Assessment of Nutritional Status in Kidney Transplant Patients at Haukeland University Hospital

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May 2017

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ACKNOWLEDGEMENTS

There are a number of people that has made it possible for me to present this thesis.

Firstly, I would like to express my gratitude to my supervisors Prof. Dr. Jutta Dierkes and Prof. Dr. med. and Dr. h.c. Hans-Peter Marti for giving me the opportunity to work on this research project. Thank you for being available for questions, and for providing me with constructive and good feedback. Your expertise has been essential for the completion of this master thesis. Thank you in particular to Jutta Dierkes, for all your time, effort, support and encouragement through this process. Your enthusiasm and dedication have been a great motivation throughout this year!

Also, I would like to thank Kristina Sandnes, clinical dietitian, for training me in anthropometric and functional measurements and bioelectrical impedance analysis, as well as sharing from her experience from working with her master thesis. It was all so very helpful!

I also would like to thank Head physician Ingegjerd Sekse and Head nurse Liv Unni Kjørvik, and all the other physicians and nurses at the outpatient clinic for your help and interest in the project. In addition, I am thankful to PhD-student Johnny Laupsa-Borge for introducing me to the programme Filemaker, and for his contribution to the creation of the digital questionnaire used in the study. I would also like to express my gratitude to staff engineer Ingeborg Brønstad and staff engineer Liv Kristine Øysæd for your help in the laboratory.

Thank you to all the patients that accepted to participate in this study. There would be no thesis to present without your participation.

Last, but not least, I would like to thank my classmates for making the last five years at the University of Bergen an adventure, and my family and friends for your support and patience this last year.

Helene Dahl

Bergen, May 2017
ABSTRACT

Background and aims: Chronic kidney disease (CKD) may give implications of nutritional status, and studies suggest that patients with CKD have increased risk of malnutrition and nutrition related conditions such as sarcopenia. Not all implications related to CKD will disappear after kidney transplantation, and side effects from polypharmacy may give additional implications in these patients. Nutritional status in kidney transplant patients has not been reviewed in many studies. The aim of this study was to assess nutritional status in kidney transplant patients and identify which nutritional challenges are present after kidney transplantation.

Methods: A cross-sectional observational study was conducted which included kidney transplant recipients from the outpatient clinic at the department of nephrology at HUS September 2016 - January 2017. Information about disease history, lifestyle, health condition, anthropometric measurements, functional measurements, dietary intake, and chemical clinical analysis results were obtained.

Results: The study population consisted of 72 patients (71% male) with the median age of 59.5 years (IQR 49.0, 66.8). Mean BMI was 26.7 kg/m² (SD ± 4.5), with 65% of the study population being overweight or obese. Central obesity was identified in 50% of the study population. Nutritional risk was identified in 7-10% of the patients, depending on which screening tool applied. Sarcopenia was identified in 31% of the study population diagnosed by reduced muscle strength and muscle mass, measured by HGS and BIA, respectively.

Conclusion: The nutritional challenges in kidney transplant recipients are presented as overnutrition in term of overweight and obesity rather than undernutrition in this study population. Assessment of body composition and muscle strength revealed a prominent proportion of sarcopenic patients, in all BMI-categories. Results suggest that nutritional care concerning overnutrition and sarcopenia may be necessary in this patient group, and that measurement of weight and height for the calculation of BMI may not be sufficient in assessment of nutritional status and body composition.
# TABLE OF CONTENTS

Acknowledgements ........................................................................................................ iii
Abstract ............................................................................................................................. v
Table of contents .............................................................................................................. vii
List of tables ................................................................................................................... x
List of figures .................................................................................................................. xi
Abbreviations .................................................................................................................. xii

1. Introduction ................................................................................................................ 1
   1.1 The kidneys .......................................................................................................... 1
   1.2 Kidney disease ..................................................................................................... 2
      1.2.1 Chronic kidney disease .............................................................................. 2
      1.2.2 Cause of chronic kidney disease ............................................................... 3
      1.2.3 Kidney transplantation .............................................................................. 3
      1.2.4 Kidney transplantation and immunologic treatment .............................. 4
      1.2.5 Kidney transplantation and implications on health .............................. 5
      1.2.6 Kidney transplantation and nutritional care ........................................... 7
      1.2.7 Epidemiology ............................................................................................ 8
   1.3 Nutritional status .................................................................................................. 8
      1.3.1 Overweight and obesity .............................................................................. 8
      1.3.2 Nutritional risk ........................................................................................... 9
      1.3.3 Anthropometry and functional measurements ...................................... 10
      1.3.4 Bioelectrical impedance analysis ............................................................... 10
      1.3.5 Sarcopenia ................................................................................................ 11
      1.3.6 Dietary intake ............................................................................................. 12
      1.3.7 Clinical-chemical measurements ............................................................. 13

2 Objective and hypothesis ........................................................................................... 14
   2.1 Main objective ..................................................................................................... 14
   2.2 Hypothesis .......................................................................................................... 14

3 Patients and methods ................................................................................................. 15
   3.1 Study design ....................................................................................................... 15
   3.2 Sampling procedure and study size ................................................................. 15
3.3 Ethical approval ................................................................. 16
3.4 Assessment methods ......................................................... 17
  3.4.1 Questionnaires .......................................................... 17
  3.4.2 24-hour dietary recall .................................................. 17
    3.4.2.1 Identification of misreporting .................................. 18
  3.4.3 Anthropometric measurements ....................................... 19
  3.4.4 Functional measurements ............................................ 20
  3.4.5 Bioelectrical impedance analysis .................................... 21
  3.4.6 Nutritional screening .................................................. 22
3.5 Sarcopenia ........................................................................ 23
3.6 Charlson comorbidity index ............................................... 23
3.7 Blood pressure ................................................................... 23
3.8 Blood and urine samples ...................................................... 23
3.9 Data handling .................................................................... 24
3.10 Data analysis ..................................................................... 24
3.11 Ethics .............................................................................. 25

4 Results ................................................................................. 27
  4.1 Descriptive statistics ........................................................ 27
    4.1.1 Characteristics of patients included and non-responders .... 27
    4.1.2 Characteristics of study population ................................. 27
    4.1.3 Cause of CKD .......................................................... 30
    4.1.4 CKD-stage .............................................................. 30
  4.2 Dietary intake .................................................................... 31
    4.2.1 Identification of misreporting ....................................... 35
    4.2.2 Dietary restrictions ..................................................... 37
    4.2.3 Dietary advice .......................................................... 37
  4.3 Anthropometric measurements .......................................... 38
  4.4 Functional measurements .................................................. 39
  4.5 Nutritional screening ........................................................ 40
  4.6 Sarcopenia ........................................................................ 41
  4.7 Blood and urine samples .................................................... 42
  4.8 Blood chemistry according to nutritional status ................. 44
    4.8.1 Blood chemistry and nutritional risk .............................. 44
    4.8.2 Blood chemistry and sarcopenia ................................... 44
5 Discussion .......................................................................................................................... 45
5.1 Main findings ..................................................................................................................... 45
  5.1.1 Overweight and obesity ............................................................................................... 45
  5.1.2 Sarcopenia and sarcopenic obesity ............................................................................. 46
  5.1.3 Dietary assessment ....................................................................................................... 47
  5.1.4 Other findings ........................................................................................................... 49
5.2 Strengths and limitations .................................................................................................. 49
  5.2.1 Strengths .................................................................................................................... 50
  5.2.2 Limitations ................................................................................................................ 50
5.3 Clinical implications ........................................................................................................ 51
5.4 Future research ............................................................................................................... 52
5.5 Conclusion ...................................................................................................................... 52
6 References ......................................................................................................................... 53
7 Appendix ............................................................................................................................ 58
LIST OF TABLES

Table 1: Classification of stages in chronic kidney disease by NKF K/DOQI guidelines (9)... 2

Table 2: Medications frequently used in immunosuppressive regimen at kidney transplantation and their nutrient interactions and implication on health.................. 5

Table 3: Methods for identify patients with sarcopenia.......................................................... 23

Table 4: Analysis performed in routine blood and urine samples ................................. 24

Table 5: Characteristics of patients included and excluded in the study .......................... 27

Table 6: Characteristics of study population in total and according to sex ...................... 29

Table 7: Distribution of study population by CKD stage .................................................. 31

Table 8: Dietary intake presented as mean of two 24-hour dietary recalls...................... 32

Table 9: Difference in dietary intake between the recalls in total and by sex .................... 34

Table 10: Energy and protein intake by BMI categories ..................................................... 35

Table 11: Underreporting from the two 24-hour dietary recalls and the mean intake........ 36

Table 12: Energy intake by dietary restrictions ................................................................. 37

Table 13: Anthropometric measurements in relation to sex ............................................ 39

Table 14: Measurements of hand grip strength and knee extension in relation to sex ........ 40

Table 15: Identification of nutritional risk by BMI-categories ........................................... 40

Table 16: Prevalence of sarcopenia in the study population............................................... 41

Table 17: Identification of sarcopenia by BMI categories .................................................. 41

Table 18: Nutrition related blood analysis results ............................................................... 43

Table 19: Inflammation related blood analysis results ....................................................... 43

Table 20: Results from urine sample analysis by sex and in relation to reference areas...... 44
LIST OF FIGURES

Figure 1: Flowchart over the inclusion process .................................................. 16

Figure 2: Distribution of cause of chronic kidney disease in the included patients .......... 30

Figure 3: Distribution of BMI among patients considered as underreporters and patients considered as not underreporters .................................................. 36
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>24 h recall</td>
<td>24-hour dietary recall</td>
</tr>
<tr>
<td>ALM&lt;sub&gt;BIA&lt;/sub&gt;</td>
<td>Appendicular lean mass</td>
</tr>
<tr>
<td>BIA</td>
<td>Bioelectrical impedance analysis</td>
</tr>
<tr>
<td>BMR</td>
<td>Basal metabolic rate</td>
</tr>
<tr>
<td>BP</td>
<td>Blood pressure</td>
</tr>
<tr>
<td>BW</td>
<td>Body weight</td>
</tr>
<tr>
<td>CCI</td>
<td>Charlson comorbidity index</td>
</tr>
<tr>
<td>CG</td>
<td>Cockroft Gault</td>
</tr>
<tr>
<td>CKD</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>Chronic Kidney Disease Epidemiology Collaboration</td>
</tr>
<tr>
<td>CNI</td>
<td>Calcineurin inhibitor</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive Protein</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>DEXA</td>
<td>Dual energy x-ray absorptiometry</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>E%</td>
<td>Energy percent</td>
</tr>
<tr>
<td>eGFR</td>
<td>Estimated glomerular filtration rate</td>
</tr>
<tr>
<td>ESPEN</td>
<td>European Society of Clinical Nutrition and Metabolism</td>
</tr>
<tr>
<td>ESRD</td>
<td>End stage renal disease</td>
</tr>
<tr>
<td>EWSGOP</td>
<td>European Working Group on Sarcopenia in Older Persons</td>
</tr>
<tr>
<td>FFM</td>
<td>Fat free mass</td>
</tr>
<tr>
<td>FFQ</td>
<td>Food frequency questionnaire</td>
</tr>
<tr>
<td>GFR</td>
<td>Glomerular filtration rate</td>
</tr>
<tr>
<td>HGS</td>
<td>Hand grip strength</td>
</tr>
<tr>
<td>HUNT</td>
<td>Nord-Trøndelag health study</td>
</tr>
<tr>
<td>HUS</td>
<td>Haukeland University hospital</td>
</tr>
<tr>
<td>IL2-RA</td>
<td>Interleukin 2 receptor antagonist</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile range</td>
</tr>
<tr>
<td>Kcal/kg BW</td>
<td>Kilocalories per kilogram body weight</td>
</tr>
<tr>
<td>KDIGO</td>
<td>Kidney disease - Improving Global Outcomes</td>
</tr>
<tr>
<td>KE</td>
<td>Knee extension</td>
</tr>
<tr>
<td>MDRD</td>
<td>Modification of Diet in Renal Disease</td>
</tr>
<tr>
<td>MUAC</td>
<td>Mid upper arm circumference</td>
</tr>
<tr>
<td>MUAMC</td>
<td>Mid upper arm muscle circumference</td>
</tr>
<tr>
<td>MUAMA</td>
<td>Mid upper arm muscle area</td>
</tr>
<tr>
<td>MUST</td>
<td>Malnutrition Universal Screening Tool</td>
</tr>
<tr>
<td>NKF/KDOQI</td>
<td>National kidney foundation kidney disease outcomes quality initiative</td>
</tr>
<tr>
<td>NRR</td>
<td>Norwegian Renal Registry</td>
</tr>
<tr>
<td>NRS 2002</td>
<td>Nutritional Risk Screening 2002</td>
</tr>
<tr>
<td>PAL</td>
<td>Physical activity level</td>
</tr>
<tr>
<td>REC</td>
<td>Regional Committees for Medical and Health Research Ethics</td>
</tr>
<tr>
<td>RMR</td>
<td>Resting metabolic rate</td>
</tr>
<tr>
<td>RRT</td>
<td>Renal replacement therapy</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SM</td>
<td>Skeletal muscle mass</td>
</tr>
<tr>
<td>SO</td>
<td>Sarcopenic obesity</td>
</tr>
<tr>
<td>WC</td>
<td>Waist circumference</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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</table>
1. INTRODUCTION
Chronic kidney disease (CKD) is a heterogeneous group of disorders that may give implications on health and nutritional status, as a number of metabolic functions and homeostasis are dependent on kidney function. A few studies reviewed the nutritional status in patients in different CKD stages, as well as dialytic patients, and the results indicate the need of nutritional care for these patients. There are only a few studies that have included patients that have gone through kidney transplantation when assessing nutritional status.

1.1 The kidneys
The kidneys are two bean-shaped organs placed on each side of the vertebral column in the retroperitoneal space (1). The physiological functions of the kidneys include maintenance of acid-base homeostasis, and balance of fluids and electrolytes in the body. The kidneys also take care of waste products, like creatinine, uric acid and urea, in the body by producing and excreting urine. In addition, the kidneys perform functions not related to the excretion. This include regulation of blood pressure (BP) through the renin-angiotensin mechanism, production of erythropoietin, a hormone which controls the production of red blood cells (RBC), and activation of vitamin D, which influence bone maintenance and remodelling (2, 3).

The kidneys consist of about a million nephrons each. Each nephron consists of a glomerulus and a proximal and distal tubuli, which again consist of different sections responsible for secretory and resorptive processes in the kidneys. Every nephron acts independently of the other nephrons. However, at the same time they are coordinated to work together, which indicate that the kidney can function despite decreased functionality of a proportion of the nephrons. Glomerular filtration rate (GFR) is a measure of the kidney's ability to filtrate plasma, and considered the best indicator for measuring the overall function of the kidneys (4, 5).

As GFR is difficult to measure in clinical practice, GFR is estimated by algorithms, often integrating race, sex, age and plasma creatinine (2). Over the past 30 years, the Cockroft Gault (CG) equation has been used for estimating GFR, which only takes age, sex, serum creatinine and lean body mass into account (6). The CG equation was not adjusted for body surface area, which made it less accurate, especially on individuals with overweight and obesity (7). Frequently used equations today are the Modification of Diet in Renal Disease
(MDRD) study equation from 1999 and the Chronic kidney disease Epidemiology Collaboration (CKD-EPI) equation from 2009 which estimate GFR by measuring creatinine clearance. The MDRD equation is widely accepted in the purpose of assessing progression of CKD. However, the MDRD equation has been identified as being less appropriate for a normal or mild decreased GFR, which led to the development of CKD-EPI equation (5). By the end of 2015 Haukeland University Hospital (HUS) exchanged the MDRD equation for the CKD-EPI equation for estimating GFR based on this argument. For healthy adults GFR will normally be 120-130 ml/min/1.73 m² (8). It is physiological that number of well functioning nephrons decrease by age in most people, and thereby a slight decrease in GFR is also normal. GFR < 60 is considered decreased (4, p. 40).

1.2 Kidney disease

1.2.1 Chronic kidney disease

The international group Kidney disease – Improving Global Outcomes (KDIGO) has defined kidney disease as “an abnormality of kidney structure or function with implications for the health of an individual, which can occur abruptly, and either resolve or become chronic” (4, p. 13). According to KDIGO, the diagnosis criteria for CKD is impairment of kidney function present for at least three months as either abnormalities of structure or function, or measurements of GFR < 60 ml/min/1.73 m² (measured at least two times within three months). A widely used classification of CKD is found in the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF/KDOQI) guidelines from 2002, where the severity of CKD has been defined from GFR, divided into five stages, with stage five being the most severe (Table 1) (9).

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥ 90</td>
<td>Normal kidney function, but evidence of kidney damage</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td>Mildly decreased kidney function and kidney damage</td>
</tr>
<tr>
<td>3</td>
<td>30-59</td>
<td>Moderately impaired kidney function</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>Severely impaired kidney function</td>
</tr>
<tr>
<td>5</td>
<td>&lt; 15</td>
<td>ESRD</td>
</tr>
</tbody>
</table>

Abbr.: GFR = glomerular filtration rate, ESRD = end-stage renal disease

Table 1: Classification of stages in chronic kidney disease by NKF K/DOQI guidelines (9)

In the KDIGO guidelines from 2012, a new method for classification of CKD is presented, combining GFR (graded G1-G5) and albumin-to-creatinine ratio (graded A1-A3) (4). GFR
classification is identical to the NKF K/DOQI guidelines. Albumin-to-creatinine ratio is classified as albuminuria < 3 mg/mmol, 3-30 mg/mmol and > 30 mg/mmol for A1, A2 and A3, respectively. Excretion of macromolecules like albumin indicates damage of the glomerulus, which normally does not filtrate molecules > 40,000 kDa (10). At HUS, the classification from 2002 is used for classification of CKD.

1.2.2 Cause of chronic kidney disease
CKD is a heterogeneous group of disease of which CKD stage and GFR gives no information about the underlying diagnosis. There are no systematic data available on causes of CKD in the milder stages of the disease, but the annual report from the Norwegian Renal Registry (NRR) provides information about causes of CKD for those patients receiving renal replacement therapy (RRT). In 2015, the most common causes were vascular/hypertensive (32 %), diabetic nephropathy (18 %) and glomerulonephritis (12 %). Cystic kidney diseases, mainly autosomal dominant polycystic kidney disease (ADPKD), and pyelonephritis/interstitial nephritis were causes of disease in 10 % and 9 % of the patients, respectively. Other causes with lower prevalence were amyloidosis, immune/systemic, kidney tumour, myelomatosis, other causes and unknown cause of CKD (11).

