Effect of immunosuppressive treatment of glomerulonephritis on nutritional status, body composition and musculoskeletal system

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INTRODUCTION

Glomerulonephritis (GN) is a common name for numerous renal disorders caused by immune system dysregulation, most often associated with proteinuria and leached red blood cells in the urine sediment. Damage to the glomerular filtration membrane in the course of glomerulopathy leads to the loss of plasma proteins in the urine, i.a. albumins, proteins of the hemostasis system, transport proteins, hormones, enzymes, and, as a result, to numerous complications, including metabolic disorders, coagulopathy, malnutrition, muscle weakness, bone disorders, and immunity disorders. Untreated GN may lead to impaired renal function, up to end-stage chronic kidney disease requiring renal replacement therapy - dialysis or kidney transplantation.

The basis of GN treatment is nephroprotection, including angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in the maximal tolerated dose, proper blood pressure control, limiting salt and moderate protein intake. In some cases, especially in patients with persistent proteinuria > 1 g/day and preserved glomerular filtration, treatment must be supplemented with immunosuppression based on steroid therapy (glucocorticosteroids, corticosteroids) in monotherapy or, depending on the histopathological diagnosis, supplemented with immunosuppressive drugs: cyclophosphamide, calcineurin inhibitors (cyclosporin, tacrolimus) and, increasingly, biological drugs (rituximab). Such treatment should result in complete or partial remission, defined as a resolution or reduction of proteinuria and an improvement or stabilization of glomerular filtration.

IgA nephropathy is one of the most frequently diagnosed GN, the therapy of which begins with corticosteroids and, in case of persistent disease, is supplemented with other immunosuppressive drugs. The basis of its treatment is steroid therapy according to the Pozzi scheme, which includes three pulses of methylprednisolone in the 1st, 3rd, and 5th month of treatment in a cumulative dose of 9 g, supplemented with oral preparations of prednisone 0.5 g/kg of body weight every other day for 6 months (between iv infusions).Both the disease and the applied therapy can cause numerous metabolic disorders, complications, and side effects. Long-term glucocorticosteroid therapy may be associated with numerous side effects, including increased protein catabolism, skeletal muscle weakness, remodeling and excessive adipose tissue growth, osteoporosis, and glucose and lipid metabolism disorders.

This study aims to evaluate the impact of nephroprotective treatment and steroid therapy on the nutritional status, body composition and muscle strength of patients with biopsy confirmed glomerulonephritis.

STUDY GROUP

The study will include 40 patients aged 18-65 with newly diagnosed IgA nephropahy (based on the histopathology results of a core-needle kidney biopsy)

From the Department of Nephrology Barlicki Memorial Teaching Hospital in Łódź between 01/06/2022 - 30/05/2025, qualified per Polish Society of Nephrology and KDIGO 2021 guidelines to nephroprotective treatment or to nephroprotective treatment with a 6-month immunosuppressive therapy regimen in Pozzi scheme.

Study design:
- Visit 0 (W0) - a visit starting before the initiation of nephroprotective treatment or steroid therapy
- Visit 1 (W1) - 8 weeks (+- 7 days) after W0
  before administration of the 2nd cycle of methylprednisolone (Pozzi scheme)
- Visit 2 (W2) - 16 weeks (+-7 days) after W0
  before administration of the 3rd cycle of methylprednisolonein (Pozzi scheme)
- Visit 3 (W3) - final visit - 24 weeks (+- 14 days) after W0
  at the end of the 6-month treatment cycle

METHODS

The primary point will be the proportion of patients with a change in body composition defined as a 5% decrease in lean tissue mass in the bioelectrical impedance over 6 months. Additional endpoints will be changes in muscle strength, physical capacity, metabolic profile parameters, and quality of life.

