Comorbidities

Expert Opinion

Cognitive Decline in Heart Failure: More Attention is Needed

Jelena Čelutkiene, Arūnas Vaitkevičius, Silvija Jakštienė and Dalius Jatužis

1. Department of Cardiovascular Diseases, Vilnius University, Vilnius, Lithuania; 2. Department of Neurology and Neurosurgery, Vilnius University, Vilnius, Lithuania; 3. Department of Radiology, Lithuanian University of Health Sciences, Vilnius, Lithuania

Abstract

Cognitive decline is a prevalent condition and independent prognostic marker of unfavourable outcomes in patients with heart failure. The highest prevalence, up to 80%, is reported in patients hospitalised due to acute decompensation. Numerous factors contribute to cognitive dysfunction in heart failure patients, with hypertension, atrial fibrillation, stroke and impaired haemodynamics being the most relevant. Cerebral hypoperfusion, disruption of blood–brain barrier, oxidative damage and brain-derived cytokines are pathogenic links between heart failure and alteration of cognitive functioning. White matter hyperintensities, lacunar infarcts and generalised volume loss are common features revealed by neuroimaging. Typically affected cognitive domains are presented. Assessment of cognitive functioning, even by simple screening tests, should be part of routine clinical examination of heart failure patients.

Keywords

Cognitive impairment, heart failure, adherence, adverse outcomes, cognitive domains, patient self-care

Disclosure: The authors have no conflicts of interest to declare.

Received: 21 September 2016 Accepted: 13 October 2016 Citation: Cardiac Failure Review 2016;2(2):106–9. DOI: 10.15420/cfr.2016:19:2

To ensure performance of everyday tasks, adherence to treatment regimens, appointments, and following dietary requirements, cognition is crucial.1 Cognitive impairment (CI) is a broad and inclusive term used to describe dysfunction of processes in various cognitive domains, such as attention, memory, judgment, reasoning, decision-making and problem solving, comprehension and production of language.

Prevalence and Pathogenic Mechanisms

Evidence is mounting that impaired cardiac function may precipitate early-onset CI. Reported prevalence2–8 of cognitive dysfunction in the heart failure (HF) population parallels the severity of HF, being the highest in the acute decompensation settings (see Table 1).

Multiple factors contributing to cognitive decline in HF are presented in Figure 1. Hypertension is found to be independently associated with CI9–11 through compromise in auto-regulation of cerebral blood flow and cerebral ischaemia (see Figure 2). Neuroimaging has revealed structural brain abnormalities (see Figure 3) correlating with reduced cognition.

Cognitive impairment has been identified as an important clinical issue in numerous recently conducted studies, though no definite consensus has been achieved so far regarding optimal diagnostics and treatment tools in patients suffering both from HF and CI. There is a definite limitation on this issue in the literature as investigators have used plenty of different tools ranging from simple and fast tests to neuropsychological test batteries, and the assessment of cognition has not been standardised. The common approach should be thoroughly investigated and reached using existing data and future clinical studies.

Cognitive Domains and Assessment Tools

The severity of CI may range from mild symptoms to advanced dementia. Mild CI is a commonly used definition for a clinical syndrome in which a patient has subjective complaints as well as objective symptoms of cognitive decline (measured by neuropsychological tests), though daily functioning of the patient is mostly intact.11 It is established that patients with mild cognitive impairment have an increased risk of progression to dementia.12,13 Dementia is characterised by a progressive impairment in more than one cognitive domain, and compromised daily functioning is evident.

Most of the HF patients suffer from mild impairment in cognition, but some of them may have moderate-to-severe CI.14 Heart failure adversely affects various cognitive domains, including attention, learning ability and working memory, executive functions, and information processing speed (see Figure 4).15–16 Cognitive impairment in HF patients usually fulfils the criteria of vascular CI or vascular dementia.16

Being one of the most important cognitive functions, episodic memory of specific personal events and experiences was demonstrated to slowly decline in HF patients.17–19 Furthermore, deficits in initial learning as well as delayed information recall were reported in the literature.20 This suggests that CI in HF patients and CI in patients with vascular dementia could share pathophysiological mechanisms.26 Deficits in executive functioning (problem solving, planning, reasoning and flexibility) have a
Cognitive Decline in Heart Failure

Table 1: Reported Prevalence Rate of Cognitive Dysfunction (CD) in Heart Failure Patients

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Study type</th>
<th>Setting</th>
<th>N</th>
<th>Prevalence of CD (%)</th>
<th>Prevalence of mild CD (%)</th>
<th>CD test used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zuccala et al. (1997)</td>
<td>Cross-sectional</td>
<td>Mild-moderate CHF</td>
<td>57</td>
<td>53</td>
<td>NA</td>
<td>MMSE</td>
</tr>
<tr>
<td>Debette et al. (2007)</td>
<td>Prospective</td>
<td>Hospitalisation for AHF</td>
<td>83</td>
<td>61</td>
<td>30</td>
<td>MMSE</td>
</tr>
<tr>
<td>Gure et al. (2012)</td>
<td>Cross-sectional</td>
<td>Community (USA)</td>
<td>6,189</td>
<td>39</td>
<td>24</td>
<td>Telephone interview for cognitive status (patterned MMSE)</td>
</tr>
<tr>
<td>Hajiuk et al. (2013)</td>
<td>Prospective</td>
<td>Hospitalisation for AHF</td>
<td>577</td>
<td>79</td>
<td>NA</td>
<td>Specific protocol*</td>
</tr>
<tr>
<td>Dodson et al. (2013)</td>
<td>Prospective</td>
<td>Hospitalisation for AHF</td>
<td>282</td>
<td>47</td>
<td>25</td>
<td>MMSE due to AHF</td>
</tr>
<tr>
<td>Levin et al. (2014)</td>
<td>Prospective</td>
<td>Hospitalisation for AHF</td>
<td>744</td>
<td>80</td>
<td>32</td>
<td>Specific protocol*</td>
</tr>
<tr>
<td>Hyoth et al. (2016)</td>
<td>Longitudinal</td>
<td>Hospitalisation for AHF</td>
<td>565</td>
<td>45</td>
<td>NA</td>
<td>MoCA</td>
</tr>
</tbody>
</table>

