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Introduction:

Sepsis is common, deadly, and heterogeneous. Prior work proposed clinical sepsis phenotypes at presentation and explored change in phenotype over time. However, little is known about how change in phenotype is associated with outcome. We explored trajectories of phenotypes in the ProCESS trial and the association between change in phenotype and outcome.

Methods:

We analyzed a cohort of 815 adult sepsis encounters from the ProCESS trial in the Usual Care and EGDT arms that survived in-hospital for at least 72-hours post-randomization. We predicted clinical phenotypes at randomization and 72-hours post-randomization using Euclidean distance anchored to previously published cluster centroids ($\alpha, \beta, \gamma, \delta$). We defined core members as $\geq 90\%$ and marginal as $< 90\%$ probability of phenotype membership at randomization. We used logistic regression to determine the odds of phenotype transition by phenotype, treatment arm, and membership probability. We explored the relationship between treatment arm, phenotype transition, and in-hospital mortality within the δ -phenotype.

Results:

We studied 815 adult sepsis encounters from the ProCESS trial (median age 60, [IQR 50-72]; 56% male, median SOFA at arrival 7, [IQR 4-9]) surviving for at least 72hrs post-randomization. At presentation, encounters were 36% α -type, 37% β -type, 13% γ -type, and 25% δ -type. Phenotype was unchanged over 72hrs in 46% of encounters. Marginal membership was (OR 1.9, 95% CI 1.4-2.6, $p < 0.01$) but treatment arm was not (OR 0.9 95% CI 0.7-1.2, $p = 0.33$, Figure 1A) associated with increased odds of phenotype transition. Within δ -type, core membership and EGDT were associated with increased in-hospital mortality (Figure 1B).

Conclusion:

Approximately half of patients changed phenotypes within 72-hours and changes were most common in marginal members. Treatment response may differ by phenotype membership probability and is an important area for further research.

Image :

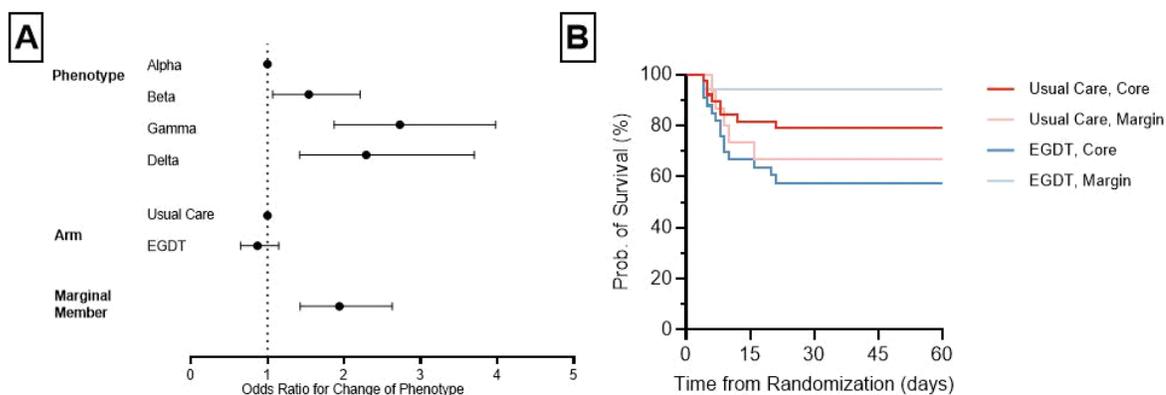


Figure 1. (A) Forest Plot showing probability of change in phenotype by phenotype, treatment arm, and probability of membership. (B) Kaplan-Meier Curve of 60-day in-hospital mortality, stratified by treatment arm and probability of

membership within the delta phenotype.