PREVENTION OF CHRONIC KIDNEY DISEASE – A PUBLIC HEALTH CHALLENGE

LĖTINIŲ INKSTŲ LIGŲ PROFILAKTIKA – VISUOMENĖS SVEIKATOS PROBLEMA

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SUMMARY

KEY WORDS: renal dysfunction, cardiovascular diseases, risk assessment, public health

With the availability of dialysis and transplantation the number of patients ending up in endstage renal failure has skyrocketed in the Western world, the annual incidence being currently 100-200 patients per million population per year, which constitutes an enormous burden on the health budget. The most common cause of endstage renal disease is today nephropathy in patients with type 2 diabetes.

Today effective treatment is available to retard, or even stop, progressive loss of renal function in patients with renal disease.

From a public health perspective even more relevant is the fact that even minor renal dysfunction causes a dramatic increase of cardiovascular events and cardiovascular death. This had not been appreciated in the past. Today, however, it is beyond doubt that even minor kidney dysfunction constitutes a major cardiovascular risk factor – irrespective of whether a primary renal disease is present or not. Assessment of renal function (serum creatinine; estimated creatinine clearance, albuminuria) should therefore today be part and parcel of the evaluation of every patient with hypertension or cardiovascular disease, particularly of patients with diabetes.

SANTRAUKA

REIKŠMINIAI ŽODŽIAI: inkstų nepakankamumas, kardiovaskulinės ligos, rizikos veiksnių, visuomenės sveikata.

Dializei ir transplantacijai tapus plačiai prieinamomis, Vakarų pasaulyje nepaprastai išaugo pacientų, sergančių terminaline inkstų nepakankamumo stadija, skaičius – tokių arvėjų metinis dažnis siekia 100-200 pacientų milijonui gyventojų, o tai tapo didžiule našta sveikatos apsaugas biudžetui. Šiuo metu dažniausia terminalinio inkstų nepakankamumo priežastis yra pacientų, sergančių antrojo tipo diabetu, nefropatija. Šiandien efektyvus gydymas gali sulėtinti ar netgi sustabdyti inkstų ligomis sergančių pacientų inkstų funkcijos pradėtą progresavimą.

Visuomenės sveikatos požiūriu dar svarbesnis yra faktas, kad netgi nedidelė inkstų disfunkcija labai lemia kardiovaskuliniių komplikacijų ir netgi mirčių skaičiaus didėjimą. Praeityje į tai nebuvo atsižvelgiama. Šiandien jau neabejojama, kad net nedidelė inkstų disfunkcija yra rimtas kardiovaskulinės rizikos veiksnys – nepriklausomai nuo to, yra ar nėra pirmos inkstų liga. Dėl to inkstų funkcijos įvertinimas (serumo kreatininas, nustatytas kreatininio klirensas, albuminurija) dabar turi būti kiekvieno paciento, sergančio hipertenzija ar kardiovaskulinė liga, ypač diabetikų, sudegamo į įvertinimo dalis.
HOW FREQUENT AND HOW COSTLY IS ENDSTAGE RENAL DISEASE AND ITS TREATMENT?

In the Western world approximately 75-200 patients per million population reach endstage renal disease [1] and require chronic dialysis or kidney transplantation to survive. Comparable figures have been found in some countries of Eastern Europe[2] including the Baltic countries (Table 1).

If one can survive on dialysis or after transplantation, why is it still absolutely necessary to prevent endstage renal disease?

For several reasons:

First, the average mortality on dialysis is 10-20 percent per year, depending on the country – a survival comparable to that of patients with metastasizing gastrointestinal carcinoma. The mortality is between several hundredfold or tenfold higher than in nonrenal individuals of the same age (Fig. 1). Furthermore although the technique of dialysis has been substantially improved, the quality of life is still markedly reduced on dialysis.

Second, kidney transplantation (which provides better quality of life if successful) is limited by the availability of donors and puts great strains on the logistics of the health care system. Nevertheless, the Baltic countries have achieved admirable success in this field which is acknowledged throughout Europe [2].