1.2.3 Kidney transplantation
If CKD progresses, it will reach CKD stage 5 or end stage renal disease (ESRD). At this stage the kidney function is impaired to a point where survival is dependent on renal replacement therapy (RRT). RRT can be either dialysis or kidney transplantation (3). For patients with ESRD, kidney transplantation is the treatment of choice. Patients that go through kidney transplantation appear to have a longer life expectancy than age-matched patients with ESRD on the waiting list for kidney transplantation. In addition, the risk of death for kidney transplant patients is considered less than half of the risk among patients receiving dialysis treatment (12, 13). Dialysis treatment is costlier for the society than renal transplantation. In 2014, dialysis patients cost the society approximately half a million Norwegian kroner each year, while transplanted patients cost approximately a quarter of this yearly after the first year post transplantation. Not all patients are suitable for kidney transplantation. Exclusion criteria for transplantation include major comorbidities that may disqualify major surgery or chronic immunosuppression after transplantation, and a cognitive status that precludes regular use of prescribed medication (14).
In most kidney transplantations the existing kidneys are not removed from the patient, and the donor kidney, the graft, is placed in the iliac fossa (15). There are a number of factors affecting the outcome of the transplantation. Matching of the human leucocyte antigens (HLA) between the transplant recipient and the donor kidney is shown to be an advantage on graft-survival. Patients with a delayed graft function, e.g. requiring a certain period of dialysis after transplantation, have a reduced survival rate of the donor kidney within the first year. According to one publication, patients between 15 and 55 years of age may have better survival prospects than children or older patients (16).

Since the first successful kidney transplantation in 1954, there has been a great development in both the actual procedure and the post-transplant care of the kidney transplant recipient (13). The short-term survival of the renal graft was in 2005 close to 90 % in the United States, and the five-year graft survival was estimated to be 70 % in 2009 (16). In Norway, acute rejection occur in 20 % of the transplant recipients (14).

In a global perspective the need of transplantation is increasing. Kidneys for transplantation may be given from living donors or from deceased donors. In Norway, donation from living donors, mostly a relative or partner, is common, with a prevalence of 25 % kidney recipients receiving kidneys from a living donor in 2015 (11). Living donors offer huge advantages for the patient and transplant survival as it is possible to plan the transplantation in advance, even avoiding dialysis (14). This is not routinely an option for kidneys from deceased donors.

More than 90 % of the Norwegian recipients receive kidneys from within Norway, and the rest receive kidneys attributed through Scandiatransplant, due to strict rules of exchange of organs between the countries. The Scandiatransplant program facilitates kidney allocation, especially for highly sensitized recipients and supports clinical research. Scandiatransplant also keeps common waiting lists for transplantation (14, 17).

1.2.4 Kidney transplantation and immunologic treatment

Receiving a kidney transplant requires lifelong suppression of the immune system of the recipient to avoid rejection of the organ (1). Rejection during the first weeks or months after transplantation is called acute rejection. Chronic rejection develops slowly over months or years post transplantation, and may lead to progressive loss of kidney function (2). It is recommended by many transplant physicians to start induction therapy consisting of a lymphocyte-depleting agent or an interleukin 2 receptor antagonist (IL2-RA) at the time of the transplantation (13). This may improve the effect of immunosuppression and be of
importance for avoidance of acute rejection. Further on, the immunosuppression regimen should consist of a combination of immunosuppressive drugs. Table 2 gives an overview of medication frequently used for this purpose. In Norway this treatment normally consists of a Calcineurin inhibitor (CNI) (cyclosporine or tacrolimus), mycophenolate mofetil and corticosteroids (Prednisolone) (14). Since tracolimus was introduced as a routinely given drug around year 2000, it has gradually replaced cyclosporine as the CNI of choice, worldwide and in Norway, although the side effect of nephrotoxicity is not resolved (14, 16).

In later years there has also appeared some replacement medication to CNIs which do not have a nephrotoxic effect. The most common group is mammalian target of rapamycin (mTOR) inhibitors, including Sirolimus and Everolimus. However, there are other side effects that limit the use of these medications, like dyslipidaemia, oedema formation, bone marrow suppression and delayed wound healing (18).

Table 2: Medications frequently used in immunosuppressive regimen at kidney transplantation and their side effects

<table>
<thead>
<tr>
<th>Medication</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNI, cyclosporine or tracrolimus</td>
<td>Sandimmune, Prograf, Advagraf Envarsus</td>
</tr>
<tr>
<td></td>
<td>Nephrotoxicity, Hypercholesterolemia, Hyperkalaemia</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Myfortic, Cellcept</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain, Diarrhoea, Leukopenia, Anaemia</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Prednisol, Predisone</td>
</tr>
<tr>
<td></td>
<td>Glucose intolerance, Lipid abnormalities, Osteoporosis, Accelerated protein catabolism, Weight gain, Mask major infections</td>
</tr>
<tr>
<td>Sirolimus and Everolimus</td>
<td>Rapamune, Certican</td>
</tr>
<tr>
<td></td>
<td>Dyslipidaemia, Oedema formation, Bone marrow suppression, Delayed wound healing</td>
</tr>
</tbody>
</table>

Abbr.: CNI = Calcineurin inhibitor.

1.2.5 Kidney transplantation and implications on health

During CKD, implications of health will appear gradually as kidney function worsen. In the first CKD stages, the patients are often asymptomatic, and it is common that patients with CKD get the diagnosis at the later stages of the disease. Kidney transplantation will cure most, but not all health implications of kidney disease. In addition, the immunosuppressive
medication required after transplantation may cause several metabolic changes and side effects. Corticosteroids are associated with hyperlipidaemia, sodium retention, increased protein catabolism, weight gain, hyperglycaemia, osteoporosis and disturbances in the electrolyte balance. CNIs are associated with elevated glucose and lipid profile as well as hypertension. In addition, CNI have a nephrotoxic effect, and concentration of CNI in the blood should be closely monitored in medical care (14).

Many patients will experience weight gain after kidney transplantation. This might be due to fewer dietary restrictions compared to before RRT and during dialysis, increased appetite, improved quality of life as well as the side effects of the medications (2, p. 530).

Hypertension and diabetes mellitus (DM) are common causes of CKD, and these conditions will remain after transplantation. About 2/3 of transplanted patients have hypertension, and use of corticosteroids and CNIs contributes to this high prevalence (14). Hypertension is defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg and is an important risk factor for cardiovascular disease (CVD) (2, 16). Medical treatment of hypertension is common among these patients. A considerable proportion of kidney transplant recipients suffer from DM, which may have been present before transplantation or DM that occur after transplantation as post transplant DM (PTDM) or DM due to use of corticosteroids. DM is similar to hypertension associated with increased risk of CVD (19).

Dyslipidaemia is a common metabolic disturbance and lipid management is therefore highly prevalent for these patients (2). Lipid-lowering medications are given to most kidney transplant patients (14).

Many of the risk factors for CVD are either already present in patients that have gone through kidney disease, or they have increased risk for these factors after transplantation. CVD is the most common cause of death in kidney transplant patients, and it is the cause of 75 % deaths in this patient group (14). Cigarette smoking will also increase the risk of CVD and kidney transplant patients are strongly recommended to quit.

CKD may lead to hyperparathyroidism due to hypophosphatemia and impaired production of active vitamin D (1,25(OH)₂D), with often lower than normal calcium levels, which affects the bone health among other organs. If the new kidney is functioning well the production of 1,25(OH)₂D resume, and the parathyroid hormone will maintain homeostasis of the calcium metabolism. If the function of the new kidney decreases, there will again be a rise of
parathyroid hormone (PTH). Kidney transplant patients have a higher risk of developing osteoporosis compared to the general population, and the risk has been reported as up to four times higher (20, 21). The use of corticosteroids will also increase the risk of developing osteoporosis.

Due to the immunosuppression all transplantation patients are, especially in their early phase, in increased risk of infections and a more serious outcome of an infection that arises. It is also quite common with viral infections, e.g. through cytomegalovirus or herpes virus, the first months after transplantation, and viral infections are found in approximately half of the kidney recipients in Norway. About 25 % of these patients will get disease caused by such infections (14). The viral diseases may lead to lesions in the mucous membrane in the oral cavity and the intestines. It may also affect the liver and the bone marrow. In rare cases it can also lead to lesions in the transplanted kidney.

Kidney transplant patients have a higher risk of malignancy than the general population (22, 23). High-dose immunosuppression and viral infections may be the cause of increased risk. Skin cancer, lymphoma and lip cancer are the most common types of cancer in this group (14).

1.2.6 Kidney transplantation and nutritional care

The metabolic effects from the progression of CKD and from immunosuppressive treatment after transplantation pose a challenge for the nutritional care of kidney transplant patients (2).

While protein restriction is more common in pre-dialysis CKD patients, increased protein intake (1.2-1.5 g/kg ideal body weight) and energy intake of 30-35 kcal/kg ideal body weight is recommended during the first weeks after transplantation to avoid a negative nitrogen balance and loss of muscle mass.

After the first six weeks of recovery, the nutritional recommendations are more similar to recommendations for the healthy population. This involves an energy intake that maintains or leads to a healthy weight and a protein intake of 0.8-1 g/kg BW (3, p. 827-828). The Norwegian department of health has presented recommendation of energy distribution among the macronutrients (24, p. 116):

- Carbohydrates: 45-60 E%
- Fat: 25-40 E%
- Protein: 10-20 E%
As many patients are overweight or increasing in weight, this is a challenge. Further, the nutritional care of kidney transplant recipients should be adjusted to each patient and the metabolic challenges that the patient may have. This may include energy restriction, attention to fat intake and fat quality and dietary supplementation of certain nutrients. Due to increased risk of vitamin D deficiency and bone disease, supplementation of vitamin D should be considered.

1.2.7 Epidemiology

By the end of 2015, 4,829 patients in Norway received RRT, which constitutes 930.5 per million inhabitants. Of these patients 3,445 patients had received RRT in terms of kidney transplantation. This contributed with 71.3 % of all RRT in Norway at that time, with a remaining 24.3 % receiving haemodialysis and 4.4 % receiving peritoneal dialysis. In 2015, 253 kidney transplantations at Oslo University Hospital Rikshospitalet were performed. This is the solitary unit of kidney transplantations in Norway. With approximately 50-60 transplantations per million inhabitants, Norway has a high number of transplantations compared to other countries, also in Scandinavia (14). In 2015, 210 patients received their first kidney transplantation, while 36 and seven patients received their second and third transplantation, respectively. By the end of 2015 the waiting list for deceased donor graft consisted of 304 patients (58.6 per million inhabitants) (11).

1.3 Nutritional status

Nutritional status is a comprehensive term assessed by several methods, often including anthropometric, functional, clinical, biochemical and dietary methods. This assessment is often carried out by a clinical dietitian (3). Methods for assessing nutritional status are further described in the following sections.

Disturbances in nutritional status can occur as either over- or undernutrition, and deficiencies of essential micronutrients. Overnutrition is defined by the BMI according to World Health Organization (WHO), while undernutrition is more difficult to measure in adults.

1.3.1 Overweight and obesity

According to WHO, the prevalence of obesity was doubled since 1980 in 2016. In 2014, 39 % of the world’s adult population were overweight, and 13 % were obese, with overweight defined as body mass index (BMI) > 25 kg/m² and obesity defined as BMI > 30 kg/m². Today more people die of causes related to overweight and obesity than causes related to
underweight, and there are more obese people than underweight people in the world (25). These numbers emphasize the gravity of the epidemic of overweight and obesity which is considered one of today’s major health challenges. Obesity is associated with increased risk of DM type II, hypertension, gallbladder disease, dyslipidaemia, sleep apnoea and certain cancer diagnoses, among others (2, p. 728).

As there has been an overall increase in prevalence of overweight and obesity, there has also been an increase in obese kidney transplant patients. In these patients, obesity is considered as an independent risk factor for adverse outcomes, also independent from diabetes (26). In addition to the general increased prevalence of overweight and obesity, transplanted patients are more prone to gain weight due to immunosuppression, as mentioned in Section 1.2.5.

1.3.2 Nutritional risk

Patients at nutritional risk include those who are already undernourished and those who are at risk of undernutrition in near future. Nutritional risk may be due to insufficient energy and nutrient intake and/or due to increased requirements because of disease or metabolic stress (27). It is well established that a considerable proportion of patients in hospitals are undernourished (27, 28). A study on inpatients at HUS revealed a prevalence of nutritional risk to be 29 %, including a prevalence of 12 % among patients with BMI > 25 (29).

The purpose of nutritional screening tools is to identify patients who would have a better clinical outcome given that they receive nutritional care. To assess the nutritional risk, a number of screening tools has been developed, and in this thesis two screening tools recommended by the European Society of Clinical Nutrition and Metabolism (ESPEN) and the Norwegian Department of Health have been used (27, 30).

Nutritional risk screening 2002 (NRS 2002) was developed in Denmark and is a screening tool for hospitalized patients. The screening tool consists of an introductory screening and a main screening. NRS 2002 consists of questions about food intake, weight, degree of morbidity and age (28).

The UK developed screening tool Malnutrition Universal Screening Tool (MUST) is suitable for outpatients and patients in primary health service, in addition to hospitalized patients (31). The purpose of MUST is to reveal undernutrition and impaired nutritional status as these factors are known to be associated with impaired function (27).
1.3.3 Anthropometry and functional measurements

Anthropometric measurements were defined by Jelliffe in 1966 as “measurements of the variations of the physical dimensions and the gross composition of the human body at different age levels and degree of nutrition” (32). Anthropometric measurements do not necessarily require advanced and expensive equipment and are easy to perform in a clinical setting, also in developing regions in the world. Today the measurements are widely used to assess nutritional status, both on individual and population level. The methods can be subdivided into two groups; The first group which measurements give information about body size and second group which measurements give information about body composition (33). Certain anthropometric measurements are especially appropriate in detecting overnutrition. In addition, waist circumference has a strong relation to metabolic syndrome and CVD risk (34). Increased waist circumference is associated with 3-4 times higher risk for CVD and is correlated with intra abdominal fat mass (35). Methods used in this thesis are weight, height, skinfold thickness, mid-upper arm circumference (MUAC) and weight circumference.

Functional measurements with the purpose of assessing protein status and muscle function can be useful when assessing nutritional status. Functional measurements can also be used to identify sarcopenia in a patient. An example of such measurement is hand grip strength (HGS), which measure muscle strength (33). Although strength in lower limbs may be of more importance concerning physical function, HGS is well correlated with relevant outcomes of physical function (36).

1.3.4 Bioelectrical impedance analysis

Bioelectrical impedance analysis (BIA) can indirectly measure body composition by measuring body water. BIA has been validated against the golden standard for assessing body composition, dual energy x-ray absorptiometry (DEXA) (37). BIA may be acceptable for assessing body composition for groups and for monitoring changes in body composition in an individual, but it is not recommended as a single measurement to assess body composition (37). BIA is easy to use due to being portable and cheap compared to DEXA, the results are easy to reproduce and the conduction of the procedure is considered easy and non-invasive for the patient (38, 39). As DEXA still is considered as the most appropriate measurement method for this objective, it is important to have this in mind when interpreting the results.

The principle of BIA is that the conductivity of each tissue in the body is specific based on the content of water and electrolytes in the tissue (40). Fat free mass (FFM) will lead electricity
better than fat mass which has an isolating function in the body. Body impedance is measured by detection of electrical current, often of 800 µA and 50 kHz (Ω), sent through the body between two electrodes e.g. on the ankle and wrist of an individual (33). By measurements of resistance, reactance and phase angle from BIA, it is possible to estimate proportion of fat mass and FFM, by using an equation for this purpose (38).

1.3.5 Sarcopenia

Sarcopenia is a condition characterized by generalized loss of skeletal muscle mass, strength and function, a condition that may cause physical disability, decrease in quality of life, increased risk of falls, fractures and even death (41). An ICD-10 code has recently been developed for the diagnosis of sarcopenia, which demonstrates the importance of this diagnosis. However, the lack of well established diagnosis criteria makes the clinical application of the diagnosis challenging (42).

The mechanisms behind sarcopenia are not fully understood, however certain processes have been associated with the condition. Insulin resistance contributes to muscle fibre atrophy and mitochondrial dysfunction, which will impair muscle function. Hormonal changes may alter muscle metabolism, and hormonal changes related to ageing are associated with decreased muscle mass and muscle strength (43). It has also been suggested that sarcopenia is an inflammatory state where proinflammatory cytokines and oxidative stress may impair protein synthesis in skeletal muscle tissue, for example by TNF-alpha, a pleiotropic cytokine (44). Inadequate nutrition or malabsorption and physical inactivity may also lead to sarcopenia. There are other syndromes concerning muscle wasting with similarities and differences to sarcopenia. Cachexia is a condition of severe muscle wasting associated with disease, such as cancer and ESRD. Most cachectic patients will also have sarcopenia, but not all sarcopenic patients will have cachexia (36).

Sarcopenia can be of age-related origin (primary sarcopenia), or of disease- or nutrition-related origin (secondary sarcopenia). In many individuals the condition will be a combination of these two, and difficult to distinguish (36). Concerning secondary sarcopenia there has been identified an association with CKD with a higher prevalence at a younger age than what is expected in the general population and an increase in sarcopenia as GFR decrease (45). A study on kidney transplant patients from Turkey has also shown this association in transplant patients (41). It has been attempted to establish diagnostic criteria for this condition, but this has not yet succeeded (46). It has however been recommended by a
joint European Working Group on Sarcopenia in Older Persons (EWGSOP) and ESPEN Special Interests Groups of Cachexia in Chronic Disease and Nutrition in Geriatrics that the criteria should contain an algorithm of assessment of muscle mass and muscle function, including both strength and performance. Estimation of muscle mass can be performed by any validated technique for this purpose, for example BIA or DEXA. Muscle performance can e.g. be assessed by measuring gait speed, a chair standing test and muscle strength can be assessed by HGS or knee extension. The report from EWGSOP also summarizes the existing suggestions for cut-off points for several of the assessment techniques that are both sex and age-dependent.

Sarcopenic obesity (SO) is a relatively newly discovered condition where body mass increase concurrent with a reduction of lean body mass, which indicate that loss of muscle mass and muscle strength may happen independently of body mass. Obesity and sarcopenia have several common pathophysiological mechanisms, such as hormonal changes, insulin resistance, elevation of pro-inflammatory cytokines and oxidative stress (43). These similarities may explain why SO is a phenomenon. Weakness among elderly has for a long time been associated with loss of muscle mass. However, it seems like fat infiltration into the muscle tissue also have an impact on muscle weakness as it implicate muscle quality and work capacity (36). As many of the pathophysiological mechanisms are common for sarcopenia and obesity, the consequences will also be similar to each other. These include increased risk for dyslipidaemia, DM type II, CVD, hypertension and frailty (43). A meta-analysis from 2016 demonstrated an association between SO and all-cause mortality 24 % higher compared to patients without SO, especially among men (47).

