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**Original Paper** 

## Renal Function Predicts Outcomes in Patients with Ischaemic Stroke and Haemorrhagic Stroke

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Key Words Stroke • Rrisk factors • Renal function

#### Abstract

Background/Aims: We evaluated renal function and the impact of renal function on inhospital outcomes in patients with ischaemic and haemorrhagic stroke. Methods: We collected data from 766 patients with stroke; 637 (83.2 %) with ischaemic and 129 with haemorrhagic one. Results: The mean serum creatinine on admission in patients with both types of stroke, who died, was significantly higher than in those who survived. Multivariate analysis showed that independent predictors of mortality in patients with ischaemic stroke were: ischemic heart disease or prior myocardial infarction, diabetes, admission glucose and eGFR on admission. Also, multivariate analysis showed that independent predictors of mortality in patients with haemorrhagic stroke were: age and admission glucose. *Conclusions:* Patients with haemorrhagic stroke, in particular with acute kidney injury during hospitalisation had significantly worse outcomes than patients with ischaemic stroke. Assessment of kidney function is prerequisite to employ the necessary measures to decrease the risk of in-hospital mortality among patients with acute stroke. Appropriate approach to patients with renal dysfunction (adequate hydration, avoidance of nephrotoxic drugs, drug dose adjustment etc) should be considered as preventive and therapeutic strategies in the management of acute stroke.

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#### Introduction

Chronic kidney disease stage 2 or higher is a major risk factor for cardiovascular diseases including stroke as shown on more than 15,000 participants in Atherosclerosis Risk in Communities (ARIC) study [1]. The Cardiovascular Health Study (CHS) has reported that patients aged 65 years or older with elevated serum creatinine were associated with higher annual mortality (7.7% vs 2.9%) and higher mortality from cardiovascular disease (3.6% vs 1.3%) compared to patients with normal serum creatinine [2]. Analysis of Heart Outcomes Prevention Evaluation Study (HOPE) has shown that mild degrees of renal dysfunction was associated with increased risk of incident ischemic stroke or TIA [3]. In addition, an independent association was observed between a reduced estimated glomerular filtration rate-eGFR and the risk of death and cardiovascular events [4]. However, in the recent study on Chinese population, proteinuria increased the risk of stroke, while eGFR was not associated with incident stroke after adjustment for established cardiovascular risk factors [5]. In many studies, reduced GFR and/or albuminuria were independently associated with cardiovascular risk factors, prevalent cardiovascular disease and all-cause mortality compared to patients without CKD [6,7]. In pooled analyses of 4 prospective communitybased cohorts low eGFR was significantly associated with increased risk of ischaemic, but not haemorrhagic, stroke risk, while high albumin/creatinine ratio was associated with both stroke types [8].

Taking all these data into consideration, the aim of this study was to evaluate renal function and the impact of renal function on in-hospital outcomes in patients with ischaemic and haemorrhagic stroke.

#### **Patients and Methods**

We collected demographic and clinical data from 766 patients with stroke; 637 (83.2 %) with ischaemic and 129 (16,84 %) with haemorrhagic who were admitted to the Department of Neurology, Medical University Hospital Bialystok, Poland from medical records. It was a retrospective analysis of prospectively collected data. Stroke was diagnosed based on neurological examination and admission computed tomography scan. Patients with subarachnoid haemorrhage, transient ischaemic attacks (TIA), after loss of consciousness, brain tumor(s), head trauma and patients with incomplete data were excluded. No patient underwent thrombolysis. Serum creatinine was measured on admission and during hospitalization (within 48 hours and more than 7 days -the last before discharge).

All laboratory parameters: total cholesterol, HDL, triglycerides, LDL, serum glucose were assessed using standard methods in central laboratory at the University Hospital. Serum creatinine was measured using a Jaffe method, alkaline picrate kinetic (Architect, Abbott, IL, USA). The method for creatinine measurement was IDMS traceable. The assessment of renal function was based on the glomerular filtration rate estimated by the MDRD equation (Modification of Diet in Renal Disease), the CKD-EPI equation (Chronic Kidney Disease Epidemiology Collaboration) [9].

