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# Psychosocial Dimensions in Hemodialysis Patients on Kidney Transplant Waiting List: Preliminary Data

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**Abstract:** Although the donation rate for deceased and living kidneys has been increasing, the donor organ availability meets only the 30% of kidney needs in Italy. Consequently, hemodialysis patients stay for a long time, an average of 3.2 years, on a waiting list for a kidney transplant with consequent relevant psychological distress or even full-fledged psychiatric disorders, as diagnosed with traditional psychiatric nosological systems. Recent studies report, however, a higher prevalence of other psychosocial syndromes, as diagnosed by using the Diagnostic Criteria for Psychosomatic Research (DCPR) in medically ill and kidney transplant patients. Nevertheless, no data regarding DCPR prevalence are available in patients waitlisted for a renal transplant (WKTs). Thus, the primary aim of this study was to identify sub-threshold or undetected syndromes by using the DCPR and, secondly, to analyze its relationship with physical and psychological symptoms and daily-life problems in WKTs. A total of 30 consecutive WKTs were assessed using the DCPR Interview and the MINI International Neuropsychiatric Interview 6.0. The Edmonton Symptom Assessment System (ESAS) and the Canadian Problem Checklist were used to assess physical and psychological distress symptoms and daily-life problems. A total of 60% of patients met the criteria for at least one DCPR diagnosis; of them, 20% received one DCPR diagnosis (DCPR = 1), and 40% more than one (DCPR > 1), especially the irritability cluster (46.7%), Abnormal Illness Behavior (AIB) cluster (23.3%) and somatization cluster (23.3%). Fifteen patients met the criteria for an ICD diagnosis. Among patients without an ICD-10 diagnosis, 77.8% had at least one DCPR syndrome ( $p < 0.05$ ). Higher scores on ESAS symptoms (i.e., tiredness, nausea, depression, anxiety, feeling of a lack of well-being and distress), ESAS-Physical, ESAS-Psychological, and ESAS-Total were found among DCPR cases than DCPR non-cases. In conclusion, a high prevalence of DCPR diagnoses was found in WKTs, including those who resulted to be ICD-10 non-cases. The joint use of DCPR and other screening tools (e.g., ESAS) should be evaluated in future research as part of a correct psychosocial assessment of WKTs.

**Keywords:** DCPR; psychiatric morbidity; distress; nephrology; hemodialysis; waiting list; kidney transplantation; illness behavior; alexithymia

## 1. Introduction

Kidney transplantation (KT) is considered a more cost-effective treatment compared to dialysis [1] due to a reduced cardiovascular risk and overall mortality, but also because of better individual health-related quality of life (HRQoL) [2–4]. However, the disparity between the shortage of available kidney and the high demand for renal allografts cause an increasing average waiting period for deceased graft [5]. In Italy, patients waitlisted for a renal transplant (WKTs) usually have an average

expectation of 3.2 years before receiving a graft [6]. The increasing waiting time could increase any form of psychological distress and/or psychiatric disorders [7–9] with rates varying according to the different nosographic classifications, such as the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD). Mood, anxiety and stress-related disorders have been found the most common psychiatric conditions in this population, with a prevalence ranging between 10 and 60% [10–12]. These disorders can be associated with potential co-morbidity, functional impairment, reduced adherence to medical care, quality of life and a negative impact on post-transplantation period [13–15].

