ORIGINAL ARTICLE

Identifying chronic kidney disease in an emergency department: a chance for an early diagnosis

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KEY WORDS

chronic kidney disease, emergency department, glomerular filtration rate, screening programs

ABSTRACT

INTRODUCTION Chronic kidney disease (CKD) has relatively asymptomatic course, but even at its onset, it worsens the prognosis of patients, mainly because of the increased risk of cardiovascular diseases. Several population-based screening programs as well as initiatives focused on certain risk groups were undertaken to better diagnose early stages of CKD. It appears that an emergency department (ED) of a hospital may be the right place to screen for early CKD.

OBJECTIVES The aim of the study was to assess the accuracy of ED practices in the detection of CKD.

PATIENTS AND METHODS The study involved 176 subjects who presented at the ED over 1 month and were subsequently admitted to one of the wards at the general hospital. Blood pressure on admission was recorded in 61% of the patients; serum creatinine and estimated glomerular filtration rate (eGFR) were measured in 50% of the subjects, urea in 42.2%, potassium in 87.5%, and glucose in 82%. Patients with previously diagnosed CKD were excluded from the study.

RESULTS Sixty-three per cent of blood pressure values exceeded 140/90 mmHg, 27.3% of all creatinine samples exceeded the upper limit of 1.2 mg/dl, and 64.8% of eGFR results were below 90 ml/min/1.73 m^2 (mean 78 ±36 ml/min/1.73 m^2). Abnormal levels of urea (>50 mg/dl) were observed in 32% of the patients. Potassium levels were within the reference range in 81.5% of the patients (3.5–5.0 mmol/l; only 10.4% exceeding 5 mmol/l). Elevated glucose levels (>110 mg/dl) were observed in 60% of the patients.

CONCLUSIONS ED practices could be used to identify a significant number of patients with undiagnosed CKD. However, these simple, widely available, and cost-effective methods of early CKD detection are underused. Our results show that there is an urgent need for a structural screening program for CKD at the level of ED.

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INTRODUCTION Chronic kidney disease (CKD) is currently considered to be an epidemic due to its increasing prevalence. However, it is very difficult to precisely estimate the occurence of the disease because only its advanced stages have clinically detectable symptoms. Due to its mild, subclinical course, the only certain fact about CKD epidemiology is the number of patients on dialysis or with a transplanted kidney. On the other hand, it is widely known that any stage of CKD (especially when glomerular filtration rate [GFR] falls below 60 ml/min) is associated with a significantly increased risk of cardiovascular complications and death.[1] The sad reality is that none of the available therapeutic interventions have been shown to change the fate of

TABLE 1 Categories of primary symptoms or diseases in the emergency department based on preliminary diagnosis

Symptom or disease	Women	Men	Total	%
trauma/injury	10	10	20	12.5
gastrointestinal bleeding	7	6	13	7.4
abdominal pain	9	9	18	10.2
suspicion of stroke	14	23	37	21.2
cardiovascular disease	18	43	61	33.5
diabetes	2	3	5	2.8
arterial hypertension	4	4	8	4.5
otolaryngological problems	2	2	4	2.3
ophthalmologic problems	2	0	2	1.1
gynecological disease	6	0	6	3.4
neoplasm	1	1	2	1.1
total	75	101	176	100

patients with overt disease or to lower the risk of death. This applies to such treatment modalities as erythropoiesis-stimulating agents, phosphate-binding drugs, lipid-lowering therapy, angiotensin-converting enzyme inhibitors, etc.[2,3] Therefore, CKD patients should be diagnosed as early as possible, so that all the available therapeutic measures can be implemented to slow down the progression of renal disease and to prevent the development of more advanced stages.

For many years, renal community has made efforts to identify CKD patients at the earliest possible stage, by implementing different screening programs. There have been population-based programs and also more "targeted" ones, namely those analyzing patient groups with certain risk factors, such as hypertension, diabetes, ethnicity, or CKD in family history. The prevalence of CKD in these programs varies from 10% to more than 50% and, obviously, the more targeted is the search, the higher the chance to identify patients at risk.[4-8] Searching for asymptomatic patients with possible CKD at early stages seems a difficult task, and it may not be very efficient (including cost-efficiency), especially in the population-based studies.

We assumed that the emergency department (ED) may be the right place to search for CKD. The advantage of screening for CKD in this setting is that no search is required, because patients (often with several comorbidities and risk factors for CKD) come on their own. On the other hand, this is an example of "non-targeted" screening, because no prespecified criteria were applied before the examination. The aim of the present study was to investigate routine ED practices, which may allow to identify patients with CKD or with major risk factors for its development.

