

Future Directions in Understanding Functional Impairment in Heart Failure

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Abstract:

The link between heart failure and reduced ability to perform activities of daily living is substantial; however, the mechanistic link between these two conditions is unclear. Understanding the underlying mechanisms of this association is difficult without joint efforts. This article discusses potential future directions for investigations focused on the link between heart failure and functional impairment. Multidirectional and multidisciplinary approaches should be taken to uncover the mechanisms that contribute to declined activities of daily living in persons living with heart failure.

Keywords: Cognitive impairment; Sensorimotor function; Heart disease; Comorbidities; Sex differences

Commentary

The number of persons living with heart failure, a complex clinical syndrome, is increasing steadily [1]. Recent interest in the connection between heart disease and impaired brain function, particularly in reference to the development of dementia, has brought together the fields of cardiovascular health and neuroscience in new and exciting ways. In particular, better understanding of the development of functional impairment—including cognitive impairment (CI) and conversion to dementia—in persons living with heart failure is an area of high interest.

Epidemiological approaches have demonstrated clear negative impacts of heart failure on the ability to perform activities of daily living; a summary can be found in Table 1 of our recent paper [2]. The risk of death in dependent persons living with heart failure is comparable with dependent persons living with heart failure and comorbidities; however, it is greater than independent persons living with heart failure and comorbidities [3]. Reduced activities of daily living in this patient population also leads to hospitalization, readmission, increased emergency department visits, and reduced quality of life. Given the detrimental repercussions of heart failure to persons living with heart failure, the need of understanding how reduced activities of daily living manifest in persons living with heart failure is increasing [4].

Heart failure mediated changes in the central and peripheral nervous systems may contribute to reduced activities of daily living

in persons living with heart failure [2]. Specifically, (CI) is strongly linked to heart failure, with up to 79% of heart failure patients demonstrating impairment in at least one cognitive domain [5]. Impairments in cognitive functions including the domains of attention, memory, verbal fluency paired with sensorimotor dysfunction is likely to be the driver of impaired ability to perform tasks of daily living in persons living with heart failure; however, strong evidence of this link is currently absent in the evidence base.

Despite the consistent finding of impaired daily functioning (including CI) in persons living with heart failure, significant variability in neuroimaging study outcomes suggest multiple pathways to the manifestation of functional impairment in persons living with heart failure. Neuroimaging findings include diffuse evidence of gray matter loss, cortical thinning, atrophy, hyperintensities, infarctions, myelin damage, and axonal integrity losses [2]. The diffuse nature of these findings suggests systemic damage that may accumulate across the lifespan. Potential cardiovascular processes that also contribute include: poor perfusion, micro-embolisms, cerebral inflammation, and endothelial dysfunction [6].

In our recent review of the evidence base [2], many studies included patients with a wide variety of heart failure subtypes along with various comorbid conditions. Given the low incidence of heart failure worldwide (0.8% as per [7]), such a conglomerate approach to heart failure assessment helps improve power for

statistical analyses at the risk of introducing high sample variability. This high sample variability may explain the inconsistencies in reported results. While it would be scientifically ideal to focus on the manifestation of a single heart failure subtype in a given study, the low incidence rate of heart failure may necessitate alternative approaches to unravel the mechanistic drivers of functional impairment in this population.

One approach to evaluation of functional impairment related to heart failure is by investigation of individual subtypes with stratification by objective measures of heart failure severity. This approach may clarify the inconsistent reports regarding interplay between CI and types of heart failure [8]. Such inconsistency can also be seen in the association between cognitive function and left ventricular ejection fraction [9]. Current available evidence supports the hypothesis of severity-dependent CI in heart failure using subjective classification criteria, such that heart failure patients with higher New York Heart Association classes (classes III and IV) exhibit poorer cognitive function compared to heart failure patients with lower New York Heart Association classes (classes I and II) [10]. This association is challenged when cognitive function is compared to objective measures of heart failure, such as left ventricular ejection fraction [9].

Another approach may be to evaluate heart failure characteristics separately by sex and/or menopausal status while still using a conglomerate approach across heart failure subtypes. This may help elucidate the impact of sex-hormones and the role of hormone replacement therapy in the manifestation of functional impairment. This approach may be particularly fruitful as women have been significantly underrepresented in heart failure research studies for decades [11–13]. Consideration of type and duration of hormone replacement therapy will be an important feature of such work, as conjugated equine estrogen have been found to negatively impact cognitive function in older women despite having no to low overall impact on cardiovascular risk [14,15].

In a similar vein, another approach may be to assess functional impairments in heart failure patients separately by comorbid condition (e.g., Type II Diabetes (DM) or chronic kidney disease (CKD)) across heart failure subtypes. For example, persons living with DM and/or CKD are at double the risk for developing heart failure as compared to healthy individuals [16–18]. This could be a fruitful approach as co-occurrence of HF and specific comorbidities likely present specific stresses on the human body that may result in consistent functional impairment patterns. For example, DM is associated with development of amnesiac mild CI concurrent with sensorimotor dysfunction, while CKD is associated with development of sensory deficits and inconsistent reports of CI in different cognitive domains [19–23]. This approach may help clarify the combined impact of heart failure and other systemic disease on specific features of functional impairment.

The proposed approaches will require a consortium or multi-

site collaborative effort, in which fosters multidirectional and multidisciplinary integration of patient-oriented research, to accumulate enough data to achieve statistical power. While there is strength in this approach, inconsistency in evaluation approaches and discrepancies in data quality may hamper overall study interpretation [24]. The involvement of principal investigators and study staff across the sites at the beginning of study planning phase is critical to ensure the adherence to study procedures that lead to consistent high-quality data across the sites.

Conclusion

Elucidating the interplay between heart failure and sensorimotor and cognitive functions is critical future direction for cardiovascular and neuroscience fields because it will contribute to reversing adverse outcomes in persons living with heart failure. Yet, several challenges exist that can hinder the better understanding of the repercussions of heart failure on daily functioning. Multidirectional and multidisciplinary efforts are necessary to overcome such challenges.

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