Correlation Between Evolution of the Cognitive Function and Mortality After Hospital Discharge in Elderly Patients with Advanced Heart Failure

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Objective - *To assess the relation between the evolution of cognitive performance and the prognosis of elderly patients after compensation of advanced heart failure.*

Methods - *Thirty-one patients older than 64 (68 ±7) years and admitted with New York Heart Association class IV heart failure and ejection fraction = 0.45 (0.38 ±0.06) were consecutively selected. They underwent cognitive tests (digit span, digit symbol, letter cancellation, trail making A and B) and the 6-minute walking test 4 days before (T1) and 6 weeks after (T2) hospital discharge, and their performances were compared using the t test. The prognostic value of the scores of the cognitive tests was analyzed with logistic regression, and the value of greatest accuracy of the tests was associated with the prognosis determined by the ROC curve.*

Results - *After 24.7 months, 17 (55%) patients had died. The performances in the 6-minute walking test and most cognitive tests improved between T1 and T2. The digit span score of the survivors ranged from 3.9 to 5.2 (P=0.003) and remained unaltered among those who died (4.1 to 3.9; P=0.496). An improvement < 0.75 points in the score was associated with mortality (relative risk of 8.1; P=0.011).*

Conclusion - *In the elderly, after compensation of advanced heart failure, the lack of evolutionary improvement in cognitive performance was associated with a worse prognosis.*

Key words: heart failure, prognosis, aging

The incidence of heart failure increases exponentially with age and is accompanied by high mortality, mainly when comorbidities are present. The identification of factors that may correlate with prognosis is important to guide possible interventions.

Some previous studies [1-3] showed the presence of cognitive impairment in patients with heart failure assessed with different tests. The possible mechanisms of the correlation between heart failure and the reduction in cognitive function are a matter of speculation. In fact, heart failure may be the cause of cognitive impairment, which influences the quality of life and the clinical evolution of the patient, because it hinders adherence to treatment and predisposes to falls and traumas. However, occasional relations between the behavior of cognitive function and clinical evolution have not been frequently studied in the elderly with advanced heart failure. As these are high-risk patients often admitted for compensation, the assessment of factors associated with their evolution is important. This study aimed at assessing the correlation between the evolution of cognitive performance and mortality after hospital discharge in these patients.

Methods

Of the 3.689 patients admitted to the Cotoxó Hospital of São Paulo Medical School from February 1995 to August 1998, the following patients were selected: those aged ≥ 64 years admitted due to decompensated New York Heart Association functional class IV heart failure, with a left ventricular ejection fraction ≤ 0.45 on echocardiography.

Patients with the following conditions were excluded from the study: depression, schizophrenia, dementia, alcoholism, drug addiction, chronic obstructive pulmonary disease, significant infection, reduction in visual acuity, stroke within the previous 6 months, acute myocardial infarction within the previous 3 months, neoplasia, urea serum levels > 120 mg/dL, creatinine serum levels > 2.4 mg/dL, and sodium serum levels < 130 mEq/L.

Based on this, 31 patients with a mean age of 68 ± 7 years and a mean left ventricular ejection fraction of 0.38 ± 0.06 were selected, 22 (71%) of whom were men. These patients underwent cognitive tests and assessment of functional capacity 4 days before (T1) and 6 weeks after (T2) hospital discharge.

After discharge, the patients were regularly followed up in the outpatient care clinic, and they were divided according to the occurrence of death into group A (dead) and group B (survivors).

The cognitive assessment comprised the following tests[4]: 1) digit span - memorization of the direct and inverse order of a 3- to 9-digit sequence verbally presented. Performance was assessed based on the number of right answers in recalling the direct and inverse sequence and the total score. The test evaluated immediate memory, concentration, and attention; 2) digit symbol substitution - symbols are designated for numbers from 1 to 9, and the patient should replace the numbers in a sequence by the corresponding symbols during a period of 90 seconds. Performance is assessed by the number of right and wrong answers. The test evaluates concentration, motor and mental velocity; 3) letter cancellation test - 2 letters of the alphabet are previously determined as target characters and the patient is asked to mark all the occurrences of the letters in a sequence of other letters of the alphabet. The task should be performed in 100 seconds. Performance is measured by the total score, the number of correct answers and omissions. The test assesses the capacity to maintain the focus of attention for a certain period of time; 4) trail making – in this test, the patient is asked to draw, as fast as possible, a line linking, in a sequence (1 - A - 2 - B -...), numbers and letters randomly distributed in a sheet. The result is measured by means of a score that varies from 1 to 300, the lower the value, the better the performance.

