**SUPPLEMENTARY CONTENT**

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**Patients and Methods**

*Statistical analysis*

Decision curve analysis (DCA) evaluates prediction models in comparison to default strategies of treating all or no patients (making all or no patients undergo diagnostic EGD in current setting).

DCA essentially estimates a “net benefit” for each of diagnostic strategies, that is defined as

*net benefit = sensitivity × prevalence – (1–specificity) × (1–prevalence) × w*

where w is the odds of true diagnosis (high-risk esophageal varices in this case) across a range of threshold probabilities. In this setting, net benefit represents a composite of the benefit gained by performing screening EGD for true VNT and risk/ discomfort incurred due to EGD in those without VNT. Threshold probability is a composite of patient and doctors’ preference that represent a theoretical risk-level where the expected benefit of treatment is equal to the expected benefit of avoiding treatment (e.g. benefit of UGIE equals risk of foregoing it). Thus, net benefit is assessed across a range of threshold probabilities to identify the best diagnostic strategy for different risk-scenarios. Test trade-off, or Δ*Net benefit* was used to assess the yield of one diagnostic strategy over other at different threshold probabilities.

**Results**

Reasons for exclusion were incomplete data records or unreliable LS measurements (n=1048), decompensation at the time of first assessment or prior decompensation events (included those with HCC) (n=3832), VBL in past (n=932), those in whom time interval between elastography measurement and EGD procedure was more than three months (n=182). and alanine aminotransferase (ALT) elevation > 2 times upper limit normal at the time of elastography (n=155).

**Decision curve analysis for prediction of VNTs in overall CLD**

Overall, Baveno-VI criteria exhibited the highest net benefit for predicting VNT when threshold probability for esophageal varices was 8% or lower. For higher threshold probabilities, i.e. from 9% to 44%, expanded Baveno-VI criteria showed maximum net benefit. Importantly, among non-elastography based methods, the platelet-albumin criteria had nearly similar net benefit as Baveno-VI criteria before 8% threshold and expanded Baveno-VI criteria beyond that, with no statistically significant differences from expanded Baveno-VI on 500-fold bootstrap validation upto threshold probability of 25%. At commonly cited risk thresholds of 5% and 10%, a test trade-off, or ΔNet benefit of 0.00388 and 0.00025 respectively was obtained in comparison to best TE based criteria at that threshold, translating to a need to subject 257 and 3958 patients at risk threshold of 5% and 10% to TE to detect one additional patient with VNT (Table 4).

**Supplementary Tables**

Supplementary Table 1: Performance characteristics of different classification criteria for predicting varices needing treatment (VNT) in overall CLD. VNT identified and missed are presented with percentages, denominator being patients with VNT.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | VNT identified | VNT missed | Misclassified High risk | Correctly spared endoscopy | Sensitivity | Specificity | PPV | NPV |
| Baveno | 262 (97.4%) | 7 (0.8%) | 536 (38.6%) | 852 (61.4%) | 97.4% (94.5% - 98.6%) | 61.4% (58.8% - 63.9%) | 32.8% (29.6% - 36.1%) | 99.2% (98.3% - 99.6%) |
| Expanded Baveno | 240 (89.2%) | 29 (10.8%) | 298 (21.5%) | 1090 (78.5%) | 89.2% (84.7% - 92.2%) | 78.5% (76.2% - 80.5%) | 44.6% (40.4% - 48.7%) | 97.4% (96.2% - 98.1%) |
| Platelet-Albumin | 247 (91.8%) | 22 (8.2%) | 373 (26.9%) | 1015 (73.1%) | 91.8% (87.7% - 94.4%) | 73.1% (70.7% - 75.3%) | 39.8% (35.9% - 43.6%) | 97.9% (96.8% - 98.6%) |
| Platelet-MELD | 156 (58.0%) | 113 (42.0%) | 240 (17.3%) | 1148 (82.7%) | 58% (51.8% - 63.6%) | 82.7% (80.6% - 84.6%) | 39.4% (34.6% - 44.2%) | 91% (89.3% - 92.4%) |

Abbreviations: VNT: Varices needing treatment, PPV: Positive predictive value, NPV: Negative predictive value