#### Statistical analyses

Due to the lack of normal distribution parameters in statistical inference, nonparametric methods were used. Mann-Whitney test was used to compare the values of variables between the 2 groups. The relationships between qualitative variables were assessed using the Fisher's exact test or the Fisher-Freeman-Halton Exact Test (compared the dichotomous variables higher than 2). Multivariate logistic regression was used to identify the independent risk factors for mortality in stroke. In analysis of the impact of mortality, variables were standardised for age by arbitrary inclusion of this variable in the model. In addition, for models with a larger number of independent variables, stepwise method was used to eliminate variables (as a criterion for accepting the value of the Wald statistics). All statistical hypotheses were verified at a significance level  $\alpha = 0.05$ . Calculations were performed using the statistical package Statistica 10.0 StatSoft, Tulsa, OK., USA. The Fisher-Freeman-Halton Exact test was used the Microsoft Excel.



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		STROKE		ischaemic	h	aemorrhagic	Р
	N	M±SD%	N	M±SD%	Ν	M/SD%	_
Age (years)	766	70,90±12,52	637	72,14±11,38	129	64,80±15,76	<0,001
female	374	48,8%	305	47,9%	69	53,5%	NS
male	392	51,2%	332	52,1%	60	46,5%	NS
Hypertension	668	87,3%	557	87,6%	111	86,0%	NS
Coronary artery disease	296	38,6%	270	42,4%	26	20,2%	<0,001
Myocardial infarction	81	10,6%	75	11,8%	6	4,7%	0,016
Diabetes	149	19,5%	137	21,5%	12	9,3%	0,001
Prior stroke	224	29,5%	204	32,3%	20	15,5%	<0,001
Atrial fibrillation	228	29,9%	213	33,6%	15	11,6%	<0,001
Valvular heart disease	34	4,5%	31	5,0%	3	2,3%	NS
Carotid artery stenosis	209	38,6%	207	39,1%	2	15,4%	NS
Blood pressure* systolic	766	155,40±27,25	637	153,56±24,81	129	164,50±35,77	0,005
Blood pressure* diastolic	766	89,22±13,32	637	88,34±12,50	129	93,57±16,17	0,001
Glucose at admission (mg/dl)	719	123,79±58,06	595	124,29±60,66	124	121,36±43,56	NS
Cholesterol (mg/dl)	571	181,48±42,59	514	181,08±41,66	57	185,09±50,43	NS
LDL (mg/dl)	556	116,69±36,13	501	116,48±35,35	55	118,58±42,92	NS
HDL (mg/dl)	560	47,31±48,83	505	47,56±51,12	55	45,01±16,89	NS
Triglycerides (mg/dl)	566	111,22±60,29	510	112,67±61,52	56	98,05±45,97	NS
* Blood pressure at admission (	[mmHg]	; M-mean, SD- sta	ndard d	eviation, NS- not si	gnifican	t	

#### Table 1. Demographic and clinical characteristics of the studied population

#### Results

#### Characteristics of the group

We collected data from 392 (51,2%) men and 374 women (48,8%). Ischaemic stroke had 52,1% men and 47,9% women, haemorrhagic stroke had 46,5% men and 53,5% women. The age of study population was between 24 and 99 (the mean age was 70,90±12,52 years). Patients with iscahemic stroke were significantly older compared to haemorrhagic (72,14± 11,38; 64,80±15,76 years respectively; p<0.001). The duration of hospitalisation was 1-65 days (the mean amounted to 16,31±14,97 days). The mean duration of hospitalisation of patients with haemorrhagic stroke was significantly longer than patients with ischaemic stroke (22.65 ± 18.70 vs 15.03 ± 13.73; p<0,05). A total of 432 (56,5%) patients were discharged home, 218 (28,5%) were transferred to other health care facilities and 115 (15,0%) died. 60.7% of ischaemic stroke patients were discharged home, 26,1% patients were transferred to other health care facilities, (13,2%) patients died. 40,6% of haemorrhagic stroke patients were on hypotensive medications, in addition 70% received statins, 80% were on acetylsalicylic acid.

Demographic and clinical characteristic of the studied population is displayed in the Table 1.

