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Nutritional Risk Index predicts mortality in hospitalized advanced heart failure patients

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BACKGROUND: Hospitalized advanced heart failure (HF) patients are at high risk for malnutrition and death. The Nutritional Risk Index (NRI) is a simple, well-validated tool for identifying patients at risk for nutrition-related complications. We hypothesized that, in advanced HF patients from the ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) trial, the NRI would improve risk discrimination for 6-month all-cause mortality.

METHODS: We analyzed the 160 ESCAPE index admission survivors with complete follow-up and NRI data, calculated as follows: NRI = (1.519 × discharge serum albumin [in g/dl]) + (41.7 × discharge weight [in kg] / ideal body weight [in kg]); as in previous studies, if discharge weight is greater than ideal body weight (IBW), this ratio was set to 1. The previously developed ESCAPE mortality model includes: age; 6-minute walk distance; cardiopulmonary resuscitation/mechanical ventilation; discharge β-blocker prescription and diuretic dose; and discharge serum sodium, blood urea nitrogen and brain natriuretic peptide levels. We used Cox proportional hazards modeling for the outcome of 6-month all-cause mortality.

RESULTS: Thirty of 160 patients died within 6 months of hospital discharge. The median NRI was 96 (IQR 91 to 102), reflecting mild-to-moderate nutritional risk. The NRI independently predicted 6-month mortality, with adjusted HR 0.60 (95% CI 0.39 to 0.93, $p = 0.02$) per 10 units, and increased Harrell's c-index from 0.74 to 0.76 when added to the ESCAPE model. Body mass index and NRI at hospital admission did not predict 6-month mortality. The discharge NRI was most helpful in patients with high (≥ 20%) predicted mortality by the ESCAPE model, where observed 6-month mortality was 38% in patients with NRI < 100 and 14% in those with NRI > 100 ($p = 0.04$).

CONCLUSIONS: The NRI is a simple tool that can improve mortality risk stratification at hospital discharge in hospitalized patients with advanced HF.

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Advanced heart failure (HF) patients are characterized by disease and symptom progression despite maximally tolerated, goal-directed therapy.[1] Such patients are frequently admitted for decompensation and are at high risk of death during and after HF hospitalization.[2] Cardiac transplantation and durable mechanical circulatory support can markedly improve quality and length of life in advanced HF, but appropriate patient selection remains challenging.[3] Patients near the end of life who are not candidates for or do not desire such aggressive interventions may derive substantial benefit from hospice referral, but predicting 6-month mortality in advanced HF can be difficult.[2,4]

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The well-described "obesity paradox" links higher body mass index (BMI) with lower short- and long-term mortality in HF; conversely, HF patients with low BMI have poorer survival.[5,6] Cardiac cachexia, a catabolic wasting state associated with inflammation and neurohormonal activation, is generally believed to mediate poor outcomes in HF patients with low BMI or weight loss. However, although often overlooked, poor nutritional status is also an important prognostic factor. Low serum albumin strongly predicts mortality across the spectrum of HF severity from ambulatory patients to left ventricular assist device (LVAD) recipients.[7,8] Detailed assessments including anthropometric and survey measures indicate that the HF obesity paradox is substantially modulated by nutritional status and that, in turn, BMI is not a good predictor of nutritional status in HF.[9–11]

The Nutritional Risk Index (NRI), an easily calculated measure that incorporates albumin and body size, predicts mortality in single-center cohorts of ambulatory[12] and hospitalized[13] HF patients. The impact of the NRI on mortality risk in advanced HF is unknown. We analyzed data from the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) study. In this well-characterized HF inpatient cohort, a bedside mortality risk prediction score (ESCAPE model) with good discrimination was developed.[14] We hypothesized that the NRI would improve risk stratification for 6-month mortality at hospital discharge in the ESCAPE study cohort, particularly in the patients at highest risk of death.

Methods

The ESCAPE trial enrolled patients from 26 academic centers in the United States and Canada with advanced HF/cardiac transplant programs. The design, end-points and results of the ESCAPE trial have been previously published.[2] In brief, the study randomized advanced HF inpatients to therapy guided by clinical assessment alone or clinical assessment plus pulmonary artery catheterization. All enrolled patients had New York Heart Association Class IV symptoms despite therapy with angiotensin-converting enzyme inhibitors and diuretics, as well as at least 1 prior HF hospitalization and/or substantial diuretic resistance during outpatient management. Other factors aimed at recruiting an advanced HF cohort included left ventricular ejection fraction $\leq$ 30%, presenting systolic blood pressure $\leq$ 125 mm Hg[15] and clinical evidence of congestion.

