Supplementary Method 1. Decision curve analysis

Decision curve analysis (DCA)

DCA is a method to assess the value of information provided by a diagnostic test by considering the likely range of patients' risk and benefit preferences, without the need for actually measuring these preferences for a particular patient. To prevent decompensation using non-selective beta-blocker (NSBB) in compensated advanced chronic liver disease (cACLD) patients, physicians must decide whether to 1) treat empirically, 2) not treat, or 3) perform further diagnostic testing before deciding between options 1 and 2. DCA evolves around 2 key concepts, namely the "net benefit" and "threshold probability".

The net benefit in DCA was assessed based on composite probabilities of the four following scenarios: 1) benefit of correctly identifying patients who merited treatment; 2) benefit of correctly excluding patients who did not merit treatment; 3) risk of incorrectly identifying patients who did not merit treatment; and 4) risk of incorrectly excluding patients who merited treatment.

Mathematically, it can be represented as: net benefit = sensitivity × prevalence − (1-specificity) × (1-prevalence) × w, with w being the odds of decompensation across a range of threshold probability.

The threshold probability is the level of diagnostic certainty, above which, physicians and patients would choose to initiate NSBB to prevent decompensation. Since the threshold probability for NSBB treatment may vary for different patients or physicians, DCA must assess the net benefit of NSBB treatment across a range of threshold probabilities to identify the best strategy for different risk scenarios. The treatment threshold is not the expected incidence of decompensation. Nevertheless, the knowledge of the expected incidence of decompensation remained relevant, because if a patient has a high risk of events (or decompensation, in this case), most physicians would prefer to treat that patient. In contrast, if a patient has a low risk of events, a test-and-treat strategy may be preferred over empirical treatment.

At a higher threshold probability for treatment, the net benefit decreases, hence the number needed to treat increases correspondingly. The median risk of decompensation in this cohort was only 10% at 5 years. For patients with a low treatment threshold of 0–3%, empirical treatment is preferred as additional diagnostic tests do not add sufficient information to change the decision to initiate treatment (NSBB), as patients seemed to be more concerned about experiencing liver decompensation than receiving unnecessary NSBB treatments. For mid-range threshold probability between 3–15%, a test-and-treat strategy based on either clinically significant portal hypertension (CSPH) or endoscopic evidence of varices is preferred. When we set a high treatment threshold of 15%, the majority of patients in this cohort would not merit NSBB treatment at a very-high risk threshold beyond 15%, hence, beyond the threshold probability of 15%, identifying CSPH has no value on the decision on NSBB treatment in these patients.

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