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Dementia and the heart failure patient

Wolfram Doehner[1,2]*

[1]*Department of Cardiology Campus Virchow, Berlin Institute of Health Center for Regenerative Therapies, Charité - Universitätsmedizin Berlin, Föhrer Str. 15, 13353 Berlin, Germany; and*
[2]*Center for Stroke Research Berlin, Charité Universitätsmedizin Berlin, Augustenburger Platz 1, 13353 Berlin, Germany*

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Heart and brain disorders more frequently co-exist than by chance alone, due to having common risk factors and a degree of interaction. In the setting of heart failure (HF) in the elderly strokes, dementia, and depression are all common and can produce a particularly difficult series of clinical problems to manage. Loss of ability to self-care can lead to very poor quality of life and a dramatic increase in health care expenditure. The Heart Failure Association of the ESC as part of its workshop on physiological monitoring of the complex multi-morbid HF patient reviewed screening, monitoring, prevention, and management of cognitive decline within the setting of HF.

Introduction

Heart failure (HF), being particularly common in the elderly, is now commonly presenting as a syndrome associated with multiorgan dysfunction and many comorbidities. This complicates our management of the condition. Comorbidities can worsen the HF, complicate its diagnosis, and make treatment more difficult and more expensive. Of these HF-related comorbidities brain disorders are some of the most prevalent and the most difficult to manage.[1] The elderly HF patient poses a complex problem for modern health care systems to look after, and foremost amongst the complexities is the issue of cognitive decline and/or dementia which makes patient self-care more difficult and which adds dramatically to the cost of health care provision for the HF itself. With the ageing of developed societies, more HF presents with these multiple comorbidities, many of which frequently dominate the clinical picture, and which have become the most frequent reason for hospitalization in HF.[2]

The heart and the brain are commonly subject to similar disease processes and pathophysiological mechanisms, and a disorder in each can affect the other. The heart and the brain are both subject to the diseases of ageing, including tissue atrophy,[3] fibrosis, ischaemia, infarction, macro- and micro-vascular dysfunction, and tissue inflammation.[4] Neurological comorbidities including stroke, depression, cognitive decline, and autonomic dysfunction have received little commentary in recent HF guidelines[5] despite being common and difficult to manage.[6] Therapeutic strategies in this setting, therefore, remain largely empirical. The haemodynamic effects of the HF state on higher cerebral function are still poorly understood,[7] but should not be underestimated.[8,9]

Dementia and cognitive impairment in heart failure

Cognitive impairment is common in HF syndromes with estimates of its prevalence varying between 25% and 75%.[10,11] Unfortunately many cases are not recognized.[12] When present it carries with it a worse prognosis, loss of independence, and a significantly impaired quality of life.[13] In HF, many aspects of higher cerebral function can be impaired, including cognition, attention, memory, language, psychomotor function, and visuo-spatial acuity.[14,15] Although the precise pathophysiological processes involved are not fully understood, poor perfusion, micro-embolic events, and other ischaemic syndromes may play a role, along with possible effects of disruptions of the blood–brain barrier, cerebral inflammation, and endothelial dysfunction. The study

*Corresponding author. Tel: +49 30 450 553507, Fax: +49 30 450 7553 507, Email: wolfram.doehner@charite.de

of subtle differences in brain function and diagnostic detection is in its infancy, with many questions remaining unanswered.[16,17] Clinical features associated with cognitive decline and dementia include hypertension as a risk factor for both, stroke, AF, metabolic abnormalities, low cardiac output, depression, anaemia, iron deficiency, and endocrine abnormalities.[18,19] Cognitive impairment in HF can have a variety of clinical manifestations from mild memory problems through to dementia requiring permanent nursing home or equivalent care and have been reported both in HFrEF and HFpEF.[20] Cognitive impairment can have an insidious onset or it can develop acutely, often associated with delirium during an admission for acute decompensated HF.[21] Delirium occurring during an admission for acute HF is associated with increased mortality and length of hospital stay. The mechanisms underlying the association between acute delirium and HF remain poorly understood however.

Monitoring cognitive function in heart failure

Multiple validated questionnaires exist to screen for, and to an extent, grade cognitive impairment. These include the Mini-Mental Status Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). Mildest on the spectrum of cognitive decline syndromes is mild cognitive impairment (MCI). It is advisable to screen for cognitive impairment, as it is similarly for depression when a patient (particularly elderly) is admitted with acute HF. Screening and review should also be regularly performed in the outpatient review setting, although primary care can often pick up earlier milder changes, perhaps being reported by carers and family members. The MMSE has been used to screen for cognitive deficits, but it is not very sensitive in detecting MCI. The MoCA has been said to be more sensitive to subtle changes.[22] These screening tools can be helpful in differentiating acute from chronic cognitive decline in HF. The questionnaires detect clinical cognitive decline, whereas the pathophysiological antecedents may be there months or years earlier. For example, cerebral atrophy, white matter hyperintensities,[23] loss of grey matter,[24] and silent cerebral infarcts[25] are frequent imaging findings in HF patients with and without cognitive dysfunction.[26,27]

