Unplanned Rehospitalizations and Depression: Time for a New Approach?

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In this issue of Circulation, Hess et al. characterize the rates, hospital variability, and patient-related risk factors for unplanned inpatient or observation rehospitalizations among all-aged patients within 30 days of discharge following an acute myocardial infarction (MI). Using data from the Treatment with Adenosine Diphosphate Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events after Acute Coronary Syndrome (TRANSLATE-ACS) Trial, Hess et al report that approximately 10% of all-aged patients with acute MI treated with PCI had at least one unplanned rehospitalization within 30 days of discharge, and these observed rates varied widely across hospitals. Consistent with prior studies, the authors find that older, female, black, and more medically complex individuals were at increased risk of having an unplanned rehospitalization. Further, beyond these typical risk factors, reporting a poor quality of life and screening positive for depression were the most powerful predictors of being rehospitalized.

These findings are interesting and important. In light of the increasing number of payers, including private insurers, shifting an increasing proportion of payments into value-based models like Accountable Care Organizations, risk-sharing quality contracts, and bundled payments, it is important for providers and policymakers to understand what is driving rehospitalizations across all populations. Much of our current understanding around this issue stems from examining readmissions in Medicare beneficiaries. Therefore, this work is an important contribution as it extends our understanding to a younger population, demonstrating that variation in and predictors of performance across observations and hospital readmissions are largely consistent.

However, one of the most striking findings of this study is one that we have actually known for a long time: screening positive for depression – on a simple, two-question screening test – was one of the strongest predictors of being rehospitalized. In this study, the odds ratio for
readmission associated with depression, at 1.31, was similar to that of prior heart failure, at 1.41. This study joins a large and growing body of research that documents the role of mental health as a powerful predictor of poor outcomes in patients with cardiovascular disease (CVD), and extends this finding to a post-MI, invasively-treated, multi-age cohort.

Not only is depression highly prevalent in patients with CVD, with as many as one in five patients suffering from depression after acute MI, but numerous studies and systematic reviews have linked depression with increased cardiovascular morbidity and mortality.\textsuperscript{5,6} Given the abundance of evidence supporting this relationship, in 2014, the American Heart Association (AHA) formally recognized depression as a risk factor for adverse medical outcomes in patients suffering from an acute coronary syndrome.\textsuperscript{5}

Many mechanisms have been postulated that might explain these relationships. For example, patients with depression have been shown to have sympathetic nervous system hyperactivity, neuro-endocrine dysfunction, higher levels of biomarkers indicating inflammation, and enhanced platelet aggregation compared to their non-depressed peers.\textsuperscript{7} Patients with depression also have lower rates of medication adherence, increased rates of substance abuse and smoking, and lower levels of physical activity, all of which may contribute to poor cardiac outcomes on top of the physiologic effects.\textsuperscript{8,9} Differential medical treatment may also be important: patients with depression and other affective disorders may be less likely to receive cardiac catheterization in the setting of an acute MI, though findings are mixed.\textsuperscript{10,11}

Interestingly, despite the increased recognition of the relationship between depression and CVD, efforts to intervene thus far have been disappointing. For example, the \textit{Sertraline Antidepressant Heart Attack Randomized Trial} (SADHART) tested the selective serotonin reuptake inhibitor (SSRI) sertraline for the treatment of major depressive disorder after acute
coronary syndrome, and found no significant reduction in cardiac events, though the trial was underpowered to do so. Similarly, the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) trial used a combination of cognitive behavioral therapy and SSRI treatment and showed no difference in clinical outcomes, including cardiovascular hospitalization. Other randomized controlled trials have confirmed the safety of pharmacologic therapy for depression in patients with other forms of CVD, including heart failure, but have also failed to show a benefit in clinical outcomes including rehospitalizations.

