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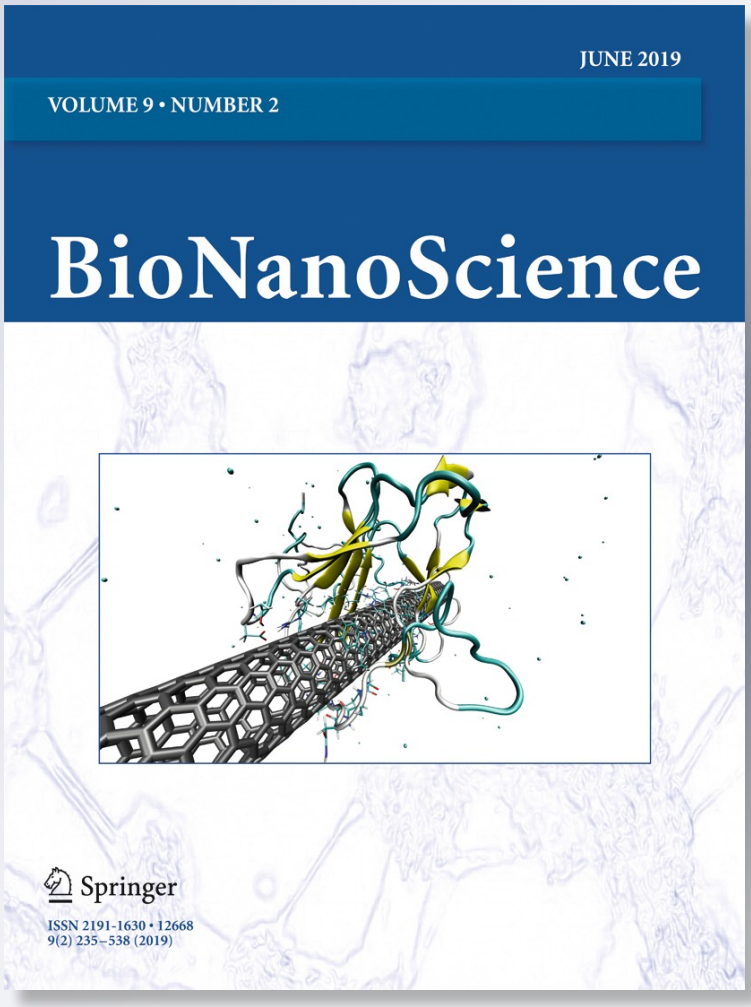

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Screening Assessment of Renal Function Status in Healthy Smoking Volunteers

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Abstract

The study objective was to evaluate the renal function status in overall healthy smokers. Renal function status was studied in 61 apparently healthy smokers aged 21–64 years (49 males and 12 females). The evaluation included taking a history with the smoking status assessment, a physical examination with assessment of systolic and diastolic blood pressure, blood and urine biochemistry, and calculation of glomerular filtration rate (GFR; CKD-EPI, 2009). The period of observation lasted for 7 days. High blood pressure and obesity had no impact on the kidney function ($p > 0.05$). Healthy smoking volunteers initially had a high GFR and a "high-normal" urine albumin level as compared to the group of healthy non-smokers ($p = 0.000$ and $p = 0.012$, respectively). The risk analysis showed that smoking increased 11-fold the risk of hyperfiltration (RR = 11.1, CI 95% 1.57–76.51, $p = 0.001$) and 5-fold the occurrence of albuminuria (RR = 5.1, CI 95% 0.71–36.99, $p = 0.009$) in smokers without initial renal pathology as compared to never-smokers. Those who abstained from smoking showed a moderate decrease of albuminuria ($p = 0.049$). Systematic tobacco consumption contributes to the development of a renal dysfunction with the occurrence of albuminuria and hyperfiltration (GFR ≥ 125 ml/min/1.73 m2). Timely smoking cessation promotes the regression of albuminuria.

Keywords Kidney · Smoking · Renal function · Albuminuria

The Global Adult Tobacco Survey carried out in the Russian Federation demonstrated that 43.9 million adult people (39.1%) are regular cigarette smokers [1]. Smoking is one of the main causes of rapid rise in mortality [2]. The role smoking plays in carcinogenesis [3] and the development of cardiovascular [3, 4] and pulmonary diseases [3, 5] has been established.

In general, the role of smoking in progression of kidney diseases has been understudied [6]; nevertheless, that it might have an adverse effect on the renal function is beyond any doubt [7].

Epidemiologic evidence suggests that smoking induces renal function impairment, that is a dose-dependent increase of the albumin (protein) excretion with urea in smokers [8–10], an increased risk of chronic kidney disease [11], including its terminal stage in male smokers in the general population [8].

