The Heart Failure Frequent Flyer: An Urban Legend

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As a clinician and teacher, I have often used the casual label frequent flyer to describe patients with chronic severe heart failure who have frequent hospital admissions. The term never fails to elicit knowing smiles and nods from audiences of experienced heart failure nurses and physicians. As with many other widely accepted labels, the term carries a number of implications. First, it reveals a mindset that says heart failure admissions reflect simple volume overload and can be treated in a straightforward manner by volume reduction. Second, it implies that these episodes have neither detrimental effect on the patient nor prognostic impact; once the volume expansion has been dealt with, the frequent flyer has returned to his or her baseline compensated state. Finally, it connotes our belief that these patients are resilient, and that they will continue to tolerate admission after admission for a prolonged time. However, as we repeatedly learn from the rigorous approach of clinical trials, we too often base our observations on patients who have merely survived our treatment, rather than on those who have actually benefited from it.

Two widely disparate sources have now given those of us important new information about the risks associated with heart failure hospitalization. The Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) investigators, who recently published a retrospective analysis of the CHARM trial data, showed a markedly increased risk of death in the first month after hospitalization for heart failure.[1] Even more interesting, although not surprising, the absolute increase in risk was clearly related to the number of previous admissions. After the first hospitalization, the hazard ratio for first-month mortality (adjusted for other known risks) increased approximately threefold above those never hospitalized or yet to be hospitalized; after the third admission, the hazard ratio for first-month mortality increased almost fifteen-fold!

My colleagues, Maria Rosa Costanzo and Janet Wynne, and I recently made similar observations using data from the Acute Decompensated Heart Failure National Registry Longitudinal Module (ADHERE-LM) registry.[2] Patients with chronic heart failure were entered into the registry on an outpatient basis while they were clinically stable. We divided the patients by number of previous heart failure hospitalizations and plotted Kaplan-Meier curves with an endpoint of death or readmission to hospital. Times to 50% of each group having experienced either death or readmission were approximately 150 d for patients with one, approximately 120 d for those with two, and approximately 60 d for those with 3 or more previous admissions.

What Lessons Can Clinicians Learn From These Data?

1. Admissions for acutely decompensated heart failure (ADHF) are not clinically benign. Each episode of hospitalization is associated with an incrementally poorer prognosis.
2. Physicians, patients, and families should be aware that ADHF patients are at markedly increased risk during the first post-discharge month. The immediate pre-discharge B-type natriuretic peptide (BNP) level may offer a useful objective indicator of the magnitude of that risk.[3]
3. The indisputable fact that mortality risk escalates dramatically with each episode of hospitalization should translate, operationally, into caregivers referring appropriate patients for specialized heart failure evaluation after the first episode of hospitalization for heart failure.

What Insights Do These Data Offer For Clinical Trialists Planning Future Heart Failure Studies?

1. Prior to randomization, patients being considered for chronic therapy trials should have a stabilization period of at least 4 to 6 wk after a heart failure hospitalization, and risk stratification should include the number of previous hospitalizations.
2. Trials focused on therapy for acutely decompensated heart failure commonly have a 30-d mortality endpoint. Future trials should carefully collect information on the number, duration, and timing of previous heart failure admissions and include that information in the statistical analysis plan.

What Basic Issues Must We Hope That Our Colleagues In The Laboratory Can Unravel?

1. What are the cellular mechanisms that account for the prolonged increase in mortality risk after an episode of acute decompensated heart failure (ADHF)?
2. Do these observations hint at very real limitations of treatment based on the neurohormonal model of heart failure? Are we beginning to understand that

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effective neurohormonal blockade can slow, but not stop, the progression of heart failure?

As practicing clinicians, the tiny minority of patients who manage to survive multiple hospital admissions for ADHF persuaded us into thinking that the natural history of chronic heart failure was clinical stability punctuated by recurrent episodes of simple volume overload. We called these patients the frequent flyers. In fact, both observational and randomized trial data have now convincingly shown that our preconceived notions were fabricated from the stuff of urban legends.

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