Besides traditional psychiatric diagnoses, however, a wide array of other psychological dimensions that can be only partially explained by the DSM and ICD diagnostic models [16,17] have been more recently reported [18]. With respect to this, over the last 20 years, the Diagnostic Criteria for Psychosomatic Research (DCPR) were introduced in medical settings to expand the traditional domains of the disease model by translating psychosocial variables that derived from psychosomatic research into operational tools [19]. In this way, the DCPR diagnostic clusters are able to identify clinically psychological dimensions which expand the range of information useful for sub-typing medical patients, identifying sub-threshold or undetected syndromes, evaluating the burden of medical syndromes, predicting treatment outcomes and identifying risk factors [20]. To date, important evidence has been accumulated on the use of the DCPR in several settings of medicine, [21] such as cardiology [22,23] oncology [24,25] gastroenterology, [26,27] dermatology [28], endocrinology [29] and in renal transplantation [18]. Indeed, we showed the presence of significant clinical undetected conditions, such as abnormal illness behavior (26.1%), irritability (31.3%), alexithymia (23.1%) and demoralization (17.2%), using the DCPR-interview in kidney transplant recipients. Furthermore, the joint use of DSM and the DCPR system was able to yield subtyping of psychosocial dimensions, to add significant information on patients' distress, and to make more efficient the role of consultation-liaison psychiatry.

Since to our knowledge, no data are available regarding the use of DCPR approach in WKTs, the aims of the present study were to investigate the distribution and characteristics of DCPR syndromes in WKTs and to identify any correlations between DCPR syndromes and psychiatric diagnoses, as registered through a traditional psychiatric nosological systems. Moreover, as a secondary aim, any associations between DCPR dimensions on one hand, and, on the other hand, physical and psychological symptoms, and daily-life problems as self-reported by the patients, were explored.

## 2. Materials and Methods

This study involved a consecutive series of WTKs who were followed in the Dialysis Center of the Ferrara University-Hospital. Inclusion criteria were a Karnofsky Performance Status Scale (KPS) indicating a sufficient level of autonomy (score  $\geq 50$ ) and absence of cognitive disorders (Mini Mental State Examination  $\geq 24$ ). The study population were approached during one of their routine hemodialytic session from January 2018 to December 2018 and were met by the same psychiatrist of the Consultation-Liaison Psychiatric Service, University Psychiatry Unit of the same S. Anna Hospital. Each patient was individually administered the DCPR interview and the Mini-International Neuropsychiatric Interview (M.I.N.I.). The two interviews took about two hours. Moreover, the Edmonton Symptom Assessment System (ESAS) and the Canadian Problem Checklist (CPC) were given as self-report instruments to be filled in.

The DCPR semi-structured interview was used [30]. It explores the presence of 12 syndromes grouped in three different clusters: abnormal illness behavior (AIB) (i.e., disease phobia, thanatophobia, health anxiety, illness denial), somatization and its different expressions (i.e., persistent somatization, functional somatic symptoms secondary to a psychiatric disorder, conversion symptoms, anniversary reaction) and irritability (i.e., irritable mood, type A behavior, demoralization and alexithymia) [31].

The M.I.N.I. [32] is a brief, structured diagnostic interview which has been validated against both the Structured Clinical Interview for DSM diagnoses (SCID-P) and the Composite International

Diagnostic Interview (CIDI) for ICD-10 diagnoses in many countries [33–35]. In this study, the ICD-10 classification to make a psychiatric diagnosis was followed.

The Edmonton Symptom Assessment System (ESAS-Revised) [36,37] was used to assess the severity of physical (i.e., pain, tiredness, nausea, drowsiness, lack of appetite, shortness of breath) and psychological symptoms (i.e., depression, anxiety, feeling of not well-being) ranging from 0 (no symptom) to 10 (the worst symptom). An optional tenth psychological symptom, the emotional distress item which corresponds to the Distress Thermometer (DT), was added [38–40]. The physical distress sub-score (ESAS-PHYS) was computed as a sum of scores for the six physical symptoms, while the psychological distress sub-score (ESAS-PSY) was calculated by summing up the scores of the four psychological symptoms. Similarly, a Global Distress score (ESAS-TOTAL) was created by summing up all the scores on the single ESAS symptoms. The ESAS has been largely used in renal, hemodialysis patients and kidney transplant recipient, showing good psychometric properties [41–43]. The Italian versions of the ESAS and the DT, which have been shown to have good levels of validity [44–47], were used in this study.

