1. INTRODUCTION

Chronic Kidney Disease (CKD) demonstrates a significant and increasingly prevalent public health problem worldwide, posing challenges to both healthcare delivery and financing systems. It occurs more frequently in individuals with diabetes and hypertension, in the elderly, in women, and in those with obesity. It affects more than 15–20% of the global population (1,2,3,4). The global prevalence of CKD in 2017 was 9.1%, corresponding to approximately 700 million cases. According to projections, by 2040, CKD will rank as the 5th most common cause of death worldwide among non-communicable diseases (5,6).

CKD itself and its progression, potentially leading to End Stage Kidney Disease (ESKD), result in several serious consequences, most notably high cardiovascular morbidity and mortality, as well as an increased need for hospital care. Cardiovascular mortality among dialysis patients with end-stage kidney disease is extremely high and may increase 500–1000-fold already in the 25–34 age group (7).

Diabetes-induced chronic kidney disease is the most common microvascular complication, affecting 40–43% of the type 2 diabetic (T2DM) population (8). Early diagnosis of diabetic kidney disease and the utilization of guideline-based pharmacological treatment options significantly improve life expectancy and result in longer survival. In T2DM, screening for CKD is recommended through monitoring eGFR and albuminuria (9,10).

CKD remains underdiagnosed even in patients with particularly high risk (diabetes, hypertension, CVD) (11,12). Unfortunately, CKD patients are typically recognised late in Hungary as well, and it is not uncommon that at the very first nephrology consultation the initiation of renal replacement therapy is immediately or soon required (11,12,13).

It is well established that in the general population, an elevated body mass index (BMI) is associated with higher mortality. In contrast, in advanced chronic kidney disease and especially in end-stage kidney disease patients requiring renal replacement therapy, certain epidemiological studies describe the so-called "obesity paradox," whereby overweight (BMI 25.0–29.9 kg/m²) or obese (BMI > 30 kg/m²) dialysis/ESKD patients have significantly lower cardiovascular and all-cause mortality risks compared to those of normal body weight. Hydration status and specific processes related to ESKD/dialysis, such as nutritional or inflammatory status, play a key role in this reverse relationship (14,15).

With respect to overall mortality, body composition is a crucial predictive factor, particularly the maintenance of adequate hydration and good nutritional status (16). Chronic fluid overload represents an independent mortality risk (17,18,19,20,21,22). For the objective determination of hydration status and body composition, three-compartment bioimpedance spectroscopy testing and its regular application are necessary (23).

In chronic kidney disease patients, malnutrition, inflammation, atherosclerosis, and cardiovascular diseases lead to the development of the malnutrition-inflammation-atherosclerosis (MIA) syndrome.

2. OBJECTIVES

2.1 **First study:** a nationwide, retrospective data analysis on the prevalence of T2DM-induced metabolic disorder and CKD in Hungary between 2016 and 2020.

"Deficiencies in the recognition and reporting of chronic kidney disease in patients with type 2 diabetes mellitus in Hungary between 2016 and 2020" (CKD–EPI– HUN) (1)

The questions of our research

1. What were the incidence and prevalence characteristics of T2DM and CKD in Hungary between 2016 and 2020?
2. What proportion of patients with T2DM had CKD according to the database of the National Health Insurance Fund of Hungary (NEAK)?
3. What were the characteristics of the sex- and age-specific distribution of the prevalent T2DM and CKD patient populations?
4. What proportion of prevalent T2DM patients had been diagnosed with CKD at the time of our study?

2.2. **Second study:** in a chronically dialyzed, haemodialysis (HD) and peritoneal dialysis (PD) treated patient population, retrospective investigation of the associations between the markers of the metabolic, hydration and inflammatory status, and all-cause mortality.

"The significance of body composition changes in chronically dialyzed patients based on retrospective data analysis"

The questions of our research

1. What were the most important differences observed in dialyzed patients who died compared with those who survived?
2. What mortality differences were observed in the studied HD- and PD-treated patient populations?
3. What associations were found between body composition test results when comparing survivors and non-survivors?
4. What trends were confirmed during the 42-month follow-up period regarding the parameters we investigated?

3. MATERIALS AND METHODS

In our CKD-EPI-HUN epidemiological study, we retrospectively analyzed, with the help of the central database of the NEAK, the age group–specific incidence and prevalence data of diabetes and CKD between 2016 and 2020 (study approval ID: I043/72-6/2020). The data were extracted from the system in anonymized form in accordance with the data protection regulations of NEAK, and thus were not identifiable in subsequent analyses. Our studies protocols were reviewed and approved by the Ethics Committee of the School of Medicine, University of Pécs (admission ID: 9005-PTE 2022) Regional Research Ethics Committee of the Clinical Centre, University of Pécs (license number: 9829-PTE 2024) as well as and the Regional/Institutional Scientific and Research Ethics Committee of the Borsod-Abaúj-Zemplén County Central Hospital and University Teaching Hospital (license number: BORS-01/2024).

In our first study, we analyzed the annual incidence and prevalence of registered CKD in different age groups of all Hungarian patients with T2DM using the NEAK database, as well as the sex- and age-specific distribution within the prevalent T2DM and CKD patient populations.

In our second study, we retrospectively analyzed the demographic, laboratory, and body composition results of all chronically dialyzed patients – haemodialysis, peritoneal dialysis – at the Miskolc Dialysis Centre, and evaluated these parameters' associations with survival.

Statistical analysis

In our first study, trends in annual changes of incidence and prevalence in T2DM and CKD were analyzed using Poisson regression. Age group–specific trends of T2DM and CKD prevalence were tested with Poisson regression, and the corresponding p-

values of each age group were established with the Bonferroni test. Chi-square test was used to compare the age-specific proportions of prevalent T2DM and CKD patients. Proportion test was used for age-specific comparison of CKD prevalence ratios in T2DM. All analyses were performed using the R programming language (version 4.0.4). A p-value of <0.05 was considered statistically significant.

