



Editorial

CHRONIC KIDNEY DISEASE – THE HIDDEN FACE OF DIABETES MELLITUS

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The epidemic evolution of chronic kidney disease (CKD) is a major health problem. CKD affects up to 10% of the adult population of Great Britain (of which 40% are in stage 3 of evolution), and 13% in the United States [1]. For the diagnosis of CKD, two consultations are necessary in a period of over 3 months, with the measurement of serum creatinine and the estimation of GFR (eGFR <60mL/min/1.73m² is considered a diagnosis element), measurements of albumin and urinary creatinine in the spontaneous urine and the calculation of albumin/ urinary creatinine ratio (ACR). ACR ≥30mg/g is another diagnosis element [2]. Therefore, at least one of these tests needs to be repeatedly modified after three months.

CKD, once installed, evolves with the steady and definitive loss of renal function, imposing a substitution therapy of renal function or, on the contrary, evolving towards death. The risk of death is very high. Thus, only one in five patients with CKD reaches end stage disease and has the chance to benefit from renal replacement therapy while four die (the majority out of cardiovascular diseases).

The therapeutic interventions may limit the progression of CKD, the appearance of complications and may reduce the risk of cardiovascular disease or acute exacerbation. In the gradual evolution, CKD associates arterial

hypertension (HTN), left ventricular hypertrophy, anomalies of mineral metabolism and of bones, anemia, acid – base and hydro-electrolytic disequilibrium, malnutrition, inflammation, uremic pericarditis, uremic encephalopathy, etc.

Most frequently, CKD is determined by another systemic diseases which affects the kidneys: first of all diabetes mellitus (DM) (49.8%) and HTN (27.3%) [3]. Diabetic CKD appears in 20-40% of DM patients and shows albuminuria, the decline of the eGFR or both modifications [4]; DM is the main cause of CKD in the final stage. The persistent albuminuria, during the interval of 30-299 mg/ 24 hours, has proved as being a starting stage of diabetic CKD in type 1 DM and a marker for the development of CKD in type 2 DM [5].

The significant improvement of anti-diabetes and anti-hypertensive therapeutic strategies has determined, for the past 30 years, a continuous decrease of the number of type 1 DM patients who need a substitution therapy for the renal function.

The worldwide pandemic evolution of type 2 DM, together with a longer life expectancy, have determined the increase of the prevalence and burden of this disease.

CKD is a powerful death predictor in DM [6]. CKD and DM independently increase the

risk of cardiovascular diseases [5]. Compared to the patients without DM, those with DM already have a high risk of cardiovascular diseases, and the additional development of diabetic CKD more and more increases the cardiovascular risk. All patients with CKD should be considered as high-risk patients for cardiovascular events and need to be treated to reduce this risk.

The progression of CKD in DM may be slowed by an intensive blood glucose control [7] and by the optimization of arterial pressure values [8]. By 1980, most patients with type 2 DM died before progressing to end-stage of CKD.

The Framingham study [9] showed the fact that patients with type 2 DM presented a decline by 69% of mortality due to cardiovascular cause, similar to patients without DM (62% decrease) for the last 25 years, compared to the previous period (1950-1975).

CKD is a disease of multifactorial etiology and needs a multidisciplinary approach. The multidisciplinary team for the integrated care of patients with CKD needs to include family doctors, nephrologists, diabetologists, and cardiologists. The CKD diagnosis in stages 1 and 2 greatly depends on family doctors and other specialists (diabetologists, cardiologists, urologists, rheumatologists, internists, gastroenterologists). Tracing CKD in initial stages also needs the involvement in a higher degree of nephrologists and the modification of medical assistance in ambulatory practice. The increase of efficiency of integrated care for patients with CKD should include a higher collaboration with family doctors and an improvement of legislation (investigation and drugs scale, prices for consultations, etc).