PATIENTS AND METHODS

Between January 1 and January 31, 2010, we analyzed the current clinical practices at the ED of a large, university-affiliated hospital serving the population of about 200,000. This analysis may become useful in the identification of patients with CKD or with certain risk factors for its development. The purpose of the study was not to create and test a "structured" screening program, but rather to take a "snapshot" of the present practices, which might help establish such a screening policy for CKD.

A total of 1146 patients have been admitted to the ED during the specified period. Most of them (934) had minor clinical problems, which were handled on an outpatient basis. In those patients no further laboratory tests or imaging procedures were performed, except for general physical examination, prescription of common drugs (oral antibiotics, pain killers, antipyretic or antidiarrheal agents, etc.) and sometimes minor surgical procedures (because of the carnival period, many patients were young people with minor injuries caused by alcohol overuse). We excluded pregnant women presenting for delivery (n = 12) and patients with critical illnesses who were immediately transferred to the operation theatre or intensive care unit without detailed diagnosis or blood sampling in the ED (n = 22). This left us with 178 patients who were preliminary diagnosed in the ED and later were nonelectively admitted to any of the hospital wards. We excluded patients with previously diagnosed CKD (based on history and medical records; n = 2). Thus, the final study group comprised 176 patients: 75 women (43%) and 101 men (57%) aged between 18 and 91 years (mean 59.6 ±20.3 years).

We investigated the frequency of those procedures performed in the ED, which may help identify the presence of CKD or the risk factors for its development. These included blood pressure measurement, urinalysis, measurement of serum urea, creatinine, glucose, potassium, and estimated GFR (eGFR) calculation. We carefully reviewed all medical records in the ED as well as the central laboratory database to obtain the true image of the current practices. The ED staff was not aware of the ongoing analysis.

All biochemical analyses were performed using the Cobas 6000 Analyser equipment (Roche Diagnostics, Basel, Switzerland), which utilizes the Jaffe method to measure serum creatinine levels. Blood pressure was measured with the certified Omron M6 Comfort electronic sphygmomanometer (Omron Ltd., Kyoto, Japan). eGFR was calculated using the abbreviated four-parameter Modification of Diet in Renal Disease (MDRD) formula; it has been calculated automatically by the laboratory in every patient with blood sampled for creatinine levels.

Statistical analysis Statistical analysis of the data was performed using the Statistica 8.0 software (StatSoft Inc., Tulsa, Oklahoma, United States). The Shapiro-Wilk's *W*-test for normality was used for data distribution analysis. Because all the variables were normally distributed, the results were presented as mean ± standard deviation. For intergroup comparisons, the *t* test for independent variables was used. We considered a *P* value of less than 0.05 as statistically significant.

TABLE 2 Wards admitting emergency patients after preliminary work-up

Ward	Number of patients	%
orthopedics	13	7.4
gastroenterology	22	12.6
neurology	38	21.6
cardiology	49	27.8
otolaryngology	4	2.3
nephrology	13	7.4
ophtalmology	2	1.1
diabetology	5	2.8
surgery	14	7.9
gynecology	6	3.4
intensive care unit	4	2.3
neurosurgery	6	3.4
total	176	100

TABLE 3 Distribution of patients with estimated glomerular filtration rate below 90 ml/min/1.73 m^2 within respective stages of chronic kidney disease

CKD stage	Number of patients	% of patients with measured eGFR
2	29	50.8
3	20	35.1
4	5	8.8
5	3	5.3
total	57	100

Abbreviations: CKD – chronic kidney disease, eGFR – estimated glomerular filtration rate

TABLE 4 Distribution of patients with estimated glomerular filtration rate below 90 ml/min/1.73 m^2 and serum creatinine above 1.2 mg/dl within individual stages of chronic kidney disease

CKD stage	Number of patients	%
2	3	12.5
3	13	54.2
4	5	20.8
5	3	12.5
total	24	100

Abbreviations: see TABLE 3

RESULTS The study group comprised 176 patients who presented at the ED and were later admitted nonelectively to one of the hospital wards between January 1 and 31, 2010. We identified 11 initial categories of preliminary diagnosis or dominating symptom, on the basis of which the patients were admitted to 11 different wards. The data are summarized in TABLE 1. As mentioned in the above section, patients with previously diagnosed CKD were excluded from the study. The wards to which emergency patients were admitted are listed in TABLE 2; cardiology and neurology units were the most frequent destinations (up to 60% of all admissions).