In our second study, distributions of individual parameters were examined with the Kolmogorov–Smirnov test. Variables with normal distribution were expressed as mean ± standard deviation, and those with non-normal distribution as median (interquartile range, IqR). For comparing survivors and non-survivors, two-sample t-test was applied for normally distributed variables, while Mann–Whitney test was applied for non-normally distributed parameters. Over the four years of follow-up, longitudinal analysis was performed separately for the HD and PD groups; for trend analysis, the Jonckheere–Terpstra test was used. A p-value of <0.05 was considered statistically significant.

For statistical analyses, we used the Statistical Package for the Social Sciences (SPSS), version 27 (IBM, Armonk, New York, USA).

4. RESULTS

4.1 "Deficiencies in the recognition and reporting of chronic kidney disease in patients with type 2 diabetes mellitus in Hungary between 2016 and 2020"

The number of incident T2DM and CKD patients between 2017 and 2020

In Hungary, during the period 2016–2020, the total number of newly registered patients with T2DM was 670,559. Among these T2DM patients during the study period, a total of 55,793 met the criteria for CKD based on ICD codes.

The number of incident T2DM patients decreased significantly ($p<0.001$) between 2017 and 2020 (from 53,398 to 28,765 cases). A significant decrease ($p<0.001$) was also observed in the number of patients with incident CKD (from 2,759 to 740 cases). Based on trend analysis, the annual incidence rate of CKD in T2DM decreased from 5.2% to 2.6%, which proved to be significant ($p<0.001$).

The number and demographic characteristics of prevalent T2DM and CKD patients between 2017 and 2020.

Between 2016 and 2020, the prevalence of T2DM increased each year at a relatively steady rate from 499,029 to 586,075 cases, with a decline observed in 2020. According to trend analysis, the annual increase in prevalence of T2DM was significant both in the period 2016–2020 and in 2016–2019 ($p<0.01$). Among T2DM patients, female predominance was observed in every study year: in 2016 women accounted for 52.8% (263,297 patients), and in 2020 for 52.3% (306,231 patients).

T2DM prevalence – age characteristics

In every study year, the prevalence of T2DM was higher in older age groups. The majority of all prevalent diabetes patients examined belonged to the 60–69 years (34.1%) and 70 years and older (36.1%) age groups throughout the entire study period. Between 2016 and 2020, the number of prevalent T2DM patients increased significantly in all age groups ($p<0.001$), except for those older than 70 years, in which age group a significant decrease was detected (from 199,698 to 183,554) ($p<0.001$).
A significant difference was observed in the age distribution of patient with T2DM from 2016 to 2020, with the proportion of patients decreasing only in the group older than 70 years (from 40.0% to 31.3%), while in all younger age groups (<20–69 years) it increased.

CKD prevalence – age characteristics

Between 2016 and 2020, the prevalence of CKD significantly dropped (from 48,902 to 38,347 cases) and reached its lowest level in 2020 ($p<0.05$). In every study year,

the proportion of women was higher among CKD patients: 27,563 (56.3%) in 2016 and 22,019 (57.4%) in 2020.

The majority of all prevalent CKD patients (64.4%) belonged to the age group older than 70 years, followed by 25.5% in the 60–69 years age group. The number of patients elevated significantly between 2016 and 2020 in the 30–39 years and 40–49 years age groups ($p<0.001$) while it did not change in the 50–59 years group. In contrast, among patients over 60 years, the number of prevalent CKD patients gradually decreased ($p<0.001$).

Between 2016 and 2020 the age distribution of prevalent CKD patients showed a significant difference, as the proportion of patients older than 70 years decreased (from 65.2% to 59.1%) however, it increased among younger patients aged 20–69 years ($p<0.001$).

Throughout the entire study period, CKD prevalence was higher in the older age groups, and differences were observed in the number of prevalent CKD patients across age groups.

In every study year, the prevalence of CKD was higher in older age groups. Considering all prevalent CKD patients, regarding the age distribution of prevalent CKD patients, we found a significant difference between 2016 and 2020. When comparing the data from the two years, the proportion of patients older than 70 years decreased (from 65.2% to 59.1%), while it increased in the younger age groups, between 20–69 years ($p<0.001$).

Age characteristics of prevalent CKD patients with diabetes

The proportion of CKD prevalence in T2DM was consistently higher at older ages in every study year. The highest value was observed in the age group over 70 years (14.85%) across the entire 2016–2020 study period.

Between 2016 and 2020, the proportion of CKD prevalence in T2DM decreased in all age groups; the decrease was significant in the over 70, 60–69, 40–49, and 30–39 age groups ($p<0.001$). At the same time, in the 30–39 and 40–49 age groups, the number of prevalent patients increased significantly in both T2DM and CKD.

When comparing by age groups, the proportion of CKD prevalence in T2DM did not differ significantly between 2016 and 2020.

Characteristics of CKD prevalence in T2DM between 2016 and 2020

The proportion of CKD prevalence in T2DM gradually decreased from 9.8% to 6.5% ($p<0.001$), which corresponded to an average of 8.3% considering all patients and the entire study period.

4.2 The significance of body composition changes in chronically dialyzed patients based on retrospective data analysis

In the study – between 2020 and 2023 – we processed and evaluated the data of a total of 765 chronically dialyzed patients. Of the 765 patients, 701 received haemodialysis or online haemodiafiltration treatment, and 64 patients received peritoneal dialysis treatment. During the study period, a total of 203 patients (26.53%) died.

Survivors versus non-survivors

When comparing the parameters of survivors and non-survivors, we found that while the mean age of survivors was significantly lower, 58 years, the mean age of non-survivors was 67 years. In both patient groups, the proportion of men was higher.

According to our results, PD treatment was associated with better outcomes, namely improved survival.

We found that non-survivors were older, more anemic, and more iron-deficient.

In non-survivors, systemic, subclinical inflammation was more pronounced, characterized by elevated CRP and ferritin (positive acute-phase proteins), decreased transferrin (negative acute-phase protein), and a consequent catabolic state (low serum albumin level) observed in this group.

