Original article

Screening for chronic kidney disease in Belgrade Primary Health Care Centers

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Summary

Introduction. Academy of Medical Science of Serbian Medical Society introduced collaboration between Belgrade nephrologists and general practitioners with the aim of examining the prevalence of chronic kidney disease (CKD) in populations at risk as well as of checking whether collaboration with general practitioners contributed to implementation of regular CKD screening.

Methods. The research encompassed two studies carried out in four Belgrade Primary Health Care Centers. The screening study involved 619 patients at risk for CKD (348 with hypertension, 206 with diabetes, 65 persons aged > 60 years without hypertension/diabetes) in whom glomerular filtration rate (eGFR) was estimated by MDRD formula, while urine dipstick test was used for detection of proteinuria and albuminuria (Micral-test® strips).The second study was retrospective analysis of medical records of 450 patients who were examined in the screening study and whose blood pressure and eGFR recording were analyzed during three-year period.

Results. In screening study, eGFR below 60 ml/min/1.73m^2 was detected in 121 (19.55%) and albuminuria in 242 (39.10%) patients. During three-year retrospective study, percentage of patients whose blood pressure and eGFR were recorded decreased from 42% to 22% and from 42% to 18%, respectively. Multivariate regression analysis selected health center, systolic blood pressure and hypertension as the variables significantly associated with the number of years in which blood pressure was recorded, while male gender, health center, hypertension and basal eGFR as variables associated with the number of years in which eGFR was recorded.

Conclusion. Despite collaboration between nephrologists and general practitioners in screening study, the retrospective three-year study revealed insufficient recording of blood pressure and eGFR in patients' medical records.

Keywords: chronic kidney disease, screening, primary health care

Introduction

In the last decades of the 20th century, a steady increase in the overall incidence rate of end-stage renal disease (ESRD) was observed in developed countries. The highest increase was registered in ESRD due to hypertension and diabetes, as well as in the older age groups [1]. However,

ERA-EDTA Registry data showed a stabilization of the overall incidence rate of RRT in developed European countries starting from 2000, but since 2008 the incidence rate has even been decreasing [1, 2]. Similar trends were described in other developed countries of the world [3, 4]. This change in incidence rate of RRT was partly explained by a well-organized program for prevention, early detection and treatment of chronic kidney disease (CKD) [1, 5]. Data of Registry on Dialysis and Kidney Transplantation in Serbia showed that changes in incidence rate of ESRD in Serbia were comparable with changes in developed countries, but with approximately ten years of delay: the incidence has begun to increase since 2002, and the stagnation was recorded in 2011 [6].

General practitioners have the main role in prevention and early detection of CKD, as well as in timely referral of patients to nephrologists [7, 8]. Academy of Medical Science of the Serbian Medical Society (AMS SMS) has undertaken several activities to improve the knowledge of general practitioners about the importance of prevention and early detection of CKD [9]. In the present study, we describe these activities and present the results of collaboration between Belgrade nephrologists and general practitioners from four Belgrade Primary Health Care Centers. The aim of the study was to determine prevalence of CKD in persons at risk examined in the screening study that was carried out in four centers as well as to check whether education of general practitioners and their collaboration with nephrologists contributed to the regular CKD screening.

Methods

The paper presents the results of two studies carried out in four Belgrade Primary Health Care Centers by the collaboration between general practitioners and nephrologists. Before the first screening study, AMS SMS organized educational meeting for general practitioners about prevention and screening of CKD (Scheme 1). The screening study involved 619 consecutive patients selected in three-month period from three populations at risk for CKD: patients with hypertension, those with type 2 diabetes mellitus, and persons aged > 60 years without hypertension or diabetes. Patients with previously known kidney disease, malignant diseases, congestive heart failure or any acute illness, persons aged ≤ 20 years, as well as pregnant women, were not included in the study. All persons included in

2007/2008	Educative meeting of AMS SMS on CKD prevention for GPs
April – Jun 2009	CKD screening in 13 Belgrade Primary Health Care Centers
November 2009	Meeting of nephrologists and GPs Presentation on screening results
2013	Retrospective analysis of medical records in 4 Belgrade Primary Health Care Centers, 2010-2012

AMS SMS – Academy of Medical Science of Serbian Medical Society; CKD – chronic kidney disease; GPs – general practitioners

Scheme 1. Activities of Academy of Medical Science of Serbian Medical Society concerning general practitioner education about necessity for regular CKD screening in populations at risk

the study were subjected to an interview, an objective review, laboratory examinations consisting of serum and urine creatinine measurement (kinetic Jaffé method), estimation of glomerular filtration rate (eGFR) by the use of the original Modification of Diet in Renal Disease (MDRD) Study formula [10], and urine dipstick detection of proteinuria as well as detection of urine albumin using Micral-test® strips (ACCU-CHEK product, Roche Diagnostics). All applied methods are described in detail elsewhere [11] and only patients with complete results of screening are analyzed in the study.

