



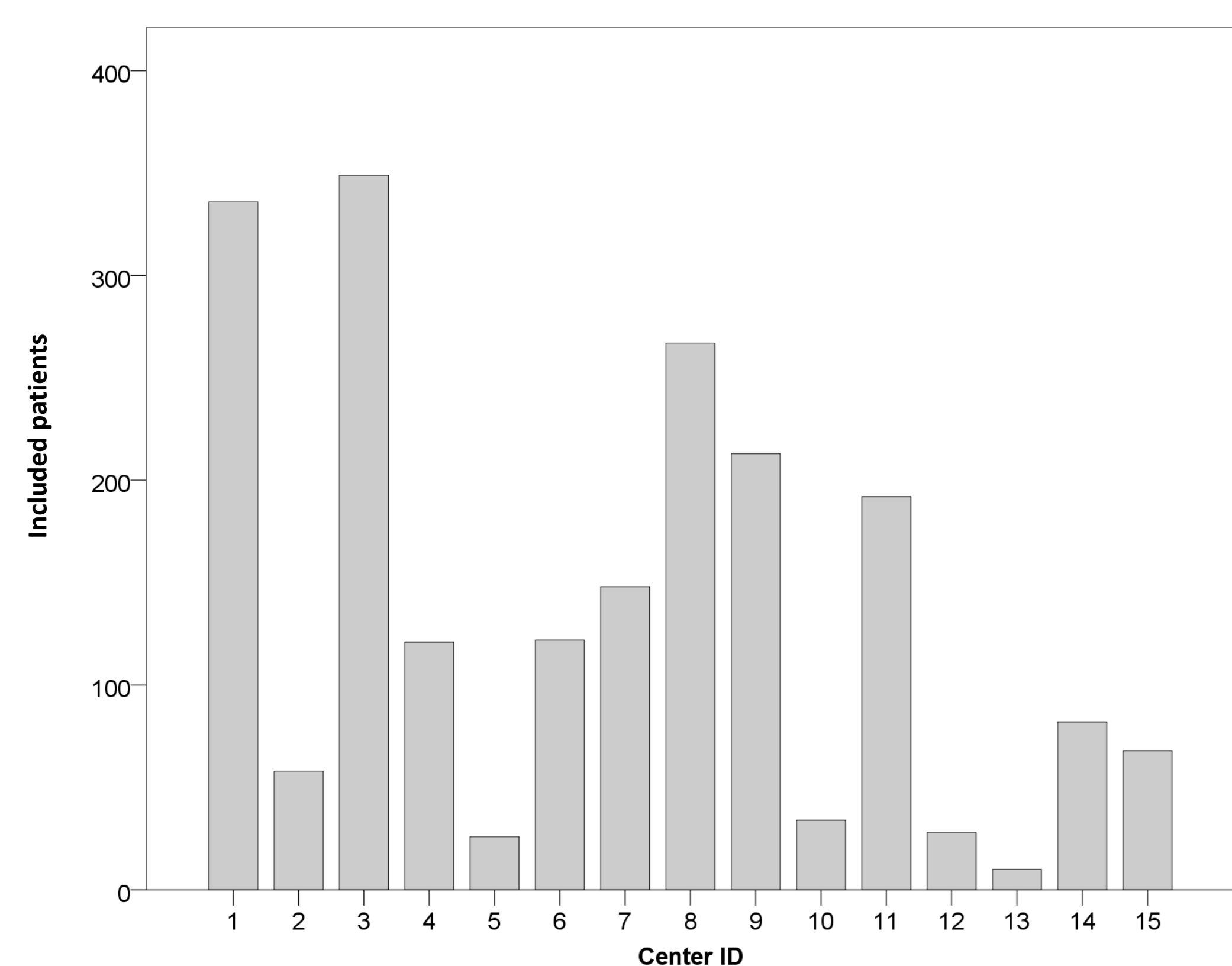
# 2D-SWE predicts survival in advanced chronic liver disease



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Figure 1:



