

## **STUDY PROTOCOL**

### **Exploring Predictors of Quality of Life in Older Adults with End-Stage Kidney Disease Receiving In-Center Hemodialysis: A Cross-Sectional Analysis of Sociodemographic, Dialysis-specific, Biopsychosocial, and Activity-Related Factors**

#### **Overview**

The global prevalence of end-stage kidney disease (ESKD) is increasing, particularly among older adults. Maintenance in-center hemodialysis (ICHD), while life-sustaining, imposes significant treatment and symptom burdens that disproportionately affect older patients with coexisting frailty, multimorbidity, and psychosocial challenges.

While older adults with ESKD consistently prioritize quality of life (QoL) over survival, this outcome remains underrepresented in clinical research. Health-Related Quality of Life (HRQoL) measures are often used as proxies but may not fully capture what matters most to patients, especially during major transitions like dialysis initiation. Differences in HRQoL instruments also create variability in evaluations and cost-effectiveness estimates.

This study seeks to address these gaps by examining overall QoL using an individualized, validated instrument, and identifying its key determinants among older ICHD patients.

#### **Study objectives**

##### Primary Objective:

To identify key factors associated with overall QoL, as measured by the Amnestic Comparative Self-Assessment (ACSA) and a range of sociodemographic, dialysis-specific, biopsychosocial, and activity-related factors, in older adults receiving ICHD.

##### Secondary Objectives:

To examine the relationship between overall QoL (ACSA) and HRQoL instruments (EQ-5D-3L, EORTC QLQ-C30, QLQ-MY20).

To explore clusters of patients with similar QoL profiles using multivariate and cluster analysis.

#### **Study design**

Type: Observational

Model: Cross-Sectional

Time Perspective: Prospective

Reporting Guidelines: STROBE

#### **Study population**

##### Inclusion Criteria

Adults aged  $\geq 65$  years

Receiving maintenance in-center hemodialysis (ICHHD)

Able to provide informed consent

Sufficient cognitive and language ability to complete questionnaires in Dutch

#### Exclusion Criteria

Undergoing ICHHD due to an acute hospital admission

Formal diagnosis of severe psychiatric or cognitive disorders (e.g., dementia)

Inability to understand or respond adequately to study assessments

#### **Study setting and recruitment**

Participants are recruited from four hospitals in Flanders, Belgium. Hospitals are selected to represent a mix of urban, rural, academic, and regional settings. Recruitment and data collection occurs during one to three consecutive dialysis sessions, depending on the participant's condition.

#### **Study procedures and data collection**

Assessments are administered face-to-face by an independent researcher unaffiliated with the dialysis units. The assessment session lasts approximately 45 minutes and includes validated instruments across several domains.

#### **Ethical considerations**

This study was approved by the Ethical Committee of Ghent University Hospital (B670201837264) and is conducted in accordance with the Declaration of Helsinki. All participants receive detailed information about the study and provide written and verbal informed consent prior to participation.

#### **Outcome measures**

##### Primary outcome/measure

Measure: Overall Quality of Life (QoL)

Instrument: Amnestic Comparative Self-Assessment (ACSA)

Description: Participants self-rate their current QoL on a scale from -5 (worst time in life) to +5 (best time), anchored to their own past experiences.

##### Secondary outcomes/measures

Measure: Dialysis and sociodemographic characteristics

Instrument: Medical records

Description: Age, marital status, living situation, (grand)children, dialysis vintage, hospital admissions

Measure: Comprehensive Geriatric Assessment

Instrument: Multi-domain assessment

Description: Includes (risk of) falls using St. Thomas's Risk Assessment Tool in Falling Elderly Inpatients (STRATIFY), risk of dementia using Mini-Cog, nutritional risk using the NRS-2002, pain using a VAS-scale, questions about vision, hearing, and continence

Measure: Frailty

Instrument: Groningen Frailty Indicator (GFI)

Description: A multidimensional frailty measure including biopsychosocial factors

Measure: Activity

Instrument: Brussels Integrated Activity Scale (BIA)

Description: Measures basic-, instrumental-, and advanced activities of daily living

Measure: Health-Related Quality of Life

Instruments: EuroQol 5-Dimension 3-Level questionnaire (EQ-5D-3L), the EORTC QLQ-C30, the EORTC QLQ-MY20

Description: the EORTC QLQ-C30 is a multidomain HRQoL instrument validated in chronic illness populations focusing on symptom and functioning scales, the EORTC QLQ-MY20 is often used as a supplemental module, focusing on disease burden, side effects, future perspective, body image

## STATISTICAL ANALYSIS PLAN

### General

Statistical analysis consists of four stages: descriptive analysis, univariate analyses, multivariate analyses, and cluster analysis. Two-tailed tests are used, with  $p < 0.05$  considered statistically significant unless otherwise specified. Data distributions to be assessed for normality using the Shapiro-Wilk test. Missing data are handled using listwise deletion per questionnaire, with the assumption that missingness was random. All statistical analyses are performed using IBM SPSS Statistics version 29.0.2.0.

### Stage 1: Descriptive analysis

Descriptive statistics are calculated for all demographic, clinical, functional, psychosocial, and quality of life variables. This includes:

- Overall QoL (ACSA)
- Participant demographics (age, sex, dialysis vintage, hospital setting)
- Comprehensive Geriatric Assessment (STRATIFY, Mini-Cog, GDS-4, NRS-2002, Pain VAS-scale, Questioning on vision, hearing, continence)
- Frailty score (GFI)
- ADL functioning (BIA; basic, instrumental, advanced activities of daily living)
- HRQoL scores (EQ-5D-3L, EORTC QLQ-C30, QLQ-MY20)

### Stage 2: Univariate analyses

Univariate analyses are conducted to identify associations between the independent variable (ACSA) and the dependent variables (secondary outcomes).

Analyses are stratified based on variable type: Dichotomous variables: Mann-Whitney U test; Categorical variables with  $\geq 3$  groups: Kruskal-Wallis test; Ordinal and continuous variables: Spearman's rank correlation coefficients

Variables with a p-value  $< 0.05$  in univariate testing are considered for multivariable modeling.

Additional exploratory analyses examine the relationship between the ACSA score and HRQoL instruments/domains, including the EQ-5D utility index.

### Stage 3: Multivariate Analysis

A stepwise multiple linear regression analysis is performed to identify independent predictors of overall QoL (ACSA score). Variables significantly associated with the ACSA in univariate analysis are entered sequentially using forward selection. Multicollinearity is assessed, and variables with high collinearity were excluded.

The model is evaluated using Adjusted  $R^2$  to assess the proportion of explained variance. Regression coefficients (unstandardized B), standardized beta weights, t-values, and significance levels are reported for each step.

#### Stage 4: Cluster Analysis

To explore subgroups of participants with distinct QoL profiles, a two-step cluster analysis is performed:

- Hierarchical clustering using Ward's method to determine the optimal number of clusters based on the dendrogram.

- K-means clustering to define group composition using the dependent variable (ACSA) and significant independent variables identified in prior analyses.

#### Sensitivity Analyses

The robustness of regression findings is checked using alternative model orders and bootstrapping methods. Variance inflation factors (VIF) are used to monitor multicollinearity.