#### Assessment of renal function

The mean serum creatinine of study population on admission was  $1,12\pm0,78$ mg/dl. Among patients with ischaemic stroke the mean serum creatinine was significantly higher compared to patients with haemorrhagic (p<0,001). Estimated GFR rate using the MDRD equation on admission among patients with hemorrhagic stroke was significantly higher compared to patients with ischemic (83,49±34,84 ml/min/1,73m<sup>2</sup> vs 70,33±23,89 ml/min/1,73m<sup>2</sup>; (p<0,001). Also, eGFR rate using the CKD-EPI equation on admission among patients with hemorrhagic stroke was significantly higher compared to patients with ischemic (77,61±26,03 ml/min/1,73m<sup>2</sup> vs 67,45±23,80 ml/min/1,73m<sup>2</sup>; (p<0,001). There were no significant differences between eGFR using the MDRD and the CKD-EPI equations in men with both types of stroke and normal level of serum creatinine, thus we report further data using CKD-EPI formula. At admission 81,4% of patients with ischaemic stroke and 90,6%

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Table 2. The mean serum creatinine level and type of stroke

	STROKE TYPE OF STROF		STROKE	Р		
				ischaemic	haemor-	-
					rhagic	
Serum	Within normal ranges	Ν	560	464	96	
creatinine	< 1,2 (mg/dl) females	%	82,8	81,4	90,6	
at	< 1,4 (mg/dl) males					_
admission	elevated	Ν	116	106	10	
	≥ 1,2 (mg/dl) females	%	17,2	18,6	9,4	<0,05
	$\geq$ 1,4 (mg/dl) males					
total		N	676	570	106	-
		%	100,0	100,0	100,0	

**Table 3.** eGFR by CKD-EPI at admission in patients with normal serum creatinine with regard to gender

TYPE OF			GENDER				
STROKE	STROKE (TOTAL)			males	females		
				(creatinine< 1,4		eatinine< 1,2	
				(mg/dl)	(mg/dl)		
	Ν	N eGFR N		eGFR	Ν	eGFR	
		CKD-EPI		CKD -EPI		CKD-EPI	
		ml/min/1,73m <sup>2</sup>		ml/min/1,73m <sup>2</sup>		ml/min/1,73m <sup>2</sup>	
ischaemic	464	75,34±18,23	239	82,79±18,16	225	67,43±14,65	
haemorrhagic	96	82,40±21,85	44	88,16±23,61	52	77,52±19,16	
Р		<0,05		NS		<0,001	

of patients with haemorrhagic stroke had normal levels of serum creatinine (<1,2mg/dl in females and <1,4 mg/dl in males- according to WHO). Elevated serum creatinine (p<0,05) occurred more frequently in patients with ischaemic stroke. (Table 2).

The mean serum creatinine among men on admission was comparable in both types of stroke (1,20  $\pm$  0,62 vs 1,22  $\pm$ 1,15 mg/dl). The mean serum creatinine among women with ischaemic stroke on admission was significantly higher compared to women with haemorrhagic stroke (1,08 $\pm$ 0,89 vs 0,87 $\pm$ 0,42 mg/dl mg/dl (p<0,001). Among patients with haemorrhagic stroke aged less than 65 years of age, the mean serum creatinine on admission was significantly higher compared to ischaemic stroke patients (1,07 $\pm$ 1,19 mg/dl vs 0,98  $\pm$ 0,29 mg/dl (p<0,05). The mean serum creatinine on admission among patients aged 65 and older with ischaemic stroke was 1,17 $\pm$ 0,84mg/dl and with haemorrhagic was 1,01 $\pm$ 0,468 mg/dl (p=0,059). Table 3. shows eGFR by CKD-EPI at admission in patients with normal serum creatinine with regard to gender.

CKD was defined as the eGFR <60 mL/min/1.73 m2 (according to KDIGO). A total of 184 (32,3%) patients with ischaemic stroke and 26 (24,5%) patients with haemorrhagic stroke had on admission the eGFR < 60 mL/min/1.73 m2 (using the MDRD equation). The GFR < 60 mL/min/1.73 m2 (using the CKD-EPI equation) on admission had 208 (36,5%) patients with ischaemic stroke and 28 (26,4%) with haemorrhagic stroke.