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Table 1:

| Parameters                                 | N    | Value                       |
|--|------|-----------------------------|
| Height (m)                                 | 1576 | 1.7 (1.4 - 2)               |
| Age  | 2084 | 55 (15 - 84.9)              |
| Follow Up [month]                          | 1675 | 34.8 (0 - 116)              |
| ALT (U/L)                                  | 2020 | 45 (3 - 1982)               |
| AST (U/L)                                  | 1954 | 44 (3 - 2507)               |
| Alkaline phosphatase (U/L)                 | 1794 | 92 (2 - 146000)             |
| Bilirubin (mg/dl)                          | 2006 | 0.76 (0.1 - 23.2)           |
| Creatinine (mg/dl)                         | 1800 | 0.8 (0.2 - 13)              |
| CRP (mg/l)                                 | 910  | 3.1 (0.2 - 184.5)           |
| Albumin (g/l)                              | 1851 | 40.7 (10 - 71)              |
| Platelets (G/l)                            | 1906 | 182 (6 - 785)               |
| INR  | 1888 | 1.06 (0.13 - 6.5)           |
| SWE (kPa)                                  | 2017 | 11 (1 - 155.5)              |
| MELD                                       | 1701 | 7.7 (6 - 40)                |
| Child (A/B/C)                              | 1773 | 1375 / 285 / 113            |
| Cause of chronic liver disease             | 1535 | 332 / 245 / 181 / 374 / 403 |
| AFLD / HepC / HepB / NAFLD / other         |      |                             |
| Gender (female / male)                     | 2057 | 886 / 1191                  |
| Esophageal varices (grade 0-IV)            | 1004 | 729 / 138 / 102 / 33 / 2    |
| Fundal varices (absent / present)          | 882  | 848 / 34                    |
| History of HRS (absent / present)          | 1226 | 1186 / 40                   |
| History of SBP                             | 1225 | 1192 / 33                   |
| Ascites (0=absent, 1=mild, 2=tense)        | 2086 | 1844 / 139 / 103            |
| Hepatic encephalopathy Grade (grade 0-III) | 2086 | 1871 / 168 / 42 / 5         |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; INR, international normalized ratio; SWE, shear wave elastography; Child, Child-Pugh-Score; MELD, Model End Stage Liver Disease; HRS, hepatorenal syndrome; AFLD, alcoholic fatty liver disease; HepC, viral hepatitis C; HepB, viral hepatitis B; NAFLD, Non-alcoholic fatty liver disease; HRS, hepatorenal syndrome; SBP, Spontaneous bacterial peritonitis

## Background:

Measurement of liver stiffness is an established technique to assess significant fibrosis in patients with chronic liver disease. Moreover, it might be a useful surrogate marker to diagnose or rule out clinically significant portal hypertension. However, the value of 2-dimensional shear wave elastography (2D-SWE) to predict mortality in cirrhotic patients is unknown. The aim of this multicentre retrospective study was to assess the value of 2D-SWE using Aixplorer to predict mortality in chronic liver disease patients.

## Methods:

Inclusion criteria were presence of chronic liver disease, valid 2D-SWE at baseline, no previous events of decompensation at baseline and at least one year of clinical follow up after the index 2D-SWE measurement. Clinical and laboratory parameters were assessed at baseline. The primary outcome was overall mortality of the patients. For the selection of cutoff values, receiver operating characteristics (ROC) analysis with survival as endpoint was calculated. Kaplan-Meier curves were used to compare the survival rates of patients using the log-rank test. Univariate time-to-event analysis and multivariate Cox regression analysis was performed to identify independent predictors of survival.