Blood pressure was measured in the whole study group but recorded in the medical files of only 108 patients (61%). Most of these 108 patients were later admitted to the departments of cardiology (44%) and neurology (32%). The mean blood pressure was 148.6 ±35.8 mmHg (systolic) and 83.3 ±17.4 mmHg (diastolic). In 68 patients, (63% of those with known blood pressure) the values exceeded 140/90 mmHg.

Serum creatinine was measured in 88 patients (50% of the study group). The mean serum creatinine was 1.3 ±1.4 mg/dl (1.6 ±2.1 for women and 1.1 ±0.5 mg/dl for men); in 24 patients it exceeded the upper normal value of 1.2 mg/dl (27.3% of all creatinine samples and almost 14% of the study group). Seventy one percent of patients with elevated serum creatinine were admitted to the departments of nephrology, cardiology, and neurology (with equal distribution between the three). By definition, in all 88 patients with creatinine assessment, MDRD-eGFR was also available. Mean eGFR was 78 ±36 ml/min/1.73 m^2 (64 ±34 ml/min/1.73 m^2 for women and 88 ±35 ml/min/1.73 m^2 for men). Fifty-seven eGFR results (64.8% of the patients with assessed eGFR and 32.4% of all patients) were below 90 ml/min/1.73 m^2, i.e., fulfilled one of the general criteria for CKD diagnosis (of at least stage 2). A detailed distribution of patients within the ranges of eGFR and the corresponding stages of CKD are shown in TABLE 3 (we omitted stage 1 patients on purpose because using the available data we were unable to detect kidney damage in patients with normal eGFR – urinalysis was performed only in 5 of 176 subjects). Because low serum creatinine in older people with sarcopenia may artificially decrease eGFR, we also analyzed the number of patients with eGFR ml/min/1.73 m^2 below 90 and serum creatinine exceeding 1.2 mg/dl to increase the potential "sensitivity" of CKD diagnosis. As can be concluded from TABLE 4, even using more restricted criteria we still were able to identify 24 patients with CKD in stages 2 to 5 (13.6% of all admitted patients). As can be predicted, this adjustment dramatically reduced the number of patients with CKD stage 2, decreased the number of patients with CKD stage 3 by roughly 40%, and did not affect the most advanced stages 4 and 5. Differences between patients with CKD (eGFR <90 ml/min/1.73 m^2) and those without (eGFR >90 ml/min/1.73 m^2) are shown in TABLE 5.

Urea was assessed in 83 subjects (42.2% of the study group) and exceeded the normal value of 50 mg/dl in 32% of the cases. Potassium was measured in 154 patients (87.5% of the study group), and in 82.5% of the assays the results were within the reference range of the local laboratory (3.5–5.0 mmol/l). Mean serum potassium was 4.3 ±0.8 mmol/l, with only 10.4% exceeding 5 mmol/l (however, 2 critically high values of 7.11 and 7.96 mmol/l were observed).

TABLE 5 Comparison of patients with known estimated glomerular filtration rate and with or without chronic kidney disease

Parameter	CKD n = 57	No CKD n = 31	*P*
age, y	69.2 ±15.6	55.0 ±20.7	<0.01
eGFR, ml/min/1.73 m^2	55.6 ±20.5	118.5 ±21.5	<0.001
glucose, mg/dl	153.7 ±71.9	144.8 ±85.6	NS
urea, mg/dl	68.4 ±68.2	33.9 ±12.7	<0.01
creatinine, mg/dl	1.6 ±1.6	0.7 ±0.1	<0.01
potassium, mmol/l	4.4 ±0.9	4.2 ±0.5	<0.05
systolic blood pressure, mmHg	141.3 ±34.4	153.1 ±32.2	NS
diastolic blood pressure, mmHg	78 ±18.2	86.4 ±16.2	<0.01

Abbreviations: NS – nonsignificant, others – see TABLE 3

Serum glucose was measured in 145 patients (82% of the study group). In 87 patients (60% of the assays), increased glucose levels were observed (>110 mg/dl). Interestingly, only 27 patients had previously diagnosed diabetes. Certainly, these results should be interpreted with caution because in many patients serum glucose might not have been measured in the fasting state.

We also looked at the number of computed tomography (CT) scans performed in the study group. Forty-three patients (27% of the study group) underwent CT examination ordered by ED prior to subsequent hospital admission. There were 25 of 38 patients admitted later to the department of neurology, 6 of 49 to cardiology, and 4 of 6 to neurosurgery. The main indication for a CT scan was the suspicion of stroke. Serum creatinine and eGFR measurements were available only in 20 patients referred for CT (less than 50%); the results were 1.11 ±0.57 mg/dl and 89.9 ±32.8 ml/min/1.73 m^2, respectively, indicating lack of advanced CKD in all but 1 patient from this group (serum creatinine, 3.3 mg/dl; eGFR, 19 ml/min/1.73 m^2).