Pre-dialysis serum urea and creatinine levels, as well as dry weight, normal hydration weight, and pre- and post-dialytic body weight were lower in non-survivors. Paradoxically, the body mass index of non-survivors was higher, most likely influenced by the fact that these patients were shorter in height.

Compared with survivors, non-survivors were significantly more hyperhydrated, primarily in the post-dialytic period and in the extracellular compartment.

Interestingly, both the weekly average pre-dialytic systolic (AW preSBP) and pre-dialytic diastolic blood pressure (AW preDBP) values were lower among non-survivors.

In non-survivors, the urea distribution volume (Vurea), total body water (TBW), extracellular water (ECW), and intracellular water (ICW) were lower.

Non-survivors had lower lean tissue index (LTI), lean tissue mass (LTM), relative lean tissue mass (relative LTM), and body cell mass (BCM), while the fat tissue index (FTI) was higher; however, body fat and adipose tissue mass (ATM) did not differ.

In some cases, particularly in patients with low muscle mass, high FTI may have adverse consequences, as it increases cardiovascular risk and worsens quality of life. In other cases – especially in severely malnourished or catabolic patients – it may exert a protective effect (obesity paradox).

Although some significant differences were confirmed in terms of dry weight, ICW, and ECW, which may have clinical relevance, these were not consistent across the entire study period; therefore, far-reaching conclusions cannot be drawn.

Regarding normal hydration status, we observed no difference between the two treatment modalities, and somewhat surprisingly, the advantage of PD over HD was not entirely clear with respect to overhydration either. Nevertheless, the significant findings tended to suggest a more favorable effect of PD, even if the picture was not entirely uniform. In terms of overhydration and total body water, PD proved to be more favorable at several time points.

No significant difference was confirmed in BMI results between the two dialysis modalities; therefore, no conclusions can be drawn.

Presentation of the time kinetics of results between 2020 and 2023

During the study period (2020–2023), we examined which time-dependent trends could be confirmed for HD and PD patients, respectively.

While haematocrit showed an increasing trend in both treatment groups, haemoglobin decreased in HD patients but remained unchanged in PD patients. The trend of serum iron was the same as that of haemoglobin. Interestingly, regarding transferrin, we observed a decrease in HD patients, whereas in PD patients a significant increase was found, which should be interpreted in light of transferrin being a negative acute-phase protein.

A difference was also found in CRP: in HD patients, an increasing trend was observed, whereas in the PD group no significant trend was detected.

BMI decreased in the HD group and remained unchanged in PD.

All post-dialytic overhydration indicators (bOH post, dOH post, eOH ECW post, dOH ECW post) showed an increasing trend in HD, while in PD they did not change.

In the HD group, the fat tissue index (FTI) and relative body fat decreased, while relative lean tissue mass (LTM) increased; these parameters did not change in PD.

5. DISCUSSION

Based on our study "Deficiencies in the recognition and reporting of chronic kidney disease in patients with type 2 diabetes mellitus in Hungary between 2016 and 2020" (1) we make the following conclusions:

In our study, we were the first to process and evaluate epidemiological data covering the entire Hungarian population regarding CKD associated with T2DM. Based on our study, we conclude the following:

i) CKD associated with T2DM decreased significantly from 2017 to 2020;

ii) Considering all prevalent cases, the majority of patients were older than 60 years, 70% in T2DM and 90% in CKD;

iii) Between 2016–2020, the annual prevalence of T2DM increased significantly;

iv) The proportion of CKD prevalence in T2DM was low and decreased significantly between 2016–2020. These results suggest insufficient recognition and/or insufficient reporting of CKD.

In our study, it was found that the incidence of CKD in T2DM was already low and decreased gradually. A significant decrease was detected from 5.2% to 2.6% in the time period 2017-2020.

Based on our results, the prevalence of T2DM showed an increasing trend, and according to previously published data, the prevalence of T2DM also increased in Hungary between 2001 and 2016. It is well known that the global prevalence of DM is rising progressively every year (24), which was also confirmed in our study. The decrease in incidence alongside the simultaneous increase in prevalence may suggest that the survival of patients with T2DM is improving, likely due to decreasing mortality (25).

The prevalence of T2DM increases with advancing age and affects 20–25% of patients older than 65 years (24,26,27). In line with this, we also found that a greater proportion of prevalent T2DM patients belonged to the older age groups, with their proportion reaching 34.1% among those aged 60–69 years and 36.1% among those older than 70 years. In these elderly patients, underlying CKD occurs more frequently, even without T2DM, affecting about one-third of the general population over the age of 65 (1,2,3,4). CKD is present in approximately 50% of patients with T2DM (28,29,30,31,32,33,34,35), and its prevalence could be even higher (about 60%) in those with age over 65 years (36). Our study also confirmed that the prevalence of CKD in T2DM is higher in the older age groups, with the majority of patients belonging to the 60–69 years (25.8%) and over 70 years (64.4%) categories.

Based on our results, from 2016 to 2020 the prevalence of CKD in patients with T2DM decreased gradually and significantly from 9.8% to 6.5%, and this decrease was observed in most age categories. The negative effect of the COVID-19 in 2020 cannot be excluded; while the prevalence of T2DM continued to increase between 2016 and 2020, CKD prevalence showed a decline during the same period.

With the introduction of newer antidiabetic therapies (e.g., SGLT-2 inhibitors, GLP-1 analogues), effective renoprotection has become possible to prevent CKD or slow its progression (10,37,38,39), but it is unlikely that this could explain the low number of identified CKD cases, given that their use has only been possible for a relatively short time.

A true decrease in CKD prevalence is also improbable. Our findings rather suggest that CKD was underdiagnosed. This is despite the fact that attention to CKD generally improves with more frequent eGFR measurement in older patients, especially in DM, where annual CKD screening is recommended (13,37,39,40,41).