Of the subjects enrolled in ESCAPE who were not lost to follow-up, 20% died and 65% died or were re-admitted within 6 months, confirming that the cohort represented advanced HF. Noting substantial clinical differences between survivors and non-survivors, several investigators derived a risk model for 6-month post-discharge mortality. Based on Cox model coefficients, a simplified integer risk score (hereafter referred to as the ESCAPE model) was developed that assigned 1 point each for age $>$ 70 years, blood urea nitrogen (BUN) $>$ 40 mg/dl and BUN $>$ 90 mg/dl, 6-minute walk distance $<$ 300 feet, serum sodium $<$ 130 mEq/liter, daily diuretic dose at discharge $>$ 240 mg furosemide equivalent and absence of β-blocker at discharge and discharge BNP $>$ 500 pg/mmol; 2 points for cardiac arrest or mechanical ventilation during the index hospitalization; and 3 points for discharge BNP $>$ 1,300 pg/mmol. In the ESCAPE cohort, overall discrimination was good and 6-month mortality increased in a stepwise fashion with this integer score.[14]

The NRI was calculated as: NRI = (1.519 × serum albumin [in g/dl]) + (41.7 × weight [in kg] / ideal body weight [in kg]). The ideal body weight (IBW) was calculated with the Devine formula for men (IBW [kg] = 50 kg + 2.3 kg for each inch of height $>$ 5 feet) and the Robinson formula for women (IBW [kg] = 48.67 kg + 1.65 kg for each inch of height over 5 feet).[16] As in other previous studies, in patients with discharge weight greater than IBW, we set this ratio to 1.[17,18] Typically, NRI $\geq$ 100 indicates no evidence of malnourishment, and 97.5 to 100 indicates mild, 83.5 to 97.5 moderate and $<$ 83.5 severe risk of malnourishment-related complications. Given the expectation that many ESCAPE patients were volume-overloaded at hospital admission and also that the ESCAPE model uses discharge data, we used albumin and body weight data at the time of hospital discharge to calculate NRI. In the ESCAPE patients assigned to pulmonary artery catheter monitoring, we explored the relationship between NRI, serum albumin and hemodynamic factors.

We calculated the ESCAPE model integer score in patients who were not lost to follow-up and the NRI in all patients with complete data. We used Cox proportional hazard modeling to evaluate the primary outcome of all-cause mortality over 6 months of follow-up, first for the ESCAPE model and the NRI alone, then in combination. We then evaluated for differential efficacy of NRI in high- and low-risk ESCAPE patients with log-rank testing, creating 4 sub-groups dichotomized at an NRI value of 100 and a predicted 6-month mortality risk of 20% (corresponding to an ESCAPE model integer score $\geq$ 2). We reviewed the performance of the model after excluding patients who underwent transplant and/or LVAD placement within 6 months. We performed a sensitivity analysis adjusting for changes in serum hemoglobin during hospitalization, as hemoconcentration may affect both discharge weight and albumin values.

Results

Baseline characteristics of the 160 patients with calculated NRI and the remaining 254 ESCAPE study patients are shown in Table 1. The NRI group was slightly younger, but was otherwise nearly identical to the remainder of the ESCAPE cohort. In addition to clinical characteristics, the observed 6-month mortality and incidence of transplant or LVAD placement were very similar between groups.

Across the entire ESCAPE cohort, 82 of 414 (20%) patients died within 6 months; in the NRI group, 30 of 160 (19%) patients died. The ESCAPE risk model retained good discrimination in the NRI cohort, with c-statistic = 0.74 and a stepwise increase in mortality hazard with increasing integer score. On a univariable basis, increasing NRI score showed a strong trend toward lower mortality hazard (hazard ratio [HR] 0.67, 95% confidence interval [CI] 0.44 to 1.02, $p = 0.06$). With respect to individual components of the NRI, there was no significant change in albumin (admission 3.7 ± 0.5 vs discharge 3.7 ± 0.5 g/dl, $p = 0.85$ by paired t-test), but weight decreased between hospital admission and discharge (86.5 ± 22 to 82.8 ± 21 kg, $p < 0.001$ by paired t-test).

When added to the ESCAPE model, NRI predicted 6-month mortality independent of the ESCAPE integer