Improved cognitive function after kidney transplantation compared to hemodialysis

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1 INTRODUCTION

Stress as a physical, mental, or emotional factor that may result in bodily or mental damage is defined as an objective or perceived imbalance within a person, with the environment, or other individuals. Chronic stress may affect cognitive function and physical capacities and has been shown to result in endocrine changes; in addition, stress is associated with an increased risk for cardiovascular events. The human stress response involves a complex signaling system; for example, environmental stressors lead to the secretion of corticotrophin-releasing hormone (CRH) from the hypothalamus and subsequent elevation of ACTH levels and cortisol [1]. Furthermore, stress may lead to increased activity of the sympathetic nervous system and the adrenal medulla resulting in a secretion of epinephrine and norepinephrine [2]. Catecholamine biosynthesis in the adrenal medulla is partly regulated by glucocorticoids, whereas the secretion of CRH is stimulated by cytokines such as tumor necrosis factor alpha, interleukin-1, interleukin-6, and various peptides [2]. A variety of physical changes have been identified in the response to stress. Monitoring heart rate variability (HRV), for example, is an important approach to assess

Abstract
End-stage renal disease is associated with chronic stress that in turn may result in endocrine changes, affect cognitive, and physical capacities and increase the risk for cardiovascular events. The objective of this study was to evaluate and characterize possible stress parameters and compare cognitive function in those patients. Physiological and biochemical stress parameters as well as cognitive function were assessed in 17 hemodialysis and 18 renal transplant patients and both groups were compared. Serum cortisol and interleukin-6 levels were elevated in both groups but showed no significant difference. Cholesterol and low-density lipoprotein levels were significantly higher in patients following renal transplantation. While heart rate variability was comparable in both groups, most cognitive tests showed better results in renal transplant patients. We showed that: (1) cognitive function may improve following renal transplantation; (2) standard biochemical stress parameters are not useful to discriminate stress in patients with chronic kidney disease; and (3) heart rate variability is unaltered in this setting.

KEYWORDS

cognitive function, hemodialysis, quality of life, renal transplantation, stress parameters
stress by identifying variations in the time interval between heartbeats, measured by the variation of the beat-to-beat interval. In fact, decreased HRV has been shown to be linked to stress and a strong predictor of increased mortality, for example, after myocardial infarction [3].

Furthermore, patients may suffer from cognitive changes such as impaired attention and memory function due to increased levels of stress [4]. Cognitive changes are generally evaluated using memory and attention function tests. Chronic diseases may lead to long-lasting stress as patients need to take medication regularly, visit their physician frequently and adapt their lifestyle to the underlying disease. This applies especially to patients with end-stage renal disease (ESRD). Up to 35% of patients receiving renal replacement therapy (RRT) suffer from cognitive impairment [5]. Cognitive function may also be impaired even before starting hemodialysis due to changes related to chronic kidney disease [5]. After all, previous studies have described improved cognitive function in patients with chronic kidney disease following renal transplantation [6]. The aim of this study was to determine biochemical and clinical stress parameters as well as cognitive function in patients with ESRD and to identify potential differences with respect to hemodialysis or renal transplantation as RRT.

2 | PATIENTS AND METHODS

A total of 35 patients with ESRD (12 female and 23 male) were included in this study. Eighteen patients had a prior renal transplant as RRT while 17 patients were on hemodialysis. Mean age of the study population was 59.6 years (range 44–78 years) with most patients having glomerulonephritis \( (n=14) \), diabetic nephropathy \( (n=7) \), or hypertensive nephropathy \( (n=8) \) as underlying renal disease; other causes were present in six individuals. Patients with a renal transplant were younger than those on hemodialysis patients (mean age 56 ± 11 vs. 63 ± 10 years, \( P < 0.05 \)), had experienced a longer time on RRT, while body mass index was significantly higher in the dialysis patients \( (28.55 ± 5.56 \text{ vs. } 23.92 ± 3.08 \text{ kg/m}^2, P = 0.005, \text{ Table 1}) \). Both groups were comparable with respect to sex and blood pressure. All patients had a history of arterial hypertension, while diabetes was more common in the hemodialysis group \( (58.8\% \text{ vs. } 16.7\%, P < 0.05) \). Biochemical stress parameters to be determined included cortisol, interleukin-6, growth hormone, epinephrine, norepinephrine, glucose, glucagon, insulin, triglycerides, cholesterol, high- and low-density lipoprotein, uric acid, urea, and thyroid stimulating hormone. In addition, parathyroid hormone, C-reactive protein, blood count, creatinine, and electrolytes were assessed. Physiological parameters determined included heart rate and blood pressure. In addition, a 12-lead electrocardiogram was taken and heart rate variability (HRV) was evaluated according to the guidelines of the Task Force for Pacing and Electrophysiology [7]. Following a continuous 20-min electrocardiogram in a quiet and temperature-controlled room (Cardio Scan 4.0, Firma MTM, Hünfelden, Germany), HRV was recorded as beat-to-beat intervals with subsequent analysis using frequency-domain parameters.