Considering the number of registered patients with T2DM in our current study, and assuming a prevalence rate of approximately 40% (4,36,42,43), the number of CKD patients with T2DM in Hungary would be around 230,000, which is close to the internationally estimated figure (44). This patient number is far from the estimated

national figure (9). The difference is due to undetected T2DM and the unknown but estimatedly high proportion of prediabetes.
In contrast, it was found that in T2DM prevalence of CKD ranged from 48,902 to 38,347 during the study period 2016–2020, corresponding to a prevalence of 9.8% to 5.6%. Based on this comparing our data to the international results a 5-6 fold lower prevalence of CKD was detected in our study(36,44). The average proportion was 8.3%.

Our results show that even among patients with T2DM, awareness regarding CKD is low, with therapeutic inertia being typical, which may explain the failure to screen for, recognise, or report CKD. The main reasons behind this are the lack of adequate knowledge and failure to follow clinical practice guidelines (45,46,47). Furthermore, in many cases, CKD diagnosis coding is not carried out even for patients at high risk of developing CKD or those with persistently reduced eGFR values (45,48,49,50,51). Screening for albuminuria and measuring eGFR are recommended at least annually in patients with T2DM (37,39,41). While eGFR testing is performed much more frequently, albuminuria screening is generally applied less often (~50%) for detecting CKD in T2DM patients (45,46,47).
In Hungary, assessment of kidney function is part of the routine clinical laboratory testing of diabetic patients. Given that eGFR appears to be the main fundamental screening parameter for CKD, we believe that in our study the insufficient recognition and underreporting of CKD, rather than inadequate testing of T2DM patients, was the underlying issue.
The strengths of our study include that it was conducted on a national level, processing a big data volume from the central registry, and analyzing age- and sex-specific distributions.
Our study also has limitations. CKD was defined on the basis of diagnosis codes, in the absence of laboratory eGFR and albuminuria measurement data, which may underestimate the true number of cases. It is well known that data derived from administrative sources have low sensitivity in CKD research (52,53,54). However,

even such non-validated data are valuable for describing epidemiological trends. In this retrospective, database study, we did not have clinical data available regarding lifestyle habits, e.g. glycemic control, duration of DM, CKD stages, nor did we examine mortality. Patients with T2DM treated only with lifestyle modification were not included in our analysis.

In summary, we can conclude that this CKD-EPI-HUN trial is the first which provides nationwide data in Hungary upon the epidemiology of CKD in T2DM using database analysis. Both the incidence and prevalence of CKD proved to be low and decreased significantly among patients with T2DM in Hungary between 2016 and 2020, which indicates insufficient recognition and/or reporting of CKD in Hungary. Our results support the urgent need to improve CKD awareness and to bring attention to identifying affected CKD patients among patients with T2DM.

5.2 The significance of body composition changes in chronically dialyzed patients based on retrospective data analysis

Based on the associations between body composition and mortality data in dialyzed patients, our findings are as follows:

i) Of the 765 chronically dialyzed patients studied, a total of 203 patients (26.5%) died during the 42-month observation period. Their average age was significantly higher than that of survivors; they were more anemic, more hyperhydrated, and more iron-deficient. The sex ratio was the same between survivors and non-survivors, with a predominance of men.

ii) Regarding mortality, PD treatment was associated with better outcomes, i.e. improved survival, compared to HD.

iii) In non-survivors, the urea distribution volume (Vurea), total body water (TBW), extracellular water (ECW), and intracellular water (ICW) were lower. Lean tissue index (LTI), lean tissue mass (LTM), relative lean tissue mass (relative LTM), and body cell mass (BCM) were also lower, while fat tissue

index (FTI) was higher, although body fat and adipose tissue mass (ATM) did not differ.

iv) In HD treatment, laboratory results indicative of subclinical inflammation showed an increasing trend compared with PD. In the HD group, fat tissue index (FTI) and relative body fat decreased, while relative lean tissue mass (LTM) increased; these parameters did not change in PD.

Based on our 42-month retrospective analysis, significantly better survival was confirmed with PD treatment. In non-survivors, systemic subclinical inflammation was more pronounced, with elevated CRP and ferritin (positive acute-phase proteins), decreased transferrin (negative acute-phase protein), and a consequent catabolic state (low serum albumin). It is well known that dialysis-related infections and chronic inflammation caused by oxidative stress accelerate catabolic processes, further reduce muscle mass, and lead to the development of malnutrition-inflammation-atherosclerosis (MIA) syndrome, which markedly increases mortality (55,56).

In our study, paradoxically, the body mass index of non-survivors was higher compared to survivors, which could largely be explained by the shorter stature of deceased patients (17).

Non-survivors had lower lean tissue index (LTI), lean tissue mass (LTM), relative lean tissue mass (relative LTM), and body cell mass (BCM), but higher fat tissue index (FTI), while body fat and adipose tissue mass (ATM) did not differ (17). This may be detrimental – especially in the presence of low muscle mass – because it increases cardiovascular risk, but in other cases it may have a protective effect (the obesity paradox), particularly in severely malnourished or catabolic patients.

In non-survivors, lower dry weight, serum urea nitrogen, and creatinine results were observed.

Interestingly, the weekly average of both the pre-dialytic systolic blood pressure (AW preSBP) and the pre-dialytic diastolic blood pressure (AW preDBP) were lower among non-survivors (17,18,57).

Regarding the parameters examined between 2020 and 2023, haematocrit, haemoglobin, and serum iron levels were consistently higher in the PD group compared to the HD group. There was no difference regarding normal hydration. Serum ferritin levels were consistently lower in the PD group, suggesting that in this analysis ferritin behaved more as a positive acute-phase protein than as a marker of iron metabolism.

With respect to dialysis adequacy (Kt/V), there was no difference between survivors and non-survivors. It is important to emphasize that Kt/V values were appropriate, well within the target range (17).

In our study – consistent with the literature – intact parathyroid hormone (iPTH) levels were lower in the PD group compared to HD.

Limitations and strengths of the study

Our study had several limitations. The study period was determined arbitrarily; during this time, all patients chronically dialyzed at our center were included, and their data were processed without forming specific subgroups in advance. Another limiting factor was that the study period overlapped with the COVID pandemic.