Third, dialysis and transplantation are costly procedures. Survival on dialysis in Germany costs approximately 40,000 Euros per year which puts an immense burden on the public health system. Renal transplantation is less costly after the first year, but current transplantation rates do not catch up with the inflow of new patients.

CAN ONE PREVENT PROGRESSION OF RENAL DISEASE?

Against this background one must raise the question: can one prevent kidney disease and in the patients who are already afflicted by this condition can one halt its progression to endstage renal disease?

Table 2 shows that today in the USA (www.USRDS.org) and in Heidelberg [3] diabetes has become the single most frequent cause of endstage renal dis-

TABLE 1 INCIDENCE OF PATIENTS ADMITTED FOR RENAL REPLACEMENT THERAPY IN CENTRAL AND EASTERN EUROPE (AFTER RUTKOWSKI AND RITZ [2])

<table>
<thead>
<tr>
<th>Country</th>
<th>ppm</th>
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<tbody>
<tr>
<td>Russia</td>
<td>15</td>
</tr>
<tr>
<td>Estonia</td>
<td>28</td>
</tr>
<tr>
<td>Bielorussia</td>
<td>31</td>
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<tr>
<td>Yugoslavia</td>
<td>37</td>
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<tr>
<td>Romania</td>
<td>53</td>
</tr>
<tr>
<td>Latvia</td>
<td>59</td>
</tr>
<tr>
<td>Macedonia</td>
<td>73</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>77</td>
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<tr>
<td>Lithuania</td>
<td>77</td>
</tr>
<tr>
<td>Poland</td>
<td>103</td>
</tr>
<tr>
<td>Bosnia-Herzegovina</td>
<td>110</td>
</tr>
<tr>
<td>Croatia</td>
<td>118</td>
</tr>
<tr>
<td>Hungary</td>
<td>128</td>
</tr>
<tr>
<td>Slovakia</td>
<td>139</td>
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<tr>
<td>Slovenia</td>
<td>144</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>171</td>
</tr>
</tbody>
</table>

ease – obviously every measure to prevent type 2 diabetes (lifestyle changes, treatment of the prediabetic metabolic syndrome) as well as improved care of the diabetic patient (normalization of blood glucose, blood pressure lowering, reduction of proteinuria ..) are well indicated[4], particularly since these measures are effective and have recently stopped the past inexorable continuous increase in the number of diabetic patients admitted with endstage renal disease both in the USA (www.USRDS.org)[5] and in Europe at least in Denmark[6]. In early stages of diabetic nephropathy glycemic control is of greatest importance, while in established diabetic nephropathy blood pressure lowering to target, blockade of the renin-angiotensin system and reduction of proteinuria are of overriding importance. At all stages cessation of smoking is highly beneficial. (Table 3)

Even in nondiabetic renal disease, however, one can successfully interfere with progressive loss of renal function by the same measures as listed in Table 3 with the obvious exception of glycemic control.

Are these measure effective? What is the evidence? One interesting piece of evidence has recently been provided by a study [7] which compared the frequency of chronic kidney disease and the incidence of patients admitted for renal replacement therapy between Trondheim (Norway) and white inhabitants of the USA. Although early kidney failure was similarly frequent in the 2 countries, the rate of admission with endstage kidney disease was significantly less in Norway. With good reason the authors ascribed this to good medical care in Norway of renal patients in the preterminal phase of their disease. So it pays off to devote a great effort to halting progression of renal disease – and this also saves the health budget a lot of money.

**How many individuals do have reduced kidney function and how can reduced kidney function be diagnosed?**

It has recently been recognized that minor renal dysfunction, i.e. reduced glomerular filtration rate (GFR), is by no means rare, particularly in the elderly, and is grossly underestimated by relying only on the serum creatinine value as the index of renal function. The serum creatinine concentration depends not only on the GFR, but also on a number of confounding factors, particularly muscle mass, consumption of cooked meat and tubular secretion of creatinine. To circumvent this dilemma and to obtain a more precise estimate of reduced renal function, the so-called MDRD (modification of diet in renal disease study) formula has been introduced in order to estimate GFR on the basis of serum creatinine concentration, body mass index and gender as shown in Table 4.

