Depressive and anxiety symptoms in Dutch chronic kidney disease patients

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Chapter 1

General introduction

GENERAL INTRODUCTION

Chronic kidney disease and chronic dialysis treatment

Chronic Kidney disease (CKD) is a major health problem. It has been estimated that over 50% of Americans born today will develop CKD during their lifetime.[1] CKD is defined as abnormalities of kidney structure or function, present for at least 3 months, with implications for health.[2] Main causes of CKD are diabetes mellitus, hypertension, renal vascular disease and glomerulonephritis.[3]

The severity of CKD is classified into 5 stages, with stage 5 (i.e. end-stage renal disease (ESRD)) being the final stage during which patients need renal replacement therapy (RRT) to sustain life.[2] RRT consists of either kidney transplantation or chronic dialysis treatment. Kidney transplantation is considered as the best renal replacement therapy for most patients.[4] However, not all stage 5 CKD patients are treated with kidney transplantation due to waiting lists[5], contraindications for transplantation[6], or graft failure after kidney transplantation.[7] Those patients depend on chronic dialysis treatment for their survival. In 2012, the incidence rate of patients who received a kidney transplant was 14.9 per million population (pmp), and the incidence rate for starting dialysis treatment was 98.1 pmp in the Netherlands.[3]

Modalities of chronic dialysis treatment are haemodialysis and peritoneal dialysis. Haemodialysis purifies the blood of waste products and superfluous water by using the non-biological membrane of an artificial kidney outside the body. A haemodialysis patient is treated approximately three times a week for three to eight hours. Peritoneal dialysis purifies the blood of waste products and superfluous water through the abdominal peritoneal membrane.[8]

Despite medical and technical improvement of dialysis treatment mortality rates of dialysis patients remain high, with respectively a one and five year mortality rate of 20% and 60%.[9] Several factors are associated with morbidity and mortality, such as comorbid conditions[10], metabolic abnormalities[11], nutritional status[12], and psychosocial factors.[13] The latter, and more specifically, depressive and anxiety symptoms, are the main focus of this dissertation.

Depressive and anxiety symptoms in CKD patients

Depressive symptoms are highly prevalent in dialysis patients with an estimated prevalence of 39% as was shown by a recent meta-analysis.[14] These symptoms are

independently associated with mortality[15] and impaired health related quality of life (HRQOL).[16] Depressive symptoms often co-occur with anxiety symptoms.[17] In contrast to the attention for depressive symptoms, anxiety symptoms in dialysis patients are underexposed. Available literature shows that anxiety symptoms are also highly prevalent in dialysis patients with a prevalence that varies from 13% to 50%.[18-23] Anxiety symptoms are also associated with impaired HRQOL in dialysis patients, and seem to contribute to the relationship between depressive symptoms and impaired HRQOL.[18]

The gold standard for diagnosing a depression or anxiety disorder is a structured interview often performed by a psychiatrist. However, such a structured interview takes time and specific expertise which makes a diagnosis of depression in large patients groups less feasible. Therefore, the assessment of depressive and anxiety symptoms is often measured by a self-report questionnaire. These questionnaires take a few minutes to fill out and the outcome represents a severity score of depressive or anxiety symptoms. Thereafter, a cut-off point is used to give an indication of the presence or absence of a depressive disorder. Several questionnaires have been validated and used in patients with chronic kidney disease.[14] A possible problem with some questionnaires is that they contain questions about physical complaints that could be an expression of depression as well as caused by ESRD e.g. fatigue, sleeplessness and less appetite.[24;25]

In the past decades clinical studies have focused especially on depressive symptoms. Several subgroups such as haemodialysis versus peritoneal dialysis, men versus women, or old versus young were investigated to explore risk factors for the high prevalence of depressive symptoms in CKD patients.[15;26] A recent meta-analysis[26] showed that the female and marital status are risk factors for a higher prevalence of depressive symptoms. Ethnicity was not defined as a risk factor in this meta-analysis.[26] Ethnic origin was often defined as self-perceived ethnicity[26], and in these predominantly United States (US) dialysis populations ethnic origin is divided into two major groups: African American or black patients and Caucasian or white patients. In the Netherlands and in many European countries the ethnic composition is different and diverse compared to the US population. In the Netherlands for example ethnic minority groups largely consist of immigrant patients who migrated to the Netherlands in the sixties and seventies.[27] In both the general population and the hospital setting it has been shown that the prevalence of depressive and anxiety symptoms is higher in immigrants than in natives.[28;29] Immigrant status was never assessed as a potential risk factor in CKD patients.