The strength of our study lies in its homogeneity, which in our case means that patients were treated by the same professional team, under identical medical principles, perspectives, quality indicators, and expectations.

6. CONCLUSIONS

The CKD-EPI-HUN trial is the first national, retrospective, database-based analysis in Hungary, which gives new data on the epidemiology of CKD associated with T2DM. We examined the incidence and prevalence of T2DM, CKD, and CKD developing in T2DM from 2016 to 2020.

Based on our results, we found that CKD awareness is lower in T2DM patients, CKD screening is often omitted, and the recognition of the disease is insufficient. Diabetic chronic kidney disease qualifies as an underdiagnosed condition, with inertia, deficiencies in reporting and coding, insufficient adherence to guidelines, and the effect of the COVID-19 being potential contributing factors.

Our findings indicate the need for better evaluation and identification of CKD patients with T2DM. Early recognition of CKD is a key strategy in preventing kidney disease, its progression, and associated complications, which have serious consequences for survival, quality of life, and healthcare expenditures.

Our research highlights the importance of CKD screening and recognition in T2DM and emphasizes that urgent action is required in this field. Awareness of kidney disease must be increased. It is essential to regularly update clinical guidelines and ensure full compliance. A monitoring system needs to be established and the introduction of new therapies encouraged.

In our dialysis population, we studied the end stage of CKD, the metabolic status of chronically dialyzed patients, mortality, and the associations of hydration and inflammatory markers. We examined mortality differences between HD and PD patient populations and evaluated body composition test results between survivors and non-survivors.

Our findings concerning dialyzed patients provide evidence – supported also by the literature – that in the treatment of dialysis patients, simultaneous consideration of body composition, nutritional status, and the characteristics of systemic subclinical inflammation can contribute to better management and improved survival.

Based on these results, we consider it essential to regularly perform comprehensive and comparative assessments of body composition – objective evaluation of muscle mass, fat mass, and dry weight – since this is crucial in the treatment of dialysis patients. It is also important to note that this method is simple to carry out and inexpensive.

The main significance of the study data lies in showing that with knowledge of these parameters, nutritional and metabolic status, SHPT, and uraemic metabolic and hydration status can be improved in an individualized and complex way through adequate and high-quality dialysis treatment.

With these measures, the survival of dialysis patients can be substantially influenced, primarily through the prevention of CVD – the factor most critical to life expectancy – by slowing disease progression and reducing complications, thereby making the treatment of dialysis patients more cost-effective.

7. THESES

I. "Deficiencies in the diagnosis and reporting of chronic kidney disease among patients with type 2 diabetes mellitus in Hungary between 2016 and 2020" (1)

1. The number of incident T2DM patients decreased significantly, while the number of incident CKD patients decreased gradually during the study period. The prevalence of T2DM increased gradually between 2016 and 2020, then declined in 2020.

2. The prevalence of CKD in T2DM decreased significantly between 2016 and 2020 and was lowest in 2020.

3. Regarding sex distribution, the proportion of women was higher among prevalent T2DM patients in every study year, and similarly, in every study year the proportion of women was greater among CKD patients as well.

4. With respect to age, the prevalence of T2DM was higher in the older age groups in every study year. The biggest proportion of all prevalent T2DM patients belonged to the 60–69 years and over 70 years age groups, with 36.1% in the latter.
   In every study year, the prevalence of CKD was higher in older age groups. Considering all prevalent CKD patients, the majority were over 70 years old, followed by the 60–69 years age group.
   In patients over 70 years, the prevalence of CKD in T2DM patients was higher in older age groups in every study year, with the highest values observed.

5. Based on data from the NEAK database, the recognition of diabetic chronic kidney disease was characterized by the fact that the prevalence ratio of CKD

in T2DM decreased gradually and significantly from year to year from 2016 to 2020.

II. The significance of body composition changes in chronically dialyzed patients based on retrospective data analysis

1. Non-survivors were significantly more anemic, more iron-deficient, and more hyperhydrated compared to survivors.
2. Serum ferritin and CRP levels were consistently lower in the PD group, while serum albumin levels were lower at several time points compared with HD.

3. In non-survivors, the urea distribution volume (Vurea), total body water (TBW), extracellular water (ECW), and intracellular water (ICW) were lower.

   Lean tissue index (LTI), lean tissue mass (LTM), relative lean tissue mass (relative LTM), and body cell mass (BCM) were also lower, while fat tissue index (FTI) was higher, although body fat and adipose tissue mass (ATM) did not differ.
4. In HD treatment, laboratory results indicative of subclinical inflammation showed an increasing trend compared with PD.

   In the HD group, FTI and relative body fat decreased, while relative LTM increased; these parameters did not change in PD.

Publications forming the basis of this dissertation:

Ladányi E, Salfer B, Balla J, Kárpáti I, Reusz Gy, Szabó L, Andriska P, Németh L, Wittmann I, Laczy B. Deficiencies in the recognition and reporting of chronic kidney disease in patients with type 2 diabetes mellitus; A Hungarian nationwide analysis. *Int J Public Health 68:1606151. doi: 10.3389/ijph.2023.1606151*

Ladányi E, Csurgyók R, Kun Sz, Wittmann I. A miskolci dialíziscentrum betegeinek jellemzése, különös tekintettel a halálozásra, a testösszetételre és a kezelési módra. *Hypertonia és Nephrologia 2024;(28)3:101-111. doi:10.33668/hn.28.013*

8. ACKNOWLEDGEMENTS

First of all, I would like to express my gratitude and deepest appreciation to my supervisor, Professor **Dr. István Wittmann**, for his support, trust, continuous and careful guidance in my scientific work, and for his constructive criticism and valuable feedback. Without his invaluable advice and guidance, this dissertation could not have been completed.

I would like to express my special thanks to my co-authors, who played an active role in carrying out the research, thereby supporting my work.