In addition, neurocognitive functions were assessed by using various tests of attentiveness (German version of a computerized attentional test [Go/NoGo, vigilance, alertness] [8] and divided attention [d2 letter cancellation test] [9]). Intrinsic alertness, representing the internal control of wakefulness and arousal in the absence of a preceding warning stimulus, as well as phasic alertness to describe the ability to increase response readiness subsequent to external cueing were evaluated [10]. The d2 letter

| Variable                          | Dialysis patients | Kidney transplant patients | \( P \)-value |
|-----------------------------------|-------------------|---------------------------|--------------|
| Number of participants            | 17                | 18                        |              |
| Female                            | 6 (35%)           | 6 (33%)                   | 0.903        |
| Male                              | 11 (65%)          | 12 (67%)                  |              |
| Age (years)                       | 63.35 ± 9.64      | 56.11 ± 10.88             | 0.05         |
| Height (m)                        | 1.69 ± 0.07       | 1.71 ± 0.09               | 0.56         |
| Weight (kg)                       | 81.12 ± 16.86     | 70.28 ± 13.19             | 0.04         |
| Body mass index (kg/m\(^2\))      | 28.55 ± 5.56      | 23.92 ± 3.08              | 0.005        |
| Time from start RRT (years)       | 4.91 ± 5.34       | 16.3 ± 9.03               | <0.001       |
| Hospitalization in previous 12 months (months) | 0.69 ± 0.73 | 1.01 ± 1.28 | 0.39 |

Abbreviation: RRT: renal replacement therapy.

\(^{a}\)Data are mean ± SD.
cancellation test as a timed-based test of divided attention was used to measure individual processing speed, rule compliance, and quality of performance [11]. Visual attention and task switching were assessed by the Trail-making test (TMT A and B) [12], while memory functions were determined using the Digit Span (short-term memory) [13] and Digit-Symbol-Substitution test (DSST, memory, and speed of processing) [13].

To assess quality of life in the study participants several questionnaires (scl-90, sleeping questionnaire, Beck Depression Inventory [BDI], Zerssen’s list of somatic complaints, Kidney Disease Quality of Life Short form