1.3.6 Dietary intake
In a clinical setting the purpose of collecting information about dietary intake is to assess the actual dietary intake, and further to be able to give relevant advice to the patient in order to improve the diet and thereby also their health. In a research setting dietary assessment in a population can give information about challenges concerning diet in e.g. an age group or disease group, and thereby potential for improvement in this group. Dietary intake can be registered by a number of different methods with different purposes, strengths and limitations (3, p. 137).

A food frequency questionnaire (FFQ) gives information about intake frequency of chosen food items in a given time period. FFQs are easy to conduct and are suitable for obtaining
information from large groups, but are not accurate enough to estimate nutrient intake. A 24-hour dietary recall (24 h recall) collect information about dietary intake the preceding 24 hours. 24 h recall is an inexpensive, easy and quick method, that does not demand much of the participant. Dietary history uses a 24 h recall as a starting point, and then the interviewer asks about general dietary habits, as well as a FFQ for clarification. Dietary history can be accurate, but demands a skilled interviewer and is time consuming. FFQ, dietary history and 24 h recall are methods that collect the information retrospectively.

Food records are a method where the patient or study participant is asked to record all food and drink consumed as they consume it in a period given in advance. Food records can either be estimated, with information given in household measures, or it can be weighed, with information given in grams, which minimize the risk of estimation errors (48). This method can be accurate if done properly, but is demanding for the participant. Food records are prospective dietary assessment methods (33, ch. 3).

1.3.7 Clinical-chemical measurements
Biomarkers can be useful in the purpose of assessing and monitoring nutritional status. It is, however, important to have in mind that several biomarkers can change rapidly, and may also be influenced by non-nutritional factors, like age, sex, inflammation and other states of disease. One example is albumin, which can be used as an overall nutritional status, but will among others be affected by inflammation and state of hydration. It is therefore necessary to assess albumin together with C-reactive protein (CRP), which will elevate in inflammatory state, to say something about nutritional status according to serum albumin (2). On the other hand, some micronutrients deficiencies, like vitamin B12 and iron, are diagnosed by biochemical measurements alone. These two examples show that biochemical measurements can be useful, but they have to be assessed correctly.
2 OBJECTIVE AND HYPOTHESIS

2.1 Main objective
The main objective of this thesis is to assess nutritional status in kidney transplant patients.

2.2 Hypothesis
Nutritional assessment can identify nutritional disturbances, including, a) underweight or overweight and obesity, b) undernutrition or risk of undernutrition, c) nutrition related conditions, e.g. sarcopenia. Kidney transplant recipients are at increased risk for nutritional disturbances due to their renal disease, polypharmacy and prevalent comorbidities.
3 PATIENTS AND METHODS

3.1 Study design
This is a cross-sectional observation study that aims to describe the nutritional status of kidney transplant patients.

3.2 Sampling procedure and study size
No formal power calculation was performed for this study, as this is a cross-sectional assessment that has not been done in this patient population before. This study therefore aimed to include as many patients as possible from the eligible group. Similar studies have been conducted earlier on patients with kidney disease, where 30-60 % of the possible patient population was included.

Inclusion criteria for participation in the study was age > 16 years, ability to speak and understand either Norwegian or English, and of course that they had undergone kidney transplantation.

The national register of kidney transplant patients from 2015 with patients having their follow-up at Haukeland University hospital (HUS) was used to invite eligible patients to the study. This register consisted of 264 patients in 2015, of whom ten patients had passed away the previous year. 254 invitations were sent out by mail, of which four letters came in return, and three of the patients were > 16 years.

The patients were contacted while waiting for their routine follow-up at the nephrology outpatient clinic, and they were given the opportunity to accept or decline participation in the study. If the patient agreed to join the study, they were interviewed and assessed just after their appointment with the physician, as a rule. Some of the patients returned to the hospital at a later point to participate in the study. 35 patients declined participation in the study, two patients did not speak Norwegian or English, and two patients were not eligible to participate due to their health condition. At some days three nephrology specialists had patient appointments at the same time, and it was therefore not possible to ensure that all patients were asked about participation, as there was only one study investigator. Due to this, and to patients not showing up for their appointment, 135 patients were not asked about participation at the hospital. All patients that accepted the participation in the study, gave a written consent
in advance of participation. In conclusion, 72 patients participated in the study, giving a participation rate of 29%. Figure 1 gives an overview of the inclusion process.

![Flowchart over the inclusion process](image)

**Figure 1: Flowchart over the inclusion process**

*NRR = Norwegian renal registry. HUS = Haukeland University Hospital
Patients with no response were mostly patients that did not get the opportunity to give an answer about participation due to more than one nephrology specialist working at the same time. Some patients did not meet for their doctor’s appointment and was therefore not asked about participation.*

### 3.3 Ethical approval

All new medical and health related research projects with an aim of investigating human beings, human biological material and health information have to send an ethical application to Regional Committees for Medical and Health Research Ethics (REC) according to the legislation of Health Research (49). An ethical application was sent to REC in August 2014. This was approved in November 2014 (Appendix 1).
3.4 Assessment methods

3.4.1 Questionnaires
The participation in the study consisted of a structured interview about social and economic background, medical history, lifestyle habits, physical activity and a 24 h recall of the preceding day. The results from the anthropometric measurements were also entered into the questionnaire. The questionnaire (Appendix 4) was created and filled out in the programme FileMaker Pro 15.0 (FileMaker, Inc., California, United States). Additional information on BP, clinical-chemical measurements and disease history was registered from the patients’ electronic journal after the interview.

3.4.2 24-hour dietary recall
In previous investigations involving CKD patients at HUS, a single 24 h recall has been used for dietary assessment. This was associated with under-reporting and also criticized by the reviewers. Therefore, in the current study, a second 24 h recall by phone was added, however, in order to allow comparisons with the former investigations, both 24 h recalls are shown separately, but the mean values of both recalls are used for calculations.

A 24 h recall method consists of the subject or patient being interviewed about the exact intake of food and fluids the preceding day (the last twenty-four hours) (33). The patient was asked to report the food and fluid intake the day before the interview in a 24 h recall. Details about brand and amounts were asked about, as well as snacking and drinking between meals. A folder of portion sizes created by University of Oslo, Norwegian Food Safety Authority and Norwegian Directorate of Health was used to improve the estimation the amount of different kinds of foods.

In addition to the 24 h recall performed at the hospital during the interview, the patients were asked if they would give another 24 h recall approximately a week later by phone. The patients did not get the exact day of the phone call in advance to make sure that the day was as representative as possible of what they usually consumed. They were also asked to continue eating and drinking as normal and not make any changes in their dieting habits due to the phone call.

All patients were interviewed by the same person and the person conducted both interviews of the same patient. There is evidence that dietary assessment is not influenced whether the interview was face-to-face or by phone (50).
The information about the dietary intake was registered in Kostholdsplanleggeren (51), a diet tool developed by the Norwegian Directorate of Health and the Norwegian Food Safety Authority. This is a tool for calculating intake of macro- and micronutrients, energy percent from macronutrients as well as intake of fluids.

3.4.2.1 Identification of misreporting

Misreporting of dietary intake, both as underreporting and overreporting, is common in nutritional research and assessment of dietary intake (52-55).

One method of identifying underreporting is the comparison of the basal metabolic rate with registered energy intake. This has been suggested by Goldberg for estimating underreporting (55). There are different scenarios for the use of this method, either by evaluating the group mean energy intake reported, or the individual reported energy intake.

\[ EI_{\text{rep}} - \text{BMR} > \text{PAL} \times \exp \left( \frac{s.d._{\text{min}} \times (S/100)}{\sqrt{n}} \right) \]

Parameters in the equations: \( EI_{\text{rep}} \) = mean reported energy intake; BMR = estimated basal metabolic rate; PAL = mean physical activity level; s.d.\(_{\text{min}}\) = -2 for the lower 95 % confidence limit, \( n \) = number of subjects in the study; \( S \) = factor that takes variation of BMR, energy requirement and intake into account and is expressed as

\[ S = \sqrt{\frac{\text{CV}_{\text{wEl}}^2}{d} + \text{CV}_{\text{wB}}^2 + \text{CV}_{\text{ip}}^2} \]

where the following parameters are included: \( \text{CV}_{\text{wEl}} \) = within-subject coefficient of variation in energy intake; \( d \) = number of days of dietary intake obtained; \( \text{CV}_{\text{wB}} \) = coefficient of variation of repeated BMR measurements/precision of estimated compared with measured BMR; \( \text{CV}_{\text{ip}} \) = coefficient of variation derived from the mean and standard deviation (SD) of a study, including true between subject variation and methodological errors.

Black’s evaluation of the Goldberg cut-off reviewed the values for variation used in the original paper. The suggested values from Black have been used in this study. This include \( \text{CV}_{\text{wEl}} = 23 \% ; \text{CV}_{\text{wB}} = 8.5 \% ; \text{CV}_{\text{ip}} = 15 \% \) (55).
As measurement of the basal metabolic rate (BMR) was not a scope of this study, BMR was calculated as resting metabolic rate (RMR) by the Mifflin St Jeor equation\(^1\) (56). Physical activity level (PAL) was assessed for each patient according to PAL-categories presented in Kosthåndboken, a nutritional care guide book from the Norwegian Directory of health (24). This assessment was based on questions in the questionnaire obtained from a questionnaire from HUNT 3 (57). There was not performed an evaluation of over-reporters in the current study, as true energy requirement is needed for this purpose (58).

3.4.3 Anthropometric measurements

Anthropometric measurements conducted in this study included measurements of height, weight, MUAC, triceps skinfold thickness, biceps skinfold thickness and waist circumference. These measurements were again used to calculate BMI, MUAMC and MUAMA.

*Height:* The patient’s height was measured with a free-standing stadiometer (Seca model 217, Seca Hamburg, Germany). The measurement was conducted with the patient wearing light clothing and no shoes. The patient was asked to stand straight with their heels and knees together and arms hanging loosely along the body. They were asked to look straight ahead and the measurer ensured that their head was kept in Frankfurt plane. The measurement was taken once to the nearest 0.5 cm.

*Weight:* To measure the patients weight a portable electronic scale was used (Seca, model 877, Seca Hamburg, Germany). Patients were measured with the patient wearing light clothing and no shoes. The measurement was taken once to the nearest 0.1 kg. Due to the weight being taken with light clothing 1 kg was subtracted from every patient’s weight to avoid systematic bias. The same scale was used for weighing all patients.

*BMI* was calculated as weight (kilograms) divided by height (meters) squared.

*Mid upper arm circumference (MUAC):* The patient was asked to remove any clothing from their non-dominant arm. The mid point between acromion process on the shoulder blade and olecranon process of the ulna was marked. A flexible non-stretch tape was wrapped firmly around this point to measure the circumference of the upper arm while the patient had their

\[ \begin{align*}
\text{Men: } & 10 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 5 \times \text{age (years)} + 5 \\
\text{Women: } & 10 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 5 \times \text{age (years)} - 161
\end{align*} \]
arm hanging loosely by their side without flexing any muscles. The measurement was taken once to the nearest 0.5 cm.

Skinfold thickness triceps: The measurement was taken at the same point as the MUAC on the non-dominant arm, at the mid point between the acromion process and the olecranon process using a Lange skinfold calliper (Quick Medical, Issaquah, USA). The investigator grasped the skinfold approximately two cm over the marked point on the dorsal side of the arm. The measurement was taken three times to the nearest 0.01 cm.

Skinfold thickness biceps: This measurement was taken with the same method as skinfold thickness triceps, except that this measurement was performed on the frontal side of the arm. The measurement was taken three times to the nearest 0.01 cm.

Mid upper arm muscle circumference (MUAMC) and mid upper arm muscle area (MUAMA): A formula was used to calculate MUAMC of the non-dominant arm, by using the mean measurements from MUAC and skinfold thickness triceps. MUAMC was used to calculate MUAMA (33):

\[
MUAMC = MUAC (\text{mm}) - (\pi \times TSF (\text{mm}))
\]

\[
MUAMA = MUAMC (\text{mm})^2 / 4\pi
\]

Waist circumference was measured on bare skin at the mid point between the lower costal arch and the iliac crest. Patients were asked to breathe normally and the measurement was taken on outbreath to the nearest 0.5 cm. Measurement of waist circumference was repeated three times. Cut-off values for increased waist circumference, indicating central obesity, were set to 102 cm for men and 88 cm for women, the same cut-off values in the national guidelines on prevention, investigation and treatment of overweight and obesity from the Norwegian Directory of Health (35, 59).

3.4.4 Functional measurements

Functional measurements are measurements taken to determine the physical performance of the body of an individual. This can reflect nutritional status and determine whether an individual has sarcopenia.

Hand grip strength (HGS): A JAMAR hydraulic hand dynamometer (Sammons Preston, Bolingbrook, IL, USA) was used to measure HGS. The patients were asked to sit down and grasping as hard as they managed around the device. The dynamometer could be adjusted
according to hand size. The investigator tried to encourage the patient to get as good results as possible. The results were measured in kilograms to the nearest 1.0 kg. This was repeated three times on each side, with alterations between the arms at each measurement.

*Knee extension:* To measure the strength in the muscles of the legs a hand-held digital force gauge (Chatillion-Ametek DFE Series II) was used. This measurement was taken on the non-dominant side, without shoes. The patients sat on a chair with their knees flexed to 90 degrees. The examiner, kneeling, placed the device just below the patient’s knee. The patient then led their non-dominant foot along the floor while the investigator used its body weight and muscle strength to resist the movement of the patient. The measurement was repeated three times and the results were measured in newton, N.

3.4.5 **Bioelectrical impedance analysis**

A single frequency tetrapolar BIA 101 Anniversary Sport Edition (AKERN) was used in the for indirectly measuring body composition by BIA. The measurement was conducted on the non-dominant side with the patient in a supine position at an examination table with their limbs abducted from the body and from each other. Watches, jewelleries and belts were removed, but the patients were not fasting, having had their skin cleaned or had not gone to the toilet in advance of the examination as a routine.

The current electrodes were placed on bare skin on the dorsal side of the hand and foot, proximal to the phalangeal-metacarpal joint and the metatarsal phalangeal joint respectively. The voltage detection electrodes were placed on the pisiform prominence of the wrist and between medial and lateral malleoli of the ankle (37). Contraindications to this measurement are implanted pacemaker and pregnancy, and in these cases the measurement was not carried out (n = 3).

Concerning prediction of muscle mass, there are several equations to choose from, and most of them include information about sex, age and height of the patient. In this thesis an equation by MacDonald et al. (2006) has been used to predict appendicular lean mass (ALM\textsubscript{BIA}), as this has been validated to predict muscle mass in patients with CKD (60).

\[
\text{ALM}\textsubscript{BIA} = -11.626 + (0.292 \times \text{height}^2 / \text{resistance}) + (0.06983 \times \text{reactance}) \\
+ (0.08553 \times \text{height}) + (-2.092 \times \text{sex}) + (-0.05 \times \text{age})
\]

Parameters in the equation: height (cm); resistance and reactance at 50 kHz (Ω); sex, 0 = male, 1 = female; age (years).
3.4.6 **Nutritional screening**

Two nutritional screening tools, NRS 2002 and MUST, were applied in the purpose of detecting patients at nutritional risk in the study population. The nutritional screening was conducted by the same investigator on all patients and it was performed on the same day as the interview.

*NRS 2002* consists of an initial screening section and a main screening section. The initial screening section consists of four questions:

1. Is BMI < 20.5 kg/m$^2$?
2. Has the patient lost weight within the last three months?
3. Has the patient had a reduced dietary intake in the last week?
4. Is the patient severely ill? (e.g. in intensive therapy)

If the answer to at least one of these questions is yes, the screening continues to the main screening section. In this section there are two categories, one regarding nutritional status and one on severity of disease. Points from 0-3 are given in each category dependent on the severity of the impairment in each category. The points of the two categories are added together and an extra point is given if the patient is aged 70 years or older. If the total score from the main screening section is three or higher the patient is considered at nutritional risk and should be followed up by developing a nutritional plan and initiating nutritional treatment. See Appendix 7 for the screening tool as a whole.

*MUST* consists of three categories each in which it is possible to gain 0-2 points. The categories are

1. BMI
2. Unintentional weight loss
3. Acute disease

The points from these categories are summed up, and a score of one is considered medium risk of undernutrition, and a score of two or more is considered high risk of undernutrition. One-point score indicates need of closer observation, with a three-day dietary intake registration. An inadequate intake should be followed by nutritional treatment. A score of two points or more should be followed by nutritional treatment (61). The screening tool is presented in Appendix 8.
3.5 Sarcopenia

As recommended by ESPEN and EWGSOP, a combination of measurements of skeletal muscle mass and muscle function has been used to identify patients with sarcopenia in this study (36, 46). The methods applied are presented in Table 3, including cut-offs for each method.

Muscle function was measured by HGS and cut-offs set at < 30 kg for men and < 20 kg for women to define reduced muscle function. These cut-offs are based on statistical analysis on 1,030 individuals (62). The cut-offs for muscle mass is based on 2 SD below mean result study group of 200 young adults (63).

Table 3: Methods for identify patients with sarcopenia

<table>
<thead>
<tr>
<th>Method</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>SM/HT² + HGS</td>
<td>SM/HT² ≤ 8.87 kg/m² + HGS &lt; 30 kg</td>
<td>SM/HT² ≤ 6.42 kg/m² + HGS &lt; 20 kg</td>
</tr>
</tbody>
</table>

Abbr.: HGS = hand grip strength, HT² = height squared, SM = skeletal muscle mass by BIA.

3.6 Charlson comorbidity index

Charlson comorbidity index (CCI) is an established index for assessing the morbidity of a patient and to assess the probability of survival. This index is based on 19 point-giving categories, and the sum of these points can predict the patient’s survival chances (64).

3.7 Blood pressure

BP was registered from the patients’ electronic journal from the appointment on the medical outpatient ward. BP from two weeks in advance and one week after the examination was accepted. If the BP was noted as a range the mean value was registered in the dataset.

3.8 Blood and urine samples

The patients’ electronic journal was used to obtain information about major clinical-chemical variables. Usually, these variables were analysed in a blood sample obtained the same day as the patient’s physician appointment, but some patients had their blood drawing earlier.

An overview of analysis preformed in routine blood and urine samples collected from the patients’ electronic journals is shown in Table 4. Samples taken more than two weeks in
advance of or two weeks after the interview, were not included. Information about coefficient of variation and methods used can be found on www.analyseoversikten.no (65).