DISCUSSION The main finding of our study is that the ED does not fully utilize the available tools that might be helpful in the early detection of CKD. The parameters that are critical for early identification of CKD or CKD risk were usually assessed in less than 50% of the patients who presented at the ED and were subsequently admitted to different hospital wards, although their clinical profile strongly suggested high probability of CKD. While serum creatinine (and eGFR calculation) was measured in 50% of the patients and urea in 42%, urinalysis was performed only in 2.84% of the study group. Based exclusively on the criterion of eGFR, 64.8% of the patients with known eGFR and 32.4% of all patients admitted nonelectively to the hospital had CKD stages 2 to 5; when criterion of elevated serum creatinine was added, these figures decreased to 27.3% and 13.6%, respectively.

The latter numbers are in line with most of the epidemical data published to date. According to one of the latest reports from the Third National Health and Nutrition Examination Survey (NHANES III) database, CKD defined as eGFR between 15 and 60 ml/min (stages 3 and 4) affected 1651 of 8829 patients (18.9% of the studied population). In this particular study, the analysis of CKD prevalence was limited to patients with hypertension; patients with CKD stages 1, 2, and 5 were excluded to avoid misclassification of CKD in its extremes (due to relatively low sensitivity of the MDRD formula in the lowest and highest ranges of GFR).[6] In one of the early NHANES III reports, 11% of all noninstitutionalized adults aged 20 years and older were considered to suffer CKD of any stage.[8] In the landmark study of Król et al.,[4] albuminuria was detected in 15.6% of 2471 people from the Polish general population when the dipstick test was used; it was confirmed in 11.9% by the turbidimetric method. Based on his prescreening, 481 people were consulted by a nephrologist; of these, 96% were diagnosed with any stage of CKD (9% of this population had MDRD-eGFR <60 ml/min/1.73 m^2).

Our study cannot be directly referred to the population-based epidemiological studies. Most of our patients suffered from cardiovascular or cerebrovascular diseases and were subsequently admitted to the neurology or cardiology wards, so this was the group with significant comorbidities. Hence, we should rather compare our data to the studies describing populations with such comorbidities. For example, the Kidney Early Evaluation Program (KEEP) focused more specifically on patients with increased risk of CKD (i.e., hypertension, diabetes, or family history of renal disease). According to one of the early KEEP reports, CKD was present in as many as 47.4% of screened patients.[9] As can be expected, presence of CKD was directly associated with increased risk of cardiovascular events and mortality.[5] Prevalence of CKD among patients with cardiovascular comorbidity is a well-known phenomenon with bidirectional cause-effect relationship: patients with atherosclerotic cardiovascular disease have higher risk for developing CKD and CKD is one of the strongest risk factors for cardiovascular complications. In a recently published analysis of the NHANES III, CKD of any stage was found in 63.7% of patients with a history of stroke (and in 34.9% eGFR was <60 ml/min/1.73 m^2). Mean eGFR in this population was 69.0 ±20.8 ml/min/1.73 m^2.[10] In a recent report from China, CKD was diagnosed in 34.1% of patients who were at least 50 years old and had a history of coronary artery disease, stroke, peripheral vascular disease, or 2 or more risk factors for developing cardiovascular disease.[11]

The MDRD formula has recently been criticized by several authors because it significantly overestimates the true values of GFR in patients with advanced CKD and underestimates in those with normal renal function or incipient CKD. The error associated with using the MDRD formula is further enhanced by imprecision in serum creatinine measurement.[12] This prompted several groups of

experts to develop and validate alternative, anthropometry-based formulas, which are expected to be better correlated with true GFR. Among the most popular and widely used is the Chronic Kidney Disease Epidemiology Collaboration formula.[13] This formula, used in a number of studies and various populations with renal disease, seems to have the best performance as compared with other methods of GFR calculation, although it cannot be used at this stage as a reference formula.[14-17] Considering all drawbacks of the MDRD formula, it is possible to misclassify patients with normal renal function as having CKD stage 2 or even stage 3. By applying the criterion of low eGFR combined with elevated serum creatinine, we significantly decreased the number of patients with CKD with a shift towards its more advanced stages, which we believe greatly reduced the possibility of such a misclassification.