The functional capacity was assessed with the 6-minute walking test[5]. The test consists in asking the patient to walk as fast as possible on a flat track for 6 minutes. Performance is measured by the distance walked in meters.

The continuous variables were expressed as mean and standard deviation; the nonpaired Student t test was used for comparison between the groups, and the paired test was used for comparison between the moments T1 and T2. The categorical variables were expressed in proportion, and the chi-square or Fisher exact tests were used for comparison between the groups. The survival curve was built using the Kaplan-Meier method[6]. The occurrence of death was analyzed as a function of cognitive performance using the logistic regression method[7]. The confidence interval used was 95%. The most accurate cut point for cognitive performance was determined by the receiver operating characteristic (ROC) curve. The value of $P < 0.05$ was considered statistically significant.

Results

The basal characteristics of the patients, according to the occurrence of death or lack thereof (groups A and B, respectively), are shown in table I. The groups did not differ in regard to age, etiology of cardiomyopathy, and ejection fraction. Using bivariate analysis, a statistically significant difference in regard to renal function was observed between the groups.

The cognitive performance of the patients as a whole, when comparing the moments T1 and T2, showed a similarity in regard to the digit span score (4.0 ± 1.5 vs $4.5+1.7$; respectively T1 and T2) and the trail making B score (79.3 ± 81.4 vs 58.1 ± 55.1; respectively T1 and T2). Differently, an improvement in the number of right answers was observed in the digit symbol substitution (12.2 ± 8.6 and 15.8 ± 9.4, respectively T1 and T2; P=0.0002) and in the letter cancellation test score (32.8 ± 16.3 vs 44.2 ± 21.0; respectively, T1 and T2; P<0.0001).

The distance walked in the 6-minute walking test of the patients selected significantly improved from T1 to T2 (314 ± 111 vs 401 ± 117 meters, P<0.0001).

After a follow-up of 24.7 ± 2.9 months, 17 (55%) patients died (group A), 11 (65%) in the first 12 months of follow-up. The comparison between groups A and B showed a difference in the evolutionary behavior only in the digit span test (tab. II).

The logistic regression analysis included the cognitive variables and the renal function data. This multivariate

Table I - Characteristics of the population			
	Group A (n=17)	Group B (n=14)	Total (n=31)	P
Male sex n (%)	12 (70.6)	10 (71.4)	22 (71.0)	1.000
Etiology				
Ischemic n (%)	6 (35.3)	8 (57.1)	14 (45.2)	0.224
Hypertensive n (%)	8 (47.1)	6 (42.9)	14 (45.2)	0.815
Chagasic n (%)				
Dyslipidemia n (%)	2 (12.5)	2 (14.3)	4 (13.3)	1.000
Diabetes n (%)	8 (47.1)	4 (28.6)	12 (38.7)	0.293
Age (years)	68.1 ± 7.6	67.1 ± 5.3	67.6 ± 6.5	0.648
Ejection fraction (%)	37.8 ± 6.8	37.2 ± 4.7	37.5 ± 5.9	0.779
Sodium (mEq/L)	136.4 ± 4.2	138.5 ± 3.9	137.3 ± 4.14	0.170
Potassium (mEq/L)	4.53 ± 0.47	4.42 ± 0.59	4.49 ± 0.52	0.570
Urea (mg/dL)	72.1 ± 25.3	55.5 ± 15.6	64.9 ± 22.9	0.037*
Creatinine (mg/dL)	1.62 ± 0.34	1.32 ± 0.33	1.49 ± 0.36	0.024*

Table II - Evolution of the cognitive and functional performance according to the occurrence of death			
Variation between T1 and T2	Group A (n=17)	Group B (n=14)	P
Digit span forward (score)	-0.2 ± 1.4	1.3 ± 1.3	0.011
Digit symbol (score)	2.7 ± 4.8	4.7 ± 4.6	0.250
Letter cancellation (score)	10.1 ± 11.6	12.8 ± 13.3	0.556
Trail making B (score)	-5.3 ± 27.8	- 36.7 ± 105.5	0.297
6-minute walking test (m)	67.3 ± 52.2	121 ± 107.4	0.130

model confirmed that the only predictive variable of death was the difference in the digit span score between moments T1 and T2 (P= 0.015).

Using the ROC curve, the difference in the digit span score between the moments T1 and T2 was defined as 0.75; this value had the greatest accuracy to predict death, with a relative risk of 8.13 (95% confidence interval: 1.6 – 40.8). The survival curve, according to the improvement in the score, showed the difference in evolution (fig. 1).