### TABLE 2
Biochemical parameters in the study population

| Parameters                  | Dialysis patients | Renal transplant patients | P-value | Normal values          |
|-----------------------------|-------------------|---------------------------|---------|------------------------|
| **Clinical chemistry**      |                   |                           |         |                        |
| Sodium                      | 137.53 ± 2.94     | 137 ± 4.61                | 0.69    | 133–146 (mmol/L)       |
| Potassium                   | 4.95 ± 0.77       | 4.27 ± 0.34               | 0.002   | 3.5–5.1 (mmol/L)       |
| Calcium                     | 2.24 ± 0.18       | 2.21 ± 0.31               | 0.683   | 2.10–2.60 (mmol/L)     |
| Chloride                    | 103.76 ± 2.66     | 106.5 ± 5.02              | 0.054   | 97–108 (mmol/L)        |
| Phosphate                   | 1.8 ± 0.57        | 1.17 ± 0.33               | 0.0003  | 0.85–1.45 (mmol/L)     |
| HCO₃⁻                       | 21.37 ± 3.15      | 20.57 ± 2.96              | 0.445   | 22–28 (mmol/L)         |
| Glucose                     | 7.52 ± 4.69       | 6.27 ± 2.83               | 0.343   | 4.22–6.05 (mmol/L)     |
| Creatinine                  | 640.86 ± 220.25   | 205.16 ± 92.28            | <0.001  | 50–98 (µmol/L)         |
| Urea                        | 13.43 ± 4.42      | 15.81 ± 10.83             | 0.407   | 1.7–8.3 (mmol/L)       |
| Uric acid                   | 290.35 ± 75.53    | 476.33 ± 143.78           | <0.001  | 140–340 (µmol/L)       |
| Cholesterol                 | 3.94 ± 1.05       | 5.06 ± 0.97               | 0.002   | 3.4–6.7 (mmol/L)       |
| HDL cholesterol             | 1.01 ± 0.45       | 1.06 ± 0.34               | 0.719   | 0.75–2.10 (mmol/L)     |
| LDL cholesterol             | 2.1 ± 0.83        | 2.96 ± 0.82               | 0.006   | 1.9–5.2 (mmol/L)       |
| Triglycerides               | 1.83 ± 0.86       | 2.45 ± 1.00               | 0.062   | <2.3 (mmol/L)          |
| Albumin                     | 29.76 ± 4.19      | 30.91 ± 5.04              | 0.481   | 33–50 (g/L)            |
| CRP                         | 31.88 ± 29.28     | 23.31 ± 29.00             | 0.39    | <5 (mg/L)              |
| **Blood count**             |                   |                           |         |                        |
| Leukocytes                  | 6910 ± 2285.43    | 6055.56 ± 2372.95         | 0.286   | 4000–9000 (/µL)        |
| Hemoglobin                  | 115.59 ± 13.34    | 109 ± 14.16               | 0.167   | 140–180 (g/L) (m)      |
| |                               |                   |                           |         | 120–160 (g/L) (f)      |
| MCV                         | 95.82 ± 5.75      | 90.31 ± 4.25              | 0.003   | 80–96 (fL)             |
| MCH                         | 31.9 ± 2.03       | 30.29 ± 1.68              | 0.015   | 28–33 (pg)             |
| MCHC                        | 333 ± 5.95        | 335.33 ± 8.94             | 0.373   | 320–360 (g/L)          |
| Thrombocytes                | 217.94 ± 78.65    | 202.06 ± 56.58            | 0.496   | 150–400 (/nL)          |
| **Endocrinology**           |                   |                           |         |                        |
| TSH                         | 1.49 ± 1.41       | 1.65 ± 1.39               | 0.745   | 0.27–4.20 (mL/L)       |
| Insulin                     | 198.40 ± 272.91   | 50.62 ± 40.48             | 0.04    | 12.5–99.3 (pmol/L)     |
| Glucagon                    | 86.59 ± 19.74     | 50.12 ± 20.83             | <0.001  | <100 (ng/L)            |
| Cortisol                    | 585.59 ± 270.88   | 575.6 ± 649.64            | 0.955   | 171–535 (nmol/L)       |
| Epinephrine                 | 280.53 ± 234.83   | 270.76 ± 342.67           | 0.925   | <464 (pmol/L)          |
| Norepinephrine              | 2275.35 ± 2340.36 | 2264.24 ± 1898.17         | 0.988   | <2364 (pmol/L)         |
| PTH                         | 181 ± 89.67       | 127.06 ± 147.55           | 0.232   | 15–65 (ng/L)           |
| STH                         | 1.74 ± 1.44       | 1.87 ± 2.91               | 0.867   | 0–8 (µg/L)             |
| Interleukin-6               | 17.06 ± 9.75      | 21.98 ± 33.97             | 0.581   | <10 (ng/L)             |

Abbreviations: CRP, C-reactive protein; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; PTH, parathyroid hormone; STH, human growth hormone; TSH, thyroid-stimulating hormone.