Causes of cognitive decline in heart failure

Stroke in patients with heart failure

Stroke, in particular, multiple mini-strokes is a common cause of disability, cognitive decline, and dementia in HF, as it is in the general population.[28,29] Strokes are more likely in the setting of HF because HF is prone to hypercoagulability of the blood, endothelial dysfunction, inflammatory activation, and malfunctioning of cerebral autoregulation along with a higher incidence of atrial fibrillation. Heart failure is implicated in nearly 10% of all strokes,[30,31] and when they occur subsequent strokes and death are more likely to follow.[32,33] Silent strokes are also extremely common in the setting of HF and may be responsible for a progressive deterioration of cognitive function. In the Framingham Study, HF leads to a 4.1 for men, and 2.8 for women, greater risk of stroke compared to those without HF.[34] AF further increases this risk, as does an ischaemic aetiology of the HF. Other comorbidities including peripheral arterial disease, hypertension, valvular heart disease, diabetes, chronic kidney disease can further increase the risk. Dementia can be delayed or prevented if strokes can be prevented or treated very early, to limit cerebral tissue loss. Oral anticoagulants are indicated in HF patients with atrial fibrillation but the balance of benefit and risk in patients with HFrEF with maintained sinus rhythm is less clear. The ESC 2016 guidelines[5] state that there is no compelling reason to use warfarin in HF patients who are not in AF. The recently published COMMANDER-HF trial as well did not show a benefit of oral anticoagulation with rivaroxaban to improve the composite primary endpoint of death, myocardial infarction, or stroke, however, a reduction of the endpoint component stroke was observed (HF 0.66, 95% confidence interval 0.47–0.95).[35] Early thrombolytic treatment of an ischaemic stroke within the first 9 h of symptom onset can improve outcomes,[36] although an increased bleeding risk after thrombolysis in HF should be taken into consideration.[37,38] Another option in ischaemic stroke is mechanical thrombectomy.

Impaired cerebral perfusion

Cerebrovascular autoregulation both globally and regionally in response to functional activity and local oxygen demands is impaired in HF. This vascular variability is locally controlled by pericytes, perivascular cells with contractile capacity at the capillary level.[39] The resulting hypoperfusion seen with both acute and chronic HF may cause or worsen cognitive decline in HF.

Management of cognitive decline in heart failure

Very little is said in most HF guidelines concerning the management of cognitive decline, dementia, or delirium. The 2016 ESC guidelines recommend only appropriate treatment of HF and team working with dementia specialists. Further research is clearly needed to investigate preventive and interventional strategies to improve outcomes, especially self-care. Depression is also a frequent accompaniment of HF and cognitive decline in this setting. Many studies have suggested worse outcomes, a poorer quality of life, and increased hospitalization rates in HF patients with coincident depression.[40–42] Depression should also be screened for in elderly HF patients using one of the validated instruments, such as the Beck Depression Inventory and the Hospital Anxiety and Depression Scale. Depression can also contribute to poor self-care, failing compliance, and low usage of life-saving medication. Although remission from depression may improve cardiovascular outcomes, effective intervention strategies have not been proven. Most antidepressants are safe in HF, but monoamine oxidase inhibitors and tricyclic antidepressants are usually avoided and two major randomized trials (SADHEART[43] and MOOD-HF[44]) did not show significant differences in outcomes with the use of selective serotonin re-uptake inhibitors.

Autonomic function in heart failure

Autonomic control of the heart and blood vessels and cardiopulmonary control can affect blood pressure, heart rate, cardiac output, peripheral blood flow, ventilation, V/Q matching, arterial blood gases, and the metabolic state of the metabolizing tissues, all of which can be put at risk in HF. Cardiopulmonary instability can result from peripheral receptor dysfunction affecting the baro-, metabo-, or chemoreceptor systems leading to disturbances such as central sleep apnoea,[45] postural hypotension, episodic hypertension, and syncope. The integrated behaviour of these reflex systems can be studied by power spectral analysis of heart rate, blood pressure, and breathing rhythms but this has not found a role in clinical practice. Routine monitoring of these autonomic abnormalities has never been taken up in routine practice despite some theoretical value for doing this.[46]

Treating cognitive decline in heart failure

ACE inhibitors and angiotensin receptor blockers and beta-blockers

ACE inhibitors and angiotensin receptor blockers have been shown to improve cognitive function in both hypertension and HF.[47–50] Beta-blockers worsen dizziness and hypotension in HF which is a theoretical risk for worsening cognitive function in fragile elderly HF patients. Sacubitril/valsartan in the PARADIGM-HF trial, whilst reducing mortality and morbidity was associated with more hypotension compared to patients randomized to enalapril,[51] and there is an as yet unresolved concern about its potential to promoting Alzheimer's disease[52] via inhibition of NEP degradation of β-amyloid (Aβ) and the potential accumulation of Aβ in the brain. However, analyses of PARADIGM did not find any increased risk of dementia or Alzheimer's.[53,54]

Devices used to treat HF such as left ventricular assist devices carry an increased risk of embolic stroke, bleeding, and thrombotic complications.[55] Changes in systemic immune state, platelet function, and acquired von Willebrand syndrome may potentially lead to cerebral infarction and haemorrhage. Other devices such as Veno-arterial extracorporeal membrane oxygenation are similarly thought to lead to an increased risk of thrombosis, bleeding, and neurologic events.

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