The mind of a failing heart: a systematic review of the association between congestive heart failure and cognitive functioning

O. P. ALMEIDA¹ and L. FLICKER²

¹Department of Psychiatry and Behavioural Science and ²Department of Medicine, University of Western Australia, Perth, Western Australia, Australia

INTRODUCTION

Congestive heart failure (CHF) is a common complication of most diseases of the heart. Its prevalence increases exponentially from age 60 years,¹ such that CHF is now one of the leading causes of hospitalization, morbidity and mortality in western societies.² The findings of several surveys indicate that physical, social, work and leisure activities are significantly impaired among CHF subjects.³ Psychological distress is also frequent, although data on this important aspect of the quality of life of patients remain sparse and difficult to interpret. Depression rates, for example, seem to be high (up to 58%) in both inpatient and outpatient settings.⁴ ⁵ Another important, but neglected, aspect of the quality of life of...
patients with CHF is cognitive functioning. Early reports indicated that up to 80% of patients with severe CHF display deficits in memory and other cognitive abilities. The consequences of these deficits are not clear, but it is conceivable that patients with cognitive impairment have even higher morbidity and mortality rates. For example, Cline et al. reported that 10 of their 22 patients were unable to name the medication they were receiving for the treatment of CHF, 11 of 22 could not state the doses and 14 of 22 failed to remember when to take their tablets. All subjects were surveyed 30 days after receiving detailed verbal and written information about their treatment regimen. Failing to take the prescribed medication, in such cases, may increase the frequency of clinical complications associated with CHF.

We designed the present study with the aim of reviewing all available medical information on the association between CHF and cognitive functioning.

METHODS

We searched Medline using the following strategy: #1. exp heart failure, congestive/; #2. esp cognition disorders/; #3. esp memory/or exp memory disorders/ or exp memory, short-term/; #4 exp attention/; # 5. 2 or 3 or 4; #6. 1 and 5; limit 6 to human. This search strategy returned a total of 35 papers for the period between 1966 and June 2000. Another five papers were retrieved through a manual search of references quoted by other papers. Criteria for inclusion of studies were: (i) case-control or cross-sectional surveys designed to investigate the association between CHF and cognitive impairment; (ii) the use of valid measures of general cognitive functioning, memory or attention; and (iii) reported data suitable for analysis (i.e. mean and SD, or proportions). Studies published in languages other than English were excluded. Reports on heart transplant candidates were considered to indicate the presence of CHF even when clinical criteria or physiological measures (such as ejection fraction) were not explicitly described. In the case of general cognitive measures, the following priority sequence was used: Mini Mental State Examination (MMSE), Blessed Dementia Scale and Wechsler Adult Intelligence Scale (WAIS) full IQ. Delayed memory scores had precedence over immediate recall or general memory measures; verbal memory had precedence over visual memory. This hierarchical approach was used to increase the homogeneity between studies and give priority to the cognitive measures most commonly used to describe impairment in general cognitive functioning and memory. Cognitive impairment was recorded as present for cases with MMSE < 24, because this cut-off point has been used by other studies of patients with CHF.

Data were analysed using the software Review Manager 4.1 (Cochrane Collaboration, Oxford, UK). The standardized mean difference (SMD = (x - x)/SD) was estimated for cognitive ratings and the weighted total SMD calculated. A pooled odds ratio (OR) was calculated for proportions (fixed-effect model).

RESULTS

Thirteen studies reported cognitive information on patients with CHF, but only five met inclusion criteria for systematic review. Table 1 describes the characteristics of studies included in the analyses. Three reports described attention and memory scores, two measures of general cognitive functioning and one the rate of cognitive impairment. Memory scores represent the performance of patients on the Rey Complex Figure Test and Logical Memory subtest of the Wechsler Memory Scale. Attention scores indicate results on tests of Attention Matrices and Trail Making B. Finally, overall cognitive performance was assessed with the MMSE and WAIS. One study described that 50 of 88 patients with CHF and 197 of 987 controls had MMSE scores lower than 24 (OR = 5.28; 95% confidence interval (CI) = 3.37–8.25), although CHF subjects were older and more depressed than controls. Results of the pooled analyses are summarized in Fig. 1.