In addition to socio-demographic and clinical parameters, type D personality could also be seen as a risk factor. Type D (distressed) personality patients have the tendency to experience negative emotions across time (negative affectivity) and inhibit emotional

expression because of fear for social rejection (social inhibition).[30] In patients with cardiovascular disease, type D personality is associated with higher morbidity and mortality rates independently of depressive and anxiety symptoms.[31] In more than half of CKD patients mortality is due to cardiovascular disease[32], which makes it reasonable to explore the relevance of type D personality in CKD patients. In dialysis patients type D personality has previously been assessed in two relatively small cohorts with a prevalence of 27%.[33;34] Patients with Type D personality experienced more depressive and anxiety symptoms and had a decreased HRQOL. Type D personality, which is seen as a psychological trait, is assumed to be stable over time. It should therefore be sufficient to make its assessment only once. On the other hand the prevalence of depressive and anxiety symptoms can vary over time with a different effect on clinical outcome.[35-37] Therefore, these symptoms can be seen as a psychological state and should preferably be assessed with multiple measurements. Consequently, it seems important to know if one type D measurement will indeed suffice in clinical practice or research setting.

Depressive symptoms in CKD patients are associated with a higher hospitalization rate, mortality rate, and a shorter time to dialysis (pre-dialysis patients).[15;26;38] The role of anxiety symptoms on these adverse outcomes remains largely unknown. Recently, two reviews/meta-analysis summarized the existing data regarding the association between depressive symptoms and mortality.[15;26] This association was stronger in incident patients, in a time-varying analysis, in patients < 60 years, and in non-USA studies.[15;26] The relative risk for progression from CKD stages 3 or 4 to ESRD in white US patients compared with Norwegian patients was found to be 2.5, despite a similar CKD prevalence.[39] This difference might be the consequence of varying risk factors for the initiation of dialysis between continents. In pre-dialysis patients only US studies showed an association between depressive symptoms and mortality and starting with dialysis.[26]

Aim and outline of this dissertation

The main topic of this dissertation is depressive and anxiety symptoms in CKD patients. The first aim (part one) is to investigate the use of self-report questionnaires to assess these symptoms and HRQOL in dialysis patients. The second aim (part two) is to investigate the relevance of depressive and anxiety symptoms in Dutch CKD patients. Special attention is given to the prevalence of depressive and anxiety symptoms in immigrant compared to native dialysis patients, the interplay of depressive and anxiety symptoms with type D personality, and the effect of depressive and anxiety symptoms on adverse events such as mortality.

Chapter 2

In dialysis patients complaints of uraemia may overlap with somatic complaints of depression, thereby hampering screening for depression. Therefore, in this chapter our aim was to validate a questionnaire with and without somatic complaints of depression. The study is based on data collected in 2008 from the dialysis department of the Sint Lucas Andreas Hospital in Amsterdam.

Chapter 3

Depressive and anxiety symptoms are associated with decreased HRQOL. Short Form 36 (SF-36) is an elaborate generally used self-report questionnaire for the assessment of HRQOL. For practical and patient friendly reasons a shorter questionnaire was developed (Short Form 12 (SF-12)). The aim of this study was to investigate if SF-12 can be used to assess HRQOL in dialysis patients instead of SF-36. For this study we used data from the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD). NECOSAD is a prospective, longitudinal, observational multicenter cohort study that was performed among 2,051 incident dialysis patients aged 18 years or above in 38 dialysis centres in the Netherlands between 1997 and 2008.

Chapter 4

In this chapter we investigated the prevalence of depressive and anxiety symptoms in immigrant compared to native dialysis patients. Patient characteristics were taken into account in order to explore possible differences. In this study data was used from the Depression related factors In dialysis patients with Various Ethnicities and Races Study (DIVERS), which is an observational prospective cohort study among dialysis patients in four urban teaching hospitals and one university hospital in the Netherlands. DIVERS started in 2012 and inclusion is still ongoing.

Chapter 5

In patients with cardiovascular disease type D personality is a risk factor for morbidity and mortality above depressive and anxiety symptoms. In this study we explored the prevalence of type D personality, the possible association between type D personality and depressive and anxiety symptoms, and the stability of type D personality over time. For this study data from two measurements from DIVERS were used.

Chapter 6

In this chapter we investigated the prevalence of depressive and anxiety symptoms in CKD patients not on dialysis. We also investigated what the association is between depressive and anxiety symptoms and initiation of dialysis treatment, hospitalization, and mortality. The study described in this chapter is based on data collected from the outpatient clinic of the Nephrology department of the Sint Lucas Andreas Hospital in 2011.

Chapter 7

The results from the previous chapters will be discussed in depth, in this chapter with recommendations and implications for future research.

Chapter 8 and 9

In these chapters the results of this dissertation will be summarized in English (chapter 8) and Dutch (chapter 9).

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