The Canadian Problem Checklist (CPC) is composed of a list of 21 possible problems, which are rated in a yes/no (0–1) format and collected into six categories (practical, social/family, emotional, spiritual, informational, and physical problems) [48].

Socio-demographic, clinical data and routine biochemistry were collected. Daugirdas' formula was used for standard Kt/V urea calculation, a DOQI-approved method [49]. The study was approved by the Local Institutional Review Board (approval code is 151297, on 17 March 2016). The procedures were in agreement with the Declaration of Helsinki and written informed consent was obtained from all patients.

### *Statistical Analysis*

Statistical analysis was performed using the SPSS-27 package. Continuous variables were reported as either mean  $\pm$  standard deviation (SD) or median and interquartile range (IQR) based on their distribution. Categorical variables were showed as frequencies (%). Moreover, the association between DCPR and ICD cases was evaluated with a chi-square test, while the relationship of DCPR and ICD cases, ESAS symptoms and CPC problems with socio-demographic characteristics was evaluated by means of the T test and chi-square test. The correlation among ESAS scores, CPC score and sociodemographic characteristics was assessed by Pearson's correlation coefficient for parametric data and Spearman's correlation coefficient for non-parametric data.

## **3. Results**

### *3.1. Characteristics of the Sample*

Data pertaining to 30 out of 35 consecutive WKTs outpatients were collected. Five patients declined to participate (four for work or family reasons and one because of health reasons). The detailed socio-demographic and clinical characteristics of the sample is shown in Table 1. In summary, 53.3% were men and the mean age was 50 ( $\pm 10.7$ ) years. Eight (26.7%) patients reported previous psychological disorders, of which mood disorders (13.3%) were more prevalent diagnosis compared to anxiety disorders (6.7%) and reaction to severe stress and adjustment disorders (6.7%).

**Table 1.** Socio-demographic and clinical variables of the sample.

Age, Years	50.1 ± 10.7	<i>Marital Status</i>	
Education, years	10.1 ± 3.9	Single, n (%)	8 (26.7)
Males, n (%)	16 (53.3)	Married, n (%)	19 (63.3)
Peritoneal dialysis, n (%)	12 (40)	Divorced, n (%)	3 (10)
Duration of dialysis, months	36.1 ± 35.1		
Time on kidney waiting list, months	25.1 ± 31.48	<i>Occupation</i>	
Systolic Blood Pressure, mmHg	126.3 ± 18.5	Employed, n (%)	11 (36.6)
Diastolic Blood Pressure, mmHg	79.1 ± 7.0	Unemployed, n (%)	6 (20)
		Retired, n (%)	5 (16.7)
<i>Blood Test Values</i>		Housewives, n (%)	3 (10)
Hemoglobin, g/dL	11.3 ± 0.9	Other, n (%)	5 (16.7)
Albumin, g/dL	5.6 ± 0.6		
Calcium, mmol/L	2.3 ± 0.1	<i>Living Situation</i>	
Phosphorus, mg/dL	5.6 ± 1.5	Family, n (%)	22 (73.3)
Vitamin D, ng/mL	17.1 ± 8.8	Parents, n (%)	1 (3.3)
KT/V	1.4 ± 0.3	Alone, n (%)	2 (6.7)
		Others, n (%)	5 (16.7)
<i>Previous psychological disorders</i>			
Yes, n (%)	8 (26.7)		
No, n (%)	22 (73.3)		

BMI: Body Mass Index. ±: Standard Deviation.

### 3.2. DCPR and ICD Diagnoses and Distribution

The distribution of the DCPR and ICD diagnoses are presented in Table 2.

**Table 2.** Ranking order of DCPR and ICD-0 diagnoses (%).

Rank DCPR Multiple Diagnosis		Rank ICD Diagnosis	
AIB Cluster, n (%)	7 (23.3)	No diagnosis, n (%)	15 (50)
Irritability Cluster, n (%)	14 (46.7)	Reaction to severe stress and adjustment disorders, n (%)	6 (20)
Somatization Cluster, n (%)	7 (23.3)	Anxiety disorders, n (%)	7 (23.3)
		Mood [affective] disorders, n (%)	2 (6.7)

AIB: abnormal illness behavior; DCPR: Diagnostic Criteria for Psychosomatic Research; ICD: International Classification of Diseases.

