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Cognitive Deficits and Related Brain Lesions in Patients With Chronic Heart Failure

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ABSTRACT

OBJECTIVES This study sought to determine the spectrum of brain lesions seen in heart failure (HF) patients and the extent to which lesion type contributes to cognitive impairment.

BACKGROUND Cognitive deficits have been reported in patients with HF.

METHODS A total of 148 systolic and diastolic HF patients (mean age 64 ± 11 years; 16% female; mean left ventricular ejection fraction 43 ± 8%) were extensively evaluated within 2 days by cardiological, neurological, and neuropsychological testing and brain magnetic resonance imaging (MRI). A total of 288 healthy, sex- and age-matched subjects sampled from the Austrian Stroke Prevention Study served as MRI controls.

RESULTS Deficits in reaction times were apparent in 41% of patients and deficits in verbal memory in 46%. On brain MRI, patients showed more advanced medial temporal lobe atrophy (MTA) (Scheltens score) compared to controls (2.1 ± 0.9 vs. 1.0 ± 0.6; $p < 0.001$). The degree of MTA was strongly associated with the severity of cognitive impairment, whereas the extent of white matter hyperintensities was similar in patients and controls. Moreover, patients had a 2.7-fold increased risk for presence of clinically silent lacunes.

CONCLUSIONS HF patients exhibit cognitive deficits in the domains of attention and memory. MTA but not white matter lesion load seems to be related to cognitive impairment. (J Am Coll Cardiol HF 2018;■:■–■)

Chronic heart failure (HF) constitutes a serious health care problem with increasing incidence and prevalence. In particular, improved survival after myocardial infarction has contributed to the rise in the prevalence of left ventricular systolic dysfunction (1). Longer-term outcome, quality of life, and health care costs depend not only on left ventricular function but also on the severity of secondary impairment of other organ systems, including the brain (1).

There is consistent evidence that HF patients frequently develop cognitive deficits as disease evolves (2–5). Such impairment may interfere with disease control because HF treatment and monitoring both require a high degree of comprehension, self-control, and adherence to treatment

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ABBREVIATIONS AND ACRONYMS

6-MWT = 6-min walk test

AF = atrial fibrillation

CI = confidence interval

HF = heart failure

LVEF = left ventricular ejection fraction

MRI = magnetic resonance imaging

MTA = medial temporal lobe atrophy

OR = odds ratio

PVH = periventricular hyperintensity

WMH = white matter hyperintensity

recommendations. In stable HF outpatients, lower left ventricular ejection fraction (LVEF) and deficits in various cognitive domains predicted 1-year mortality risk (3).

To date, information on the prevalence, type, and severity of cognitive impairment in HF patients is limited. Data on the spectrum of brain lesions that contribute to cognitive dysfunction are particularly sparse (6-9).

In this study we report on the associations between cognitive performance and brain lesions at baseline among patients followed in the prospective Cognition.Matters-HF study. Moreover, the extent of medial temporal lobe atrophy (MTA), white matter hyperintensities (WMHs), and clinically silent lacunes in HF patients were compared with those of an age-matched healthy population sampled from the ASPS (Austrian Stroke Prevention Study) and ASPS-Fam (Austrian Stroke Prevention Family Study) trials (10,11).

METHODS

STUDY DESIGN AND ETHICAL CONSIDERATIONS. The Cognition.Matters-HF study is an investigator-initiated, prospective monocentric follow-up study. The study protocol was approved by the local ethics committee and complies with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

PATIENT SELECTION CRITERIA. Patients with clinically confirmed chronic HF were eligible. HF was defined according to established criteria in the guidelines of the European Society of Cardiology at the time of study entry (12). Patients with de novo or acutely decompensated HF were not eligible. Other exclusion criteria were a history of clinical stroke, apparent psychiatric disease (including depression or dementia), carotid artery stenosis >50%, or any implant or device impeding brain magnetic resonance imaging (MRI) (Online Table 1).

STUDY FLOW. Figure 1 shows the time schedule of study-related investigations. Echocardiography was used as the initial screening procedure. Baseline investigations (and iterative follow-up examinations after 12, 36, and 60 months) comprised comprehensive evaluation by a cardiologist, neuropsychologist, neurologist, and neuroradiologist. Care was taken to complete all diagnostic procedures per visit within 2 days.

DIAGNOSTIC PROCEDURES. Cardiological evaluation and laboratory. Clinical examination, electrocardiography, echocardiography, 24-h Holter electrocardiography, 24-h blood pressure measurement, and 6-min walk test (6-MWT) were all performed according to standard operating procedures at the Comprehensive Heart Failure Center Würzburg. Blood samples for routine clinical chemistry investigations were tested at the certified facility of the University Hospital Würzburg.

Neuropsychological test battery. All patients completed a comprehensive neuropsychological test battery, which was performed between 9 AM and 11 AM. A detailed description of the test battery is provided in the Online Methods and Online Table 2. The modifying effect of age, sex, and educational level had been investigated in validation studies of these tests in healthy volunteers. Respective influencing factors per test were then considered in the test outputs, which were given by T-standardized values (mean = 50, SD = 10 as mean reference comparator). As such, a T ≤40 indicates performance below average according to the test-specific control group. Reliability of tests ranged between 0.60 and 0.99 (13). Selection of tests was based on taxonomy of attention dimensions from Sturm et al. (14). The applied sequence prevented learning effects by arranging attention tests at the beginning and avoiding the overlap of memory spans and contents. Verbal and visual performances were measured separately within the domains of memory and executive functions.

Neurological examination. The neurological evaluation included clinical examination, Barthel index (15), modified Rankin scale (15), National Institutes of Health Stroke Scale (16), Mini-Mental State Examination (17), and cerebrovascular ultrasound (18) (for details, see the Online Methods).

Cerebral MRI. ***Image acquisition.*** Brain MRI was performed on a 3-T scanner (Siemens MAGNETOM Trio; Siemens Healthcare, Erlangen, Germany) using a 12-channel head coil involving T_1W FLASH, T_1W 3D TFL, T_2W FLAIR, T_2W TSE, DWI, localizers, SV spectroscopy, and ASL perfusion (for detailed protocol and definition of terms, see the Online Methods and Online Table 3).

Image analysis. MRI analysis was performed according to the study protocols of ASPS and ASPS-Fam (10,11). ASPS, commenced in 1991, and its extension ASPS-Fam are prospective single-center community-based studies on the cerebral effects of vascular risk factors in the normal elderly population of Graz, Austria. Images from HF patients were read and documented by an expert neuroradiological reader (B.A.) focusing on brain atrophy, white matter lesions, and brain infarctions. The findings were formally approved by a second senior