This study and its results reflect not only my own work, but also the joint efforts of my colleagues at the Miskolc Nephrology Centre – our shared work as a team.I would like to thank all my colleagues for their helpful collaboration, especially the nurses, whose work played an active role in carrying out the examinations. I am glad to have been leading for decades such a team of colleagues, clinicians, nurses, and dietitians.
I owe special thanks to my secretary, Nikoletta Krajnyákné Szűcs, who worked on the preparation of this dissertation with immense patience and attention.
I am grateful to my children – for their encouragement and support, even from afar.
I also wish to thank everyone not listed above, who contributed to my work or supported me in my personal life.

9. REFERENCES

1. Xie Y, Bowe B, Mokdad AH, Xian H, Yan Y, Li T, et al. Analysis of the Global Burden of Disease Study Highlights the Global, Regional, and National Trends of Chronic Kidney Disease Epidemiology From 1990 to 2016. *Kidney Int. 2018;94(3):567–81. doi:10.1016/j.kint.2018.04.011*

2. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, Regional, and National Burden of Chronic Kidney Disease, 1990-2017: A Systematic Analysis for the Global Burden of Disease Study 2017. *Lancet 2020;395(10225):709–33. doi:10.1016/S0140-6736(20)30045-3*

3. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-Analysis. *PLoS One 2016;11(7):e0158765. doi:10.1371/journal.pone. 0158765*

4. United States Renal Data System USRDS Annual Data Report. Epidemiology of Kidney Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases (2021). *https://adr.usrds.org/2021/chronic-kidney-disease/1-ckdin-the-general-population.*

5. Ladányi Erzsébet Magyarország a másfél millió krónikus vesebeteg országa. *Metabolizmus 2023. XXI.(3):126-30.*

6. GBD Chronic Kidney Disease Collaboration Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet 2020;395:709–733.*

7. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis. 1998;32(suppl 3):S112-S119.*

8. Gheith O, Farouk N, Nampoory N, Halim MA, Al-Otaibi T. Diabetic Kidney Disease: Worldwide Difference of Prevalence and Risk Factors. *J Nephropharmacol. 2015;5(1):49–56.*

9. A Belügyminisztérium egészségügyi szakmai irányelve a felnőttkori idült vesebetegség diagnózisáról és kezeléséről. *EÜ Közlöny 2025. LXXV. évf. 7. 789-952.*

10. Provenzano M, Puchades MJ, Garofalo C, Jongs N, D'Marco L, Andreucci M, et al. Albuminuria-Lowering Effect of Dapagliflozin, Eplerenone, and Their Combination in Patients With Chronic Kidney Disease: A Randomized Crossover Clinical Trial. *J Am Soc Nephrol. 2022;33(8):1569–80. doi:10. 1681/ASN.2022020207*

11. Kim V, Zhakhina G, Gusmanov A, Sakko Y. et al. Late diagnosis of CKD and associated survival after initation of renal replacement therapy in Kazakhstan: analysis of nationwide electronic healthcare registry 2014-2019. *Renal Failure 2024;46(2):2398182 doi: 10.1080/ 0886022X.2024.2398182*

12. Baer G, Lameire N, Biesen VM. Late referral of patients with end-stage renal disease: an in-depth review and suggestion s for further actions. *NDT Plus 2010;3:17-27. doi.org/10.1093/ndtplus/sfp050*

13. Ladányi E, Salfer B, Balla J, Kárpáti I, Reusz Gy, Szabó L, Andriska P, Németh L, Wittmann I, Laczy B. Deficiencies in the recognition and reporting of chronic kidney disease in patients with type 2 diabetes mellitus; A hungarian nationwide analysis. *Int J Public Health 68:1606151. doi: 10.3389/ijph.2023.1606151*

14. Ladányi Erzsébet. A tápláltság hatása a predialízis szakban a vesebetegség progressziójára és prognózisára. *Hypertonia és Nephrologia 2002;6(S3):74-77.*

15. Ladányi Erzsébet, Mácsai Emília, Klenk Nóra, Fodor Bertalan. Szérum-prealbuminszintek összehasonlító vizsgálata dializált betegekben. *Hypertonia és Nephrologia 2005;9(1):30-34.*

16. Stuard S, Ridel C, Cioffi M, Trost-Rupnik A, Gurevich K, Bojic M, Karibayev Y, Mohebbi N, Marcinkowski W, Kupres V, Maslovaric J, Antebi A, Ponce P, Nada M, Baro Salvador ME, Rosenberger J, Jirka T, Enden K, Novakivskyy V, Voiculescu D, Pachmann M, Arkossy O. Hemodialysis Procedures for Stable Incident and Prevalent Patients Optimize Hemodynamic Stability, Dialysis Dose, Electrolytes, and Fluid Balance. *Journal of Clinical Medicine 2024;13:3211. Doi.org/10.3390/jcm13113211*

17. Ladányi E, Csurgyók R, Kun Sz, Wittmann I. A miskolci dialíziscentrum betegeinek jellemzése, különös tekintettel a halálozásra, a testösszetételre és a kezelési módra. *Hypertonia és Nephrologia 2024;(28)3:101-111. doi:10.33668/hn.28.013*

18. Wizemann V, Wabel P, Chamney P et al. The mortality risk of overhydration in haemodialysis patients. *Nephrol Dial Transplant. 2009;24:1574-1579. doi:10.1093/ndt/gfn707*

19. Kalantar-Zadeh K, Regidor DL, Kovesdy CP, et al. Fluid retention is associated with cardiovascular mortality in patients undergoing long-term hemodialysis. *Circulation 2009;119:671-79.*

20. Movilli E, Gaggia P, Zubani R, et al. Association between high ultrafiltration rates and mortality in uraemic patients on regular haemodialysis. A 5-year prospective observational multicentre study. *Nephrol Dial Transplant. 2007;22:3547-52.*

21. Flythe JE, Kimmel SE, Brunelli SM. Rapid fluid removal during dialysis is associated with cardiovascular morbidity and mortality. *Kidney Int. 2011;79;250-57.*

22. Wizemann V, Moissl U, Rode C, et al. Interdialytic weight gain or chronic fluid overload which is more dangerous for chronic HD patients? *ASN 2009, 2010San Diego, CA*