Of the total the sample, 18 patients (60%) presented symptoms meeting the criteria for at least one DCPR diagnosis (DCPR cases), with six subjects (20%) reporting one DCPR diagnosis (DCPR = 1) and 12 (40%) more than one (DCPR > 1) (total number of DCPR diagnoses = 39; mean = 1.3 per patient). Alexithymia (n = 9, 30%), irritable mood (n = 9, 30%), persistent somatization (n = 7, 23.3%), demoralization (n = 5, 16.7%), health anxiety (n = 4, 13.3%) and functional somatic symptoms (n = 4, 13.3%) were the most frequent DCPR diagnoses.

There was an overlap between DCPR and ICD diagnoses for 13 patients (13/15 patients with an ICD-10 diagnosis were also DCPR cases, 86.6%), while 14/18 patients with a DCPR diagnosis were also ICD-10 cases, 77.8%. Among those who had no formal ICD psychiatric diagnosis, "ICD non-cases" (n = 15, 50% of the total sample), five received a DCPR diagnosis (5/15 = 33.4%, false ICD-10 negative). Only two patients with a formal ICD diagnosis were not identified by the DCPR (2/15 "DCPR non-cases", 13.4%). There were 10 patients (33.3% of the total sample) who did not report any DCPR or ICD diagnosis ("non-cases") ( $\chi^2 = 8.89, p < 0.05$ ) (Table 3).

**Table 3.** Relationship between DCPR and ICD diagnosis.

	ICD Cases	ICD Non-Cases	Total
DCPR non-cases, n (%)	2 (13.3)	10 (66.7)	12 (40)
DCPR cases, n (%)	13 (86.7)	5 (33.3)	18 (60)
Total, n (%)	15 (50)	15 (50)	30 (100)

$\chi^2 = 8.89$ ,  $df = 1$ ,  $p < 0.05$  DCPR: Diagnostic Criteria for Psychosomatic Research; ICD: International Classification of Diseases.

Patients receiving an ICD-10 diagnosis of adjustment disorders reported mainly a DCPR diagnosis of demoralization, alexithymia and irritability cluster; those with anxiety and stress-related disorders mainly had a DCPR diagnosis of AIB cluster; those with a mood disorder mainly had an equal distribution of demoralization and irritability cluster. Among ICD-10 non-cases, alexithymia and irritability cluster were the most frequent DCPR diagnosis.

3.3. Relationship of the DCPR and ICD Diagnoses with the ESAS/CPC

Mean and standard deviations on the ESAS for the different groups of patients, according to DCPR and ICD diagnoses, are presented in Tables 4 and 5.