## Results:

2084 patients from 15 centres were screened and 1434 patients fulfilled the inclusion criteria and were included in the analysis with a median follow up of 34.8 months. The median age of the population was 55 (range: 15-85) years, with 58% male patients. The main aetiology was viral hepatitis (27%), while 21% suffered of chronic alcoholic liver disease. The median of liver 2D-SWE was 11kPa (range: 1-156). The AUC of SWE for mortality within 24 months was 0.815 (CI: 0.773-0.857) with the best Cut-off of 20.6 kPa (sensitivity 76%, specificity 80%). In univariate analysis age, MELD, Child Score, creatinine, bilirubin, albumin, platelets, AST and SWE>20.6 kPa were significantly associated with overall mortality. In the cox-regression multivariate analysis SWE>20.6 kPa was independently associated with over all mortality (HR: 2.17 (0.991-4.76)), besides albumin (HR: 0.93 (0.89-0.978)), MELD (HR: 1.08 (1.013 - 1.146)) and age (HR: 1.01 (1.007-1.065)).

## Conclusions:

This study shows for the first time that liver stiffness measured by 2D-SWE predicts mortality in patients with chronic liver disease. 2D-SWE of more than 20.6 kPa might be helpful to stratify risk and guide patient management.

Table 2: Univariate time to event analysis

|                          | p      | HR    | 95.0% confidence interval for HR |        |
|--------------------------|--------|-------|----------------------------------|--------|
|                          |        |       | Under                            | Upper  |
| Age                      | <0.001 | 1.05  | 1.032                            | 1.075  |
| ALT (U/L)                | 0.016  | 0.997 | 0.988                            | 0.999  |
| AST (U/L)                | 0.6    | 0.99  | 0.996                            | 1.002  |
| Bilirubin (mg/dl)        | <0.001 | 1.18  | 1.129                            | 1.241  |
| Creatinine (mg/dl)       | 0.048  | 1.18  | 1.002                            | 1.399  |
| CRP                      | 0.003  | 1.01  | 1.004                            | 1.022  |
| Albumin (g/l)            | <0.001 | 0.85  | 0.823                            | 0.881  |
| Platelets (G/l)          | <0.001 | 0.99  | 0.988                            | 0.994  |
| INR                      | <0.001 | 1.09  | 1.051                            | 1.12   |
| SWE < 20.6 kPa           | <0.001 | 11    | 6.901                            | 19.894 |
| MELD                     | <0.001 | 5     | 3.650                            | 6.831  |
| Child                    | <0.001 | 1.11  | 1.087                            | 1.144  |
| Gender (female / male)   | 0.34   | 0.79  | 0.505                            | 1.262  |
| Esophageal varices grade | <0.001 | 1.52  | 1.206                            | 1.918  |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; INR, international normalized ratio; SWE, shear wave elastography; Child, Child-Pugh-Score; MELD, Model End Stage Liver Disease