The second study was retrospective analysis of medical records of patients included in the first study who visited their doctors at least once in the period covered by the study (2010-2012). Out of a total of 619 patients included in the first study, medical records of 460 patients, who fulfilled the previous criterion, were available. In the retrospective analysis, demographic data on patients, body weight and height, smoking habit, blood pressure, use of ACEI, serum creatinine levels and eGFR were obtained from patients' medical records. Data on proteinuria were rarely found in medical records and therefore were not analyzed.

The Ethic Committee of each health center, as well as of the Clinical Center of Serbia, evaluated and approved both studies, and patients gave their informed consent.

The results are expressed as mean with standard deviations for the continuous variables or as frequencies for categorical variables. The comparison of the variables recorded in two studies was drawn by the Student-t test and Chi-square test as appropriate, while the comparison of the frequencies of recorded variables in the examined years was made by the Chi-square test.

Multivariate stepwise linear regression analysis was performed to determine variables associated with number of years in which blood pressure and eGFR were found in medical records during three-year period, using $p < 0.10$ for variable retention. All analyses were performed using SPSS statistical software package (Version 21; SPSS Inc., Chicago, IL, USA).

Results

Demographic data on patients included in both screening and retrospective study, as well as their BMI, blood pressure, use of ACEI and smoking habit are presented in Table 1. The only statistically significant difference was in systolic blood pressure and in the number of patients treated with ACEI, which were lower in patients included in retrospective study.

Table 2 shows that the majority of patients included in the screening study were in the second

Table 1. Data on patients obtained in screening study and at the beginning of retrospective study

	Patients included in		
	Screening study 2009	Retrospective study 2010-2012	P
Number of patients	619	460	
Patient gender – males	247 (39.9)	182 (39.57)	0.439
Patient age, years	63.33 ± 10.17	64.02 ± 9.99	0.261
Patients with diabetes	206 (33.28)	176 (38.26)	0.104
Patients with hypertension	348 (56.22)	249 (54.13)	0.535
Patients > 60 yrs without DM/HTA	65 (10.5)	35 (7.6)	0.130
BMI, kg/m^2	28.04 ± 4.52	28.31 ± 4.03	0.257
Systolic BP, mmHg	140.6 ± 13.32	138.82 ± 14.23	0.033
Diastolic BP, mmHg	85.6 ± 7.84	85.02 ± 8.59	0.232
ACEI treated	407 (65.75)	211 (45.87)	0.0001
Smokers	134 (21.65)	102 (22.17)	0.895

Data are presented as number (%) or as mean ± standard deviation. BMI - body mass index; DM - diabetes; HTA - hypertension; BP - blood pressure

stage of chronic kidney disease, while 121 (19.55%) patients had eGFR below 60 ml/min/1.73m². Using Micral-test® strips, albuminuria was detected in 242 (39.10%) patients.

During three-year period covered by retrospective study, systolic and diastolic blood pressure decreased and the mean values of both systolic and diastolic blood pressure in the second (p< 0.01) and third year (p < 0.005) were significantly lower compared with the values in screening study. However, blood pressure values were recorded in only 42% of patients' medical records in the first year of retrospective study and over the next two years this percentage was almost halved (Figure 1).

Figure 2 presents the changes of mean eGFR and percentage of patients with recorded eGFR in the screening study as well as in three-year period of retrospective study. No significant difference was found between mean eGFR obtained in screening study and in the first (Table 1) and second (76.73 ± 24.29 ml/min/1.73m²) year of retrospective study, while in the third year the mean eGFR (66.17 ± 17.44 ml/min/1.73m²) was significantly lower in comparison with the value in screening study (p = 0.0001). The percentage of patients with eGFR found in medical records

declined year after year and was only 18% in the third year.