Smoking is an independent predictor of albuminuria and a decreased renal function in patients with arterial hypertension. It is a risk factor of albuminuria occurrence and its progression to proteinuria and the development of a chronic kidney disease in type 1 and 2 diabetes mellitus; it increases the risk of renal graft loss and plays an important role in the development of atherosclerotic renal artery stenosis and ischemic nephropathy [9, 12–15].

The study objective To evaluate the renal function status in overall healthy smokers.

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Table 1 Clinical and laboratory characteristics of healthy volunteer smokers (main group) and non-smokers (control group)

Group Parameters	Main group $n = 61$ (M ± m)	Control group $n = 24$ (M ± m)	p*
Age, years	34.5 ± 1.3	39.1 ± 4.1	0.166
Gender			
Male	49	18	$\chi^2 = 0.061$
Female	12	6	0.805
BMI, kg/m^2	24.2 ± 0.8	22.3 ± 0.6	0.158
SBP, mmHg	125.5 ± 1.2	120.2 ± 6.1	0.216
DBP, mmHg	75.5 ± 1.3	76.1 ± 0.7	0.778
Serum creatinine, μmol/L	74.8 ± 1.5	91.5 ± 1.8	*0.000*
Sodium, mmol/L	141.4 ± 0.3	138.1 ± 0.6	*0.000*
Potassium, mmol/L	4.6 ± 0.1	4.5 ± 0.1	1.000
Serum albumin, g	52.6 ± 0.3	51.7 ± 0.5	0.119
Urine albumin, mg/g	15.7 ± 2.6	5.0 ± 0.1	*0.012*
Protein, mg/day	0.05 ± 0.03	0.00	*0.000*
Specific gravity	1.022 ± 0.001	1.020 ± 0.001	0.237
GFR, ml/min/m^2	123.1 ± 1.6	112.1 ± 1.9	*0.000*

The italicized entries represent statistically significant difference

*p— a significance when comparing the groups with the analysis of variance

1 Materials and Methods

A renal function status was studied in 61 apparently healthy smokers (the main group) aged 21–64 years old (the mean age (M ± m) 31.5 ± 1.3 years; 49 males and 12 females). The inclusion criteria are the following: smoking at least 10 cigarettes per day within the last 4 weeks and the history of smoking for at least 3 years. The exclusion criteria are the following: an acute disease and/or an exacerbation of chronic diseases during the study period, a history of an acute and/or chronic kidney disease. A control group consisted of 24 apparently healthy subjects without the history of smoking, who were age- and gender-matched with the main group (the mean age 39.1 ± 4.1 years, $p = 0.227$; 18 males and 6 females, $\chi^2 = 0.0$, $p = 0.996$).

The evaluation included taking a history with the smoking status assessment, a physical examination (an assessment of systolic (SBP) and diastolic (DBP) blood pressure, a body mass index (BMI)), and blood (creatinine, cholesterol, sodium, potassium) and urine (albumin, protein, specific gravity) biochemistry. A glomerular filtration rate (GFR) was calculated using the CKD-EPI equation (NKF 2009). The period of observation including the assessment of (Δ) SBP, DBP, GFR, and urine albumin dynamics lasted for 7 days.

Statistical analysis was performed using parametric and non-parametric methods such as a mean value (M), a standard error (m), a median (Me), 25;75 percentiles, a relative risk (RR) and confidence interval (CI), a χ^2 test, a Student's t test with the Bonferroni correction, and the Pearson correlation coefficient (r). Sample differences were considered statistically significant at $p < 0.05$.

2 Results and Discussion

Physical examination results are given in Table 1. There were no differences in SBP and DBP levels between the main and control groups ($p > 0.05$); therefore, a factor of high BP had no impact on the kidney function in both groups. No obesity as an unfavorable factor of exposure to the renal function was observed: the BMI was slightly higher ($p > 0.05$) in the main group (24.2 ± 0.8 kg/m^2) than in the control one (22.3 ± 0.6 kg/m^2). Healthy smoking volunteers initially had a higher blood Na level (141.4 ± 0.3 mmol/L), a high GFR (123.1 ± 1.6 ml/min/1.73m^2), and a "high-normal" urine albumin level (15.7 ± 2.6 mg/g) as compared to the group of healthy non-smokers (138.1 ± 0.6, $p = 0.000$; 112.1 ± 1.9, $p = 0.000$; and 5.0 ± 0.1, $p = 0.012$, respectively). No differences in potassium levels ($p = 0.237$) or urine-specific gravity ($p = 1.000$) were observed, that is there were no tubulointerstitial abnormalities. The data obtained suggest that smoking affects the renal function with the development of hyperfiltration [10] and the occurrence of high normoalbuminuria.