The diagnosis of CKD in DM is usually a clinic/laboratory diagnosis and does not need renal biopsy if there are no doubts regarding the diagnosis. In adults, the screening for CKD in

DM needs to be run using the ACR and eGFR (grade D, Consensus) [10]. For patients with type 1 DM of more than 5 years, screening needs to take place annually, while in those with type 2 DM the screening will take place when DM is diagnosed and then annually. Potential causes for transient albuminuria are represented by: recently intensive physical exercise, febrile disease, infections of urinary tract, menstruation, congestive cardiac insufficiency, severe acute increases of blood glucose, severe acute increases of arterial pressure values [10].

Patients with DM and CKD should have a test of ACR and an eGFR at least once every 6 months (grade D, Consensus) [10].

Adults with DM and persistent albuminuria (ACR >2,0 mg / mmol for men, > 2,8 mg/ mmol for women) should receive an angiotensin-converting enzyme inhibitor (ACE inhibitor) or an angiotensin receptor blocker (ARB) to delay the progression of CKD, even when HTN is missing (grade A, Level 1A) [10]. Patients with DM who receive ACE inhibitor or ARB will be checked for the serum creatinine and serum potassium levels in 1 or 2 weeks from the initiation of therapy and also during acute periods (grade D, Consensus) [10].

Sending patients to nephrologists needs to be taken into consideration when: there is a progressive chronic decline of renal function (eGFR is <30 ml / min; ACR is over 60 mg/mmol, persistent; the patient is unable to reach the goal of arterial pressure; when adverse effects appear (hyperkalaemia or an increase of > 30% of serum creatinine in a period of 3 months from the beginning of treatment), for patients on renal protection therapies such as ACE inhibitor or ARB) (grade D, Consensus) [10].

Don't forget key messages: Most frequently CKD is determined by another disease that affects the kidneys, first of all, DM

(49.8%) and HTN (27.3%); approximately 1 of 2 patients with type 2 DM will have CKD; for the diagnosis of CKD two consultations are needed in a period of more than 3 months; for adults with type 1 DM of over 5 years duration the screening needs to be run annually, and for those

with type 2 DM when the DM is diagnosed and afterwards annually; CKD and DM independently increase the risk of cardiovascular diseases; CKD is a powerful predictor of death in DM patients.

REFERENCES

1. **Hajhosseiny R, Khavandi K, Goldsmith DJ.** Cardiovascular disease in chronic kidney disease: untying the Gordian knot. *Int J Clin Pract* 67: 14- 31, 2013.
2. *** KDIGO 2012 Guideline for Evaluation and Management of CKD. *Kidney Int Suppl* 3: 19–62, 2013.
3. **O'Hare AM, Batten A, Burrows NR et al.** Trajectories of kidney function decline in the 2 years before initiation of long-term dialysis. *Am J Kidney Dis* 59: 513–522, 2012.
4. **American Diabetes Association.** Standards of medical care in diabetes-2014. *Diabetes Care* 37 [Suppl.1]: S14-S80, 2014.
5. **Wang Y, Katzmarzyk PT, Horswell R, Zhao W, Johnson J, Hu G.** Kidney function and the risk of cardiovascular disease in patients with type 2 diabetes. *Kidney Int.* 85: 1192-1199, 2014.
6. **Afkarian M, Sachs MC, Kestenbaum B et al.** Kidney disease and increased mortality risk in type 2 diabetes. *J Am Soc Nephrol* 24: 302-308, 2013.
7. **Wang PH, Lau J, Chalmers TC.** Meta-analysis of effects of intensive blood- glucose control on late complications of type I diabetes. *Lancet* 341: 1306-1309, 1993.
8. **Maki DD, Ma JZ, Louis TA et al.** Long-term effects of antihypertensive agents on proteinuria and renal function. *Arch Intern Med* 155: 1073-1080, 1995.
9. **Preis SR, Hwang SJ, Coady S et al.** Trends in all-cause and cardiovascular disease mortality among women and men with and without diabetes mellitus in the Framingham Heart Study, 1950 to 2005. *Circulation* 119: 1728–1735, 2009.
10. **McFarlane Ph, Gilbert RE, MacCallum L, Senior P, Canadian Diabetes Association Clinical Practice Guidelines Expert Committee.** Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: chronic kidney disease in diabetes. *Can J Diabetes* 37[suppl 1]: S129-S136, 2013.