**Table 4.** Mean  $\pm$  SD scores on the ESAS between DCPR groups.

ESAS	DCPR Cases (n = 18)	DCPR Non-Cases (n = 12)	Statistics	Cohen's d (95% CI)
Pain	3.67 $\pm$ 3.40	0.83 $\pm$ 1.60	F = 9.96, $p < 0.05$	0.98 (1.75; 0.20)
Tiredness	4.78 $\pm$ 3.65	2.08 $\pm$ 1.97	F = 4.77, $p < 0.05$	0.86 (1.62; 0.96)
Nausea	2.56 $\pm$ 2.87	0.12 $\pm$ 1.16	F = 46.23, $p < 0.05$	1.14 (1.92; 0.34)
Depression	2.83 $\pm$ 3.03	0.58 $\pm$ 1.37	F = 29.18, $p < 0.05$	0.89 (1.65; 0.12)
Anxiety	4.83 $\pm$ 2.81	0.92 $\pm$ 1.50	F = 4.99, $p < 0.05$	1.64 (2.47; 0.78)
Drowsiness	1.67 $\pm$ 2.52	1.33 $\pm$ 1.77	F = 1.20, $p = 0.28$	0.14 (0.87; 0.58)
Lack of appetite	1.33 $\pm$ 2.70	0.7 $\pm$ 0.47	F = 14.21, $p = 0.01$	0.63 (1.37; 0.12)
Feeling of not well-being	2.56 $\pm$ 1.88	0.17 $\pm$ 0.57	F = 20.47, $p < 0.05$	1.57 (2.40; 0.73)
Shorten of breath	0.78 $\pm$ 1.35	0.25 $\pm$ 0.86	F = 6.31, $p < 0.05$	0.44 (1.18; 0.29)
Distress	3.94 $\pm$ 3.26	1.50 $\pm$ 1.50	F = 10.78, $p < 0.05$	0.90 (1.66; 1.27)
ESAS PHYS	14.17 $\pm$ 7.65	3.17 $\pm$ 3.66	F = 13.33, $p = 0.05$	1.72 (2.56; 0.85)
ESAS PSY	14.78 $\pm$ 10.91	4.50 $\pm$ 3.14	F = 13.83, $p = 0.05$	1.17 (1.96; 0.37)
ESAS Total	28.94 $\pm$ 14.89	7.67 $\pm$ 6.42	F = 4.06, $p < 0.05$	1.73 (2.57; 0.86)
CPC Total	4.33 $\pm$ 2.99	1.08 $\pm$ 1.37	F = 7.09, $p < 0.05$	1.30 (2.10; 0.49)

CI: Confidence Interval; CPC: Canadian Problem Checklist; DCPR: Diagnostic Criteria for Psychosomatic Research; ESAS: Edmonton Symptom Assessment System, ESAS-PSY: psychological distress sub-score, ESAS-PHYS: physical distress sub-score.

**Table 5.** Mean  $\pm$  SD scores on the ESAS between ICD groups.

ESAS	ICD Cases (n = 15)	ICD Non-Cases (n = 15)	Statistics	Cohen's d (95% CI)
Pain	3.20 $\pm$ 3.40	1.87 $\pm$ 2.82	F = 1.79, $p = 0.19$	0.42 (0.30; 1.14)
Tiredness	4.73 $\pm$ 3.65	2.67 $\pm$ 2.71	F = 1.87, $p = 0.18$	0.64 (0.09; 1.37)
Nausea	2.80 $\pm$ 2.98	0.27 $\pm$ 1.03	F = 25.99, $p < 0.05$	1.13 (0.35; 1.90)
Depression	3.78 $\pm$ 2.59	0.07 $\pm$ 0.25	F = 43.15, $p < 0.05$	1.89 (1.00; 2.74)
Anxiety	5.40 $\pm$ 2.58	1.13 $\pm$ 1.16	F = 2.29, $p = 0.14$	1.95 (1.06; 2.82)
Drowsiness	2.13 $\pm$ 2.74	0.93 $\pm$ 1.38	F = 7.02, $p < 0.05$	0.51 (0.18; 1.27)
Lack of appetite	1.07 $\pm$ 2.52	0.53 $\pm$ 1.80	F = 1.64, $p = 0.21$	0.24 (0.47; 0.96)
Feeling of not well-being	2.33 $\pm$ 1.95	0.87 $\pm$ 1.59	F = 1.66, $p = 0.20$	0.82 (0.07; 1.56)
Shorten of breath	0.73 $\pm$ 1.35	0.40 $\pm$ 1.05	F = 1.92, $p = 0.17$	0.27 (0.44; 0.99)
Distress	4.67 $\pm$ 3.08	1.27 $\pm$ 1.43	F = 15.68, $p < 0.05$	1.41 (0.59; 2.20)
ESAS PHYS	16.20 $\pm$ 6.85	3.30 $\pm$ 2.87	F = 13.67, $p < 0.05$	2.44 (1.47; 3.39)
ESAS PSY	14.67 $\pm$ 11.58	6.67 $\pm$ 6.18	F = 6.75, $p < 0.05$	0.86 (0.10; 1.60)
ESAS Total	32.6 $\pm$ 13.36	10.00 $\pm$ 8.50	F = 3.47, $p < 0.05$	1.69 (0.84; 2.53)
CPC Total	4.87 $\pm$ 2.85	1.2 $\pm$ 1.560	F = 4.97, $p = 0.07$	1.59 (0.75; 2.41)