Table 4: Analysis preformed in routine blood and urine samples

<table>
<thead>
<tr>
<th>Blood analysis</th>
<th>Urine analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-Albumin</td>
<td>U-Creatinine</td>
</tr>
<tr>
<td>B-Haemoglobin</td>
<td>U-Albumin (mg/mmol creatinine)</td>
</tr>
<tr>
<td>B-Leucocytes</td>
<td>U-Protein (mg/mmol creatinine)</td>
</tr>
<tr>
<td>B-HbA1c</td>
<td></td>
</tr>
<tr>
<td>S-Glucose</td>
<td></td>
</tr>
<tr>
<td>S-CRP</td>
<td></td>
</tr>
<tr>
<td>S-Creatinine</td>
<td></td>
</tr>
<tr>
<td>S-eGFR*</td>
<td></td>
</tr>
<tr>
<td>S-Urea</td>
<td></td>
</tr>
<tr>
<td>S-Uric acid</td>
<td></td>
</tr>
</tbody>
</table>

Note: *Calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Abbr: CRP = C-reactive protein, S = Serum, B = Full blood, U = Urinary, eGFR = estimated glomerular filtration rate.

3.9 Data handling

Most of the data was collected straight from the digital questionnaire made in Filemaker. During the interview most of this data was plotted directly into the questionnaire by the investigator. Some data were manually plotted into the questionnaire at a later time, from Kostholdsplanleggeren and the patients’ electronic journal. Every value from Kostholdsplanleggeren plotted into the questionnaire, was double checked by a fellow student. The patients’ identities were not revealed to this student. The values from the patients’ electronic journals concerning biochemical samples were double checked by the investigator and partly by a fellow master student. The majority of the calculations for the calculated variables were either performed in Filemaker or in SPSS Statistics. It was possible to extract a choice of fields from the questionnaire in FileMaker and export it as an Excel file, which again could be imported to SPSS Statistics which was used to perform the statistical tests that are presented in the thesis.

3.10 Data analysis

All data analysis was performed in SPSS Statistics. Independent samples t-test was used to compare two groups with normal distribution, and the non-parametric Mann Whitney-U test was used when there was a lack of normal distribution. Parametric one-way ANOVA was used to assess differences between three or more groups, assuming normal distributions of the data. The non-parametric Kruskal Wallis was used when at least one of the groups did not
have normal distribution. To check the association between two categorical variables Chi-Squared test was used. Paired-samples t-test, also called dependent t-test was used to assess the difference between two dependent variables assuming normal distribution. Wilcoxon signed-rank test was utilized when this assumption was not met.

3.11 Ethics

The patients that participated in the study were exposed to a low risk and the workload for the patients was small. Few studies have been conducted on this patient group for this purpose and the results from this study may therefore be of importance for the treatment of the patient group in the future. As a routine, the patients were interviewed at the same day as their routine appointment with their nephrologist at HUS, they were already were present at the hospital. The interview and examination together lasted for about 45 minutes. In addition, the patients were asked to answer some questions by telephone about a week later. This phone call usually took 5-10 minutes.

The patients were also asked to give blood samples and urine samples for a bio bank for later studies. These samples were, if possible collected at the same time as their routine samples, which did not lead to extra time spent on waiting or extra distress of retaking the blood samples. As a routine, many of the transplanted patients had their blood samples taken in advance of their appointment with the nephrologist, which made it impossible to coordinate the samples. If this was the case, the patients were asked if they were comfortable with taking a new round of blood samples and there was no enforcement from the examiners side. The urine samples for the bio bank were delivered directly to the examiner.

The patients were not required to give an answer on the letter sent out by mail as to whether they wanted to participate in the study or not, and they could give their answer directly to the examiner when they registered at the hospital for their appointment with the nephrologist. All patients participating in the study was offered to receive information about their personal results from the examination as well as a copy of this master thesis.
4 RESULTS

4.1 Descriptive statistics

4.1.1 Characteristics of patients included and non-responders

Characteristics of patients included and those not included in the study by age and sex are shown in Table 5. The groups were compared by the use of independent t-test (age) and Chi squared test (sex). Patients included and excluded from the study did not differ significantly by age and sex. Based on these parameters, the patients included in the study can be regarded as representative for kidney transplant patients at HUS, and the results from this study may therefore be generalized to the general population of kidney transplant patients at HUS.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Included patients</th>
<th>Excluded patients</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>n = 72</td>
<td>n = 175</td>
<td></td>
</tr>
<tr>
<td>median (IQR)</td>
<td>59.5 (49.0, 66.8)</td>
<td>58.0 (45.0, 68.0)</td>
<td>0.494</td>
</tr>
<tr>
<td>range</td>
<td>21-81</td>
<td>17-80</td>
<td></td>
</tr>
<tr>
<td>Sex, women</td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>21 (29)</td>
<td>60 (34)</td>
<td>0.436</td>
</tr>
</tbody>
</table>

Note: n (%) = percentage of column, p-value for age from conducting a Mann-Whitney U test, p-value for sex from conducting a Chi-squared test. Abbr: IQR: inter quartile range.

4.1.2 Characteristics of study population

Characteristics of the population of the study are presented in Table 6. The majority of the patients included in the study were men (71 %) and the median age was 59.5 years, with a range from 21 to 81 years. Ten patients (14 %) had gone through more than one kidney transplantation. Dialysis treatment had occurred in 50 patients (69 %) prior to kidney transplantation. Median time since the last transplantation was 8.9 years. Mean GFR was 54.0 ml/min/1.73 cm\(^2\) (SD ± 21.8). Serum urea was elevated in 64 % of the.

Mean BMI was 26.7 kg/m\(^2\) (SD ± 4.47) in the total study population and there was no significant difference between men and women. The mean estimated PAL was 1.639 (SD ± 0.175) in the total population, and there was no difference when comparing PAL in male patients with female patients. Hypertension was diagnosed in 28 of the patients (39 %), of whom 18 were male (36 %) and 10 were female (48 %). DM was diagnosed in 11 patients (15 %), with 2 patients (3 %) with DM type I and 9 patients (13 %) with DM type II. Bone mineral disorders were reported as osteopenia and osteoporosis in 6 (8 %) and 17 (24 %)
patients, respectively. The overall prevalence of bone mineral disorders was higher in female patients compared to male patients (30 % vs. 39 %).

Eight patients (11 %) were current smokers, and additionally 28 patients (39 %) were ex-smokers. Median number of prescribed medication was 9 (interquartile range (IQR) 7, 11). In total there were 14 patients (19 %) identified with oedema, of whom 7 patients (10 %) had pitting oedema (non-visible oedema), and 7 patients (10 %) had visible pitting oedema. Median systolic BP was 130 mmHg and median diastolic BP was 80 mmHg (IQR 120-140 and 71-81.5 for systolic and diastolic BP, respectively). There was no significant difference in these variables between men and women.
<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients</th>
<th>Male</th>
<th>Female</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (% of total)</strong></td>
<td>n = 72 (100)</td>
<td>n = 51 (71)</td>
<td>n = 21 (29)</td>
<td></td>
</tr>
</tbody>
</table>
| **Age (years)**               | median (IQR) | 59.5 (49.0, 68.8) | 62.0 (49.0, 68.0) | 58.0 (49.0, 61.0) | 0.110*
| **BMI (kg/m²)**               | mean ± SD    | 26.7 ± 4.5 | 27.1 ± 4.3 | 25.6 ± 4.8 | 0.219
| **PAL**                       | mean ± SD    | 1.639 ± 0.175 | 1.639 ± 0.174 | 1.638 ± 0.180 | 0.980
| **No. of tx**                 |              | n (%)   |        |          |
| 1                             |              | 61 (86) | 43 (84) | 19 (90) | 0.492*
| 2                             |              | 10 (14) | 8 (16)  | 2 (10)  |          |
| **Time since KTx (years)**    | median (IQR) | 8.9 (5.9, 15.5) | 9.1 (6.7, 16.6) | 8.3 (4.3, 14.3) | 0.540†
| **Hypertension**              | n (%)        | 50 (69) | 37 (73) | 13 (62) | 0.373
| **DM**                        | n (%)        | 28 (39) | 18 (35) | 10 (48) | 0.330*
| **DM1**                       | n (%)        | 2 (3)   | 2 (4)   | 0 (0)   | 0.357*
| **DM2**                       | n (%)        | 9 (13)  | 7 (14)  | 2 (10)  | 0.624*
| **Bone mineral disorder**     |              |        |        |          |
| **Osteopenia**                | n (%)        | 6 (8)   | 4 (8)   | 2 (10)  | 0.815*
| **Osteoporosis**              | n (%)        | 17 (24) | 11 (22) | 6 (29)  | 0.525*
| **Smoking habits**            |              |        |        |          |
| **Current smoker**            | n (%)        | 8 (11)  | 5 (10)  | 3 (14)  | 0.501*
| **Ex-smoker**                 | n (%)        | 28 (39) | 22 (43) | 6 (29)  |          |
| **No. of drugs**              |              |        |        |          |
| **Oedema**                    |              |        |        |          |
| **Pitting oedema**            | n (%)        | 7 (10)  | 6 (12)  | 1 (5)   | 0.146*
| **Visible oedema**            | n (%)        | 7 (10)  | 7 (14)  | 0 (0)   | 0.109*  
| **Systolic BP (mmHg)**        | median (IQR) | 130 (120, 140) | 130 (120, 140) | 138 (125, 145) | 0.105†
| **Diastolic BP (mmHg)**       | median (IQR) | 80 (71, 81.5) | 80 (70, 82) | 80 (75, 80) | 0.372†
| **S-Creatinine (µmol/L)**     | median (IQR) | 114.0 (95.5, 163.5) | 122.0 (99.0, 166.5) | 105.0 (83.3, 138.8) | 0.140*
| **eGFR (mL/min/1.73 m²)**     | mean ± SD    | 54.0 ± 21.8 | 54.3 ± 21.3 | 53.3 ± 23.4 | 0.862
| **S-Urea**                    | median (IQR) | 9.3 (6.7, 13.8) | 9.5 (6.9, 14.3) | 8.7 (6.3, 12.7) | 0.273†
| **S-Albumin (g/L)**           | mean ± SD    | 43.1 ± 3.0 | 42.7 ± 3.0 | 43.8 ± 3.0 | 0.186
| **B-Haemoglobin (g/L)**       | mean ± SD    | 13.6 ± 1.9 | 14.0 ± 1.8 | 12.7 ± 1.8 | 0.009
| **S-CRP (mg/L)**              | median (IQR) | 2.00 (1.00, 4.00) | 2.25 (1.00, 4.00) | 1.00 (1.00, 2.75) | 0.037*
| **U-Albumin per mmol creatinine (mg/mmol)** | median (IQR) | 2.70 (0.90, 17.00) | 2.80 (0.85, 18.10) | 1.95 (0.95, 20.8) | 0.900*
| **HbA1c (%)**                 | median (IQR) | 5.70 (5.50, 6.10) | 5.70 (5.50, 6.25) | 5.70 (5.45, 5.80) | 0.544†

4.1.3 Cause of CKD

Causes of CKD among the study population are shown in Figure 2. The most frequent cause of CKD was glomerular disease, reported in n = 26 (36 %) of the patients. Polycystic disease was reported as cause of CKD in n = 14 (20 %) and hypertension and diabetes nephropathy was reported as cause of disease in n = 13 (18 %). Renal tubule-interstitial disease and other causes of CKD were reported as causes of disease in n = 6 (8 %) in each category. In n = 7 (10 %) patients the cause of CKD was unknown.

![CAUSE OF CKD](image)

**Figure 2: Distribution of cause of chronic kidney disease in the included patients**
*Abbr: CKD: chronic kidney disease.*

4.1.4 CKD-stage

Distributions of study population by CKD stage defined by GFR and albuminuria are presented in Table 7. One patient had GFR correspondent with CKD stage 5 or ESRD. 11 patients (15 %) were identified in CKD stage 4, and 28 patients were in CKD stage 3. Of the patients with a GFR > 60, 28 patients (39 %) were in CKD stage 2, and three patients (4 %) in
CKD stage 1. When classifying according to albuminuria, 29 patients (40%) were classified in stage A1, 16 patients (22%) in stage A2 and 10 (14%) in stage A3.

Table 7: Distribution of study population by CKD stage

<table>
<thead>
<tr>
<th>GFR (mL/min/1.73 m²)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  ≥ 90</td>
<td>3 (4)</td>
</tr>
<tr>
<td>2  60-89</td>
<td>28 (39)</td>
</tr>
<tr>
<td>3  30-59</td>
<td>28 (39)</td>
</tr>
<tr>
<td>4  15-29</td>
<td>11 (15)</td>
</tr>
<tr>
<td>5  &lt; 15</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Albuminuria (mg/mmol)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  &lt; 3</td>
<td>29 (40)</td>
</tr>
<tr>
<td>2  3-30</td>
<td>16 (22)</td>
</tr>
<tr>
<td>3  &gt; 30</td>
<td>10 (14)</td>
</tr>
<tr>
<td>Missing</td>
<td>17 (24)</td>
</tr>
</tbody>
</table>

Note: n (%) = percentage of group, Abbr.: GFR: glomerular filtration rate

4.2 Dietary intake

Dietary intake of the total study population and stratified by sex, is presented in Table 8. Mean energy intake was 1,840 kcal (SD ± 558) or 24.1 kcal/kg BW (SD ± 8.6). Daily energy intake in kcal/d was significantly higher among male patients compared to female patients (p = 0.014), but the energy intake per kg body weight was similar in both sexes (p = 0.694).

Reported energy intake was low when compared to the recommendations for the healthy population. In general, intake of energy as fat or protein was high, while contribution of carbohydrates to total energy intake was lower than recommended. This distribution of energy intake was similar to the Norwegian population in Norkost 3, a national diet survey in the adult population in Norway from 2010-2011 (66).

Regarding protein recommendations adjusted for body weight, 25% of the patients had a protein intake according to the recommendations. A quarter of the patients had protein intake below recommended protein intake and the remaining 50% had an intake exceeding the recommendations for protein intake per kg bodyweight.

On average, saturated fat contributed to > 10% of the energy intake in both men and women. The fibre intake was in general low, with a mean daily intake of 20 g (SD ± 8). Calculated salt intake was comparable to the intake that was reported in the general Norwegian population in Norkost 3 (66).
### Table 8: Dietary intake presented as mean of two 24-hour dietary recalls

<table>
<thead>
<tr>
<th></th>
<th>All patients n = 72</th>
<th>Male n = 51</th>
<th>Female n = 21</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>kJ</strong></td>
<td>7719 ± 2344</td>
<td>8149 ± 2438</td>
<td>6674 ± 1743</td>
<td><strong>0.014</strong></td>
</tr>
<tr>
<td><strong>Kcal</strong></td>
<td>1840 ± 558</td>
<td>1943 ± 580</td>
<td>1592 ± 417</td>
<td><strong>0.014</strong></td>
</tr>
<tr>
<td><strong>Kcal/kg BW</strong></td>
<td>24.1 ± 8.6</td>
<td>23.8 ± 8.3</td>
<td>24.7 ± 9.5</td>
<td>0.694</td>
</tr>
<tr>
<td><strong>CH E%</strong></td>
<td>44.8 ± 8.6</td>
<td>44.0 ± 8.4</td>
<td>46.5 ± 8.9</td>
<td>0.262</td>
</tr>
<tr>
<td><strong>Fat E%</strong></td>
<td>36.4 ± 8.1</td>
<td>36.7 ± 8.3</td>
<td>35.7 ± 7.9</td>
<td>0.615</td>
</tr>
<tr>
<td><strong>Protein E%</strong></td>
<td>18.9 ± 4.1</td>
<td>19.3 ± 4.2</td>
<td>18.0 ± 3.5</td>
<td>0.208</td>
</tr>
<tr>
<td><strong>CH (g)</strong></td>
<td>214.5 ± 83.5</td>
<td>224.9 ± 89.9</td>
<td>189.1 ± 59.7</td>
<td>0.098</td>
</tr>
<tr>
<td><strong>Fibre (g)</strong></td>
<td>20.2 ± 8.3</td>
<td>20.7 ± 8.7</td>
<td>19.0 ± 7.3</td>
<td>0.436</td>
</tr>
<tr>
<td><strong>Fat (g)</strong></td>
<td>74.6 ± 25.9</td>
<td>78.8 ± 25.7</td>
<td>64.6 ± 24.1</td>
<td><strong>0.034</strong></td>
</tr>
<tr>
<td><strong>Saturated fat (g)</strong></td>
<td>29.3 ± 11.4</td>
<td>30.9 ± 11.3</td>
<td>25.4 ± 10.7</td>
<td>0.060</td>
</tr>
<tr>
<td><strong>MUFA (g)</strong></td>
<td>25.9 ± 10.3</td>
<td>27.7 ± 10.3</td>
<td>21.5 ± 9.1</td>
<td><strong>0.020</strong></td>
</tr>
<tr>
<td><strong>PUFA (g)</strong>*</td>
<td>11.68 (7.20, 14.94)</td>
<td>11.75 (7.45, 16.65)</td>
<td>9.90 (4.30, 13.95)</td>
<td>0.152*</td>
</tr>
<tr>
<td><strong>Trans fat (g)</strong>*</td>
<td>0.60 (0.45, 1.05)</td>
<td>0.60 (0.45, 1.05)</td>
<td>0.60 (0.43, 1.05)</td>
<td>0.980*</td>
</tr>
<tr>
<td><strong>Protein (g)</strong></td>
<td>85.0 ± 27.9</td>
<td>91.0 ± 28.5</td>
<td>70.3 ± 20.4</td>
<td><strong>0.004</strong></td>
</tr>
<tr>
<td><strong>Protein/kg BW</strong></td>
<td>1.10 ± 0.38</td>
<td>1.11 ± 0.39</td>
<td>1.07 ± 0.34</td>
<td>0.677</td>
</tr>
<tr>
<td><strong>Salt (g)</strong>*</td>
<td>6.65 (4.65, 8.31)</td>
<td>6.95 (4.85, 8.40)</td>
<td>5.30 (3.65, 8.13)</td>
<td>0.126*</td>
</tr>
<tr>
<td><strong>Alcohol (g)†</strong></td>
<td>9 (13)</td>
<td>6 (12)</td>
<td>3 (14)</td>
<td>0.769</td>
</tr>
<tr>
<td><strong>Water (g)</strong></td>
<td>2075 ± 673</td>
<td>2075 ± 646</td>
<td>2076 ± 751</td>
<td>0.996</td>
</tr>
</tbody>
</table>

Note: In 7 patients (3 males, 4 females), only one 24 h recall was obtained and results were used from this recall. *variables presented as median (interquartile range), p-value from conducting a Mann Whitney U-test. †variables presented as n (%) patients who reported alcohol intake, p-value from conducting a Chi-Square test. Abbr.: kJ = kilojoule, kcal = kilocalories, /kg BW = per kilogram body weight, CH = carbohydrates, including fibre, E% = energy percentage, MUFA = mono unsaturated fatty acids, PUFA = poly unsaturated fatty acids.