So, what now? The findings of the Hess et al study should inspire both clinical leaders and researchers to focus on post-MI patients with depression as a particularly important group for intervention, given their high event rates and the high prevalence of this comorbidity. However, in light of previous trials showing little effect of treating depression in CVD patients, successfully intervening to reduce rehospitalizations in depressed patients, as well as those with poor quality of life, will likely require a more complex approach than pharmacotherapy alone.

What might the future hold for concurrent management of depression and CVD? For clinical leaders, whose practices and hospitals increasingly operate in an environment in which payment is based on outcomes such as readmissions, the results of this study may spur interest in linking behavioral health providers with the medical, and cardiovascular, community in a more meaningful way. Historically, mental health providers have operated in separate siloes from primary care physicians and medical subspecialists. Sharing of relevant information rarely occurred, in part related to restrictive privacy laws around mental health. Patients with depression, however, might benefit more from a comprehensive, coordinated system. Integration of mental health services in primary care and cardiovascular practices offers one such possibility. Integrated care-delivery models facilitate communication between multi-
disciplinary providers and allow for greater concordance in patients’ care plans; they also better ensure that patients have access to necessary care when they need it. This is particularly relevant in patients with mental illness, where follow-up and adherence to complex medical regimens can be poor. Additionally, given the known strong interrelatedness between socioeconomic factors and depression, social workers, care coordinators, and others with knowledge of community organizations and resources may have a particularly important role to play in this population.

For researchers, the results of this study may remind us how much we still have to learn about the pathophysiology of mental illness. Depression is a complex, genetically and phenotypically heterogeneous disorder. As such, our understanding may need to become more refined for us to make real inroads into its treatment. For example, screening positive using the Patient Health Questionnaire-2 (PHQ-2) Depression score, as used to assess depression in the study by Hess et al, does not distinguish between mild depression and severe major depressive disorder; while of great use as a screening tool, this instrument provides little insight into the clinical reality for any individual patient. Prior work has shown that there may be distinct subtypes of depressed patients that are at higher risk for cardiac morbidity and mortality, and that these subgroups may respond differentially to treatment with SSRIs or other therapies – but currently, many of our screening tools do not recognize these subtleties. On the other end of the spectrum, short-term depressive symptoms may be difficult to differentiate from a more severe, persistent condition in the setting of a medical event, which could dilute the potential benefit of therapy for depression. For example, roughly half of the patients in the placebo group in both SADHART and ENRICHD demonstrated a reduction in depressive symptoms during the study period despite receiving no pharmacologic therapy. It is possible that a tool that allowed
better differentiation between depression that is likely to remit and depression that is likely to be severe and persistent might allow better matching of patients to therapy.

Ongoing efforts and increasing sophistication in bringing large and disparate datasets together, leading to the ability to combine genetic or genomic data, metabolomic or proteomic data, traditional biomarkers, and patient-reported data with clinical outcome data, may allow us to learn more about the relationship between depression and CVD at the molecular level. Such understanding could potentially spur different approaches to treatment. For example, if certain types of depression are more powerfully associated with platelet aggregation, prolonged antiplatelet therapy may be appropriate; if associated with inflammation, high-intensity statins may have a key role. In order for such insights to occur, it is critical that clinical trials and observational studies in CVD collect data on mental health to the fullest degree possible; it is a credit to the designers of the TRANSLATE-ACS that depression and quality of life data were available for analysis in this particular case. Additionally, we as clinicians and researchers should continue to encourage collaborative efforts between health systems, professional societies, academic institutions, and payers that allow and promote the creation of complex data systems that can elucidate patterns and treatments, and ultimately, improve care.

Conclusion

Hess et al have reminded us that depression and quality of life are key predictors of 30-day rehospitalization, above and beyond our patients’ medical comorbidities. As we reflect on the current state of care for patients with comorbid depression and CVD, and as we seek to improve their quality of care and outcomes in an era of new financial incentives to reduce readmissions, focusing on both the unique clinical needs and the underlying biology of patients with these two complex conditions will be critical.
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References:


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