Figure 3 confirms insufficient blood pressure and eGFR recording in patients' medical

Table 2. Estimated glomerular filtration rate (eGFR) and distribution of patients included in the screening study according to their eGFR and albuminuria

eGFR, ml/min/1.73m²	72.25 ± 16.45
Number (%) of patients with eGFR:	
1. > 90 ml/min/1.73m²	86 (13.89)
2. 60-89.9 ml/min/1.73m²	412 (66.56)
3a. 45-59.9 ml/min/1.73m²	102 (16.48)
3b. 30-44.9 ml/min/1.73m²	17 (2.74)
4. < 30 ml/min/1.73m²	2 (0.32)
Number (%) of patients with u-albumin	
0 mg/l	377 (60.84)
20 mg/l	181 (29.37)
50 mg/l	31 (5.00)
100 mg/l	30 (4.90)
Number (%) of patients with eGFR < 60 mm/min/1.73m² + u-albumin ≥ 20 mg/l	36 (5.82)
Number (%) of patients with eGFR > 60 mm/min/1.73m² + u-albumin ≥ 20 mg/l	206 (33.28)

U-albumin detected by Micral-test® strips (ACCU-CHEK product, Roche Diagnostics)
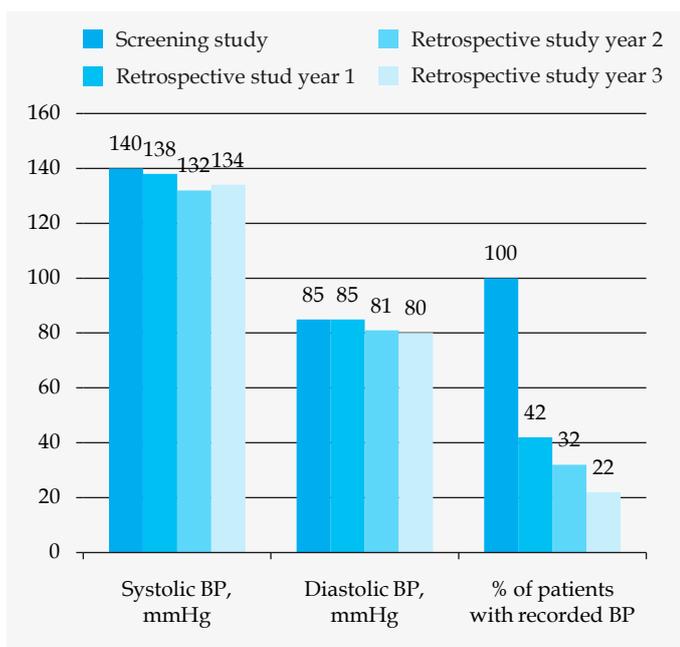

Figure 1. Mean systolic and diastolic blood pressure (BP) and percentage of patients with recorded blood pressure in both screening study and three-year period of retrospective study
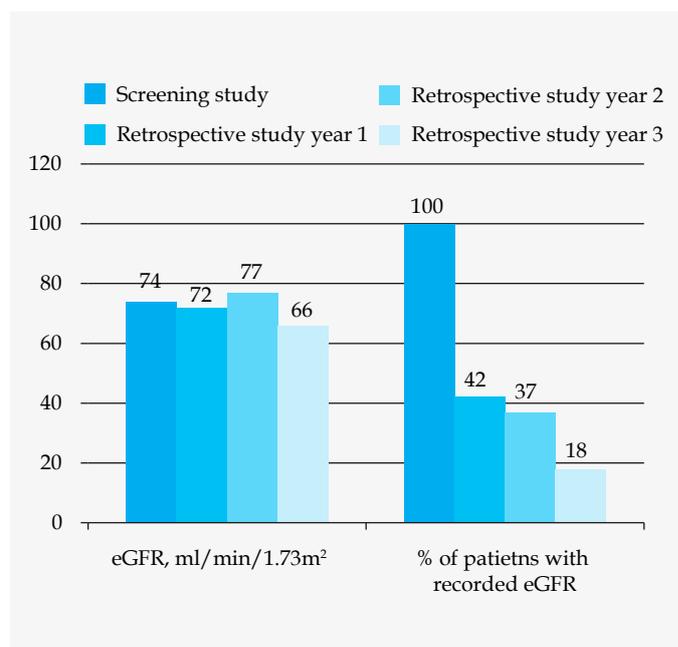

Figure 2. Mean eGFR and percentage of patients with recorded eGFR in both screening study and three-year period of retrospective study

Table 3. Variables associated with number of years in which blood pressure and eGFR were found in medical records during three-year period (multivariate stepwise linear regression analysis)