*Data are mean ± SD.
[KDQOL-SF]) were used in both groups: The scl-90 is a 90-item self-report symptom inventory developed by Derogatis [14], designed to reflect psychological symptom patterns in psychotherapeutic clients or medical patients. The scl-90 is scored and interpreted in terms of nine primary symptom dimensions and three global indices of distress, referring to the last 7 days. The sleeping questionnaire indicates sleeping behavior and sleeping quality in a non-standardized self-report inventory, while the BDI is a 21-question multiple-choice self-report inventory, measuring the severity of depression. Zerssen's list of somatic complaints represents a screening instrument to gather self-reported bodily symptoms. Finally, study participants had to work with the SF-36 assessment tool, a multi-purpose, short-form health survey with 36 questions that consists of eight scaled scores regarding functional and mental health. Including an extension specifically addressing further illness-specific issues in

| Neurocognitive test          | Dialysis patients | Renal transplant patients | P-value |
|-----------------------------|-------------------|---------------------------|---------|
| Digit symbol test           |                   |                           |         |
| Raw (number)                | 23.76 ± 9.75      | 30.22 ± 11.48             | 0.083   |
| SW                          | 92.29 ± 14.74     | 100.72 ± 17.15            | 0.130   |
| Digit span test             |                   |                           |         |
| Raw (number)                | 7.82 ± 1.59       | 9 ± 2.06                  | 0.068   |
| SW                          | 86.24 ± 11.50     | 94.72 ± 15.05             | 0.071   |
| d2 test b                   |                   |                           |         |
| GZ                          | 271.76 ± 88.01    | 332.94 ± 84.32            | 0.047   |
| GZ_SW                       | 80 ± 9.59         | 86.71 ± 9.41              | 0.048   |
| GZ-F                        | 251.59 ± 87.81    | 316.18 ± 85.53            | 0.037   |
| GZ-F_SW                     | 79.53 ± 10.57     | 87.76 ± 10.07             | 0.026   |
| KL                          | 95.88 ± 39.97     | 122.47 ± 38.17            | 0.056   |
| KL_SW                       | 83.59 ± 8.60      | 87.06 ± 11.10             | 0.316   |
| Trail-Making test           |                   |                           |         |
| Raw A (s)                   | 65.18 ± 30.40     | 45.72 ± 19.60             | 0.030   |
| PR A                        | 25.88 ± 24.25     | 34.44 ± 26.62             | 0.269   |
| Raw B (s)                   | 181.06 ± 125.73   | 125.22 ± 78.30            | 0.122   |
| PR B                        | 28.82 ± 23.15     | 30 ± 16.45                | 0.364   |
| Benton test b               |                   |                           |         |
| Mistakes group 1            | 3.76 ± 1.35       | 3.88 ± 1.83               | 0.833   |
| Mistakes in total           | 8.29 ± 3.44       | 7.12 ± 2.55               | 0.266   |
| Alertness                   |                   |                           |         |
| RZ without audible warning (ms) | 380.24 ± 119.53 | 345.33 ± 175.72          | 0.499   |
| RZ with audible warning (ms) | 360.59 ± 98.11   | 331.11 ± 162.58           | 0.524   |
| Value phasic A.             | 0.02 ± 0.12       | 0.04 ± 0.10               | 0.593   |
| Go/Nogo                     |                   |                           |         |
| RZ (ms)                     | 496.65 ± 95.92    | 448.78 ± 109.42           | 0.179   |
| Auditive vigilance c        |                   |                           |         |
| RZ 1. part (ms)             | 686.35 ± 103.73   | 618.67 ± 121.07           | 0.086   |
| RZ 2. part (ms)             | 771.18 ± 184.23   | 672.67 ± 138.32           | 0.082   |
| RZ in total (ms)            | 726.24 ± 143.83   | 638.56 ± 107.49           | 0.048   |

Abbreviations: GZ, total number; GZ-F, GZ minus mistakes; KL, concentration performance; PR, percentile rank; RZ, reaction time; SW, standard-value. Data are mean ± SD. Missing data for 1 individual in the renal transplant group. One subject in the renal transplant group finished the test prematurely.
patients with renal disease, the tool forms the KDQOL-SF.

The study protocol was approved by the Ethics Committee of the University of Lübeck, Germany (No. 10-098). All participants gave written informed consent before participating.

Results in both groups were compared using the Student’s paired t-test in case of normally distributed data. The nonparametric Wilcoxon signed-ranks test was applied in all other cases. A P-value of less than 0.05 was considered significant.