As presented in table Table 8, the amount alcohol consumed was small in the total population. There was a question about drinking habits in the questionnaire, and almost half of the patients reported that the either never drink alcohol (n =17, 24 %) or less than once a month (n = 17, 24 %). The proportions of patients drinking alcohol less than once a week, and drinking alcohol 1-2 times a week were the same, with 19 patients (26 %) in each category.

On the recall performed at the hospital three patients (4 %) reported that they had consumed alcohol the preceding day with intake between 1.3-23.0 g. At the recall conducted by phone eight patients (12 %) reported intake of alcohol the day in advance with intakes between 1.3-92.0 g. In total, nine patients reported intake of alcohol from at least one of the days of the recalls, with a range from 0.65-46.0 g as mean daily intake. The patients reporting alcohol intake had reported drinking less than once a week or 1-2 times a week, indicating that the questionnaire and dietary recall resulted in comparable results.
The differences in dietary intake of macro- and micronutrients from the two 24 h recalls are presented in Table 9. In the total population there were no significant differences in dietary intake between the two days (p > 0.05). However, there were some differences at 0.05 < p > 0.1, including kcal/kg BW, fat, saturated fat and alcohol. When dividing into groups by sex, women’s intake of carbohydrates (including fibre) and energy intake, including kcal, kJ and kcal/kg body weight (kcal/kg BW) differed significantly from hospital and phone recall. The highest reported intake was obtained from the recall by phone. In men, the intake of fibre was significantly higher on the recall at the hospital compared to the recall by phone (p = 0.035).
Table 9: Difference in dietary intake between the recalls in total and by sex

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 65)</th>
<th></th>
<th>Male (n = 48)</th>
<th></th>
<th>Female (n = 17)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospital</td>
<td>Phone</td>
<td>P-value</td>
<td>Hospital</td>
<td>Phone</td>
<td>P-value</td>
</tr>
<tr>
<td>kJ</td>
<td>7380 ± 2601</td>
<td>7959 ± 2868</td>
<td>0.100</td>
<td>8073 ± 2476</td>
<td>8291 ± 3000</td>
<td>0.543</td>
</tr>
<tr>
<td>Kcal</td>
<td>1759 ± 620</td>
<td>1899 ± 684</td>
<td>0.097</td>
<td>1924 ± 589</td>
<td>1978 ± 714</td>
<td>0.529</td>
</tr>
<tr>
<td>Kcal/kg BW</td>
<td>22.4 ± 8.0</td>
<td>24.5 ± 9.8</td>
<td>0.069</td>
<td>23.7 ± 8.4</td>
<td>24.3 ± 9.9</td>
<td>0.611</td>
</tr>
<tr>
<td>CH E%</td>
<td>44.9 ± 9.1</td>
<td>44.1 ± 10.8</td>
<td>0.683</td>
<td>44.6 ± 9.3</td>
<td>43.6 ± 10.4</td>
<td>0.489</td>
</tr>
<tr>
<td>Fat E%</td>
<td>35.8 ± 8.9</td>
<td>37.5 ± 11.0</td>
<td>0.297</td>
<td>35.8 ± 8.8</td>
<td>37.7 ± 11.2</td>
<td>0.246</td>
</tr>
<tr>
<td>Protein E%</td>
<td>19.3 ± 5.5</td>
<td>18.5 ± 5.0</td>
<td>0.245</td>
<td>19.6 ± 5.5</td>
<td>18.8 ± 5.4</td>
<td>0.417</td>
</tr>
<tr>
<td>CH (g)</td>
<td>208 ± 91</td>
<td>215 ± 96</td>
<td>0.429</td>
<td>227 ± 95</td>
<td>224 ± 105</td>
<td>0.806</td>
</tr>
<tr>
<td>Fibre (g)</td>
<td>20.8 ± 9.9</td>
<td>19.3 ± 8.0</td>
<td>0.187</td>
<td>21.9 ± 10.5</td>
<td>18.9 ± 8.2</td>
<td>0.035</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>69.9 ± 28.4</td>
<td>79.4 ± 36.6</td>
<td>0.079</td>
<td>75.9 ± 26.8</td>
<td>82.7 ± 36.6</td>
<td>0.206</td>
</tr>
<tr>
<td>Saturated fat (g)</td>
<td>26.9 ± 12.9</td>
<td>31.8 ± 16.7</td>
<td>0.068</td>
<td>29.4 ± 12.3</td>
<td>32.8 ± 16.4</td>
<td>0.193</td>
</tr>
<tr>
<td>MUFA (g)</td>
<td>24.2 ± 11.6</td>
<td>27.9 ± 13.9</td>
<td>0.071</td>
<td>26.5 ± 11.6</td>
<td>29.6 ± 14.1</td>
<td>0.154</td>
</tr>
<tr>
<td>PUFA (g)*</td>
<td>9.5 (6.1, 15.2)</td>
<td>9.8 (6.25, 15.45)</td>
<td>0.966</td>
<td>9.95 (6.93, 16.95)</td>
<td>10.10 (6.83, 15.85)</td>
<td>1.000</td>
</tr>
<tr>
<td>Transfat (g)*</td>
<td>0.60 (0.20, 0.80)</td>
<td>0.70 (0.40, 1.05)</td>
<td>0.081</td>
<td>0.60 (0.23, 0.88)</td>
<td>0.70 (0.40, 1.00)</td>
<td>0.186</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>84.5 ± 37.5</td>
<td>85.0 ± 32.0</td>
<td>0.967</td>
<td>93.1 ± 37.3</td>
<td>89.0 ± 31.9</td>
<td>0.484</td>
</tr>
<tr>
<td>Protein/kg BW</td>
<td>1.08 ± 0.50</td>
<td>1.09 ± 0.43</td>
<td>0.949</td>
<td>1.15 ± 0.53</td>
<td>1.08 ± 0.40</td>
<td>0.335</td>
</tr>
<tr>
<td>Salt (g)*</td>
<td>6.00 (4.15, 7.20)</td>
<td>5.60 (3.80, 8.90)</td>
<td>0.365</td>
<td>6.35 (4.65, 7.78)</td>
<td>6.80 (4.03, 9.20)</td>
<td>0.343</td>
</tr>
<tr>
<td>Alcohol* (g)</td>
<td>0 (0, 0)</td>
<td>0 (0, 0)</td>
<td>0.058</td>
<td>0 (0, 0)</td>
<td>0 (0, 0)</td>
<td>0.293</td>
</tr>
<tr>
<td>Water (g)</td>
<td>2092 ± 753</td>
<td>2005 ± 836</td>
<td>0.457</td>
<td>2129 ± 753</td>
<td>1972 ± 861</td>
<td>0.275</td>
</tr>
</tbody>
</table>

Note: Results presented as mean ± SD and p-value from a paired samples test. *results presented as median (inter quartile range) and p-value from Wilcoxon Signed Rank test. CH = Carbohydrates including fibre, MUFA = mono unsaturated fatty acids, PUFA = poly unsaturated fatty acid.
An overview of mean energy and protein intake according to BMI categories is shown in Table 10, both in kcal/d and kcal/kg BW. The patients with normal weight had the highest mean energy intake of 2050 kcal/day. The lowest energy intake was found in the group of obese patients, with an intake of 1688 kcal/day. Intake of kcal/kg BW decreased as BMI category increased, from 40 kcal/kg BW in underweight patients to 17 kcal/kg BW in obese patients. Exclusion of patients with oedema did not change the energy intake in the different BMI-categories substantially. There were significant differences among the groups in kcal/kg BW, kcal/kg ALM and protein/kg BW. Exclusion of patients with oedema (n = 14) did not change these results.

Table 10: Energy and protein intake by BMI categories

<table>
<thead>
<tr>
<th></th>
<th>Underweight</th>
<th>Normal weight</th>
<th>Overweight</th>
<th>Obesity</th>
<th>P (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (% of total)</td>
<td>3 (4)</td>
<td>22 (31)</td>
<td>31 (43)</td>
<td>16 (22)</td>
<td></td>
</tr>
<tr>
<td>Kcal mean ± SD</td>
<td>1818 ± 468</td>
<td>2050 ± 654</td>
<td>1760 ± 366</td>
<td>1688 ± 695</td>
<td>0.186</td>
</tr>
<tr>
<td>Kcal/kg BW mean ± SD</td>
<td>40.4 ± 13.7a</td>
<td>28.9 ± 8.5b</td>
<td>22.7 ± 4.8c</td>
<td>17.3 ± 6.0c</td>
<td>0.000</td>
</tr>
<tr>
<td>Kcal/kg ALM mean ± SD</td>
<td>127.6 ± 35.3a</td>
<td>89.2 ± 24.4a,b</td>
<td>92.9 ± 25.0a,b</td>
<td>74.3 ± 23.9b</td>
<td>0.007</td>
</tr>
<tr>
<td>Protein (g) mean ± SD</td>
<td>66.5 ± 11.9</td>
<td>91.4 ± 34.9</td>
<td>81.7 ± 21.9</td>
<td>86.1 ± 29.1</td>
<td>0.406</td>
</tr>
<tr>
<td>Protein/kg BW (g)</td>
<td>1.48 ± 0.40a</td>
<td>1.28 ± 0.45a</td>
<td>1.05 ± 0.28a,b</td>
<td>0.88 ± 0.29b</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Note: Differences between the BMI categories were tested by one-way ANOVA with post hoc Tukey comparison. Different superscript letters show differences by the post hoc comparison. Abbr.: Kcal = kilo calories, kcal/kg BW = kilo calories per kilogram bodyweight. ALM = appendicular lean mass.

4.2.1 Identification of misreporting

The mean quotients of reported energy intake and RMR from the recall at the hospital and the recall by phone were 1.16 ± 0.36 and 1.24 ± 0.44, respectively. Applying the Goldberg equation, 33% of the dietary assessments in the hospital and 32% of the phone assessments may be considered as underreporting. When looking at the mean intake from the two recalls, 18 dietary assessments (28%) can be considered as underreporting (Table 11).
Table 11: Underreporting from the two 24-hour dietary recalls and the mean intake

<table>
<thead>
<tr>
<th></th>
<th>Total population, n</th>
<th>Underreporting, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital</td>
<td>72</td>
<td>24 (33)</td>
</tr>
<tr>
<td>Phone</td>
<td>65</td>
<td>21 (32)</td>
</tr>
<tr>
<td>Mean</td>
<td>65</td>
<td>18 (28)</td>
</tr>
</tbody>
</table>

Note: n (%) = percentage of total population of each row.

The mean BMI in the underreporting group was 29.2 kg/m² (SD: ± 4.3) and significantly higher than the mean BMI in the group without underreporting on 26.0 kg/m² (SD: ± 4.0), p= 0.006. The distribution of BMI in the two groups is presented in Figure 3. There was also a significant age difference (p= 0.049) with patients who underreported their dietary intake being older (median 66.5 vs. 59.0 years). Underreporters were not significantly different in GFR and in the distribution of gender.

Figure 3: Distribution of BMI among patients considered as underreporters and patients considered as not underreporters

Abbr.: BMI = body mass index,
4.2.2 Dietary restrictions

In the study populations, 15% of the patients (n = 11) reported having dietary restrictions advised from a health professional, mostly their physician. A proportion of 22% (n = 16) of the patients followed self-imposed dietary restrictions while 63% (n = 45) reported having no dietary restrictions. Among the patients that reported dietary restrictions advised from a medical perspective there was one patient that reported restriction of phosphate intake, two patients reported restriction of potassium intake, one patient reported restriction of protein intake, four patients reported restriction of salt intake, four patients reported restriction of sugar intake and one patient reported restriction of vitamin K intake. Some of the patients have reported multiple dietary restrictions.

Table 12 presents the energy intake in the groups of patients that reported self-imposed dietary restrictions, no dietary restrictions and dietary restrictions advised from a medical perspective. The group that reported self-imposed dietary restrictions had the highest energy intake, and the group of patients reporting having medical advised dietary restrictions had the lowest energy intake, both for kcal and kcal adjusted for body weight. However, there were no significant differences in either kcal or kcal/kg BW between the groups. There were no differences in BMI-categories by dietary restriction categories.

Table 12: Energy intake by dietary restrictions

<table>
<thead>
<tr>
<th></th>
<th>Self-imposed dietary restriction</th>
<th>No dietary restriction</th>
<th>Medical advised dietary restriction</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>16 (22)</td>
<td>45 (63)</td>
<td>11 (15)</td>
<td></td>
</tr>
<tr>
<td>Kcal mean ± SD</td>
<td>2082</td>
<td>1777</td>
<td>1717</td>
<td>0.137</td>
</tr>
<tr>
<td>Kcal/kg BW mean ± SD</td>
<td>25.3</td>
<td>23.9</td>
<td>22.8</td>
<td>0.765</td>
</tr>
</tbody>
</table>

Note: P-values from conducting a parametric one-way ANOVA. Abbr.: SD = standard deviation, Kcal = kilocalories, kcal/kg BW = kilocalories per kilogram bodyweight.

4.2.3 Dietary advice

The major proportion of the study population (78%) reported that they had received dietary advice regarding their kidney disease. A proportion of 80% of these patients (n = 45) reported receiving dietary advice from a clinical dietitian, mostly at seminars of management of everyday life with kidney disease. The remaining 20% received the advice from either a physician, nurse or booklet.
4.3 Anthropometric measurements

The anthropometric measurements of the total study population and stratified by sex are presented in Table 13. Mean weight in male and female patients were 83.8 kg (SD ± 13.0) and 67.5 kg (SD ± 13.6), respectively (p < 0.001). BMI was not different between men and women (p = 0.219). When grouping patients according to BMI category, the group of underweight patients consisted only of women and represented 14% of the female study population. The prevalence of normal weight was higher among men (37%) compared to women (14%), and the prevalence of overweight among women is nearly twice the prevalence of overweight among men (62% and 35%, respectively). Obesity was more prevalent among men than women, with a prevalence of 28% in the female population against 10% in the male population. Six of the nine patients with DM type II were overweight and the remaining three patients with DM type II were obese. DM type I were found in one patient with normal weight and one patient with overweight.

Waist circumference had a mean of 101.3 cm (SD ± 13.3) among male patients and 90.4 cm (SD ± 14.0) among female patients (p = 0.003). Half of the study population (n = 36) was identified with an increased waist circumference according to sex-specific cut-off values. Among male patients, 45% had an increased waist circumference and among the female patients 62% had an increased waist circumference, indicating central obesity. One patient with normal weight was identified to have central obesity, while the remaining patients were obese or overweight according to BMI. All obese patients were identified to have central obesity.

Regarding MUAC, the mean measurements in male patient were significantly higher compared to female patients (p = 0.007). Biceps and triceps skinfold thickness were significantly higher in female patients compared to male patients (p = 0.040 and 0.025, respectively). Both MUAMC and MUAMA were significantly higher in male patients compared to female patients, with p-values < 0.001.

The measurements from BIA were significantly higher among female patients compared to male patients concerning reactance and resistance, with p-values 0.008 and < 0.001, respectively. Phase angle was higher in male patient compared to female patients, but the difference was not significant. Appendicular lean mass was higher in male patients compared to female patients (p < 0.001).
### Table 13: Anthropometric measurements in relation to sex

<table>
<thead>
<tr>
<th>Variables</th>
<th>All patients</th>
<th>Male</th>
<th>Female</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>mean ± SD</td>
<td>79.0 ± 15.0</td>
<td>83.8 ± 13.0</td>
<td>67.5 ± 13.6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>mean ± SD</td>
<td>172.0 ± 8.8</td>
<td>176.1 ± 6.2</td>
<td>162.1 ± 5.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>mean ± SD</td>
<td>26.7 ± 4.5</td>
<td>27.1 ± 4.3</td>
<td>25.6 ± 4.8</td>
</tr>
<tr>
<td><strong>BMI categories</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight n (%)</td>
<td>3 (4)</td>
<td>0 (0)</td>
<td>3 (14)</td>
<td>0.002</td>
</tr>
<tr>
<td>Normal weight n (%)</td>
<td>22 (31)</td>
<td>19 (37)</td>
<td>3 (14)</td>
<td></td>
</tr>
<tr>
<td>Overweight n (%)</td>
<td>31 (43)</td>
<td>18 (35)</td>
<td>13 (62)</td>
<td></td>
</tr>
<tr>
<td>Obesity n (%)</td>
<td>16 (22)</td>
<td>14 (28)</td>
<td>2 (10)</td>
<td></td>
</tr>
<tr>
<td>WC (cm)</td>
<td>mean ± SD</td>
<td>98.0 ± 14.3</td>
<td>101.3 ± 13.3</td>
<td>90.4 ± 14.0</td>
</tr>
<tr>
<td>Central obesity n (%)</td>
<td>36 (50)</td>
<td>23 (45)</td>
<td>13 (62)</td>
<td>0.195*</td>
</tr>
<tr>
<td>MUAC (cm)</td>
<td>mean ± SD</td>
<td>30.5 ± 3.4</td>
<td>31.2 ± 3.0</td>
<td>28.8 ± 3.7</td>
</tr>
<tr>
<td>SFT B (mm)</td>
<td>median (IQR)</td>
<td>7.3 (5.0, 12.0)</td>
<td>7.0 (4.3, 10.5)</td>
<td></td>
</tr>
<tr>
<td>SFT T (mm)</td>
<td>median (IQR)</td>
<td>18.0 (11.7, 25.7)</td>
<td>16.5 (11.6, 23.2)</td>
<td>25.0 (12.4, 28.2)</td>
</tr>
<tr>
<td>MUAMC (mm)</td>
<td>mean ± SD</td>
<td>244.7 ± 29.4</td>
<td>256.3 ± 23.7</td>
<td>217.1 ± 22.4</td>
</tr>
<tr>
<td>MUAMA (mm²)</td>
<td>mean ± SD</td>
<td>4832 ± 1137</td>
<td>5271 ± 978</td>
<td>3788 ± 744</td>
</tr>
<tr>
<td>BIA Resistance mean ± SD</td>
<td>487.2 ± 86.3</td>
<td>452.8 ± 60.2</td>
<td>566.0 ± 86.2</td>
<td>0.000</td>
</tr>
<tr>
<td>BIA Reactance mean ± SD</td>
<td>50.0 ± 12.9</td>
<td>47.4 ± 11.4</td>
<td>56.1 ± 14.2</td>
<td>0.008</td>
</tr>
<tr>
<td>BIA Phase angle mean ± SD</td>
<td>5.86 ± 1.03</td>
<td>5.95 ± 1.06</td>
<td>5.63 ± 0.94</td>
<td>0.240</td>
</tr>
<tr>
<td>ALM_BIA mean ± SD</td>
<td>21.4 ± 4.8</td>
<td>24.2 ± 2.8</td>
<td>15.2 ± 1.6</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Note: underweight = BMI < 18.5, normal weight = BMI 18.5-25.0, overweight = BMI 25.0-30.0, obesity = BMI >30.0. *P-value from conducting a Chi Squared test. n (%) = percentage of column. Abbr.: IQR = interquartile range. WC = waist circumference, MUAC = middle upper arm circumference, SFT B = skinfold thickness biceps, SFT T = skinfold thickness triceps, MUAMC = middle upper arm muscle circumference, MUAMA = middle upper arm muscle area, BMI = body mass index

