.1 – 0.3) |  |  |  | 47.3 (39 – 55.6) | 9.2 (3.2 – 14.5) |
| **BMI<30 (n=120; F3-F4 fibrosis 36.6%)** |
| **LSM XL probe** | **9,3** | 56.8 (41.9 – 72.1) | 90.8 (84.4 – 97.7) | 78.1 (63.9 – 92.9) | 78.4 (70.2 – 87.3) | 6.2 (3.3 – 18.7) | 0.5 (0.3 – 0.6) | 27.5 (19.2 – 35.8) | 63.3 (55 – 72.5) | 9.1 (3.3 – 14.2) | 9.2 (2.3 – 15.6) | 43.2 (27.9 – 58.1) |
|  | **5,7** | 90.9 (83.8 – 100) | 67.1 (57.1 – 77.6) | 61.5 (49.6 – 73.1) | 92.7 (87 – 100) | 2.8 (1.5 – 3.5) | 0.1 (0.0 – 0.3) |  |  |  | 32.9 (22.4 – 42.9) | 9.1 (2 – 19.1) |
| **LSM M probe** | **9,6** | 79.5 (68.4 – 92.4) | 86.8 (79.8 – 95.1) | 77.8 (65.8 – 90.6) | 88 (81.1 – 95.7) | 6 (3.6 – 13.5) | 0.2 (0.1 – 0.4) | 11.7 (5 – 17.5) | 73.3 (65 – 81.7) | 11.7 (5.8 – 16.7) | 13.2 (4.9 – 20.2) | 20.5 (7.6 – 31.6) |
|  | **7,9** | 90.9 (83.8 – 100) | 69.7 (59.7 – 80.3) | 63.5 (52 – 75.5) | 93 (87.6 – 100) | 3 (1.4 – 3.8) | 0.1 (0.0 – 0.3) |  |  |  | 30.3 (19.7 – 40.3) | 9.1 (2 – 18.6) |
| **BMI>=30 (n=124; F3-F4 fibrosis 43.5%)** |
| **LSM XL probe** | **9,3** | 59.3 (45.4 – 72.5) | 81.4 (72.5 – 90.8) | 71.1 (58.2 – 84.7) | 72.2 (62 – 82.6) | 3.2 (0.1 – 4.4) | 0.5 (0.3 – 0.7) | 41.9 (33.9 – 50.8) | 43.5 (34.7 – 52.4) | 13.7 (7.3 – 19.4) | 18.6 (9.2 – 27.5) | 40.7 (27.5 – 54.6) |
|  | **5,7** | 92.6 (86.9 – 100) | 31.4 (20.8 – 42.3) | 51 (41.3 – 61.6) | 84.6 (72.7 – 99.2) | 1.4 (1.1 – 1.6) | 0.2 (0.0 – 0.5) |  |  |  | 68.6 (57.7 – 79.2) | 7.4 (1.7 – 15.1) |
| **LSM M probe** | **9,6** | 77.8 (67.2 – 89.5) | 55.7 (44.3 – 67.3) | 57.5 (45.8 – 69.2) | 76.4 (64.9 – 88.8) | 1.8 (1.1 – 2.2) | 0.4 (0.1 – 0.6) | 17.7 (10.5 – 24.2) | 53.2 (44.4 – 62.1) | 29 (21 – 37.1) | 44.3 (32.7 – 55.7) | 22.2 (10.5 – 32.8) |
|  | **7,9** | 90.7 (83.6 – 98.8) | 34.3 (23.1 – 45.4) | 51.6 (41.5 – 61.7) | 82.8 (69.9 – 97.7) | 1.4 (1.1 – 1.6) | 0.3 (0.1 – 0.6) |  |  |  | 65.7 (54.6 – 76.9) | 9.3 (1.2 – 16.4) |

**Supplemental Table 4.** Accuracy of Serial Combination of FIB-4 and NAFLD Fibrosis Score with Fibroscan, for the Diagnosis of Severe Fibrosis in Patients with Nonalcoholic Fatty Liver Disease Stratified According to BMI and ALT Values.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Tools** | **Uncertainty area (%)** | **Accuracy (%)** | **Wrong classification (%)** | **False positive (%)** | **False negative (%)** | **Negative Predictive Value (%)** | **Positive Predictive Value (%)** |
| **BMI<30 & ALT<=100 (n=472; F3-F4 fibrosis 20.9%)** |  |  |
| **NFS→LSM in NFS [-1.455; 0.676]** | 5.93 (3.81; 7.84) | 83.26 (79.87; 86.86) | 10.81 (7.84; 13.56) | 6.36 (4.03; 8.47) | 4.45 (2.33; 6.14) | 94.12 (91.84 – 96.78) | 65.52 (55.39 – 75.35) |
| **FIB4→LSM in FIB4 [1.30;2.67]** | 5.51 (3.39; 7.42) | 84.11 (80.72; 87.29) | 10.38 (7.42; 13.14) | 6.14 (3.81; 8.26) | 4.24 (2.33; 5.93) | 94.41 (92.17 – 96.84) | 67.05 (56.98 – 77.17) |
|  |  |  |
| **BMI<30 & ALT>100 (n=119; F3-F4 fibrosis 27.7%)** |  |  |
| **NFS→LSM in NFS [-1.455; 0.676]** | 4.2 (0; 7.56) | 78.99 (72.27; 86.55) | 16.81 (10.08; 23.53) | 15.13 (8.4; 21.01) | 1.68 (0; 3.36) | 97.59 (95.18 – 100.0) | 41.94 (24.50 – 59.53) |
| **FIB4→LSM in FIB4 [1.30;2.67]** | 4.2 (0.84; 7.56) | 73.11 (65.55; 81.51) | 22.69 (15.13; 30.25) | 14.29 (7.56; 20.17) | 8.4 (3.36; 13.45) | 87.80 (81.17 – 95.36) | 46.88 (28.38 – 66.18) |
|  |  |  |
| **BMI>=30 & ALT<=100 (n=295; F3-F4 fibrosis 38.3%)** |  |  |
| **NFS→LSM in NFS [-1.455; 0.676]** | 9.49 (6.1; 12.88) | 66.78 (61.36; 71.86) | 23.73 (18.98; 28.47) | 9.49 (6.1; 12.54) | 14.24 (10.17; 17.97) | 74.39 (68.04 – 80.96) | 72.82 (64.50 – 81.41) |
| **FIB4→LSM in FIB4 [1.30;2.67]** | 7.46 (4.41; 10.17) | 72.2 (67.12; 77.29) | 20.34 (15.59; 24.75) | 13.9 (9.83; 17.63) | 6.44 (3.39; 9.15) | 88.76 (84.22 – 93.56) | 60.58 (51.15 – 69.64) |
|  |  |  |
| **BMI>=30 & ALT>100 (n=82; F3-F4 fibrosis 37.8%)** |  |  |
| **NFS→LSM in NFS [-1.455; 0.676]** | 10.98 (3.66; 17.07) | 68.29 (58.54; 78.05) | 20.73 (12.2; 29.27) | 10.98 (3.66; 17.07) | 9.76 (2.44; 15.85) | 82.61 (72.53 – 94.76) | 66.67 (49.34 – 83.33) |
| **FIB4→LSM in FIB4 [1.30;2.67]** | 4.88 (0; 8.54) | 68.29 (58.54; 78.05) | 26.83 (17.07; 36.59) | 14.63 (7.32; 21.95) | 12.2 (4.88; 18.29) | 80.00 (69.26 – 92.00) | 57.14 (38.42 – 76.05) |