3 | RESULTS

Most biochemical stress parameters did not differ significantly in the hemodialysis and renal transplant group, showing comparable results regarding cortisol, epinephrine, norepinephrine, glucose, C-reactive protein, and interleukin-6 levels (Table 2). However, low-density lipoprotein levels were significantly lower in hemodialysis patients (2.1 mmol/L ± 0.83 vs. 2.96 mmol/L ± 0.82; \( P = 0.006 \)), while glucagon levels were much higher in patients on dialysis when compared to those after kidney transplantation (86.59 ng/L ± 19.74 vs. 50.12 pg/mL ± 20.83; \( P < 0.001 \)). Similarly, insulin levels were higher in the dialysis group (198.40 pmol/L ± 272.91 vs. 50.62 pmol/L ± 40.48; \( P = 0.04 \)). Expected, serum phosphate and creatinine levels were significantly lower following renal transplantation (\( P < 0.001 \)).

Physiological parameters as blood pressure, heart rate, and heart rate variability did not differ significantly between both groups (data not shown).

Of interest, most tests of attentiveness (e.g., digit symbol test, digit span test, word pair test, and clock test, Table 3) tended to be better in renal transplant patients, while the trail-making test A (\( P = 0.03 \)), as well as the auditory vigilance (\( P = 0.048 \)), and d2 test (\( P = 0.047 \)) significantly improved in this group. However, no significant differences could be noted with respect to the trail-making test B, Benton-test, Alertness, and Go/NoGo.

Concerning quality of life (QoL), no significant differences were observed in both groups with different RRTs with respect to scl-90, Zerssen’s list of somatic complaints, and the SF-36. Nevertheless, QoL analysis using the KDQOL-SF showed significant differences regarding daily life performance (\( P = 0.001 \)), burden of disease (\( P = 0.042 \)), and sexual functions (\( P = 0.001 \)) with betters scores within the transplant group. Of note, quality of sleep tended to be worse in the hemodialysis group (\( P = 0.072 \)) with depression—as assessed with the BDI—being more likely prominent in this group (\( P = 0.08 \)). Of note, two patients in each group scored more than 18 points suggesting severe depression.

4 | DISCUSSION

ESRD is a global health burden with high prevalence and incidence worldwide, warranting RRT for survival; hemodialysis represents a therapeutic choice in this setting—usually consisting of three weekly sessions of 4–5 hours each. Unfortunately, chronic dialysis therapy is associated with multiple psychological, physical, and financial burdens and challenges. If possible, kidney transplantation is the preferred method to treat patients with ESRD, since several studies have shown that renal transplantation is associated with better survival and less morbidity in suitable candidates while QoL increases [15]. Furthermore, long-term costs are lower after renal transplantation when compared to hemodialysis treatment [16].

After kidney transplantation, various parameters may reflect the restoration of endocrine and exocrine functions, for example, lower potassium, phosphate, and creatinine levels. On the other hand, increased concentrations of uric acid are common in renal transplant recipients, as noted above, possibly due to an immunosuppressive regimen with cyclosporine or metabolic syndrome as a potential side effect of corticosteroids [17].

In the present study, no differences in biochemical stress parameters could be observed between hemodialysis and renal transplant patients. In fact, in accordance with findings of Cueto-Manzano et al. [18], values for C-reactive protein and interleukin-6 were comparable and not very high, despite a suggested chronic inflammatory status at least in hemodialysis patients. While increased inflammatory markers and anemia have been reported to be closely associated with a reduced QoL in patients with chronic kidney disease [19], the present data do not support this idea in our study population. In addition, in contrast to a previous study [20], we did not find any significant differences with regard to cortisol, epinephrine, and normetanephrine.

Of interest, significantly higher levels of LDL cholesterol in the renal transplant cohort may be partly attributed to high dose steroid treatment. Possibly due to the immunosuppressive regimen, Spinelli et al. showed increased levels of LDL cholesterol 1 year after kidney transplantation compared to \( P \)-values before transplantation [21]. The significantly higher levels of glucagon and insulin in the present hemodialysis group were most likely explained by the fact that patients in the dialysis group were more obese than those with a kidney transplant.
Overall, classical biochemical stress parameters seem not to be useful to discriminate stress in patients with ESRD, possibly due to various external factors, for example, medication, chronic inflammation, endocrine, and exocrine changes, that may hamper the interpretation.