### 4.4 Functional measurements

The results from functional measurements are shown in Table14. Mean maximum HGS was 32.0 kg (SD ± 11.2) in the total population, and 36.6 kg (SD ± 9.7) and 21.0 kg (SD ± 5.0) in male and female patients, respectively. As expected, there was a significant difference between the sexes in HGS, concerning both maximum and mean value from the dominant hand. Mean knee extension max was 195.4 N (SD ± 38.8) in the total population. There was, however, no statistical difference between the sexes in the knee extension test.
Table 14: Measurements of hand grip strength and knee extension in relation to sex

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Male</th>
<th>Female</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HGS max (kg)</td>
<td>mean ± SD</td>
<td>32.0 ± 11.2</td>
<td>36.6 ± 9.7</td>
<td>21.0 ± 5.0</td>
</tr>
<tr>
<td>HGS mean (kg)</td>
<td>mean ± SD</td>
<td>30.0 ± 11.0</td>
<td>34.6 ± 9.6</td>
<td>19.0 ± 4.4</td>
</tr>
<tr>
<td>KE, max (N)</td>
<td>mean ± SD</td>
<td>195.4 ± 38.8</td>
<td>198.4 ± 39.0</td>
<td>188.2 ± 38.4</td>
</tr>
<tr>
<td>KE, mean (N)</td>
<td>mean ± SD</td>
<td>182.7 ± 37.1</td>
<td>185.4 ± 36.2</td>
<td>176.1 ± 39.2</td>
</tr>
</tbody>
</table>

Note: P-value from conducting an Independent Samples T-test. HGS measurements taken the dominant hand. Abbr.: HGS = Hand grip strength, KE = Knee extension. SD= standard deviation

4.5 Nutritional screening

Nutritional risk was identified by the screening tools NRS 2002 and MUST. According to NRS 2002, five patients (7%) were at nutritional risk by scoring > three points in the main screening, indicating a need of nutritional treatment. When screening with MUST, seven patients (10%) were identified with nutritional risk with a score > one point, indicating need of closer attention and assessment of dietary intake, possibly followed by nutritional treatment, if necessary. The results from the two screening tools applied are presented in Table 15 divided into BMI-categories.

Table 15: Identification of nutritional risk by BMI-categories

<table>
<thead>
<tr>
<th></th>
<th>Underweight</th>
<th>Normal weight</th>
<th>Overweight</th>
<th>Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRS 2002</td>
<td>n (% of total)</td>
<td>3 (4)</td>
<td>22 (31)</td>
<td>31 (43)</td>
</tr>
<tr>
<td>0 n</td>
<td>0</td>
<td>15</td>
<td>28</td>
<td>16</td>
</tr>
<tr>
<td>1 n</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2 n</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>3 n</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4 n</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>MUST</td>
<td>n (% of total)</td>
<td>0</td>
<td>19</td>
<td>30</td>
</tr>
<tr>
<td>0 n</td>
<td>0</td>
<td>19</td>
<td>30</td>
<td>16</td>
</tr>
<tr>
<td>1 n</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2 n</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>


The two screening tools agreed about three patients being at nutritional risk and 63 patients not being at nutritional risk. NRS 2002 identified two patients at risk who were not identified by MUST, and four patients at risk according to MUST were not at risk according to NRS 2002.
4.6 Sarcopenia

When including measurements of both HGS and SM/HT$^2$, 22 patients were identified with sarcopenia, which constitutes 31% of the study population, as described in Table 16. Due to contraindications, 3 patients (4%) were not eligible to measure muscle mass by BIA, and they are therefore only included in the identification of sarcopenia by HGS. The prevalence of sarcopenia was higher among female patients with a prevalence of 48% compared to a prevalence of 24% among male patients. The different definitions of sarcopenia resulted in very different prevalence rates (Table 16).

Table 16: Prevalence of sarcopenia in the study population

<table>
<thead>
<tr>
<th>Cut-off defined by</th>
<th>Diagnosed with sarcopenia</th>
<th>All patients n = 72</th>
<th>Male n = 51</th>
<th>Female n = 21</th>
</tr>
</thead>
<tbody>
<tr>
<td>HGS n (%)</td>
<td>23 (32)</td>
<td>13 (26)</td>
<td>10 (48)</td>
<td></td>
</tr>
<tr>
<td>SM/HT$^2$ n (%)</td>
<td>69 (96)*</td>
<td>46 (90)*</td>
<td>19 (91)</td>
<td></td>
</tr>
<tr>
<td>HGS and SM/HT$^2$  n (%)</td>
<td>22 (31)*</td>
<td>12 (24)*</td>
<td>10 (48)</td>
<td></td>
</tr>
</tbody>
</table>

Note: n (%) = percentage of group. *n = 3 missing measurements from BIA due to contraindication concerning pacemaker. Abbr.: HGS = hand grip strength, SM/HT$^2$ = skeletal muscle mass divided by height squared.

When dividing the study population into groups by BMI category, there were identified sarcopenic patients in all BMI categories. The highest prevalence was found in the underweight group (67%), but the prevalence in the overweight group was also high (47%).

The underweight group consisted of female patients only, of whom 2/3 patients had sarcopenia. None of the female patients in the normal weight group were sarcopenic, while 28% of male patients with normal weight were identified to have sarcopenia. Among female patients with overweight the prevalence of sarcopenia was 62% while the prevalence was 35% among male, overweight patients. In the obesity group, the prevalence of sarcopenia was 48% among female patients and 25% among male patients. Table 17 gives an overview of the distribution of sarcopenia by BMI categories.

Table 17: Identification of sarcopenia by BMI categories

<table>
<thead>
<tr>
<th>BMI category</th>
<th>No sarcopenia</th>
<th>Sarcopenia</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%) of total</td>
<td>50 (69)</td>
<td>22 (31)</td>
<td>0.021</td>
</tr>
<tr>
<td>Underweight n (%)</td>
<td>1 (33)</td>
<td>2 (67)</td>
<td></td>
</tr>
<tr>
<td>Normal weight n (%)</td>
<td>16 (76)</td>
<td>5 (24)</td>
<td></td>
</tr>
<tr>
<td>Overweight n (%)</td>
<td>16 (53)</td>
<td>14 (47)</td>
<td></td>
</tr>
<tr>
<td>Obesity n (%)</td>
<td>14 (93)</td>
<td>1 (7)</td>
<td></td>
</tr>
</tbody>
</table>

Note: P-value from conducting a Chi-square test. Abbr.: BMI = body mass index.
Regarding dietary intake in patients with or without sarcopenia, was there no difference in intake of carbohydrates (including fibre) or fat. In male patients identified with sarcopenia, intake of protein was lower than in patients without sarcopenia \((p = 0.070)\). When adjusting protein intake to body weight, there was no difference in protein intake neither in male or female patients.

In women, there was no difference in the results of anthropometric measurements according to the presence of sarcopenia, with the exception that the phase angle was significantly lower in sarcopenic women compared to non-sarcopenic female patients \((5.1 \pm 0.6 \text{ vs } 6.1 \pm 0.9, p < 0.02)\). In men, phase angle was also different according to sarcopenia, but in addition, MUAC, MUAMC and MUAMA were significantly lower in sarcopenic male patients.

Patients with sarcopenia were not significantly older than patients without sarcopenia in the total patients group, however, when analysed by gender, it appeared that male patients with sarcopenia were significantly older than male patients without sarcopenia \((64 \pm 15 \text{ years versus } 56 \pm 13 \text{ years, } p = 0.05)\), but there was no significant difference in age according to sarcopenia in female patients \((p = 0.551)\).

There was no difference in comorbidities in patients identified with sarcopenia compared to patients not identified with sarcopenia according to the CCI. However, sarcopenic patients used significantly more medications than non-sarcopenic patients, with 14 of 22 sarcopenic patients using more than nine medications, compared to 14 of 47 non-sarcopenic patients using more than nine medications \((p = 0.01)\).

### 4.7 Blood and urine samples

Information about routine samples of blood and urine obtained from the patients’ journal is presented in Tables 18-20. Samples from eleven patients were excluded due to samples taken more than 14 days apart from the interview date. One exception was made; GFR was included from all patients, independent of time between sample taken and interview performed.

Table 18 gives an overview of nutrition related blood results. Full blood haemoglobin results were below the cut-off in 34 % of the patients, thus indicating anaemia, while 3 % of the patients had results exceeding the cut-off. Levels of haemoglobin were significantly higher among male patients compared to female patients \((p = 0.009)\). Glucose was measured within
the reference range in 55 % of the patients, whereas the remaining 41 % and 4 % were exceeding and below the cut-off, respectively. HbA1c was elevated in 19 % of the patients (n = 9), including one patient not diagnosed with DM. All patients with DM that had HbA1c measured had levels exceeding the cut-off. Serum albumin was below cut-off in 3 % of the patients. Serum creatinine was elevated in 66 % of the patients. Uric acid results were found below cut-off in 2 % of the patients while results exceeding the cut-off were found in 42 % of the patients.

**Table 18: Nutrition related blood analysis results**

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Below cut-off</th>
<th>Exceeding cut-off</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-Hb (g/dL)</td>
<td>13.6 ± 1.9</td>
<td>14.0 ± 1.8</td>
<td>12.7 ± 1.8</td>
<td>34 %</td>
<td>3 %</td>
</tr>
<tr>
<td>S-Glucose</td>
<td>5.6 (5.1, 7.0)</td>
<td>5.6 (5.0, 7.7)</td>
<td>5.4 (5.2, 5.9)</td>
<td>4 %</td>
<td>41 %</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.70 (5.50, 6.10)</td>
<td>5.70 (5.50, 6.25)</td>
<td>5.70 (5.45, 5.80)</td>
<td>-</td>
<td>17 %</td>
</tr>
<tr>
<td>S-Albumin (g/L)</td>
<td>43.1 ± 3.0</td>
<td>42.7 ± 3.0</td>
<td>43.8 ± 3.0</td>
<td>3 %</td>
<td>2 %</td>
</tr>
<tr>
<td>S-Creatinine</td>
<td>114.0 (95.5, 163.5)</td>
<td>122.0 (99.0, 166.5)</td>
<td>105.0 (83.3, 138.8)</td>
<td>0 %</td>
<td>66 %</td>
</tr>
<tr>
<td>S-Uric acid</td>
<td>431.1 ± 104.4</td>
<td>445.9 ± 100.4</td>
<td>400.0 ± 108.5</td>
<td>2 %</td>
<td>42 %</td>
</tr>
</tbody>
</table>

**Note:** Variables presented as mean ± SD *Variables presented as median (IQR). Abbr.: S = serum, B = full blood, Hb = haemoglobin, IQR = interquartile range.

Table 19 gives an overview on the markers of inflammation C-reactive protein (CRP) and leucocytes. An elevation of CRP, > 5 mg/L, was found in 17 % of the patients. CRP was significantly higher in male patients compared to female patients (p = 0.037). There was no difference in CRP by BMI-categories (p = 0.279). Leucocyte counts were decreased in 2 % of the patients and increased in 17 % of the patients.

**Table 19: Inflammation related blood analysis results**

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Below cut-off</th>
<th>Exceeding cut-off</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-Leucocytes</td>
<td>7.7 ± 2.8</td>
<td>8.1 ± 3.0</td>
<td>6.9 ± 2.1</td>
<td>2 %</td>
<td>17 %</td>
</tr>
<tr>
<td>(10^9/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S-CRP (mg/L)*</td>
<td>2.00 (1.00, 4.00)</td>
<td>2.25 (1.00, 4.00)</td>
<td>1.00 (1.00, 2.75)</td>
<td>-</td>
<td>17 %</td>
</tr>
</tbody>
</table>

**Note:** Variables presented as mean ± standard deviation. *variables presented as median (interquartile range). Abbr.: CRP = C-reactive protein. B = full blood. S = serum.
Table 20 gives an overview of results from urine sample analysis. U-creatinine was not found elevated in any patient. Thirty patients, constituting 55 % of the patients, had levels of U-albumin per mmol creatinine exceeding the cut-off. Proteinuria, identified by increased U-protein per mmol creatinine, was found in 25 % of the patients.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Below cut-off</th>
<th>Exceeding cut-off</th>
</tr>
</thead>
<tbody>
<tr>
<td>U-Creatinine (mmol/L)</td>
<td>5.9 (4.2, 8.7)</td>
<td>6.4 (4.5, 8.5)</td>
<td>5.0 (4.2, 9.5)</td>
<td>2 %</td>
<td>0 %</td>
</tr>
<tr>
<td>U-Albumin per mmol creatinine (mg/mmol)</td>
<td>2.70 (0.90, 17.0)</td>
<td>2.80 (0.85, 18.10)</td>
<td>1.95 (0.95, 20.8)</td>
<td>-</td>
<td>55 %</td>
</tr>
<tr>
<td>U-Protein (mg/mmol creatinine)</td>
<td>0.0 (0.0, 26.0)</td>
<td>0.0 (0.0, 32.9)</td>
<td>0.0 (0.0, 21.0)</td>
<td>-</td>
<td>25 %</td>
</tr>
</tbody>
</table>

*Note: Variables presented as median (interquartile range). Abbr.: U = urinary.*

### 4.8 Blood chemistry according to nutritional status

#### 4.8.1 Blood chemistry and nutritional risk

There were no significant differences in CRP, S-Albumin or U-protein per mmol creatinine in patients identified at nutritional risk compared to patients identified not at nutritional risk. This was tested both NRS 2002 and MUST. It should be noticed that the lack of significant differences may be due to a low sample size, resulting in a power problem.

#### 4.8.2 Blood chemistry and sarcopenia

There was no difference in GFR in patients identified with sarcopenia compared to patients not identified with sarcopenia (p = 0.060). When adjusting for sex, there was a significant difference in GFR in male patients identified with sarcopenia compared to male patients not identified with sarcopenia (p = 0.029). There was no difference in female patients regarding GFR and sarcopenia. Haemoglobin levels were significantly lower in patients identified with sarcopenia compared to patients not identified with sarcopenia (p < 0.001). The difference remained in male patients when stratifying by gender, but female patients with sarcopenia did not show differences in haemoglobin from female patients without sarcopenia. There was no difference in CRP in patients identified with sarcopenia compared to patients not identified with sarcopenia (p = 0.563).
5 DISCUSSION

The current study aimed to investigate the nutritional status in kidney transplant patients followed up at HUS. Nutritional status can be defined in several ways, which were applied in the current thesis: a) according to body mass index, patients can be classified as underweight, normal weight, overweight or obese; b) according to nutritional screening, patients can be classified either as being well-nourished or being undernourished or at nutritional risk; c) nutritional status can be described according to the presence or absence of sarcopenia, a state of diminished skeletal muscle mass and strength. These categories use different criteria and there may be an overlap in the categories, thus, a patient can be overweight, being at nutritional risk and can have sarcopenia at the same time. This example illustrates the complexity of nutritional status assessment, and may also explain different prevalence rates in different settings.

The discussion will be divided into three sections. The first section will discuss the main findings of this study, and compare the results to related studies. The strengths and limitations of the study design and methods used will be discussed in the second section. The third section will concern an evaluation of clinical impact from this study, the requirement for further research on the subject and finally a conclusion.

5.1 Main findings

The aim of this study was to investigate the nutritional status of kidney transplant recipients followed up at HUS. The main findings were a) that a large proportion (65 %) of the patient group were overweight or obese; b) less than 10 % of the patients were at nutritional risk and c) that 31 % of the patients had sarcopenia. Sarcopenia prevalence was differently between the sexes and more prevalent in female patients. The prevalence of sarcopenia in the study population was independent of BMI-categories and seemed to have strong meaning for the health status of the patients, especially in the male sarcopenic patients.

5.1.1 Overweight and obesity

There was a prevalence of 43 % and 22 % of overweight and obesity, respectively, in the study population, concluding with 65 % of the patients with BMI > 25 kg/m². All patients with DM type II were either overweight or obese. In addition, 50 % of the study populations were classified to have central obesity, which is a strong risk factor for metabolic disturbances and increases the risk for CVD (34).
It has been suggested that waist circumference is a better predictor for cardiovascular and DM risk than BMI, but not a better prediction for hypertension (67). This indicates that BMI measurement alone might not be sufficient in assessment of obesity and the associated risk factors, and that BMI and waist circumference measurements together may give a better clinical picture of obesity.

As oedema is known to be a potential issue in patients with kidney disease, clinical signs of oedema were assessed in the study population. A proportion of 19 % (n = 14) of the study population was identified with oedema, with half of these patients (n = 7) with visible/severe pitting oedema. The patients identified with oedema were normal weight (n = 5), overweight (n = 7) and obese (n = 2). Exclusion of patients with oedema did not change the distribution of patients in the different BMI-categories substantially.

Corticosteroids were used by 97 % of the study population, and one known side effect of corticosteroids is weight gain. The use of these medications may partly explain the high prevalence of overweight and obesity in the study population.

5.1.2 Sarcopenia and sarcopenic obesity

There was a prevalence of 31 % of patients identified with sarcopenia in the study population when combining results from both HGS and BIA. The prevalence of sarcopenia was 24 % and 48 % among male and female patients, respectively. Sarcopenia can easily be overlooked in patients with high BMI, and in this study were sarcopenic patients identified in all BMI categories, with the highest prevalence among underweight patients (67 %), followed by patients with overweight (47 %). Central obesity was identified in 41 % of the patients with sarcopenia. This demonstrates that assessment of sarcopenia should be performed in all patients, and that a regularly screening for sarcopenia in kidney transplant patients may be discussed.