Procedures:
- Medical history including comorbidities and concomitant medications
- Anthropometric data - sex, age, height, weight, waist, hip, arm circumference, blood pressure
- Body composition analysis with bioelectrical impedance - Body Composition Monitor Fresenius™ - estimation in unique, 3 compartment model adjusted to patients with renal disease and fluid retention, including lean tissue mass, fatty tissue mass and overhydration

- Muscle strength assessment - analysis of the isometric strength of the six muscles/muscle groups of the lower limbs using a hand-held dynamometer
- Assessment of nutritional status (Malnutrition-Inflammation Score), diet (Staring The Conversation Questionnaire), appetite (Council on Nutrition Appetite Questionnaire), level of physical activity (General Practice Physical Activity Questionnaire)
- Assessment of the subjectively perceived quality of life (Short Form 36)
- From routine laboratory tests performed during hospitalization: complete blood count, lipid profile, serum concentration of: glucose, HBA1C, potassium, sodium, CRP, aminotransferases, urea, creatinine, albumin, total protein, TSH; general urine test; loss of protein in the 24-hour urine collection
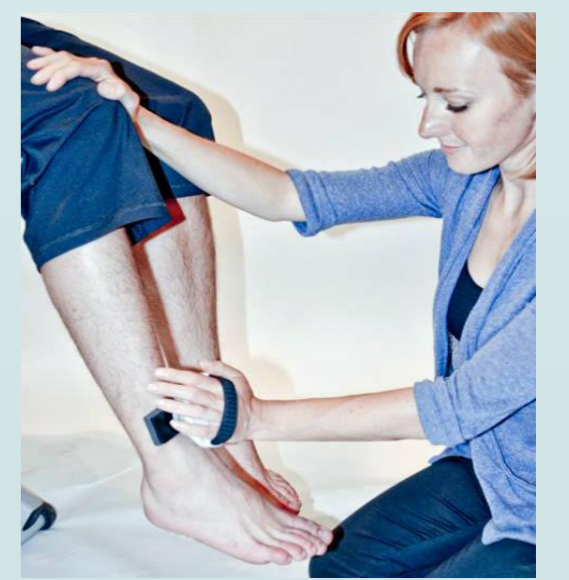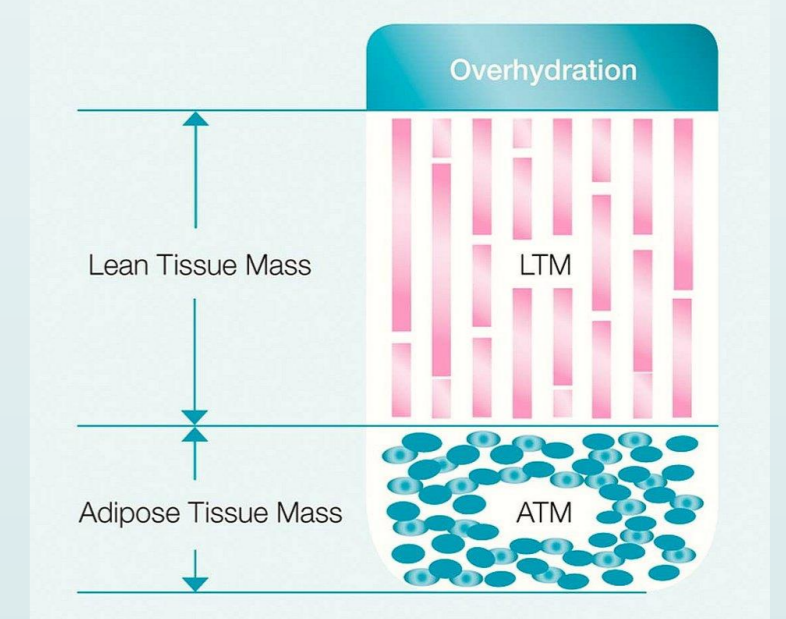
POPULATION ANALYSIS