Table 3: Multivariate time to event analysis

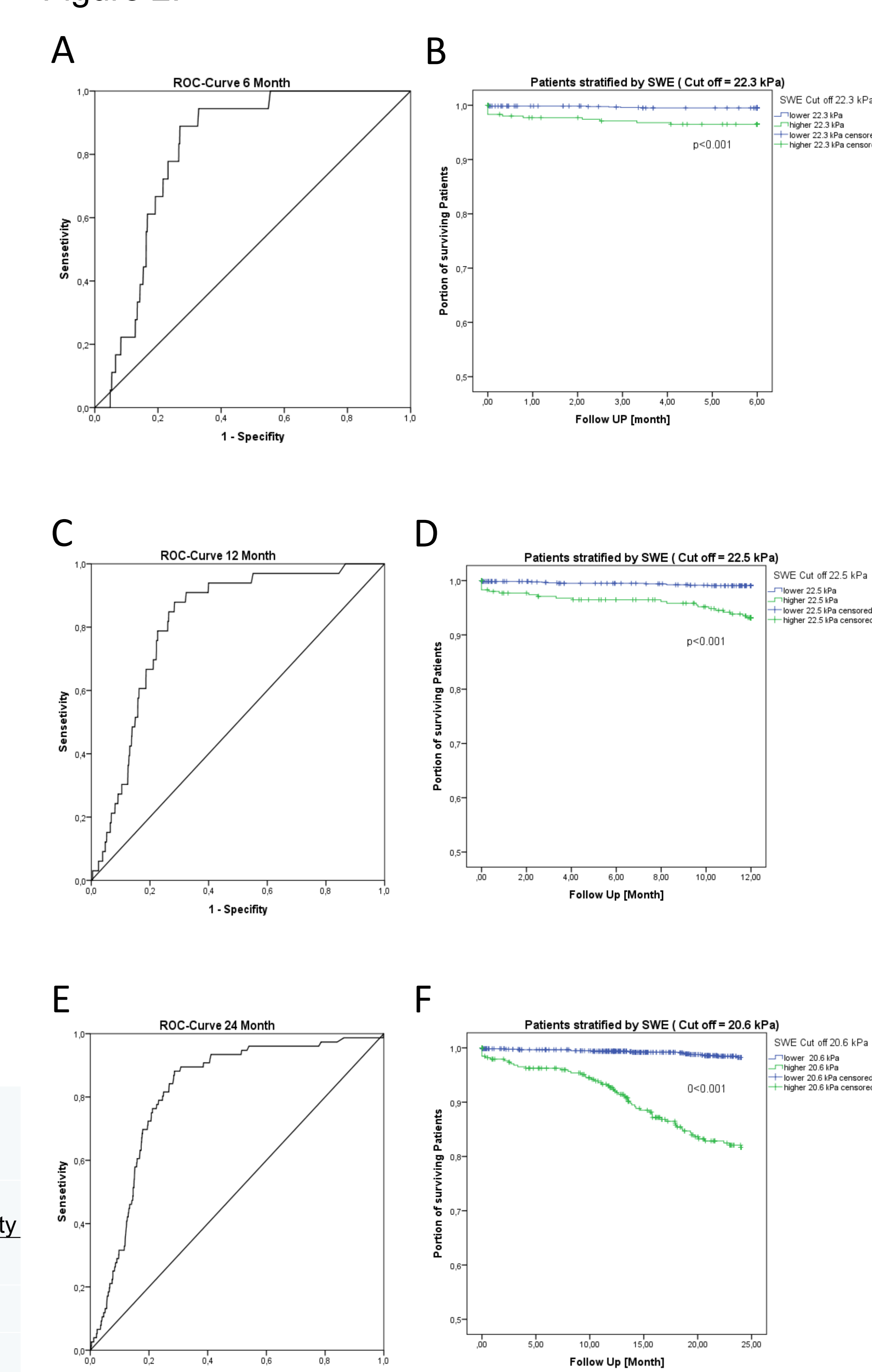
|                           | P     | HR   | 95.0% confidence interval for HR |       |
|---------------------------|-------|------|----------------------------------|-------|
|                           |       |      | Under                            | Upper |
| Age                       | 0.013 | 1.01 | 1.007                            | 1.065 |
| Albumin (g/L)             | 0.004 | 0.93 | 0.89                             | 0.978 |
| MELD                      | 0.017 | 1.08 | 1.013                            | 1.146 |
| SWE Best Cut off 20.6 kPa | 0.053 | 2.17 | 0.991                            | 4.76  |

SWE, shear wave elastography; Child, Child-Pugh-Score; MELD, Model End Stage Liver Disease

Table 4: ROC analysis

|          | AUC   | P      | Asymptotic 95% confidence interval |       | Best Cut Off | Sensitivity | Specificity |
|----------|-------|--------|------------------------------------|-------|--------------|-------------|-------------|
|          |       |        | Under                              | Upper |              |             |             |
| 6 month  | 0.814 | <0.001 | 0.758                              | 0.869 | 22.3         | 70 %        | 80 %        |
| 12 month | 0.813 | <0.001 | 0.756                              | 0.870 | 22.5         | 67 %        | 80 %        |
| 24 month | 0.815 | <0.001 | 0.773                              | 0.857 | 20.6         | 76 %        | 80 %        |
| Over all | 0.745 | <0.001 | 0.708                              | 0.781 | 25.0         | 53 %        | 80 %        |

Figure 2:



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