Male sarcopenic patients were older, had lower GFR and lower haemoglobin levels, and also lower phase angle and lower MUAC measurements. MUAC measurements could offer an easy tool to assess sarcopenia in these patients where BIA measurements are not available. A study on elderly patients in Turkey have similar results with significant differences in MUAC in sarcopenic and non-sarcopenic male patients (68). More research is required on the association of MUAC and sarcopenia in these patients.
The lack of a common definition for diagnosis of sarcopenia limits the clinical application of sarcopenia and SO with regard to metabolic disorders and CVD (43). In this study sarcopenia was identified by measurements of BIA and HGS, recommended methods for clinical practice (69). DEXA is however considered as a more accurate measurement method of body composition, and a problem with BIA is that the results can be affected of presence of oedema (70). Seven patients identified with sarcopenia had oedema, and the accuracy of this measurement in these patients may be questioned. However, BIA can be used as a transportable, easy method that is cheap, does not expose the patient to radiation and that can be applied at bedside or in the outpatient clinic. DEXA measurements, although nowadays more common and available, are still expensive and are not widely available.

There is also a challenge in comparing the results from this study to other studies due to different methods for identifying sarcopenia. A study on kidney transplant patients in Turkey that identified sarcopenia in 21% of the study population of kidney recipients used only cut-offs of HGS measurements as diagnostic criteria for sarcopenia. In addition, the cut-offs used in this study were different from the present study, as they in addition to sex-specific cut-offs included BMI-specific cut-offs (41). A definition for sarcopenia diagnostic criteria is necessary to identify sarcopenia and to make comparison between different studies and populations more accurate.

The applicability of the cut off measurements can also be discussed, as use of HGS or SM/HT\(^2\) alone resulted in very different prevalence rates of sarcopenia, compared to when the two measurements were combined (Table 16). Further research on the diagnosis of sarcopenia is required as this reflects an important risk factor for health in these patients.

### 5.1.3 Dietary assessment

The mean energy intake from both recalls in the study population was 1840 kcal/d or 24.1 kcal/kg BW, which is quite low. This becomes especially evident when taking into account that the majority of the study population was either overweight or obese. Underreporting may an explanation to the reported energy intake. The prevalence of patients considered as underreporters on mean intake from the two recalls performed was 28%, and there was an association between underreporting and high BMI. Other studies have also shown that BMI may be a consistent determinant of misreporting of energy intake (71).

In the previous studies on kidney patients at HUS one 24 h recall was used to assess dietary intake of the study population. This has been criticized, as one 24 h recall will not give
accurate information about nutrient intake (33). In this present study two 24 h recalls were therefore used to assess dietary intake. Use of two 24 recalls reduced the proportion of underreporting from 32-33 % to 28 %, however, still a large proportion of underreporting was observed. Opposite results were found in an American study, where underreporting was identified in 25 % of the study population when including two recalls and underreporting was identified in 21 % of the study population when including only the first recall (54). A few other studies have assessed the prevalence of underreporting of energy intake, but they included other methods for obtaining dietary information, e.g. seven days of food diary and FFQs (72-74). Nonetheless, the prevalences of underreporting in these studies were similar to the present study.

The Goldberg cut-off equation has been used in several studies to identify individuals reporting low or high energy intake which might not be plausible, and the sensitivity of application of the equation on an individual level has been considered as low. Identification of underreporters based on the Goldberg cut-off equation, compare reported energy intake to estimated energy requirement adjusted to physical activity. RMR was adjusted by weight among others, but weight was not adjusted according to presence of oedema. This may have caused bias regarding evaluation of dietary intake. However, when excluding patients with oedema, there was no difference in the result of BMI by underreporting.

PAL was estimated from questions asked about physical activity habits. The questions were obtained from the questionnaire from HUNT 3 (57) regarding physical activity. However, there is a lack of standardized questions for the purpose of estimating PAL, and validation of self-reported habits of physical activity have given limited results (75, 76). The estimation of PAL may therefore not be as accurate as it could have been with other questions asked regarding physical activity. Kosthåndboken recommends estimation of PAL based on patients’ activity level at work (24). A major proportion of the patients included in the study was no longer working, ant the usefulness of these descriptions of PAL may therefore be questioned.

When comparing information on dietary intake obtained 24 h recall at the hospital with the recall on the phone, there were no significant differences in the entire patient group. However, when stratifying the population by gender, there was a significant higher intake of energy and carbohydrates (including fibre) from the recall performed by phone compared to the recall at the hospital among women. We have chosen to do the second 24 hour dietary recall by phone,
as this was more practical and because a Norwegian study have investigated whether there is a difference in dietary intake reported face to face and by phone, found no difference in reported intake in the different methods of conducting the interview (50). One possible explanation for the difference in energy intake in the present study may be caused by the patient being more disciplined the day before their hospital visit than what they usually are. Research is required on the dietary behaviour of patients with chronic diseases in relation to appointments in health services.

5.1.4 Other findings
There was only a small proportion of the patients that were identified in nutritional risk by NRS 2002 and MUST in the present study. The nutritional status of other patients with CKD has been investigated in projects preceding the present one, applying similar methods. Thus, prevalence rates of obesity, sarcopenia and nutritional risk can be compared among these groups. Welland reported among ESRD patients treated with haemodialysis, a prevalence of 33 % in nutritional risk (77). In pre-dialysis patients with CKD, 3 % of the patients were reported to be at nutritional risk and 16 % were reported to have sarcopenia (78). All together, these results show that there is cause for concern on the nutritional status of renal patients at HUS and that more attention should be paid to nutritional status.

A major proportion of the study population reported receiving dietary advice, and most of these patients received advice from a clinical dietitian. However, most of these patients received advice from a clinical dietitian once, at a seminar about management of daily life with kidney disease prior to transplantation. Dietary advice given in the long run after kidney transplantation was not prevalent in the study population. This might have been favourable, as nutritional disturbances related to kidney transplantation may appear gradually and over time after transplantation due to side effects of immunosuppresion, e.g. sarcopenia and osteoporosis.

5.2 Strengths and limitations
The design for this study was a cross-sectional observational study, which in itself bring some strengths and limitations. This kind of study design is useful when the object of the study is to investigate exposures and outcomes, which was the aim of this study. However, cross-sectional studies are not suitable to give information about causality (79). A longitudinal study would be more appropriate for this purpose, but this was beyond the scope of this
master thesis. However, there are also advantages with a cross-sectional study, in term of minimal loss of follow-up and often being easy and inexpensive to perform.

5.2.1 Strengths

The assessment of nutritional status in this study is based on a number of different methods, which can be considered as a particular strength of the study. Conditions as sarcopenia and central obesity would not be identified by measurements of e.g. weight and height alone. The measurements were standardized and performed by a trained examiner, thus the results can be compared with other results, e.g. the previous studies performed on CKD patients and ESRD patients on haemodialysis at HUS.

By using a registry for the invitation process for the study, it was ensured that all patients were invited to participate in the study. The use of a digital questionnaire minimized the risk of type errors, and a large proportion of the data was typed directly into the questionnaire as the patient was interviewed and was converted to SPSS without typing the values again. Most of the data that was typed into the questionnaire after the interview, e.g. calculated dietary intake and clinical chemical results were double checked to ensure minimisation of type errors.

In this study, two nutritional screening tools were applied with purpose of identifying nutritional risk in the study population. NRS 2002 was used by previous studies on kidney patients at HUS, and was therefore included in the present study. As NRS 2002 is adjusted for hospitalized patients, it is not entirely correct to use this tool in identification of nutritional risk in a population of outpatients. MUST was designed for this purpose and may therefore be more accurate in this setting.

The prevalence of underreporting was improved when including both 24 h recalls compared to estimating underreporting in just one of the recalls, and information on dietary intake in kidney transplant patients in this study will therefore be more accurate than if only one 24 h recall was used for this assessment. By obtaining two recalls it was also possible to assess whether there was a difference in dietary intake in the day prior to the hospital appointment compared to an occasional day.

5.2.2 Limitations

The limited size of the study population may be a limitation of the study, especially when stratifying the population in groups by e.g. gender and BMI-categories.
Concerning the study population size, there was no formal calculation of sample size beforehand, but we had an aim of including at least 100 patients. This aim was not met, and the population size ended up at 72 patients, representing 29% of the eligible patients. However, a comparison of age and sex of included patients showed that the included patients are representative for this patient group (Table 4). In general, there was a positive attitude concerning participation among the patients that were asked about participation. The impression was that many patients declining participation did not have the time for participating that day or that they had participated in other studies. Of course, there were some patients that did not want to participate in the study as well. The relative high number of not asked patients can partly be explained of time constraints, as the duration of the interview for the study endured for a longer time than the routine examination at the nephrologist. In addition, there was a strike among Norwegian physicians the first six weeks of the inclusion of patients, and leading to reduced activity in the nephrology outpatient clinic.

The assessment methods included in the study were standardized as much as possible. However, some standardization goals were not met. There was for example no routine of toilet visits in advance of BIA and weight measurements. Most of the patients were not fasting, which would be preferred to get measurements like waist circumference, weight and BIA as accurate as possible.

Regarding routine samples of blood and urine, many patients took their samples in advance of their physician appointments, this made it impossible to take the study samples simultaneously. Some patients were not fasting when giving blood for routine samples, and the high prevalence of serum glucose exceeding reference cut off may be partly biased due to this.

5.3 Clinical implications

The findings of nutritional status in kidney transplant patients indicate need of nutritional care and education. The high prevalence of overweight and obesity as well as other adverse metabolic effects due to immunosuppressive medication should be paid attention to. There is need for more closely follow-up of nutritional status and improved treatment of disturbances of nutritional status. Inclusion of a clinical dietitian in the staff of the nephrology outpatient clinic may be favourable for patients with kidney disease, including kidney transplant patients.
Also, the number of non-medical dietary restrictions may be a reason for concern, limiting the dietary variation of patients. The sample size, however, was not high enough to evaluate this in more detail. As the patient group has increased risk of CVD, osteoporosis and sarcopenia, nutritional advice to prevent or minimize these factors should also take this into consideration. We did not investigate the long term consequences of nutritional status in this patient group. However, it would be worth to investigate the long term health effect of sarcopenia, obesity or nutritional risk in this patient group.

5.4 Future research
The need of more studies on the assessment of nutritional status in kidney transplant recipients is clear, as there are only a few studies existing today. Both studies with a cross-sectional design including a larger study population and studies with a longitudinal design may be useful in the investigation of nutritional status in kidney transplant patients. Intervention studies aiming on prevention of malnutrition, both as undernutrition/nutritional risk and overnutrition (overweight and obesity), sarcopenia may be of interest in this patient group, as there is a high prevalence of all mentioned above.

5.5 Conclusion
Overweight and obesity was highly prevalent in kidney transplant recipients. There was a high prevalence of sarcopenia in the patient group, and the proportion of patients with both sarcopenia and overweight or obesity was high. Medical nutrition therapy and assessment of nutritional status may be necessary in this patient group, with focus on a healthy weight, lipid status and bone and muscle status. More and improved nutritional treatment is required in this patient group, also in the long run after kidney transplantation.
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7 APPENDIX
1. Ethical approval (REC)
2. Study protocol
3. Information sheet and informed consent
4. Questionnaire
5. Number of patients according to measurement methods
6. Reference areas for blood- and urine analysis
7. NRS 2002
8. MUST
Appendix 1: Ethical approval (REC)

Jutta Dierkes
Klinisk Institutt 1

2014/1790 Underernæring ved pasienter med nyresvikt

Forskningsansvarlig: Universitetet i Bergen, Klinisk Institutt 1
Prosjektleder: Jutta Dierkes

Vi gir til søknad om forhandlingsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK vest) i møtet 23.10.2014. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10, jf. forskningsetikkloven § 4.

Prosjektomtale
Hovedformålet med denne studien er å øke kunnskapsnivået om ernæringsstatus blant pasienter med nyresvikt og sammenhengen mellom ernæringsstatus og risiko for å utvikle hjert- og karsykdom. 300 pasienter med ulik grad og drøm av nyresvikt skal inkluderes og blir spurt om matinnat og restriksjoner i forbindelse med matinnat ved baseline. Antropometriske, biokjemiske og kliniske målinger tas til lege, blant annet om kalsifiseringsstendensen i blodet. Forskergruppen ønsker å følge opp pasientene longitudinelt.

Vurdering

Søknad/protokoll
Komiteen mener at prosjektet er viktig. Komiteen har ingen merknader til søknad eller protokoll, og anser derfor prosjektet som forsvarlig å gjennomføre.

Forskningsbiobank

Det er oppgitt i informasjonsskrivet til deltakerne at opplysninger fra intervjuer og sykehusopphold også skal inkluderes i forskningsbiobanken. Komiteen legger imidlertid til grunn at kun grunnleggende metadata kan oppbevares sammen med det biologiske materialet i forskningsbiobanken.


Informasjonsskriv
Informasjonsskrivet mangler opplysninger om at forskningsbiobanken er en generell forskningsbiobank og at man da også samtykker til at materialet kan brukes i fremtidige prosjekter. Komiteen setter som vilkår at
informasjonsskrivet revideres ut fra denne merknaden og ettersendes REK for arkivformål.

Vilkår

- Revidert informasjonsskriv sendes til REK vest for arkivformål.

Vedtak

REK vest godkjenner prosjektet på betingelse av at ovennevnte vilkår tas til følge.

Sluttmelding og søknad om prosjektendring
Prosjektleder skal sende sluttmelding til REK vest på eget skjema senest 31.03.2020, jf. hfl. § 12. Prosjektleder skal sende søknad om prosjektendring til REK vest dersom det skal gjøres vesentlige endringer i forhold til de opplysninger som er gitt i søknaden, jf. hfl. § 11.

Klageendang

Med vennlig hilsen

Angar Berg
Prof. Dr. med
Komiteleder

Trine Anikken Larsen
førstekonsulent

Kopi til: postmottak@uib.no
Appendix 2: Study protocol

ASSESSMENT OF NUTRITIONAL STATUS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Professor Jutta Dierkes, Department of Clinical Medicine, Clinical Nutrition, UiB.  
Professor Hans-Peter Marti, Department of Clinical Medicine, Nephrology, UiB

Introduction
Patients with chronic kidney disease often suffer from malnutrition, due to dietary restrictions, losses of small molecules due to hemodialysis (Heinz et al., 2008) or due to uremic toxins. Thereby, etiology and consequences of protein energy wasting (PEW) in chronic kidney disease (CKD) are manifold, as shown below in Figure 1 (Alp Ikizler et al. Kidney Int 2013).

![Figure 1. Etiology and Consequences of protein energy wasting](image)

In addition, CKD patients suffer from accelerated vascular disease. Importantly, the relationship between the nutritional status and vascular calcification is poorly understood. The extent of vascular calcification represents a known predictor of cardiovascular events and mortality risk in patients with CKD.

Recently, a novel in vitro blood test that provides an overall measure of calcification propensity by monitoring the maturation time (T50) of calciprotein particles in serum was described (Smith ER et al, JASN, 2014). In that study, increased serum calcification propensity was independently associated with progressive aortic stiffening and an augmented mortality risk.

Main hypotheses:
1) Patients at Haukeland University Hospital with chronic kidney disease (CKD), including patients who have undergone kidney transplantation or who are on maintenance dialysis, demonstrate multiple signs of malnutrition and related vascular disease.
2) Malnutrition is associated with increased mortality in patients with chronic kidney disease

Objectives
1) To evaluate the nutritional status of the CKD population at Haukeland University Hospital
2) To assess the degree of vascular disease of these CKD patients in relation to their nutritional status by measurements of pulse wave velocity (PWC) and calcification propensity in serum

3) To investigate the association of nutritional status, renal disease progression, cardiovascular disease and mortality in patients with chronic kidney disease

Description of work and role of participants

Patients with chronic kidney diseases of various degrees/stages will be included. At baseline, nutritional status, disease history, and clinical measurements will be performed. These measurements will be used for a cross-sectional investigation of the association of nutritional status and vascular stiffness. In addition, the patients will be followed longitudinally to investigate the role of nutritional status and vascular stiffness on disease progression and mortality.

Interviews and anthropometric measurements will be taken by master students in clinical nutrition. Patients with chronic kidney disease, patients with end-stage renal disease who are treated with hemodialysis and after transplantation will be included. Dietary assessment will focus on dietary restrictions and assess dietary intake by 24 h recalls. Body composition will be measured by skinfold thickness and bioelectrical impedance measurements. The students will be also responsible for measurement of physical function by hand grip strength and knee extension. Health personnel will draw blood samples from patients for assessment of nutritional and biochemical variables. Respective analyses of blood and urine will be conducted both by routine hospital laboratories and by research laboratories.

Pulse-wave velocity will be measured by ultrasound through collaboration with the Department of Cardiology (Prof. Eva Gerds).  

Outcomes:
The primary outcome variable is the nutritional status in the CKD patient cohort

Secondary outcome variables include:
- Degree of vascular stiffness and its relation to nutritional status
- Calcification propensity and its relation to nutritional status
- Nutritional status and vascular stiffness as risk factors of mortality

Study procedures:

Procedures related to the study include at baseline a structured interview, a clinical examination, anthropometric measurements followed by blood and urine (if applicable) sampling. These tests include the analyses of the serum calcification propensity.

The patients will undergo measurement of pulse wave velocity by ultrasound. Thereafter, the patients will be followed longitudinally to assess long-term morbidity and mortality.

Inclusion criteria:

Patients > 16 years who are able to consent and who are willing to participate in the study. Their estimated life expectancy should be more than 6 months.
Exclusion criteria:
Children and patients who lack the cognitive function to understand the study objectives are excluded. Patients with a missing informed consent cannot be included.

Power calculation
We aim to include all eligible patients with chronic kidney disease treated at Haukeland University Hospital, as there is virtually no data on the association of nutritional status, vascular stiffness and mortality. Therefore, it is difficult to provide a valid power calculation. Earlier studies with a sample size of about 100 patients showed significant effects of individual risk factors on mortality (Dierkes et al., 2000). Therefore, we aim to include about 100 patients of each stage of chronic kidney disease (pre-dialysis, dialysis, transplantation).

Feasibility
The research group has ample experience with clinical nutrition (Prof. Jutta Dierkes) and with clinical trials (Prof. Jutta Dierkes and Prof. Hans-Peter Marti).

Safety and patients' issues
The study does not put the patients at risk, as blood samples are taken from routine blood collections. Measurement of body composition and anthropometry are non-invasive and safe for the patients. Measurement of pulse-wave velocity is non-invasive and safe. All data will be stored and processed after de-identification, to ensure that no conclusion can be drawn on individual patients. No individual patient data will be published or made available for persons who are not in charge of the study. In case of life-threatening results of clinical tests, the physician in charge of the patient will be immediately informed about the result.

Role of participants

Principal investigators
Prof. Jutta Dierkes (clinical nutrition) and Prof. Hans-Peter Marti: Writing of the study protocol, supervision of the trial, supervision of master students, writing of reports.

Master students (three)
Assignments include study organization, conduction of study procedures (dietary assessment, anthropometry, disease history, analysis of blood samples and processing of questionnaires (related to secondary outcomes).