Discussion

To our knowledge, this is the first study correlating evolution of cognitive performance and mortality in the elderly with advanced heart failure.

Compared with ours, the SOLVD study [8] assessed younger patients with less advanced heart failure and better performance on digit span (score: 10.0±2.6). On the other hand, Bornstein et al [9], studying younger patients (mean age of 45 years) before undergoing heart transplantation, found a performance on the digit span test similar to that in our study (score of 4.4 ± 1.2). Newman et al [10], studying a group of patients with atherosclerotic coronary disease but no heart failure before myocardial revascularization (mean age of 61 years), reported the score of 7.3 ±2.3.

The survival curve showed that most deaths occurred within the first year after hospitalization; later on, the curves of the groups with and without cognitive deficit became parallel. Therefore, the association of cognitive dysfunction and prognosis should occur close to hospital discharge and not in the long run. Our study was not designed to clarify

Fig. 1 - Probaility of survival according to the difference in the digit span score between the moments T1 and T2.

whether cognitive performance is a cause of worse evolution or a consequence of more severe heart disease; however, some hypotheses may be elaborated.

The correlation between worse cognitive performance and clinical evolution may reflect the marked hemodynamic impairment of cerebral blood flow, not only global, but also regional. In an unpublished study carried out by our group, we observed that elderly patients with advanced heart failure have changes in regional flow, particularly in the areas related to cognition. On the other hand, the elderly may have worse cognitive performance due to changes in cerebral vascularization, which can reflect a lower degree of adaptation of the systemic circulation to heart failure.

The presence of poorer cognitive performance, however, could impair evolution, as adherence to the medicamentous treatment decreased. In agreement with this, the attentional deficit evaluated on digit span is in accordance with this hypothesis.

Renal function, assessed based on urea and creatinine levels, has been correlated with the occurrence of death through bivariate analysis. In fact, uremia may influence cognitive performance, and patients with severe renal failure were excluded from the study. In addition, through multivariate analysis, cognitive performance was correlated with mortality independently of renal function.

It is worth noting that, in our sample, the surviving patients had improved cognitive function above a level of performance similar to that in the group of the patients who died, emphasizing that reversibility of the cognitive impairment deficit correlated with a better evolution. In addition, the correlation of the evaluation using the digit span test and fatal evolution was markedly significant and had a relative risk of 8.13. The large confidence interval reflected the relatively small size of the sample; however, in the worst of cases, the relative risk was 1.6, stressing the hypothesis that cognitive impairment is associated with a worse prognosis.

Our findings confirm that the elderly with advanced heart failure have a marked reduction in performance in cognitive tests, stressing the usefulness of specific tests in these patients. The cognitive improvement observed in some patients after compensation may have resulted from the improvement in cardiovascular, hemodynamic, and clinical conditions, a fact that may have resulted in a better evolution. This possibility could not be confirmed in this study.

Our sample was limited by exclusion factors, such as the impossibility of walking, the reduction in visual acuity, and depression, which are very frequent in critically ill, elderly patients with comorbidities (eg, diabetes mellitus). The
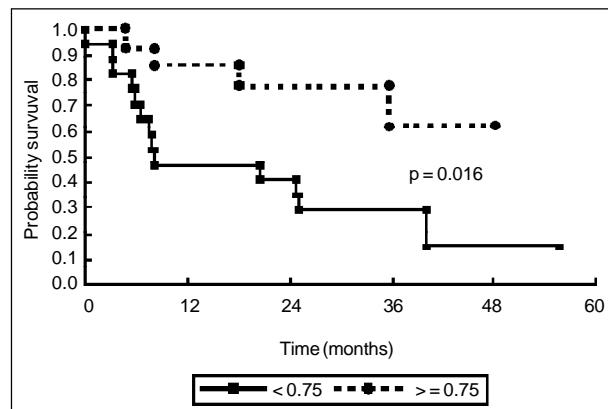
patients who died during the period of 6 weeks were not assessed. Although our sample was relatively small (n=31), the number of deaths (17) was sufficient to reduce type I error.

Our sample comprised patients with functional class IV heart failure, which does not allow us to extrapolate our findings to patients with milder disease.

The high incidence of illiteracy, most frequently functional illiteracy, in our elderly population may have influenced the results of the cognitive tests, although the design of the study, which compared 2 moments in the same patient, may have reduced this influence.

In conclusion, in the elderly with advanced heart failure, the lack of improvement in cognitive performance measured with the digit span test correlates with a poorer evolution mainly in the short run.

Acknowledgments

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