*Specific bedside protocol: test of immediate and delayed memory (subscale of MoCA), processing speed (Digit Symbol Substitution Test, DSSST) and executive function (Controlled Oral Word Association Test [COWA] for verbal fluency), AHF = acute heart failure; CHF = chronic heart failure; MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment.

Importance of Cognitive Decline for Prognosis and Self-care

Several prospective and cross-sectional studies showed a strong independent association of cognitive deterioration and increase in mortality and readmissions in acute heart failure (AHF) patients. A twofold increase in 30-day death and readmissions, almost fivefold rates of 1-year mortality, as well as increase in hospitalisation and/or death within 5 years were demonstrated. Such association with poor outcomes is observed even in cases of mild CI, which frequently remains undiagnosed. Dodson et al. found that patients with unrecognised cognitive decline exhibited a higher 6-month mortality and hospital readmissions.

Possible Ways to Prevent Cognitive Impairment

Evidence of therapeutic methods for prevention and management of cognitive decline in HF is lacking. The primary approach to the management of the HF patients with CI seems to be optimal pharmacotherapy, outlined in the HF guidelines, restoring central haemodynamics, as well as correction of vascular risks factors. Several studies demonstrated that patients with mild CI can return to normal cognitive functioning. The beneficial influence of HF treatment on cognition processes including angiotensin-converting enzyme inhibitors, diuretics, digoxin, cardiac resynchronisation therapy and heart transplantation were reported. Clinical trials (such as the Efficacy and Safety of LCZ696 Compared to Valsartan on Cognitive Function in Patients with Heart Failure and Preserved Ejection Fraction [PERSPECTIVE] trial; NCT02884206) investigating the impact of treatment with angiotensin-converting enzyme inhibitors and computerised adaptive cognitive training on cognitive function are ongoing. Non-pharmacological measures, such as physical activity, are also important and have been identified to have beneficial effects on cognition as well as protective benefits on brain plasticity in vascular CI and related conditions. The main task for physicians is to identify patients with early stages of CI in order to start corrective measures as soon as possible and also manage patients at risk of CI.
Figure 2: Pathogenic Links of Heart Failure and Cognitive Dysfunction

HEART FAILURE
- Reduced ejection fraction, cardiac output
- Impaired diastolic filling
- Low systolic blood pressure

ARTERIAL HYPERTENSION

CHRONIC/INTERMITTENT CEREBRAL HYPOPERFUSION

ATRIAL FIBRILLATION, ATHEROSCLEROSIS

HYPOXIA

HIF-1

VASCULAR REMODELING ENDOTHELIAL DYSFUNCTION

DISRUPTION OF BRAIN–BLOOD BARRIER

OXIDATIVE DAMAGE

STROKES

METABOLIC/HUMORAL ABNORMALITIES
- Elevated BNP
- Hyponatraemia
- Homocysteine

PROINFLAMMATORY CYTOKINES
- IL-1, IL-6, TNF-alpha

BRAIN-DETECTED CYTOKINES

INDIRECT CAUSES
- Diabetes
- Depression
- Anaemia
- Nutrition, etc.

COGNITIVE DYSFUNCTION

BNP = brain natriuretic peptide; HIF-1 = hypoxia inducible factor-1; IL = interleukin; TNF-alpha = tumour necrosis factor-alpha.

Figure 3: Magnetic Resonance Imaging of Structural Brain Abnormalities in Patients with Cognitive Dysfunction

A: Confluent hyperintense changes in the periventricular white matter consistent with small vessel ischaemic changes associated with generalised brain volume loss. B: Multifocal chronic small vessel ischaemic changes, predominantly affecting frontal lobes, and associated with a lacunar infarct on the right side. C: Lacunar infarcts bilaterally in the thalami and small vessel ischaemic changes affecting frontal periventricular white matter and associated generalised brain volume loss. D: Haemosiderin staining bilaterally in the thalami and left occipital lobe due to microbleeds.
Cognitive Decline in Heart Failure

There are no particular approved medicines for patients with CI in HF. Given that acetylcholinesterase inhibitors and memantine were found to be effective in vascular dementia, a similar effect might be expected in patients with HF, though no formal regulatory approvals have been received.20-21

Conclusion

Cognitive decline is a prevalent condition and an independent prognostic marker of adverse outcomes in patients with HF. Assessment of cognitive functioning, even by simple screening tests, should be part of routine clinical examinations of HF patients. Despite growing data in clinical practice, CI is still the challenge for clinicians. Future research including cognitive function as a relevant endpoint of HF studies is warranted. Better understanding of pathogenic links between CI and HF including molecular, neuroendocrine, epigenetic and psychosocial factors is needed. It is important to uncover the relationship between cognitive function and HF types and co-morbidities, use of cardiovascular drugs and devices. Further, more randomised and controlled trials should be initiated to provide additional data and implement diagnostic, prevention and management tools for CI in patients with HF. ■