DISCUSSION

The results of the present review indicate that CHF is associated with a pattern of generalized cognitive impairment that includes memory and attention deficits. They also highlight the enormous paucity of systematic information in the area, with only five studies reporting data suitable for analysis. Seven other reports described the cognitive performance of patients with CHF, but did not use suitable comparison groups (Table 2). Overall, the published studies seem to confirm that CHF is associated with cognitive impairment.

Attentional deficits are expected among patients with a severe and debilitating medical illness, such as CHF. In fact, the performance of subjects in other cognitive tasks is likely to be influenced by the presence of attentional deficits, which may partly explain the finding of memory deficits and generalized cognitive impairment.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Methods</th>
<th>Participants</th>
<th>Interventions</th>
<th>Outcomes</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Case-control study; CHF × other heart diseases</td>
<td>CHF = 183; no CHF = 684</td>
<td>None</td>
<td>MMSE, Leipad (self-memory), verbal fluency, spatial span, digit span, Rey-immediate, Rey-delayed attentional matrices</td>
<td>Scores were not adjusted for confounding variables, such as age, gender and education</td>
</tr>
<tr>
<td>8</td>
<td>Case-control study; CHF × no CHF, CHF (MMSE &lt; 24) × CHF (MMSE &gt; 23)</td>
<td>Total sample size = 1075; CHF = 88; MMSE &lt; 24 = 247</td>
<td>None</td>
<td>MMSE</td>
<td>Logistic regression with cognitive impairment used as independent variable: CHF OR = 1.96 (1.07–3.58)</td>
</tr>
<tr>
<td>11</td>
<td>Case-control study of subjects with EF &lt; 35%</td>
<td>NYFC-I versus NYFC-II/III</td>
<td>None</td>
<td>WAIS vocabulary, digit span, trail making A, trail making B</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Matched case-control study</td>
<td>44 heart transplant candidates, 44 healthy controls recruited from the community</td>
<td>None</td>
<td>Grooved pegboard, trail making A, trail making B, logical memory</td>
<td>Matching was not stringent (age, gender, ethnic origin, education)</td>
</tr>
<tr>
<td>6</td>
<td>Case-control study (subjects used as their own controls), before and after surgery</td>
<td>54 pre-operative patients, 20 pre/post cardiac transplant patients recruited from the Temple University Hospital (USA)</td>
<td>Cardiac transplant</td>
<td>WAIS full IQ, WAIS verbal IQ, WAIS performance IQ, WMS logical memory, WMS visual reproduction, HR impairment index, HR category, HR tactual performance, HR total time, HR memory, HR location, HR speech-sound, HR seashore, HR finger-oscillation</td>
<td>Subjects with more severe impairment were less likely to receive heart transplant</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure; MMSE, Mini Mental State Examination; WAIS, Wechsler Adult Intelligence Scale; EF, ejection fraction; NYFC, New York functional class; WMS, Wechsler Memory Scale; HR, Hastead–Reitan.
impairment among patients. Gorkin et al.\textsuperscript{11} showed that subjects with more severe forms of CHF (functional class II/III) have greater difficulty than controls (functional class I) on digit span and trail making A tests. They also found that performance on these tasks is associated with decreased functional capacity, as measured by the 6 min walk test. These results suggest that cognitive deficits become more prominent with increasing severity of illness, although Schall et al.\textsuperscript{6} found that cardiac transplant fails to reverse the deficits of some cognitive skills, such as memory.