CI: Confidence Interval; CPC: Canadian Problem Checklist; ESAS: Edmonton Symptom Assessment System; ESAS-PSY: psychological distress sub-score, ESAS-PHYS: physical distress sub-score; ICD: International Classification of Diseases.

A first series of analysis was conducted between patients who were DCPR non-cases ( $n = 18$ ) and DCPR cases ( $n = 12$ ). Higher scores on the ESAS symptoms (except for drowsiness) and ESAS PHYS and PSY sub-scores were found among DCPR cases than DCPR non-cases ( $F$  between 4.06 and 46.23,  $p < 0.05$ ). A second series of analysis was carried out between ICD-10 cases and ICD-10 non-cases. ICD-10 cases showed higher scores on four ESAS symptoms, namely nausea ( $F = 25.99$ ,  $p < 0.05$ ) depression ( $F = 43.15$ ,  $p < 0.05$ ), drowsiness ( $F = 7.02$ ,  $p < 0.05$ ) and distress ( $F = 15.68$ ,  $p < 0.05$ ), and ESAS PHYS, PSY and total scores ( $F = 13.67$ ,  $p = 0.05$ ;  $F = 6.75$ ,  $p < 0.05$ ;  $F = 3.47$ ,  $p < 0.05$ ; respectively), in comparison with ICD non-cases.

A further analysis was carried out among patients without any DCPR or ICD diagnoses (non-cases), patients having one ICD-10 without any DCPR diagnoses (DCPR-/ICD+), patients with at least one DCPR diagnosis without an ICD diagnosis (DCPR+/ICD-), and patients with both ICD-10 and DCPR diagnoses (DCPR+/ICD+). DCPR-/ICD+ showed higher scores on some ESAS symptoms, such as depression, anxiety, feeling of a lack of well-being ( $F$  between 5.93 and 13.52,  $p < 0.05$ ), whereas DCPR+/ICD+ reported a higher score on ESAS nausea as well as ESAS PSY and PSHY sub-scores and total score ( $F$  between 3.49 and 20.03,  $p < 0.05$ ).

In comparison with DCPR non-cases, DCPR cases reported more problems in all the problem areas, except for practical ones ( $F$  between 7.5 and 45.5,  $p < 0.05$ ), and higher CPC total score ( $F = 7.09$ ,  $p < 0.05$ ). Likewise, ICD cases also reported a higher number of problems in comparison with ICD non-cases ( $F$  between 5.1 and 112.0,  $p < 0.05$ ), with the exception of practical problems, and with a higher score on the CPC-Total ( $F = 4.97$ ,  $p < 0.05$ ). Conversely, non-cases showed lower possible problems (except practical ones) in comparison with ICD-10 or DCPR cases ( $F$  between 4.69 and 224,  $p < 0.05$ ).

#### 3.4. Relationship of DCPR, ICD, and ESAS/CPC with Socio-Demographic and Clinical Variables

No significant correlation was found between DCPR diagnosis, socio-demographic characteristics (age, sex, marital status, housing, employment) and blood chemistry, with the exception of vitamin D ( $F = 5.0$ ,  $p < 0.05$ ). KT/V was associated with both DCPR diagnosis ( $F = 5.91$ ,  $p < 0.05$ ) and ICD-10 diagnosis ( $F = 4.85$ ,  $p < 0.05$ ). Systolic blood pressure and diastolic blood pressure were positively correlated with a higher score on ESAS stress ( $r = 0.51$ ,  $r = 0.43$ , respectively; all  $p < 0.05$ ), ESAS anxiety ( $r = 0.50$ ,  $r = 0.39$ ,  $p < 0.05$ ) and ESAS-PSY ( $r = 0.55$ ,  $r = 0.40$ ,  $p < 0.05$ ), as well as hemoglobin with ESAS pain score ( $R = 0.47$ ,  $p < 0.05$ ).