Independent variables	Number of years with recorded blood pressure				Number of years with recorded eGFR			
	B	beta	95% CI	p	B	beta	95% CI	p
Age, years	0.001	0.01	-0.005– 0.007	0.704	-0.002	0.03	-0.10 – -0.005	0.525
Gender, male	-0.07	-0.004	-0.11– 0.10	0.892	**-0.24**	**-0.15**	**-0.43 – -0.05**	**0.012**
Health center	**0.31**	**0.13**	**0.13 – 0.48**	**0.001**	**-0.72**	**-0.36**	**-0.99 – -0.48**	**<0.001**
Systolic BP0, mmHg	**-0.005**	**-0.08**	**-0.009 – -0.001**	**0.019**	-0.02	-0.01	-0.02 – -0.01	0.0541
Hypertension, yes	**-1.19**	**-0.47**	**-1.38 – -1.00**	**<0.001**	**-0.53**	**-0.31**	**-0.77 – -0.28**	**<0.001**
eGFR0, ml/min/1.73m^2	0.001	0.02	-0.003 – 0.01	0.618	**0.01**	**0.18**	**0.002 – 0.02**	**0.018**
Constant	0.93		0.10 – 1.75	0.027	0.93		-0.10 – 1.75	0.027

eGFR0 – eGFR determined in screening study

records. In only 8% of patients, blood pressure was recorded in each of the three analyzed years and this percentage was even lower for eGFR recording. In one-third of patients, blood pressure and eGFR were recorded in only one of the three analyzed years.

Multivariate stepwise regression analysis selected health center, systolic blood pressure and hypertension (defined as blood pressure above 140/90 mmHg) as variables significantly associated with number of years in which blood pressure was recorded. Male gender, health center, hypertension and eGFR determined in screening study were selected as variables significantly associated with number of years in which eGFR was recorded.

Figure 3. Distribution of patients according to number of years in which blood pressure and eGFR were found in medical records during three-year period of retrospective study.

Discussion

Increase in the overall incidence rate of ESRD in Serbia, which in 2007 exceeded incidence rate in most developed European countries [6, 12], has prompted AMS SMS to undertake several activities that can improve prevention and early detection of CKD. In 2007 and 2008 educative meetings about CKD prevention and screening were organized for general practitioners. It was considered, however, that the joint work between the nephrologists and general practitioners in the screening for CKD would give better results. Therefore, in 2009 screening for CKD in population at risk was organized in thirteen Belgrade Primary Health Care Centers and carried out by physicians from these centers in collaboration with Belgrade nephrologists [11]. In the present study, the screening results obtained in four Belgrade Primary Health Care Centers are presented since only in these centers the retrospective study was carried out. The screening of three groups at risk for CKD detected eGFR below 60 ml/min/1.73m^2 in 19.5% of patients and albuminuria in 39.10% of patients. After the screening, AMS SMS organized a meeting for nephrologists and general practitioners to show the results of screening which clearly revealed the
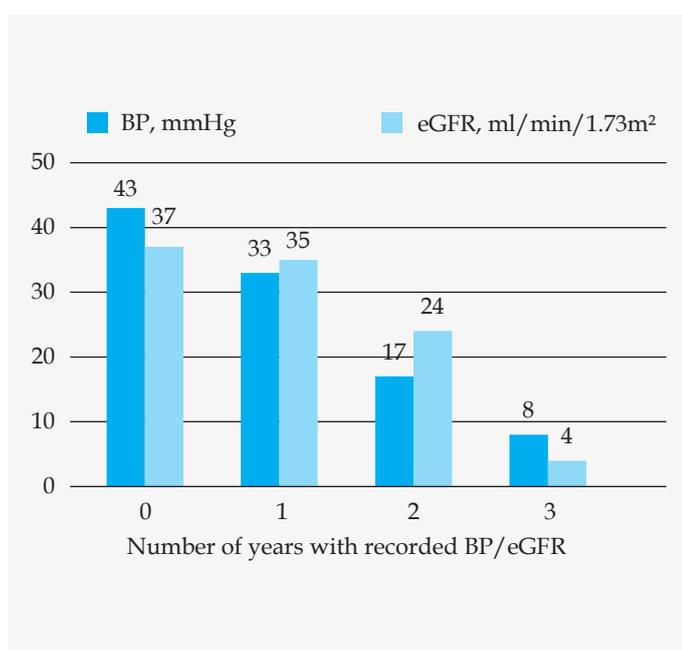
importance of regular screening in populations at risk (Scheme 1). In the same meeting, "Recommendations for prevention and early detection of CKD" for general practitioners was presented and soon published [13].