We analyzed 781 histopathological reports of renal biopsies performer in Caucasian adults in Lodzkie Voivoidship between 01.04.2018 - 30.04.2022; 675 were performer in native kidneys, out of which 587 were performer for a first time diagnosis; 506 (81.47%) revealed any glomerular changes, including 302 (59.68%) of primary GN and 180 (35.57%) of secondary GN.
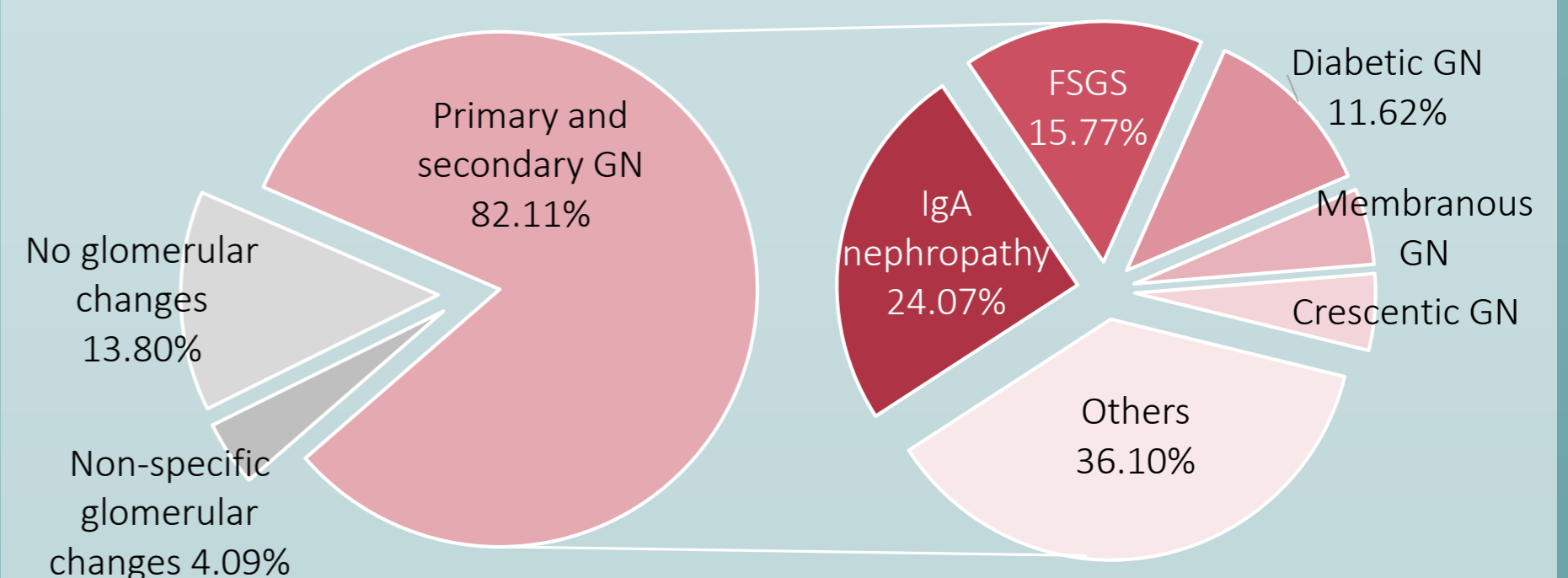
PATIENTS RECRUITMENT

The study has been approved by Medical University of Lodz Bioethical Comitee RNN/63/22/KE from 10th May 2022.

Between 06.2022 to 06.2023, 15 patients underwent screening for the study (diagnosis of IgA nephropathy in native kidney biopsy); 1 did not agree to to the study, 2 did not meet the inclusion criteria. Currently, 12 patients (6F, 6M) with a median age of 42 (33-49) years have been enrolled in the study. 7 patients were included in the study group, 5 in the control group, of which 5 and 3 patients, respectively, completed the study after W3 (final visit). We plan further recruitment until the designed size of the study group and control groups is reached, as well as preliminary statistical analysis of the results after reaching 50% of the planned recruitment.

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