23. Kyle U, Bosaeus I, De Lorenzo A, Deurenberg P, Elia M, Gómez J.M, Heitmann B.L, Kent-Smith L, Melchior J.C, Pirlich M., Scharfetter H, M W J Schols A, Pichard C, Composition of the ESPEN Working Group. Bioelectrical impedance analysis-Part I: Review of principles and methods. *Clin. Nutr. 2004;2(5)3:1226–43. doi: 10.1016/j.clnu. 2004.06.004.*

24. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and Regional Diabetes Prevalence Estimates for 2019 and Projections for 2030 and 2045: Results From the International Diabetes Federation Diabetes Atlas, 9th Edition. *Diabetes Res Clin Pract. 2019;157:107843. doi:10.1016/j.diabres.2019.107843*

25. Jermendy G, Kiss Z, Rokszin G, Abonyi-Tóth Z, Wittmann I, Kempler P. Decreasing Incidence of Pharmacologically Treated Type 2 Diabetes in Hungary From 2001 to 2016: A Nationwide Cohort Study. *Diabetes Res Clin Pract. 2019;155:107788. doi:10.1016/j.diabres.2019.107788*

26. Jermendy Gy, Kempler P, Abonyi-Tóth Zs, Rokszin Gy, Wittmann I. Changes in Features of Diabetes Care in Hungary in the Period of Years 2001–2014. Aims and Methods of the Database Analysis of the National Health Insurance Fund. *Orvosi Hetilap 2016;157(32):1259–65. doi:10.1556/650.2016. 30519*

27. Centers for Disease Control and Prevention. National Diabetes Statistics Report Website (2019). *https://www.cdc.gov/diabetes/data/ statistics-report/index.html*

28. Bramlage P, Lanzinger S, van Mark G, Hess E, Fahrner S, Heyer CHJ, et al. Patient and Disease Characteristics of Type-2 Diabetes Patients With or Without Chronic Kidney Disease: An Analysis of the German DPV and DIVE *Databases. Cardiovasc Diabetol. 2019;18(1):33. doi:10.1186/s12933- 019-0837-x*

29. Svensson MK, Cederholm J, Eliasson B, Zethelius B, Gudbjörnsdottir S, Swedish National Diabetes Register. Albuminuria and Renal Function as Predictors of Cardiovascular Events and Mortality in a General Population of Patients With Type 2 Diabetes: A Nationwide Observational Study From the Swedish National Diabetes Register. *Diab Vasc Dis Res. 2013;10(6):520–9. doi:10.1177/1479164113500798*

30. Luk AO, Li X, Zhang Y, Guo X, Jia W, Li W, et al. Quality of Care in Patients With Diabetic Kidney Disease in Asia: The Joint Asia Diabetes Evaluation (JADE) Registry. *Diabet Med. 2016;33(9):1230–9. doi:10.1111/dme.13014*

31. Pugliese G, Solini A, Bonora E, Fondelli C, Orsi E, Nicolucci A, et al. Chronic Kidney Disease in Type 2 Diabetes: Lessons From the Renal Insufficiency and Cardiovascular Events (RIACE) Italian Multicentre Study. *Nutr Metab Cardiovasc Dis. 2014;24(8):815–22. doi:10.1016/j. numecd.2014.02.013*

32. Metsärinne K, Bröijersen A, Kantola I, Niskanen L, Rissanen A, Appelroth T, et al. High Prevalence of Chronic Kidney Disease in Finnish Patients With Type 2 Diabetes Treated in Primary Care. *Prim Care Diabetes 2015;9(1):31–8. doi:10.1016/j.pcd.2014.06.001*

33. González-Pérez A, Saéz ME, Vizcaya D, Lind M, García Rodríguez LA. Impact of Chronic Kidney Disease Definition on Assessment of its Incidence and Risk Factors in Patients With Newly Diagnosed Type 1 and Type 2 Diabetes in the UK: A Cohort Study Using Primary Care Data From the United Kingdom. *Prim Care Diabetes 2020;14(4):381–7. doi:10.1016/j.pcd. 2019.11.002*

34. Mata-Cases M, Franch-Nadal J, Real J, Cedenilla M, Mauricio D. Prevalence and Coprevalence of Chronic Comorbid Conditions in Patients With Type 2 Diabetes in Catalonia: A Population-Based Cross-Sectional Study. *BMJ Open 2019;9(10):e031281. doi:10.1136/bmjopen-2019-031281*

35. Migdalis IN, Papanas N, Raptis AE, Ioannidis IM, Sotiropoulos AE, Dimitriadis GD, et al. The Prevalence of Diabetic Chronic Kidney Disease in Adult Greek Subjects With Type 2 Diabetes Mellitus: A Series From Hospital-Based Diabetes Clinics. *Diabetes Res Clin Pract. 2020;166: 108243. doi:10.1016/j.diabres.2020.108243*

36. Bailey RA, Wang Y, Zhu V, Rupnow MFT. Chronic Kidney Disease in US Adults With Type 2 Diabetes: An Updated National Estimate of Prevalence Based on Kidney Disease: Improving Global Outcomes (KDIGO) Staging. *BMC Res Notes 2014;7:415. doi:10.1186/1756-0500-7-415*

37. Shlipak MG, Tummalapalli SL, Boulware LE, Grams ME, Ix JH, Jha V, et al. The Case for Early Identification and Intervention of Chronic Kidney Disease: Conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int. 2021;99(1):34–47. doi:10.1016/j.kint. 2020.10.012*

38. Wheeler DC, Stefánsson BV, Jongs N, Chertow GM, Greene T, Hou FF, et al. Effects of Dapagliflozin on Major Adverse Kidney and Cardiovascular Events in Patients With Diabetic and Non-Diabetic Chronic Kidney Disease: A Prespecified Analysis From the DAPA-CKD Trial. *Lancet Diabetes Endocrinol. 2021;9(1):22–31. doi:10.1016/S2213-8587(20)30369-7*