Surprisingly, no significant differences between the hemodialysis and transplant groups were noted with respect to physiological stress parameters. In particular, heart rate variability did not differ between both groups, contrary to observations by Zhang et al. who demonstrated significantly reduced LF and HF levels in patients with ESRD compared to healthy controls, while heart rate variability significantly improved following kidney transplantation [22].

It is well known that progressive chronic kidney disease is associated with a decline of cognitive function [23]. This cognitive impairment persists during dialysis [24], possibly in part due to cerebrovascular disease and other structural brain abnormalities frequently seen in dialysis patients. However, it has been previously shown that cognitive functions may improve following kidney transplantation [24].

The Digit-Symbol-Substitution test (DSST) requiring response speed, sustained attention, visual-spatial skills and set shifting revealed no significant differences between both groups; however, a tendency of better scoring seemed to be present in the transplant group ($P = 0.08$). This finding is in accordance with work by Griva et al. [25] who serially tested cognitive functions in the same patient group being on dialysis and later following renal transplantation. In fact, kidney transplantation significantly improved cognitive abilities.

Auditive short-term memory testing revealed a tendency to better scoring in the group of renal transplant recipients. While comparable previous studies are lacking, impaired kidney function has been shown to be associated with a more rapid decline of cognitive functions [26]. In the present study, transplant patients scored significantly better in two of three parameters in the d2, a test to measure the attentional performance, suggesting an attention deficit in hemodialysis patients. As already reported in previous studies [25], we could demonstrate significantly more favorable results in the Trail-Making-Test (TMT) A and B following kidney transplantation when compared to patients on dialysis. Moreover, hemodialysis patients had significantly longer reaction times when performing the TMT A. To evaluate visual memory and possible organic brain damage, we performed the Benton test. Contrary to Griva et al. [27] we could not see better performance in patients with a kidney transplant. It is conceivable that improvement of cognitive functions is limited to certain subfunctions. We could not find any significant differences between the two groups regarding tests of attentional performance. However, performance was significantly improved in the subtest auditive vigilance, which measures sustained attention, as reaction time was significantly shorter in renal transplant patients. This finding supports the hypothesis that selected subfunctions are improved following kidney transplantation.

In a synopsis of the results, we demonstrated an improvement of attention following kidney transplantation (vigilance auditive, d2). Besides, there seems to be an improved memory function in connection with a higher level of intellectual flexibility (TMT). Ohman et al. [4] examined the impact of chronic stress on cognitive functions and reported significant declines in the TMT B and digit symbol test in stress-induced ill patients in comparison to a healthy control group. In addition, affected patients complained about enhanced memory deficits. Our findings could point to more stress in patients with hemodialysis therapy. However, it is still unclear, if cognitive functions recover up to the state of a healthy control group. Conceivably, there is a connection between impaired cognitive functions and an increased risk of mortality [28], which might be explained by cerebrovascular changes and/or enhanced stress. Impaired cognitive functions may also be influenced by depressive symptoms; for example, Agganis et al. [29] recently reported that 23.7% of 241 dialyzed patients suffer from depressions. In fact, evaluation of cognitive functions in depressive patients showed significantly worse scoring in the TMT B and digit symbol test.

Previous studies showed conflicting data regarding QoL in ESRD patients: Ortiz et al. [30] and Kimmel [15] reported significantly better QoL after kidney transplantation, whereas Fructuoso et al. [31] did not find any significant difference between patients on dialysis or those following renal transplantation. In the present study, we also could not find any significant differences in most questionnaires. However, when the KDQOL-SF was used, renal transplant recipients scored significantly better regarding several subscales. This notion is supported by Balaska et al. [32] and Kostro et al. [33] who also reported significant changes in various subscales (“general health perceptions,” “effects on daily life,” “burden of kidney disease,” “physical role,” “emotional role,” “vitality”). Our findings though point to a less physical impairment in kidney transplant patients. In conclusion, our observation also supports the idea that the KDQOL-SF is a more reliable and better assay to assess QoL in patients on dialysis and/or following kidney transplantation than the SF-36. As there is evidence for an association of QoL and the mortality risk [34] further studies are necessary to assess QoL and to identify potentials to restore QoL in patients with ESRD.
QoL is also often associated with the development of depression, being an independent risk factor for transplant failures or death in kidney transplant recipients [35]. Baines et al. [36] reported significant improvement in the general mood and depression, respectively, as shown with better BDI scores following kidney transplantation. However, despite a tendency to better scoring in the group of transplant patients, we could not find significant differences regarding depression between both study groups. Similarly, the quality of sleep tended to be better in the group of transplant patients, we could not find significant differences in sleeping behavior between the two groups [37], while a study by Eryilmaz et al. [38] found more sleeping disorders in dialysis patients than in those with renal transplants.