Supplementary Table 2: Etiology specific performance characteristics of different non-invasive classification criteria for predicting varices needing treatmnt (VNT) in overall CLD. VNT identified and VNT missed are presented with percentages, denominator being patients with VNT within respective etiological subgroup.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | High risk varices identified | High risk varices missed | Misclassified High risk | Correctly spared endoscopy | Sensitivity | Specificity | PPV | NPV |
| Baveno | n |  |  |  |  |  |  |  |  |
| Alcohol | 195 | 70 (100%) | 0 (0%) | 81 (64.8%) | 44 (35.2%) | 100.00% | 35.20% | 46.40% | 100.00% |
| HBV | 633 | 78 (100%) | 0 (0%) | 214 (38.6%) | 341 (61.4%) | 100.00% | 61.40% | 26.70% | 100.00% |
| HCV | 554 | 39 (100%) | 0 (0%) | 148 (28.7%) | 367 (71.3%) | 100.00% | 71.30% | 20.90% | 100.00% |
| NASH | 243 | 64 (91.4%) | 6 (8.6%) | 84 (48.6%) | 89 (51.4%) | 91.40% | 51.40% | 43.20% | 93.70% |
| Others | 32 | 11 (91.7%) | 1 (8.3%) | 9 (45.0%) | 11 (55.0%) | 91.70% | 55.00% | 55.00% | 91.70% |
|  |  |  |  |  |  |  |  |  |  |
| Expanded Baveno | | |  |  |  |  |  |  |  |
| Alcohol | 195 | 69 (98.6%) | 1 (1.4%) | 51 (40.8%) | 74 (59.2%) | 98.60% | 59.20% | 57.50% | 98.70% |
| HBV | 633 | 67 (85.9%) | 11 (14.1%) | 97 (17.5%) | 458 (82.5%) | 85.90% | 82.50% | 40.90% | 97.70% |
| HCV | 554 | 34 (87.2%) | 5 (12.8%) | 83 (16.1%) | 432 (83.9%) | 87.20% | 83.90% | 29.10% | 98.90% |
| NASH | 243 | 59 (84.3%) | 11 (15.7%) | 60 (34.7%) | 113 (65.3%) | 84.30% | 65.30% | 49.60% | 91.10% |
| Others | 32 | 11 (91.7%) | 1 (8.3%) | 7 (35.0%) | 13 (65.0%) | 91.70% | 65.00% | 61.10% | 92.90% |
|  |  |  |  |  |  |  |  |  |  |
| RECIST |  |  |  |  |  |  |  |  |  |
| Alcohol | 195 | 66 (94.3%) | 4 (5.7%) | 63 (50.4%) | 62 (49.6%) | 94.30% | 49.60% | 51.20% | 93.90% |
| HBV | 633 | 71 (91.0%) | 7 (9.0%) | 135 (24.3%) | 420 (75.7%) | 91.00% | 75.70% | 34.50% | 98.40% |
| HCV | 554 | 38 (97.4%) | 1 (2.6%) | 115 (22.3%) | 400 (77.7%) | 97.40% | 77.70% | 24.80% | 99.80% |
| NASH | 243 | 61 (87.1%) | 9 (12.9%) | 53 (30.6%) | 120 (69.4%) | 87.10% | 69.40% | 53.50% | 93% |
| Others | 32 | 11 (91.7%) | 1 (8.3%) | 7 (35.0%) | 13 (65.0%) | 91.70% | 65.00% | 61.10% | 92.90% |
|  |  |  |  |  |  |  |  |  |  |
| Platelet-MELD | | |  |  |  |  |  |  |  |
| Alcohol | 195 | 41 (58.6%) | 29 (41.4%) | 45 (36.0%) | 80 (64.0%) | 58.6% | 64.0% | 47.7% | 73.4% |
| HBV | 633 | 71 (91.0%) | 7 (9.0%) | 135 (24.3%) | 420 (75.7%) | 91.0% | 75.7% | 34.5% | 98.4% |
| HCV | 554 | 22 (56.4%) | 17 (43.6%) | 43 (8.3%) | 472 (91.7%) | 56.4% | 91.7% | 33.8% | 96.5% |
| NASH | 243 | 43 (61.4%) | 27 (38.6%) | 40 (23.1%) | 133 (76.9%) | 61.4% | 76.9% | 51.8% | 83.1% |
| Others | 32 | 10 (83.3%) | 2 (16.7%) | 8 (40%) | 12 (60%) | 83.3% | 60% | 55.6% | 85.7% |

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; NASH, non-alcoholic steatohepatitis; MELD, model for end-stage liver disease; VNT: varices needing treatment; PPV, positive predictive value; NPV, negative predictive value

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Prediction of VNT** | | | | | | |
|  | **Threshold probability 5%** | | | **Threshold probability 10%** | | |
|  | Net benefit | Test trade-off in comparison to TE based criteria | Number of additional TE for detecting 1 additional VNT | Net benefit | Test trade-off in comparison to TE based criteria | Number of additional TE for detecting 1 additional VNT |
| **TE based criteria** | | | | | | |
| **Baveno-VI** | 0.1415 |  |  | 0.1267 |  |  |
| **Expanded Baveno- VI** | 0.1358 |  |  | 0.1276 |  |  |
| **Non-TE based criteria** | | | | | | |
| **Platelet-Albumin** | 0.1376 | 0.00388 | 257 | 0.1273 | 0.00025 | 3958 |
| **Platelet-MELD** | 0.0867 | 0.05482 | 18 | 0.0801 | 0.04665 | 21 |

Supplementary Table 3: Decision curve analysis showing net benefit of different noninvasive criteria for prediction of varices needing treatment and variceal bleed in overall CLD at relevant threshold probabilities (5% and 10% for VNT/ Test trade-off along with corresponding number needed to diagnose is estimated for non-TE based methods in comparison to best performing TE based criteria at that risk-threshold

Abbreviations: TE: Transient elastography

**Supplementary figure legends**

Supplementary Figure 1: Stacked-bar plots representing number of patients correctly classified (green) or misclassified as low-risk (red) or high-risk (blue) across different etiological subgroups of overall CLD based on respective non-invasive classification criteria [A) Baveno-VI, B) Expanded Baveno-VI, C) Platelet-albumin D) Platelet-MELD]. Numbers within each stack represent number of patients given that classification.

Supplementary Figure 2: Decision curve plots demonstrating net benefit of different classification criteria for varices needing treatment in cACLD across range of threshold probabilities against default strategies of performing endoscopy for all (red) and no (brown) patients. See text for interpretation.

Supplementary Figure 3: Decision curve plots demonstrating net benefit of different classification criteria for varices needing treatment in entire CLD across range of threshold probabilities against default strategies of performing endoscopy for all (red) and no (brown) patients. See text for interpretation.