39. American Diabetes Association. 11. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes-2020. *Diabetes Care 2020;43(1):S135–S151. doi:10.2337/dc20-S011*

40. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. 2019 ESC Guidelines on Diabetes, Pre-diabetes, and Cardiovascular Diseases Developed in Collaboration With the EASD. *Eur Heart J. 2020;41(2):255–323. doi:10.1093/eurheartj/ehz486*

41. Kidney Disease Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl. 2013;3:S1–S150. doi:10.1038/ kisup.2012.76*

42. Plantinga LC, Crews DC, Coresh J, Miller ER 3rd, Saran R, Yee J, et al. Prevalence of Chronic Kidney Disease in US Adults With Undiagnosed Diabetes or Prediabetes. *Clin J Am Soc Nephrol. 2010;5(4):673–82. doi:10. 2215/CJN.07891109*

43. Wang T, Xi Y, Lubwama R, Hannanchi H, Iglay K, Koro C. Chronic Kidney Disease Among US Adults With Type 2 Diabetes and Cardiovascular Diseases: A National Estimate of Prevalence by KDIGO 2012 Classification. *Diabetes Metab Syndr. 2019;13(1):612–5. doi:10.1016/j.dsx.2018.11.026*

44. Deng Y, Li N, Wu Y, Wang M, Yang S, Zheng Y, et al. Global, Regional, and National Burden of Diabetes-Related Chronic Kidney Disease From 1990 to 2019. *Front Endocrinol (Lausanne) 2021;12:672350. doi:10.3389/fendo.2021.672350*

45. Szczech LA, Stewart RC, Su HL, DeLoskey RJ, Astor BC, Fox CH, et al. Primary care detection of chronic kidney disease in adults with type-2 diabetes: the ADD-CKD Study (awareness, detection and drug therapy in type 2 diabetes and chronic kidney disease). *PLoS One 2014;9(11):e110535. https://doi.org/10.1371/journal.pone.0110535*

46. Stempniewicz N, Vassalotti JA, Cuddeback JK, Ciemins E, Storfer-Isser A, Sang Y, et al. Chronic Kidney Disease Testing Among Primary Care Patients With Type 2 Diabetes Across 24 U.S. Health Care Organizations. *Diabetes Care 2021;44(9):2000–9. doi:10.2337/dc20-2715*

47. Bramlage P, Lanzinger S, Tittel SR, Hess E, Fahrner S, Heyer CHJ, et al. Guidelines Adherence in the Prevention and Management of Chronic Kidney Disease in Patients With Diabetes Mellitus on the Background of Recent European Recommendations - A Registry-Based Analysis. *BMC Nephrol. 2021;22(1):184. doi:10.1186/s12882-021-02394-y*

48. Tuttle KR, Alicic RZ, Duru OK, et al. Clinical Characteristics of and Risk Factors for Chronic Kidney Disease Among Adults and Children: An Analysis of the CURE-CKD Registry. *JAMA Netw Open2019;2(12):e1918169. https://doi.org/10.1001/jamanetworkopen. 2019.18169*

49. Abdel-Kader K, Greer RC, Boulware LE, Unruh ML. Primary Care Physicians' Familiarity, Beliefs, and Perceived Barriers to Practice Guidelines in Non-Diabetic CKD: A Survey Study. *BMC Nephrol. 2014;15:64. doi:10.1186/1471-2369-15-64*

50. Stevens PE, O'Donoghue DJ, de Lusignan S, Van Vlymen J, Klebe B, Middleton R, et al. Chronic Kidney Disease Management in the United Kingdom: NEOERICA Project Results. *Kidney Int. 2007;72(1):92–9. doi:10.1038/sj.ki. 5002273*

51. Schroeder EB, Powers JD, O'Connor PJ, Nichols GA, Xu S, Desai JR, SUPREME-DM Study Group, et al. Prevalence of Chronic Kidney Disease Among Individuals With Diabetes in the SUPREME-DM Project, 2005-2011. *J Diabetes Complications 2015;29(5):637–43. doi:10.1016/j.jdiacomp.2015. 04.007*

52. Zemplényi A, Sághy E, Kónyi A, Szabó L, Wittmann I, Laczy B. Prevalence, Cardiometabolic Comorbidities and Reporting of Chronic Kidney Disease; A Hungarian Cohort Analysis. *Int J Public Health 2023;68:1605635. doi:10. 3389/ijph.2023.1605635*

53. van Oosten MJM, Logtenberg SJJ, Edens MA, Hemmelder MH, Jager KJ, Bilo HJG, et al. Health Claims Databases Used for Kidney Research Around the World. *Clin Kidney J. 2020; 14(1):84–97. doi:10.1093/ckj/sfaa076*

54. Sundström J, Bodegard J, Bollmann A, Vervloet MG, Mark PB, Karasik A, et al. Prevalence, Outcomes, and Cost of Chronic Kidney Disease in a Contemporary Population of 2·4 Million Patients From 11 Countries: The CaReMe CKD Study. *Lancet Reg Health Eur. 2022; 20:100438. doi:10.1016/j. lanepe.2022.100438*

55. Filho RP, Lindholm B, Stenvinkel P. The malnutrition, inflammation, and atherosclerosis (MIA) syndrome – the heart of the matter. *Nephol Dial Transplant. 2002;17(S11):28-31. https://doi.org/10.1093/ndt/17.suppl_11. 28.*

56. Yao Q, Lindholm B, Stenvinkel P. Inflammation as a cause of malnutrition, atherosclerotic cardiovascular disease, and poor outcome in hemodialysis patients. *Hemodial Int. 2004;8(2):118-29. doi:10.1111/j.1492-7535 .2004.01085.x.*

57. Shu Y, Liu J, Zeng X, Hong HG, Li Y, zhong H, Ma L, Fu P. The effect of overhydration on mortality and technique failure among peritoneal dialysis patients: a systematic review and meta-analysis. *Blood Purif. 2018;46(4):350-58. DOI: 10.1159/000492148*