Our study has several limitations. Patients' comorbidities, past medical history, medications taken, or follow-up after admission were not assessed in detail. The "three-month" criterion of CKD diagnosis was not fulfilled – patients were not reassessed after 3 months to confirm that kidney damage was chronic. Nevertheless, the main objective of the study was to asses to what extent routine ED practices might be useful in identifying patients with CKD – it was a snapshot of these practices. Excluding patients with life-threatening conditions seemed reasonable, because many of them might have suffered from acute kidney injury rather than from CKD (our methodology did not allow us to differentiate between the two groups). However, to our knowledge, there have been no other studies on the prevalence of CKD among emergency patients.

In conclusion, ED seems to be the right place to detect CKD using simple tools and may help identify numerous patients with this clinical entity. If serum creatinine, eGFR, or even blood pressure are not measured, we risk overlooking a significant percentage of patients who might benefit from early (on-admission) identification of CKD. This means that another chance to be diagnosed with CKD is lost, at least for some patients. Renal community calls for action to detect patients with early CKD. It is of paramount importance because several clinical trials published recently have shown poor results of therapeutic interventions in advanced CKD (such as lipid or blood pressure-lowering drugs, erythropoiesis-stimulating agents, medications that correct abnormalities of CKD-related mineral and bone disorder, etc.).[18-22] On the other hand, patients who present at the ED and show a set of risk factors for CKD are not screened for this disease. Our results indicate that there is an urgent need for a structural screening program for CKD at this level of health care.

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ARTYKUŁ ORYGINALNY

Rozpoznawanie przewlekłej choroby nerek na szpitalnym oddziale ratunkowym: szansa na wczesną diagnozę

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programy przesiewowe, przewlekła choroba nerek, szpitalny oddział ratunkowy, współczynnik przesączania kłębuszkowego

STRESZCZENIE

WPROWADZENIE Przewlekła choroba nerek (PChN) ma skąpoobjawowy, niecharakterystyczny przebieg kliniczny, lecz nawet we wczesnych stadiach w istotny sposób pogarsza rokowanie pacjentów, głównie poprzez znaczny wzrost ryzyka chorób układu sercowo-naczyniowego. Aby poprawić wykrywalność PChN w jej wczesnych stadiach, zainicjowano szereg programów przesiewowych, zarówno populacyjnych, jak i adresowanych do poszczególnych grup ryzyka. Wydaje się, że szpitalny oddział ratunkowy (SOR) może być odpowiednim miejscem do wczesnego rozpoznawania tej choroby.

CELE Celem badania była ocena przydatności procedur stosowanych na SOR do wykrywania PChN.

PACJENCI I METODY W badaniu wzięło udział 176 pacjentów, którzy w ciągu miesiąca zgłosili się na SOR, a następnie zostali przyjęci na jeden z oddziałów szpitala wojewódzkiego. Ciśnienie tętnicze w chwili przyjęcia zostało udokumentowane u 61% pacjentów, u 50% dokonano pomiaru stężenia kreatyniny w osoczu i wyliczono współczynnik przesączania kłębuszkowego (*estimated glomerular filtration rate* – eGFR), stężenie mocznika zbadano u 42,2%, stężenie potasu u 87,5%, a stężenie glukozy – u 82% pacjentów. Z badania wykluczono pacjentów, u których już wcześniej zdiagnozowano PChN.

WYNIKI W 63% pomiarów ciśnienie przekraczało 140/90 mm Hg, w 27,3% pomiarów kreatyniny stwierdzono stężenie powyżej górnej wartości referencyjnej (>1,2 mg/dl), a 64,8% wyników eGFR było <90 ml/min/1,73 m^2 (średnio 78 ±36 ml/min/1,73 m^2). Nieprawidłowy mocznik (>50 mg/dl) stwierdzono u 32% pacjentów. Poziom potasu był w zakresie prawidłowym u 81,5% pacjentów (3,5–5,0 mmol/l; tylko w 10,4% wyników >5 mmol/l). Nieprawidłowy poziom glukozy (>110 mg/dl) stwierdzono u 60% pacjentów.

WNIOSKI Stosowane na SOR procedury mogłyby pozwolić na zidentyfikowanie znacznej liczby pacjentów z dotychczas nierozpoznaną PChN. Te proste, łatwo dostępne i tanie metody wczesnego wykrywania choroby są jednak wykorzystywane w niedostatecznym stopniu. Nasze wyniki wskazują na potrzebę rozwoju programów przesiewowych w kierunku rozpoznawania PChN na SOR.

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