Dissemination of the results
The results will be published in high-impact peer-reviewed international journals within the fields of nutrition and nephrology, including internal medicine. Key findings will be submitted as abstracts to relevant conferences internationally and nationally. Results will be made available to the general public, care professionals and students in nutrition and medicine at the University of Bergen during lectures and courses.
References


Ernæringsstatus hos pasienter med nyresvikt

Forespørsel om deltakelse i forskningsprosjektet

"Underernæring hos pasienter med nyresvikt"

Bakgrunn og hensikt
Dette er et spørsmål til deg om å delta i en forskningsstudie i regi av Klinisk institutt ved Universitet i Bergen og Haukeland Universitetssykehus. Hensikten med studien er å kartlegge ernæringsstatus hos pasienter med ulik grad og årsak til nyresvikt. Pasienter med nyresvikt har ofte dårlig ernæringsstatus pga. sykdom, behandling og redusert matlyst. I tillegg kan matvarerestriksjoner som en del av behandlingen begrense matintakket. Det er antatt at dårlig ernæringsstatus påvirker sykdomstillstanden negativt. Det er ukjent hvordan ernæringsstatus påvirker tilleggsykkermer som ofte forekommer med nyresvikt, som hjertekarsykdom.

Hva innebærer studien?

Mulige fordeler og ulemper
Intervju og målinger vil ta ca. 2 timer. For dialysepasienter vil dette foregå under dialysebehandling. Hvis noen resultater viser uvanlige verdier blir lege umiddelbart informert.

Hva skjer med prøvene og informasjonen om deg?

Frivillig deltakelse

Ytterligere informasjon om studien finnes i kapittel A – utdypende forklaring av hva studien innebærer.
Ytterligere informasjon om biobank, personvern og forsikring finnes i kapittel B – Personvern, biobank, økonomi og forsikring.

Samtykkeerklæring følger etter kapittel B.
Kapittel A- utdypende forklaring av hva studien innebærer

Kriterier for deltakelse er at du er en pasient med nyresvikt, eldre enn 16 år og har samtykkekompetanse.

Bakgrunnsinformasjon om studien
- Hensikten med studien er å kartlegge ernæringsstatus hos pasienter med nyresvikt og å undersøke på hvilke måte ernæringsstatus påvirker helsetilstand og sykdomsutvikling.

Følgende undersøkelser du må gjennom i studien:
- blodprøver, urinprøver (hvis mulig), veining, måling av høyde, blodtrykk, ultralyd for å måle blodets hastighet gjennom kroppen, gripe, knekkstyrke, måling av muskelmasse ved hjelp av biotimpedansmålning, hudføldtykkelsesmålning, kostholdsintervju og intervju ang matintak
- Alle undersøkelser skjer før eller under dialysebehandling (i pasienter med dialysebehandling) eller ved rutinemessig besøk på Haukeland Universitetssykehus.

Mulige fordeler og ubehag
- Undersøkelser tar ca. 2 timer
- Du må ta ekstra blodprøver i tillegg til de du tar rutinemessig på sykehuset

Pasienten vil bli orientert så raskt som mulig dersom ny informasjon blir tilgjengelig som kan påvirke pasientens villighet til å delta i studien.

Pasienten skal opplyses om mulige beslutninger/situasjoner som gjør at deres deltagelse i studien kan bli avsluttet tidligere enn planlagt.

Kapittel B - Personvern, biobank, økonomi og forsikring

Personvern
Opplysninger som registreres om deg er helseopplysninger fra din journal på Haukeland Universitetssykehus. I tillegg vil vi innhente informasjon om følgende: vekt, høyde, blodtrykk, pulse wave hastighet, blodprøver, urinprøver, fysisk funksjon, kosthold, kroppssammensetning. Formålet er å kontrollere at studieopplysningene stemmer overens med tilsvarende opplysninger i din journal. Alle som får innsyn har taushetsplikt.

Universitetet i Bergen ved administrerende direktør er databehandlingsansvarlig.

Biobank
Ernæringsstatus hos pasienter med nyresvikt – Kapittel A og B

Utlevering av materiale og opplysninger til andre
Hvis du sier ja til å delta i studien, gir du også ditt samtykke til at prøver og avidentifiserte opplysninger utleveres til samarbeidende universiteter i Europa og USA. Dette kan være land med lover som ikke tilfredsstiller europeisk personvernlovgivning.

Rett til innsyn og sletting av opplysninger om deg og sletting av prøver
Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

Økonomi
Studien og biobanken er finansiert gjennom forskningsmidler fra Klinisk institutt 1 ved Universitetet i Bergen.

Forsikring
Ved deltakelse i studien har du rettigheter i forhold til Pasientskadeerstatningsloven.

Informasjon om utfallet av studien
Som deltaker i studien har du rett til å få informasjon om resultatet av studien.

Samtykke til deltakelse i studien

Jeg er villig til å delta i studien

--------------------------------------------------
(Signert av prosjektdektaker, dato)

Jeg bekrefter å ha gitt informasjon om studien

--------------------------------------------------
(Signert, rolle i studien, dato)
## Appendix 4: Questionnaire

<table>
<thead>
<tr>
<th>ID</th>
<th>Sykdomsblide</th>
<th>Kosthold og livsstil</th>
<th>Fysisk aktivitet</th>
<th>Dietary record</th>
<th>Antropometri</th>
<th>Ernæringscreening</th>
<th>Urin- og blodprøver</th>
</tr>
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<table>
<thead>
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<th>Fødselsdato</th>
<th>Alder</th>
<th>Kjønn</th>
<th>Etnisitet</th>
<th>Sivilstatus</th>
<th>Utdannelse</th>
<th>Telefonnummer</th>
<th>Ønsker masteroppgaven tilsendt</th>
<th>Ønsker tilbakemelding om egne resultater</th>
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<tbody>
<tr>
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<thead>
<tr>
<th>ID</th>
<th>Sykdomsblide</th>
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</table>

<table>
<thead>
<tr>
<th>Årsak til nyresydom</th>
<th>Dato diagnose</th>
<th>Dato første dialyse</th>
<th>Levende donor?</th>
<th>Dato transplantasjon 2</th>
<th>Dialyse mellom transplantasjonene?</th>
<th>Medikamenter</th>
</tr>
</thead>
<tbody>
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<table>
<thead>
<tr>
<th>BT</th>
<th>Dato BT</th>
<th>Ant innleggelser siste Året</th>
<th>Ant medisiner</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>
### Sykdomsblide

<table>
<thead>
<tr>
<th>ID</th>
<th>Sykdomsblide</th>
<th>Kosthold og livsstil</th>
<th>Fysisk aktivitet</th>
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<th>Antropometri</th>
<th>Ernaeringsscreening</th>
<th>Urin- og blodprøver</th>
</tr>
</thead>
</table>

- **Motatt kostråd ved nyresykdom?**
  - Fra hvem?  

- **Nåværende kostrestriksjoner?**
  - Hvilke restriksjoner?  
  - Vann:  
  - Salt:  
  - Fosfat:  
  - Protein:  
  - Kalium:  
  - Other:  

- **Kosttilskudd?**
  - Hvilke tilskudd?  
  - Multivitamin:  
  - Vit D/Ca:  
  - Fiskeolje:  
  - Multimineral:  
  - Vit D/Ca:  
  - Næringssøkning:  
  - Trant:  
  - Other:  

- **Alkoholfrekvens**
  - Antall enheter  

- **Røyker du?**
  - Antall røyk/dag  

- **Har du tidligere røkt?**
  - Når?  

- **Tygevansker?**
  - Svelgevansker?  

### Fysiologisk aktivitet

- **Hvor ofte driver du med mosjon?**  

- **Hvor hardt mosjonerer du?**  

- **Hvor lenge mosjonerer du?**  

- **Har du 30 minutters aktivitet hver dag?**  

- **Hvor mange timer sitter du i ro i løpet av en dag?**  

- **Hvordan vil du beskrive jobb med tanke på aktivitet?**  

### Intake

<table>
<thead>
<tr>
<th>Dato</th>
<th>Ukedag</th>
<th>Weekday</th>
<th>Special</th>
<th>Inntak siste uke</th>
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<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

**Intake**

- **Telefon**
  - Water:  
  - Fat:  
  - E%:  
  - Kcal:  
  - Mettet fett:  
  - Transfett:  
  - MUFA:  
  - PUFA:  
  - CHO:  
  - KH:  
  - Protein:  
  - E%:  
  - Fiber:  
  - Salt:  
  - Alcohol:  

[Close]
### Sykdomsblide

<table>
<thead>
<tr>
<th>ID</th>
<th>Kosthold og livsstil</th>
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</tbody>
</table>

#### Åge reader
- Gripstyrke dominant hånd
  - 1 Max
  - 2 Gjennomsnitt
  - 3
- Gripstyrke ikke-dominant hånd
  - 1 Max
  - 2
  - 3
- Kneestensjon ikke-dominant ben
  - 1 Gjennomsnitt
  - 2
  - 3
- Resitens
- Reaktans
- Phase angle
- Kommentar

### Ødemer

<table>
<thead>
<tr>
<th>ID</th>
<th>Kosthold og livsstil</th>
<th>Fysisk aktivitet</th>
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</tbody>
</table>

#### Overarmssømmrets
- Hudfoldstykkeelse triceps
  - 1 Gjennomsnitt
  - 2
  - 3 MUAMC
- Hudfoldstykkeelse biceps
  - 1 Gjennomsnitt
  - 2
  - 3
- Midjeomkrets
  - 1 Gjennomsnitt
  - 2
  - 3
- Vekt
  - kg
- Vektutvikling
- Høyde
  - m
- BMI
  - Kommentar

#### Ødemer

<table>
<thead>
<tr>
<th>ID</th>
<th>Kosthold og livsstil</th>
<th>Fysisk aktivitet</th>
<th>Dietary record</th>
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</tbody>
</table>

### MUST

- Score BMI
- Score vektfall
- Score matinntak
- Totalscore

<table>
<thead>
<tr>
<th>ID</th>
<th>Kosthold og livsstil</th>
<th>Fysisk aktivitet</th>
<th>Dietary record</th>
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</table>

### Urinstik

<table>
<thead>
<tr>
<th>ID</th>
<th>Kosthold og livsstil</th>
<th>Fysisk aktivitet</th>
<th>Dietary record</th>
<th>Antropometri</th>
<th>Ernæringsscreening</th>
<th>Urin- og blodprøver</th>
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</tbody>
</table>

#### pH
#### Glukose
#### Leukocytter
#### Nitrit
#### Protein
#### Blod

#### Dato rutineprøver
- Kreatinin
- eGFR
- Hb
- Leukocytter
- Trombocytter
- HbA1C
- Glukose
- CRP
- ALAT
- AST
- ALP
- GT
- Natrium
- Kalium
- Kalsium
- Fosfat
- Bilirubin
- Albumin
- U-leu
- U-nitrit

#### U-prøver
- U-pH
- U-protein
- U-Hb
- U-glukose
- U-ketoner
- U-kreatinin
- U-protein (mg/mmol kreat)
- U-albumin (mg/mmol kreat)
Appendix 5: Number of patients according to measurement methods

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients</th>
<th>Male patients</th>
<th>Female patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total population</strong></td>
<td>72</td>
<td>51</td>
<td>21</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>71</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>Creatinine</td>
<td>61</td>
<td>41</td>
<td>20</td>
</tr>
<tr>
<td>eGFR</td>
<td>71</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>Albumin</td>
<td>58</td>
<td>39</td>
<td>19</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>59</td>
<td>39</td>
<td>20</td>
</tr>
<tr>
<td>CRP</td>
<td>60</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>Leucocytes</td>
<td>59</td>
<td>39</td>
<td>20</td>
</tr>
<tr>
<td>Uric acid</td>
<td>59</td>
<td>40</td>
<td>19</td>
</tr>
<tr>
<td>Urea</td>
<td>61</td>
<td>41</td>
<td>20</td>
</tr>
<tr>
<td>Glucose</td>
<td>54</td>
<td>37</td>
<td>17</td>
</tr>
<tr>
<td>U-albumin</td>
<td>55</td>
<td>37</td>
<td>18</td>
</tr>
<tr>
<td>U-creatinine</td>
<td>55</td>
<td>37</td>
<td>18</td>
</tr>
<tr>
<td>U-protein</td>
<td>55</td>
<td>37</td>
<td>18</td>
</tr>
<tr>
<td>HbA1c</td>
<td>47</td>
<td>33</td>
<td>14</td>
</tr>
<tr>
<td>Triceps skinfold</td>
<td>71</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>Biceps skinfold</td>
<td>71</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>MUAC</td>
<td>71</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>MUAMC</td>
<td>71</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>MUAMA</td>
<td>71</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>71</td>
<td>50</td>
<td>21</td>
</tr>
<tr>
<td>BIA</td>
<td>69</td>
<td>48</td>
<td>21</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>69</td>
<td>48</td>
<td>21</td>
</tr>
<tr>
<td>24 h recall phone</td>
<td>65</td>
<td>48</td>
<td>17</td>
</tr>
</tbody>
</table>

*Measurement methods not mentioned in the table above were conducted on the total study population.*
### Appendix 6: Reference ranges for blood- and urine analysis according to analyseoversikten.no

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Reference range</th>
</tr>
</thead>
</table>
| **B-Haemoglobin** | Male: 13.4-17.0 g/dL  
Female: 11.7-15.3 g/dL |
| **B-Leucocytes** | 3.5-11.0 $10^9$/L |
| **S-Glucose**   | 4.0-6.0 mmol/L (fasting) |
| **HbA1c**       | ≤ 6.5 (%) |
| **S-Albumin**   | < 39 years: 39-50 g/L  
40-69 years: 39-48 g/L  
> 70 years: 36-48 g/L |
| **CRP**         | < 5 mg/L |
| **S-Urea**      | Male: < 50 years: 3.2-8.1 mmol/L  
> 50 years: 3.5-8.1 mmol/L  
Female: < 50 years: 2.6-6.4 mmol/L  
> 50 years: 3.1-7.9 mmol/L |
| **S-Creatinine**| Male: 60-105 umol/L  
Female: 45-90 umol/L |
| **S-Uric acid** | Male: 230-480 umol/L  
Female: < 50 years: 155-350 umol/L  
≥ 50 years: 155-400 umol/L |
| **U-Albumin**   | 0-2.5 mg/mmol creatinine |
| **U-Creatinine**| 2.2-35.4 mmol/L |
| **U-Protein**   | < 20 mg/mmol creatinine |
### God ernæringspraksis – vurdering av ernæringsmessig risiko

#### Screening av ernæringsmessig risiko (NRS 2002)

**Innledende screening**

<table>
<thead>
<tr>
<th></th>
<th>JA</th>
<th>NEI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Er BMI &lt; 20,57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Har pasienten tappt vekt i løpet av de siste ukene?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Har pasienten hatt reduksjon i næringsinnhold de siste ukene?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Er pasienten alvorlig syk.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ja: Dersom svaret er JA på noen av disse spørsmålene, gjennomføres hovedvurderingen på neste side.
Nei: Dersom svaret er NEI på alle spørsmålene, gjennomføres innledende screening ukselget.
Genom pasienten skal gjennomgå planlagt større kirurgi, skal en forebyggende ernæringsplan vurderes for å unngå asosiert ernæringsrisiko.

#### Hovedscreening – vurdering av risikograd

<table>
<thead>
<tr>
<th>Score</th>
<th>Ernæringsstilstand</th>
<th>Sykdommens alvorlighetsgrad</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal ernæringsstilstand</td>
<td>0: Ikke syk</td>
</tr>
<tr>
<td>1</td>
<td>Vekttaug 5-10 % siste 3 måned.</td>
<td>1: En pasient med kronisk sykdom eller en pasient som har gjenomgått et mindre kirurgisk ingrep. Studier er gjort på pasienter med levercirrose, nyrevekt, kronisk lungesykdom, kreiaplusses, pasienter med osfisk narv og fraktur, etter helikoptertjekking og laparoskopiske operasjoner.</td>
</tr>
<tr>
<td>2</td>
<td>Vekttaug 10-15 % siste 3 måned.</td>
<td>2: En pasient med tydelig reduksjon tilsetnad på sin sykdom. Studier er gjort på pasienter med alvorlig pneomoni, inflamatorisk tarmkydder med følger, skritt lymfevekt, større kirurgiske ingrep som kolektomi og gastrectomi, tumor, aneviematosseknappe og gjentatte operasjoner.</td>
</tr>
<tr>
<td>3</td>
<td>Vekttaug &gt; 15 % siste 3 måned.</td>
<td>3: En pasient som er alvorlig syk. Studier er gjort på pasienter med store innspekser, alvorlig septis, intensivpaspasienter (APACHE 100, bennangtrans-plantasjoner, store osteokluder, brannskader &gt; 40 % og alvorlig akutt pancreatitis.</td>
</tr>
</tbody>
</table>
Appendix 8: MUST

**Step 1**
BMI score

- BMI kg/m²
  - >20 (>30 Obese) = 0
  - 18.5-20 = 1
  - <18.5 = 2

**Step 2**
Unplanned weight loss in past 3-6 months

- %
  - <5 = 0
  - 5-10 = 1
  - >10 = 2

**Step 3**
Acute disease effect score

- If patient is acutely ill and there has been or is likely to be no nutritional intake for >5 days, Score 2

**Step 4**
Overall risk of malnutrition

Add scores together to calculate overall risk of malnutrition.
- Score 0 Low Risk
- Score 1 Medium Risk
- Score 2 or more High Risk

**Step 5**
Management guidelines

**0 Low Risk**
Routine clinical care
- Repeat screening
- Hospital - weekly
- Care Homes - monthly
- Community - annually for special groups (e.g., those >75 yrs)

**1 Medium Risk**
Observe
- Document dietary intake for 3 days
- If adequate - little concern and repeat screening
- Hospital - weekly
- Care Home - at least monthly
- Community - at least every 2-3 months
- If inadequate - clinical concern, follow local policy, set goals, improve and increase overall nutritional intake, monitor and review care plan regularly

**2 or more High Risk**
Treat
- Refer to dietician, Nutritional Support Team or implement local policy
- Set goals, improve and increase overall nutritional intake
- Monitor and review care plan
- Hospital - weekly
- Care Home - monthly
- Community - monthly
* Unless detrimental or no benefit is expected from nutritional support e.g., imminent death

All risk categories:
- Treat underlying condition and provide help and advice on food choices, eating and drinking when necessary.
- Record malnutrition risk category.
- Record for special diets and follow local policy.

Obesity:
- Record presence of obesity. For those with underlying conditions, these are generally controlled before the treatment of obesity.

Re-assess subjects identified at risk as they move through care settings.

See the ‘MUST’ Explanatory Booklet for further details and the ‘MUST’ Report for supporting evidence.