At the beginning of 2013, retrospective analysis of medical records of patients included in screening study was performed with the aim of checking whether patients at risk for CKD were regularly controlled. The study included only those patients who visited their doctors at least once during the period covered by the study. As data on urine analysis were rarely stored in medical records, data concerning recorded blood pressure and eGFR were only taken into consideration. The results of retrospective analysis showed that the percentage of patients with recorded blood pressure and eGFR in medical records declined year after year from 42% to 22% and from 42% to 18%, respectively. Health center, systolic blood pressure and hypertension were selected as variables significantly associated with number of years in which blood pressure was recorded, while male gender, health center, hypertension and eGFR were selected as variables significantly associated with number of years in which eGFR was recorded.

Prevalence of CKD amongst the general population is estimated to be 8–16% worldwide [14, 15]. Although current guidelines recommend screening in individuals at risk for CKD [16], there are more data on the prevalence of CKD in the general population [17-20]. Nevertheless, a number of papers present the prevalence of CKD in patients with diabetes [21-23] but this is not the case with the prevalence of CKD in patients with hypertension. Although hypertension has been proven to be a risk factor for CKD and one of main causes of ESRD [24], the majority of studies present prevalence of ESRD caused by hypertension, but rarely the prevalence of early stages of CKD in patients with hypertension [25, 26]. The data from our national registry that showed faster increase in ESRD incidence caused by hypertension rather than by diabetes directed our attention to the prevention and early detection of CKD in patients with hypertension. In

the present study, we tested the prevalence of CKD in patients at risk for CKD and half of them were diagnosed with hypertension. Our aim was to acquaint general practitioners with the high incidence of CKD in patients with hypertension as well as with the importance of regular screening for CKD and its prevention in this population. The prevalence of albuminuria and reduced eGFR, two main biomarkers of CKD found in our screening study, was high and comparable with the one obtained in other studies targeting at different populations at risk [25- 28]. The screening study was followed by the meeting where the screening results were presented and several educational meetings and lectures on screening and prevention of CKD organized for general practitioners by AMS SMS. The question was raised as to whether all of these activities contributed to regular monitoring of CKD biomarkers in primary care, and this issue prompted us to undertake the retrospective study.

Retrospective analysis of medical records of 450 patients at risk for CKD showed that during three-year period percentage of patients whose blood pressure and eGFR were recorded decreased from 42% to 22% and from 42% to 18%, respectively. Similar results are obtained in studies with larger number of patients [29, 30], but there are also studies that have shown much better results [31, 32]. The results of our study on recording blood pressure and eGFR in medical records are inconsistent with the data obtained by a survey of general practitioners. The survey was carried out at the end of an educational meeting and involved 329 physicians who voluntarily and anonymously filled out the survey questionnaire on the recommendations of the national guidelines for CKD. All of them correctly answered the question about populations at risk for CKD as well as about the recommended target values of blood pressure and HbA1c. Where the question regarding regular control of kidney function was concerned, 88% of respondents answered that it should be checked once a year in patients with diabetes and 82% of them gave the same answer for patients with hypertension. While 69% of respondents wrote

that the screening for CKD included the determination of albuminuria and eGFR, the remaining percentage of physicians considered it to be only eGFR. National guidelines for CKD were used by 76% of physicians, 19% of interviewed physicians did not read it but they were at the meetings where the guidelines were presented and 5% of physicians were not acquainted with the guidelines. Although the results of the survey revealed a good knowledge of the guideline recommendations, recordings of blood pressure and eGFR were insufficient. In each of the three analyzed years, blood pressure was recorded in only 8% and eGFR in 4% of patients. This shows that physicians' knowledge of guideline recommendations is not profound enough to be applied in practice. Multivariate analysis showed that the number of years in which blood pressure and eGFR were recorded depended on health center. The variation in recording of CKD biomarkers as well as the acceptance of guidelines among different health units has already been described [33-35]. Different causes of insufficient guideline implementation have been described and the education of doctors is considered to be the most effective solution for this problem [33-35]. However, patients are a very important link in regular control and proper treatment of CKD. This is also indicated by the results of our study. Multivariate analysis showed that higher blood pressure and lower eGFR were associated with smaller number of years in which blood pressure and eGFR were recorded, indicating that irregular visits to doctors and irregular controls were associated with poorer treatment outcomes. Although insufficient patient education is justified by various factors, the lack of doctor's time to educate patients and the asymptomatic nature of the disease itself, which deceives and reduces the patient's interest in education, can be considered the main barriers [36]. In spite of all barriers, education of patients at risk for CKD has to take a very important place in guidelines for CKD. It is particularly important that both doctors and patients bear in mind that in Serbia ESRD is caused by hypertension or diabetes in every second patient, and that only strict implementation of preventive measures and regular controls can prevent it. Only regular controls can detect early signs of CKD, which enables the health professionals to slow down its progression. In addition, early detection of CKD and its proper treatment are important not only for the slowing down of CKD progression, but also for the prevention of development of comorbid conditions associated with CKD, especially cardiovascular diseases [37]. In all this, general practitioners, who treat most of the patients at risk for CKD, play the major role and must accept, understand and, in close cooperation with the patients, implement all of the measures recommended by the guidelines. In addition, the results presented in this study prompted the AMS SMS to undertake new activities that would contribute to better education of general practitioners as well as their better cooperation with nephrologists across Serbia.