Using this estimate a large national census in the USA (NHANES, national health and nutrition examination study) showed that in the USA the figure of

**Table 3** The main goals of treatment in diabetic patients with nephropathy

<p>| | |</p>
<table>
<thead>
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<tbody>
<tr>
<td>1.</td>
<td>BP &lt; 125/75 mmHg</td>
</tr>
<tr>
<td>2.</td>
<td>blockade renin-angiotensin system (ACE inhibitors, Angiotensin receptor blockers)</td>
</tr>
<tr>
<td>3.</td>
<td>proteinuria &lt; 1g/24h</td>
</tr>
<tr>
<td>4.</td>
<td>glycemic control</td>
</tr>
<tr>
<td>5.</td>
<td>cessation of smoking</td>
</tr>
<tr>
<td>6.</td>
<td>lipid lowering</td>
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**Table 4** eGFR algorithm

**MDRD formula (2005)**

\[
\text{GFR} = 175 \times (\text{standardized } S-\text{crea})^{1.154} \times (\text{age})^{-0.203} \times 0.742 \text{ (for females)}
\]


![chart](chart.png)
300,000 patients on dialysis (comprising 0.1 % of the US population) contrasts with the enormous number of 12.9 million inhabitants (7.3% of the US population) who have an estimated GFR between 89 and 30 ml/min/1.73m².

**HOW GREAT IS THE RISK OF HEART DISEASE AND STROKE IN INDIVIDUALS WITH MINOR RENAL DYSFUNCTION ?**

Do all those patients with mild to moderate reduction of GFR end up in endstage renal disease? No. It has been shown that for such a patient the risk to die from cardiovascular causes, mainly sudden death, heart failure, myocardial infarction and stroke, is 20 times greater than to end up on dialysis[8]. Meanwhile there is an overabundance of evidence that the cardiovascular risk conferred by minor renal dysfunction is comparable in magnitude to that conferred by classical risk factors such as LDL-cholesterol, hyperglycemia and others. This has been shown in the general population [9], populations at high cardiovascular risk [10], and particularly in patients with myocardial infarction [11, 12] or surviving with a history of MI or congestive heart failure [13].

But it is not only reduced GFR, but even less dramatic kidney malfunction such as proteinuria or trace albuminuria dramatically increases the cardiovascular risk. The cardiovascular risk of proteinuria had originally been shown in the Framingham study [14] and that of microalbuminuria (30-300 mg/day) or even high normal albuminuria has recently been confirmed in large studies such as the LIFE study [15, 16] or the Dutch PREVEND study [17].

**HOW CAN WE DEAL WITH THIS PROBLEM ?**

To take care of all these patients would surpass the capacity of nephrologists, the specialists in kidney disease. What is necessary is to first to raise the awareness of the nonspecialist about the importance of kidney malfunction and kidney disease. This necessitates that instead of only measuring serum creatinine laboratories must calculate the eGFR for which they require data on age, gender and body mass index and standardized methodology to measure serum creatinine.

Second at least in high risk patients (hypertension, metabolic syndrome) urinary albumin should be measured for which several procedures are available [18].

Third to reduce the patient load with progressive primary renal disease it will be necessary that general practitioners and nephrologists work closer together. Our society recommends that patients with primary renal disease and elevated creatinine are seen once per year by the nephrologist and when eGFR is higher than 30 ml/min/1.73m² the nephrologist should take care of the patient. Numerous studies documented [19] that late referral to the nephrologist causes a striking increase of mortality on dialysis or after transplantation.

Finally it would be useful to educate the general population about the importance of kidney malfunction and disease – not to frighten, but to make them conscious that early detection may ward off the tragic late stages of kidney disease. What has been so beautifully demonstrated with respect to lipids, hypertension and diabetes by our Finnish colleagues [20, 21] should also be possible with respect to kidney disease.

**REFERENCES**