The mechanisms that contribute to the development of cognitive impairment among patients with CHF remain unclear. Zuccalà et al.\textsuperscript{12} observed a linear relationship between MMSE scores and left ventricular ejection fraction rates for values lower than 40%. Similarly, Putzke et al.\textsuperscript{13} noted that Trail B, Digit Symbol Substitution and Stroop scores were all significantly associated with cardiac output. Cerebrovascular disease is another likely cause of cognitive impairment, because many patients with CHF have widespread cardiovascular problems and are at increased risk for strokes. Data derived from the

### Figure 1

Summary data of studies investigating the cognitive performance of patients with congestive heart failure (CHF) and controls. Controls include subjects with no medical conditions, subjects with other cardiovascular diseases and patients with mild CHF or CHF after cardiac transplant. The first comparison table displays the data summary for attention scores, followed by memory and general cognitive skills. SMD, standardized mean difference.
Rotterdam study,\textsuperscript{14} for example, indicate that white matter disease is associated with subjective memory impairment and lower scores on tests of cognitive function. Similarly, patients with strokes are more likely to develop cognitive deficits and dementia. Other cardiovascular problems, such as low\textsuperscript{15} and high blood pressure,\textsuperscript{16} both frequent among patients with CHF, are associated with cognitive impairment. Cognitive impairment in CHF may also be due to the abnormal hormonal response that characterizes the disease, although no direct evidence is currently available to support this hypothesis. Finally, there is still the possibility that some of the cognitive deficits of patients with CHF are secondary to the presence of depressive or other psychiatric symptoms.

In conclusion, the results of the present systematic review suggest that CHF is associated with a pattern of cognitive impairment that includes attention and memory deficits. However, the number of studies is still very small and neuropsychological information is only available for fewer than 400 subjects with CHF. Generalization of these findings is further limited by the heterogeneity of the samples selected for investigation and the absence of suitable control groups. In addition, most studies were exploratory in nature and, as a consequence, used a large number of neuropsychological tests without any \textit{a priori} hypotheses.

We expect that new case-control and cohort studies will be designed to confirm the presence of cognitive impairment in patients with CHF and trust that this information will improve the management of CHF patients and our understanding of the mechanisms associated with cognitive decline in later life.

\textbf{REFERENCES}


\begin{table}
\centering
\footnotesize
\begin{tabular}{ll}
\hline
Reference & Reason for exclusion \\
\hline
17 & Sixty-two baseline assessments of cardiac transplant candidates; only 30 survived an average of 36 months for reassessment; 11 were retested, of whom seven were operated on. Outcome is presented as change of scores compared with baseline, but data are not available. The overall result was that the change of scores between transplanted and not transplanted groups was significant ($P = 0.03$). \\
18 & The authors reported an 18-month follow-up study of an undisclosed number of subjects with CHF and other medical conditions. They reported that CHF patients’ scores on the Dementia Rating Scale deteriorated over time compared with the scores of adults with CVA. No hard data are available and the authors have obviously made multiple comparisons and no statistical correction. \\
19 & Abstract information only. Authors claimed that heart transplant was associated with improved IQ, memory and attention. \\
20 & The authors investigated the effect of age, gender, hip fracture, CVA and ethnic origin on mental status (Blessed Dementia Scale) of 212 older adults discharged from hospital. CHF was significantly associated with cognitive impairment, but no data are described in the paper. \\
13 & Cross-sectional survey of 62 heart transplant candidates. The performance of 24\% of subjects was 2SD below the mean for BNT, TMB, DSS, WMS logical memory, WMS paired associates. This study showed a positive correlation between the severity of heart failure and degree of cognitive impairment. \\
21 & Study described in the paper by Acanfora \textit{et al.}\textsuperscript{9} The number of subjects is unclear. Acanfora \textit{et al.}\textsuperscript{9} reported mean scores, but not SD; the MMSE score of patients with CHF was lower than for controls with other cardiovascular diseases (22.5 × 23.8). \\
12 & Cross-sectional exploratory study of 57 subjects with CHF. Thirty of 57 patients had MMSE < 24. There was no comparison group. This study showed a positive correlation between the severity of heart failure and degree of cognitive impairment. \\
\hline
\end{tabular}
\caption{Characteristics of excluded studies that reported cognitive functioning of patients with congestive heart failure.}
\end{table}
11 Gorkin L, Norvell NK, Rosen RC et al. Assessment of quality of life as observed from the baseline data of the studies of left ventricular dysfunction (SOLVD) trial quality-of-life substudy. Am J Cardiol 1993; 71: 1069–73.

Internal Medicine Journal 2001; 31: 290–295