## 4. Discussion

This pilot study expands the traditional domains of psychiatric disorders by examining other clinically significant psychosocial dimensions, as assessed by the DCPR, among a small cohort of patients who were waitlisted for a kidney transplant.

A first result of the study was that a high percentage of WKTs met the criteria for at least one DCPR syndrome (60%), with about half reporting more than one DCPR diagnosis. These results, by strongly confirming the relevance of psychosomatic factors in medically ill patients with chronic conditions [50,51], are in agreement with the reported prevalence of DCPR diagnoses in a kidney transplant setting and other non-medical settings, such as oncology, dermatology and gastroenterology [21,22,52,53], confirming the need for a wider perspective in the psychosocial assessment of medically ill patients, going far beyond the traditional psychiatric assessment.

In fact, a further result is that the prevalence of DCPR diagnoses was higher than the ICD-10 psychiatric diagnoses, which were found in 50% of WKTs. While WKTs who were given an ICD-10 diagnosis frequently also had an additional DCPR diagnoses (86.6%), one-third of the patients that did not meet any criteria for a definite ICD-10 psychiatric diagnosis was reported to have a DCPR syndrome (33.4%). These findings suggest that the DCPR can detect psychological dimensions which are not identified by ICD-10 criteria also in WKTs. Thus, our results also support the hypothesis that

the joint application of the DCPR and traditional psychiatric nosographic systems may improve the identification of psychological problems by 20–30% in subjects affected by medical disease.

When examining the specific DCPR diagnoses, in WKTs, the irritability cluster (46.7%) was the most represented, followed by the AIB cluster (23.3%) and the somatization cluster (23.3%).

Regarding the irritability cluster, these results are consistent with other studies reporting that this dimension is frequently present in patients with physical illness [54]. If examined with respect to specific medical disorders, WKTs were found to have similar rates to those reported in other studies of cardiac and endocrine patients [21,55], although higher than those found in cancer patients [24,25]. The irritability cluster is described as a relevant clinical dimension to be taken into account which may represent a psychological response to hospitalization, disability, pain, treatments and diagnostic procedures; it is of clinical importance as shown, for example, in heart transplant recipient where hostility (as part of the irritability cluster) has been shown to be related to higher mortality [56]. A possible explanation for its high prevalence among WKT lies in the fact that, despite the hope of new life and having a kidney transplant, irritability could be activated by stressful conditions that WKTs have to deal with, including job uncertainties, social and family integration, frequent follow-up clinic visits and multiple diagnostic procedures, as well as possible hemodialysis complications.

One of the most frequent DCPR diagnoses in WKTs was alexithymia, as shown in about one-third of all the patients. Several hypotheses can be raised, including a possible primary condition (i.e., a personality trait) or a secondary condition related to the medical illness. With respect to this, the cognitive implications of long-term hemodialysis [57] can have a role in the onset of alexithymia features [58]. It is, in fact, to be considered that alexithymia is a complex construct, particularly in medically ill patients and that, in this respect, Porcelli et al. [21] have identified, in a large sample of medically ill patients, at least five clusters of patients with alexithymia, including: those with no psychiatric comorbidity (about one third of the cases); those with a depressed somatization and alexithymic features (about one-quarter of the patients); and alexithymia associated with illness behavior, or somatization or anxiety. Indeed, the alexithymic condition also remains in a high percentage of patients after the kidney transplant, as recently shown in our study [18]. More studies and further specific analysis are necessary to understand alexithymia and its characteristics and associated features, since it seems to be quite common in patients with kidney disorders, [59] but there is a lack of research in nephrology.