5 | CONCLUSIONS

We showed that: (1) cognitive functions may improve following renal transplantation; (2) classical biochemical stress parameters are not useful to discriminate stress in patients with end-stage renal disease; and (3) heart rate variability is unaltered in transplant recipients compared to hemodialysis patients. Further studies are required to determine whether age and co-morbidities may affect stress parameters independently from the choice of renal replacement therapy.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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REFERENCES

1. Charmandari E, Tsigos C, Chrousos G. Endocrinology of the stress response. Annu Rev Physiol. 2005;67:259–84.
2. Goldstein DS. Adrenal responses to stress. Cell Mol Neurobiol. 2010;30:1433–40.
3. Cripps TR, Malik M, Farrell TG, Camm AJ. Prognostic value of reduced heart rate variability after myocardial infarction: clinical evaluation of a new analysis method. Br Heart J. 1991;65:14–9.
4. Ohman L, Nordin S, Bergdahl J, Slunga Birgander L, Stigsdotter Neely A. Cognitive function in outpatients with perceived chronic stress. Scand J Work Environ Health. 2007;33:223–32.
5. Murray AM, Tupper DE, Knopman DS, Gilbertson DT, Pederson SL, Li S, et al. Cognitive impairment in hemodialysis patients is common. Neurology. 2006;67:216–23.
6. Joshee P, Wood AG, Wood ER, Grunfeld EA. Meta-analysis of cognitive functioning in patients following kidney transplantation. Nephrol Dial Transplant. 2018;33:1268–77.
7. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Circulation. 1996;93:1043–65.
8. Zimmermann P, Fimm B. Die Testbatterie zur Aufmerksamkeitsprüfung, Manual Vs. 1.0. Eigenverlag; 1992.
9. Brickenkamp R. Test d2. Handanweisung. Göttingen: Hogrefe; 2000.
10. Sturm W, Willmes K. On the functional neuroanatomy of intrinsic and phasic alertness. Neuroimage. 2001;14:76–84.
11. Strauss E, Sherman EMS, Spreen OA. Compendium of neuropsychological tests: administration, norms, and commentary. New York: Oxford University Press; 2006.
12. Reitan RM. Der Trail making test. Göttingen: Hogrefe; 1979.
13. Tewes U. Der Hamburg-Wechsler-Intelligenztest für Erwachsene. Göttingen: Hogrefe; 1997.
14. Derogatis LR. SCL-90-R: administration, scoring and procedures manual-I for the (revised) version. Baltimore: John Hopkins University School Medicine; 1977.
15. Kimmel PL, Cohen SD, Weisbord SD. Quality of life in patients with end-stage renal disease treated with hemodialysis: survival is not enough! J Nephrol. 2008;21:554–8.
16. Tonelli M, Wiebe N, Knoll G, Bello A, Browne S, Jadhav D, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. Am J Transplant. 2011;11:2093–109.
17. Malheiro J, Almeida M, Fonseca I, Martins LS, Pedroso S, Dias L, et al. Hyperuricemia in adult renal allograft recipients: prevalence and predictors. Transplant Proc. 2012;44:2369–72.
18. Cueto-Manzano AM, Morales-Buenrostro LE, González-Espinoza L, González-Tableros N, Martín-del-Campo F, Correa-Rotter R, et al. Markers of inflammation before and after renal transplantation. Transplantation. 2005;80:47–51.
19. Farag YM, Keithi-Reddy SR, Mittal BV, Surana SP, Addabbo F, Goligorsky MS, et al. Anemia, inflammation and health-related quality of life in chronic kidney disease patients. Clin Nephrol. 2011;75:524–33.
20. Lang R, Michels J, Becker-Berke R, Lukowski K, Vlaho V, Grundmann R. Sympathetic activity in terminal renal failure and kidney transplants. Klin Wochenschr. 1984;62:1025–31.