A correlation analysis in the group of smokers showed that urine albumin was significantly associated with GFR ($r = 0.41$, $p = 0.000$), BMI ($r = 0.31$, $p = 0.015$), and DBP ($r = 0.39$, $p = 0.002$). Relationships of GFR with SBP ($r = (-0.32)$, $p = 0.013$), DBP ($r = (-0.37)$, $p = 0.004$), and BMI ($r = (-0.37)$, $p = 0.004$) levels, as well as those of the BMI with SBP ($r = 0.39$, $p = 0.002$) and DBP ($r = 0.44$, $p = 0.000$) levels were revealed. The analysis of a relative risk of BP increases higher than 130/90 mmHg when smoking showed its ninefold increase as compared to the control group (RR = 9.1, CI 95% 1.29–

Table 2 Clinical and laboratory characteristics of healthy volunteers divided into 3 subgroups according to the smoking "status"

Subgroup Parameters	Subgroup 1 $n = 15$ (M ± m)	Subgroup 2 $n = 31$ (M ± m)	Subgroup 3 $n = 15$ (M ± m)	Control $n = 24$ (M ± m)	p
Age, years	33.7 ± 3.2	30.2 ± 1.7	31.9 ± 2.4	39.1 ± 4.1	0.560
Gender					
Male	12	25	12	18	$\chi^2 = 0.036$
Female	3	6	3	6	1.000
BMI, kg/m^2	24.7 ± 1.1	24.3 ± 0.8	23.4 ± 0.8	22.3 ± 0.6	0.174
SBP, mmHg	128.5 ± 4.1	126.5 ± 2.7	123.5 ± 3.3	120.2 ± 6.1	0.573
DBP, mmHg	80.7 ± 1.9	74.6 ± 1.7	73.2 ± 1.8*	76.2 ± 0.7	*0.030*
Serum creatinine, μmol/L	64.4 ± 3.2	64.7 ± 1.9	65.1 ± 3.5	72.5 ± 1.8	0.086
Sodium, mmol/L	140.7 ± 0.3**	141.3 ± 0.5**	142.3 ± 0.8**	138.1 ± 0.6	*0.000*
Potassium, mmol/L	4.6 ± 0.1	4.4 ± 0.1	4.7 ± 0.1	4.5 ± 0.1	0.231
Urine albumin, mg/g	28.3 ± 9.6**	24.2 ± 2.5**	25.2 ± 1.4**	5.0 ± 0.1	*0.000*
Protein, mg/day	0.01 ± 0.01**	0.02 ± 0.01**	0.02 ± 0.01**	0.00	*0.000*
Specific gravity	1.020 ± 0.002	1.023 ± 0.001	1.023 ± 0.001	1.020 ± 0.001	0.117
GFR, ml/min/m^2	121.9 ± 3.6**	124.1 ± 2.1**	122.3 ± 3.8**	112.1 ± 1.9	*0.004*

The italicized entries represent statistically significant difference

p—a significance in multiple group comparison with the analysis of variance

*Significant ($p < 0.05$) difference with subgroup 1 (the Student's t test with the Bonferroni correction)

**Significant ($p < 0.05$) difference with control group (the Student's t test with the Bonferroni correction)

63.33, $p = 0.002$). The data obtained on the role of smoking in the development of kidney damage confirm the unity of risk factors for cardiovascular diseases and renal disorders.

Increased GFR-hyperfiltration (GFR ≥ 125 ml/min/1.73 m^2) and albuminuria > 10 mg/g were observed in 28 (45.9%) and 15 (24.6%) healthy smokers, respectively. Accordingly, the risk analysis showed that smoking increased 11-fold the risk of hyperfiltration (RR = 11.1, CI 95% 1.57–76.51, $p = 0.001$) and fivefold the occurrence of albuminuria (RR = 5.1, CI 95% 0.71–36.99, $p = 0.009$) in smokers without initial renal pathology as compared to never-smokers.