Regarding the AIB cluster, it was diagnosable in almost one-quarter of the patients, denoting the patients' ways of experiencing and responding to their health status. Within the AIB cluster, health anxiety was one of most represented DCPR syndromes, although its prevalence was not high (about 13.3% of the patients). It is understandable that some WKTs can be worried about their new condition because of fears of not receiving a kidney transplant, fear of infections and unpredictable outcome, with possible misinterpretation of their bodily symptoms, which might trigger a vicious circle and health anxiety.

Finally, we did not find a hierarchical relationship between DCPR clusters and ICD diagnoses in both groups. In fact, our results show that all DCPR clusters were associated with more than one ICD diagnosis, and, vice versa, every DCPR cluster was not strictly correlated to specific ICD-10 category. These findings are also consistent with other studies that showed that DCPR system evaluated distinct clinical phenomena and not merely symptomatic states of psychiatric disorders [16,17].

Interesting results emerged when examining the role of both DCPR and ICD-10 diagnoses on the single psychological and physical symptoms as measured by the ESAS and CPC problems. In fact, patients receiving either a DCPR or an ICD-10 diagnosis had higher levels of ESAS symptoms and problems in daily life. This result seems to indicate the role of psychosocial variables (and morbidity) and distress in being associated with patients' bodily and psychological feelings, with a possible negative influence, as demonstrated in breast cancer patients, by using the DCPR, on quality of life [24].

A further analysis of our study showed the correlation between the presence of DCPR diagnosis and a deficit of vitamin D, highlighting another plausible pleiotropic effect of vitamin D, not only

in developing psychiatric [60,61] disease, but also in the subthreshold syndromes detected with the DCPR interview. Moreover, higher scores of ESAS symptoms of stress and anxiety were associated with higher value of systolic or diastolic blood pressure. These data are in line with emerging evidence that considers psychological and social factors as contributors of hypertension, in hemodialysis patients [62,63].

The strength of this study is that it reported, for the first time, the distribution of DCPR syndromes in WKTs, by also comparing it with traditional psychiatric diagnoses, according to the ICD. In fact, although the DCPR has been shown to be more comprehensive than ICD criteria to identify psychological distress conditions in patients affected by medical disease [64], this has not been proved in WKTs. There are, however, limitations in our study that also should be mentioned. First, the small sample size of our population does not allow us to generalize our results. Another limit is represented by the fact that, when conducting our study, the new version of the DCPR (DCPR-R) was not available yet. Further multicenter studies on larges samples of WKTs should be considered for future research, using the DCPR-R, which might give more information about the several psychosocial domains affecting patients functioning and quality of life. A further limit of the study is that there was no control group of patients with other kidney conditions, including inpatient units and in patients with other nephrological disorders, that could have given us more details about the rate and characteristics of psychosocial morbidity in other areas of nephrology. Finally, we did not take into account the level of physical activity, an emergent factor which could affect mood and anxiety [65–67].

## 5. Conclusions

Although this pilot study was conducted among a small cohort of WKTs, it provides relevant information on the high rate of DCPR diagnoses, indicating that almost 2/3 of them present DCPR psychosocial disorders and that, among those that did not shown any ICD-10 psychiatric diagnosis, half met the criteria for a DCPR diagnosis. This suggests that future investigation should use DCPR as a complementary integration to the traditional nosographic psychiatric criteria for better understanding of psychological distress in WKTs. Moreover, the role of DCPR in influencing the series of symptom parameters investigated in terms of psychological and physical symptoms, by means of the ESAS, further underscore the importance of a careful and more comprehensive psychosocial assessment in WKTs. The study of the association of other dimensions of patients' functioning, including quality of life, interpersonal relationships, coping mechanisms with the DCPR domain and, in general, psychosocial and psychiatric morbidity, should be part of future investigation in order to improve clinical assessment, prevention and care of nephropathic patients. Moreover, further research is required to longitudinally assess the temporal stability of DCPR syndromes and to determine whether the presence of DCPR syndromes have prognostic implication in WKTs.

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