21. Spinelli GA, Felipe CR, Park SL, Mandia-Sampaio EL, Tedesco-Silva H, Medina-Pestana JO. Lipid profile changes during the first year after kidney transplantation: risk factors and influence of the immununosuppressive drug regimen. Transplant Proc. 2011;43:3730–7.
22. Zhang L, Yang S, Chen J, Ma J, Ren Y. Associations of parathyroid hormone levels and mineral parameters with heart rate variability in patients with end-stage renal disease. Int Urol Nephrol. 2017;49:1079–85.
23. Drew DA, Weiner DE, Tighiouart H, Duncan S, Gupta A, Scott T, et al. Cognitive decline and its risk factors in prevalent hemodialysis patients. Am J Kidney Dis. 2017;69:780–7.
24. Harciarek M, Biedunkiewicz B, Lichodziejewska-Niemierko M, Dębska-Sliżien A, Rutkowski B. Cognitive performance before and after kidney transplantation: a prospective controlled study of adequately dialyzed patients with end-stage renal disease. J Int Neuropsychol Soc. 2009;15:684–94.
25. Griva K, Hansraj S, Thompson D, Jayasena D, Davenport A, Harrison M, et al. Neuropsychological performance after kidney transplantation: a comparison between transplant types and in relation to dialysis and normative data. Nephrol Dial Transplant. 2004;19:1866–74.
26. Buchman AS, Tanne D, Boyle PA, Shah RC, Leurgans SE, Bennett DA. Kidney function is associated with the rate of cognitive decline in the elderly. Neurology. 2009;73:920–7.
27. Griva K, Thompson D, Jayasena D, Davenport A, Harrison M, Newman SP. Cognitive functioning pre-to post-kidney transplantation- a prospective study. Nephrol Dial Transplant. 2006;21:3275–82.
28. Raphael KL, Wei G, Greene T, Baird BC, Beddhu S. Cognitive function and the risk of death in chronic kidney disease. Am J Nephrol. 2012;35:49–57.
29. Agganis BT, Weiner DE, Giang LM, Scott T, Tighiouart H, Griffith JL, et al. Depression and cognitive function in maintenance hemodialysis patients. Am J Kidney Dis. 2010;56:704–12.
30. Ortiz F, Aronen P, Koskinen PK, Malmström RK, Finne P, Honkanen EO, et al. Health-related quality of life after kidney transplantation: who benefits the most? Transpl Int. 2014;27:1143–51.
31. Fructuoso M, Castro R, Oliveira L, Prata C, Morgado T. Quality of life in chronic kidney disease. Nefrologia. 2011;31:91–6.
32. Balaska A, Moustafellos P, Gourgiotis S, Pistolas D, Hadjiyannakis E, Vougas V, et al. Changes in health-related quality of life in Greek adult patients 1 year after successful renal transplantation. Exp Clin Transplant. 2006;4:521–4.
33. Kostro JZ, Hellmann A, Kobiela J, Skóra I, Lichodziejewska-Niemierko M, Dębeka-Ślizień A. Quality of life after kidney transplantation: a prospective study. Transplant Proc. 2016;48:50–4.
34. Molnar-Varga M, Molnar MZ, Szefert L, Kovacs AZ, Kelemen A, Becze A, et al. Health-related quality of life and clinical outcomes in kidney transplant recipients. Am J Kidney Dis. 2011;58:444–52.
35. Zalai D, Szefert L, Novak M. Psychological distress and depression in patients with chronic kidney disease. Semin Dialy. 2012;25:428–38.
36. Baines LS, Joseph JT, Jindal RM. Emotional issues after kidney transplantation: a prospective psychotherapeutic study. Clin Transplant. 2002;16:455–60.
37. Liaveri PG, Dikeos D, Ilias I, Lygkoni EP, Boletis IN, Skalioti C, et al. Quality of sleep in renal transplant recipients and patients on hemodialysis. J Psychosom Res. 2017;93:96–101.
38. Eryilmaz MM, Ozdemir C, Yurtman F, Cilli A, Karaman T. Quality of sleep and quality of life in renal transplantation patients. Transplant Proc. 2005;37:2072–6.