Based on changing the smoking "status," the main group was subdivided into 3 subgroups, and the renal function status was prospectively (within 7 days) assessed. Subgroup 1

Table 3 Dynamics of clinical and laboratory parameters depending upon the smoking "status," day 7 (5 days after changing the smoking "status")

Subgroup Parameters	Subgroup 1, $n = 15$ (M ± m)	Subgroup 2, $n = 31$ (M ± m)	Subgroup 3, $n = 15$ (M ± m)	p
SBP, mmHg, day 2	128.5 ± 4.1	126.5 ± 2.7	123.5 ± 3.3	
SBP, mmHg, day 7	126.5 ± 2.7	122.1 ± 1.2	119.1 ± 2.3	0.055
Δ SBP, mmHg/day	− 0.24	− 0.88	− 0.80	
p	0.821	0.142	0.263	
DBP, mmHg, day 2	80.7 ± 1.9	74.6 ± 1.7	73.2 ± 1.8	
DBP, mmHg, day 7	81.2 ± 2.7	72.3 ± 1.5*	71.9 ± 1.7*	*0.003*
Δ DBP, mmHg/day	0.1	− 0.46	− 0.26	
p	0.881	0.314	0.604	
Urine albumin, mg/g, day 2	28.3 ± 9.6	24.2 ± 2.5	25.2 ± 1.4	
Urine albumin, mg/g, day 7	27.1 ± 9.8	21.2 ± 4.7	16.3 ± 4.1	0.565
Δ Urine albumin, mg/g/day	− 0.24	− 0.6	*− 1.78***	
p	0.931	0.575	*0.049*	
GFR, ml/min/m^2, day 2	121.9 ± 3.6	124.1 ± 2.1	122.3 ± 3.8	
GFR, ml/min/m^2, day 7	123.8 ± 3.1	125.0 ± 1.6	122.4 ± 3.3	0.740
Δ GFR, ml/min/m^2/day	0.38	0.18	0.02	
p	0.692	0.828	0.964	

The italicized entries represent statistically significant difference

*Significant ($p < 0.05$) difference with subgroup 1 (the Student's t test with the Bonferroni correction)

**A significant ($p < 0.05$) change of the parameter against the baseline

included 15 subjects who continued smoking cigarettes, subgroup 2 consisted of 31 subjects, whose standard cigarettes were replaced by tobacco heating system, and subgroup 3 included 15 subjects who abstained from smoking completely. Characteristics of clinical and laboratory parameters (day 2 of the study, before changing the smoking "status") are showed in Table 2.

As can be seen from the data presented in Table 2, there was a higher GFR ($p < 0.05$), proteinuria ($p < 0.05$), and albuminuria ($p < 0.05$) in all subgroups as compared to the controls. The subjects of the subgroup 3 initially had a lower DBP level as compared to those who continued smoking (73.2 ± 1.8 and 80.7 ± 1.9 mmHg, respectively, $p = 0.030$).

The assessment of SBP and DBP in dynamics revealed no changes in any of the subgroups (Table 3). In subgroups 2 and 3, there was a tendency to a decrease of SBP and DBP ($p > 0.05$); however, at the end of observation, the DBP level was higher in subgroup 1 (81.2 ± 2.7, $p < 0.05$) subjects, who continued their usual smoking regime, as compared to subgroups 2 (72.3 ± 1.5) and 3 (71.9 ± 1.7). The subjects of subgroups 1 (27.1 ± 9.8 mg/g, $p > 0.05$ as against the baseline) and 2 (21.2 ± 4.7 mg/g, $p > 0.05$ as against the baseline) had "high-normal" albuminuria; those who abstained from smoking showed a moderate decrease of albuminuria to 16.3 ± 4.1 mg/g ($\Delta = (-1.78)$ mg/g/day, $p = 0.049$). There were no changes in the GFR in all subgroups studied; the GFR more than 125 ml/min persisted in all subjects ($n = 28$) with initial hyperfiltration.

A correlation analysis in subgroups 1 and 2 subjects demonstrated a persistent relation of albuminuria with the GFR ($r = 0.51$, $p = 0.041$ and $r = 0.48$, $p = 0.050$, respectively), and DBP ($r = 0.43$, $p = 0.032$ and $r = 0.39$, $p = 0.030$), and the GFR with the SBP ($r = (-0.63)$, $p = 0.010$ and $r = (-0.55)$, $p = 0.050$) and DBP ($r = (-0.38)$, $p = 0.035$ and $r = (-0.41)$, $p = 0.023$) levels. For those who abstained from smoking, albuminuria was associated with a DBP level only ($r = 0.61$, $p = 0.021$). The results obtained are consistent with the evidence that albuminuria is reversible when the exposure to the damaging factor is ceased [7].

3 Conclusion

Thus, our results confirm that smoking is one of the significant factors affecting the renal function status. Systematic tobacco consumption contributes to the development of a renal dysfunction with the occurrence of albuminuria and hyperfiltration (GFR ≥ 125 ml/min/1.73 m^2). Compared to never-smokers, smoking increases 11-fold the risk of hyperfiltration (RR = 11.1, CI 95% 1.57–76.51, $p = 0.001$) and fivefold the occurrence of albuminuria (RR = 5.1, CI 95% 0.71–36.99, $p = 0.009$). Timely smoking cessation promotes the regression of albuminuria.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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