The study has some limitations. It was carried out in only four primary health care centers, involved small number of patients, so the findings cannot be generalized. Regardless of this, the results of the study warn us of insufficient attention paid to patients at risk for CKD in primary care. On the other hand, low percentage of blood pressure and eGFR recording does not necessarily mean that these values are not checked more often but simply that they have not been recorded. It can be expected that recently introduced computerized medical records in primary care and electronic delivery of laboratory results to the doctors who have requested them will correct this shortage.

Conclusion

Academy of Medical Science of Serbian Medical Society has induced the collaboration between Belgrade nephrologists and general practitioners to undertake screening for CKD among patients at risk. Despite high percentage of patients with detected CKD biomarkers and the educational programs for general practitioners that were conducted afterwards, the retrospective study subsequently found insufficient recording of blood pressure and eGFR in patients' medical records.

The results of two described studies should warn general practitioners, as well as the institutions that deal with the health care organization, of insufficient attention paid to early detection of CKD in populations at risk.

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Skrining hronične bolesti bubrega u beogradskim domovima zdravlja

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Uvod. Akademija medicinskih nauka Srpskog lekarskog društva podstakla je saradnju beogradskih nefrologa i lekara opšte medicine sa ciljem da se ispita prevalenca hronične bolesti bubrega (HBB) u populacijama sa rizikom kao i da se proveri da li je edukacija i saradnja nefrologa i lekara opšte medicine doprinela sprovođenju redovnog skrininga HBB.

Metode. Istraživanje je obuhvatilo dve studije sprovedene u četiri beogradska doma zdravlja. Skrining studija je uključila 619 bolesnika sa rizikom za HBB (348 sa hipertenzijom, 206 sa dijabetesom i 65 osoba starijih od 60 godina bez hipertenzije i dijabetesa). Procenjena je jačina glomerulske filtracije (eGFR) pomoću MDRD formule, a pomoću test traka ispitano je prisustvo proteina i albumina u urinu (Micral-test® strips). U drugoj, retrospektivnoj studiji pregledani su medicinski kartoni 450 bolesnika ispitanih u prethodnoj skrining studiji i analizirano registrovanje krvnog pritiska i eGFR u zdravstvenim kartonima tokom trogodišnjeg perioda.

Rezultati. U skrining studiji otkrivena je eGFR ispod 60 ml/min/1,73m^2 kod 121 (19,55%) bolesnika i albuminurija kod 242 (39,10%) bolesnika. Tokom trogodišnje retrospektivne studije procenat bolesnika u čijim je kartonima registrovan krvni pritisak i eGFR se smanjivao od 42% do 22%, odnosno od 42% do 18%. Samo kod 8% bolesnika registrovan je krvni pritisak svake od tri analizirane godine, dok je za eGFR to utvrđeno samo kod 4% bolesnika. Multivarijantna regresiona analiza je izdvojila dom zdravlja, sistolni krvni pritisak i hipertenziju kao varijable značajno povezane sa brojem godina u kojima je registrovan krvni pritisak, a muški pol, dom zdravlja, hipertenziju i bazalni eGFR, kao varijable povezane sa brojem godina u kojima je registrovan eGFR.

Zaključak. Uprkos saradnji nefrologa i lekara opšte medicine u skrining studiji koja je otkrila visok procenat bolesnika sa biomarkerima za HBB, retrospektivna trogodišnja studija sprovedena posle skrininga je pokazala nedovoljno registrovanje krvnog pritiska i eGFR u zdravstvenim kartonima bolesnika sa rizikom za HBB.

Ključne reči: hronična bolest bubrega, skrining, primarna zdravstvena zaštita