#### Renal function and outcome

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The mean serum creatinine in patients with ischaemic stroke who died was significantly higher than in those who survived  $(1,4\pm0.9 \text{ mg/dl vs } 1,1\pm0.7 \text{ mg/dl}, \text{ respectively; } (p<0.05)$ . The mean serum creatinine in patients with hemorrhagic stroke who died was significantly higher than in those who survived  $(1,3\pm0.8 \text{ mg/dl vs } 1,0\pm0.9 \text{ mg/dl} \text{ respectively; } (p<0.05)$ . The eGFR using the CKD-EPI equation on admission in patients with ischaemic stroke who

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Table 4. Kidney function in patients with	h haemorrhagic and ischaemic	stroke with regard to outcome
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	END OF	IS	CHAEMIC ST	ROKE	HAEMORRHAGIC STROKE			
	TREATMENT	N	Mean±SD	Р	Ν	Mean±SD	Р	
Creatinine at	Stroke -total	570	1,14±0,77		106	1,04±0,87		
admission	survived	502	1,10±0,74	<0,05	81	0,98±0,89	<0,05	
(mg/dl)	dead	68	1,41±0,91		25	1,30±0,81		
eGFR by	Stroke -total	570	67,5±23,8		106	77,6±26,0		
CKD-EPI – at	survived	502	69,3±23,1	< 0.001	81	81,6±24,4	< 0.05	
admission	dead	68	53,9±24,8	<0,001	25	64,6±27,5	<0,05	
(ml/min/1,73m2)								

survived was significantly higher compared to patients who died (69,3±23,1 ml/  $min/1,73m^2$ VS 53,9±24,8 ml/ min/1,73m<sup>2</sup> respectively (p<0,001). There were significant differences between eGFR on admission in patients with haemorrhagic stroke depending on the outcome (p<0,05) (Table 4). Among patients with ischaemic stroke who died, 41,2% had

elevated

creatinine on ad-

serum

Table 5. Serum creatinine during hospitalization with regard to outcome

TYPE OF	END OF	CREATININE	Ν	Mean±SE
STROKE	TREATMENT			(MG/DL)
Stroke	total	At admission	676	1,12 ± 0,7
		After 48 hours	168	0,97 ± 0,4
	survived	At admission	583	1,08 ± 0,7
		After 48 hours	149	0,94 ± 0,3
	survived	At admission	93	1,37 ± 0,8
		After 48 hours	19	1,36 ± 1,1
ischaemic	total	At admission	570	1,14 ± 0,7
		After 48 hours	152	0,96 ± 0,3
	survived	At admission	502	1,10 ± 0,7
		After 48 hours	137	0,95 ± 0,3
	survived	At admission	68	1,41 ± 0,9
		After 48 hours	15	1,11±0,7
haemorrhagic	total	At admission	106	1,04 ± 0,8
		After 48 hours	16	1,12 ± 1,1
	survived	At admission	81	0,98 ± 0,8
		After 48 hours	12	0,73 ± 0,3
	survived	At admission	25	1,30 ± 0,8
		After 48 hours	4	2,30 ± 1,9

mission (according to WHO) and among those who survived 15,5% (p<0,001). Among patients with haemorrhagic stroke who died, 20,0% had elevated serum creatinine and among those who survived 6,2% (p=0,053). 29,5% of patients with ischaemic stroke who survived and 52,9% of patients who died, had on admission the eGFR < 60 mL/min/1.73 m2 (using the MDRD equation) (p<0,001). 16.0% of patients with haemorrhagic stroke who survived and 52,% of patients who died on admission had the eGFR <60 mL/min/1.73 m2 (using the MDRD equation) p<0,001). Similar differences were observed using the CKD-EPI equation in both types of stroke.

#### Assessment of renal function during hospitalization

The mean serum creatinine on admission and after 48 hours in patients with ischaemic and haemorrhagic stroke who died was higher compared to those who survived (Table 5).

In the study population the mean serum creatinine measured more than 7 days (the last before discharge) was  $1,15\pm0,74$ mg/dl. There were no significant differences between serum creatinine level, measured more than 7 days of hospitalisation and patients with both types of stroke and the outcome. Prevalence of acute kidney injury was 20% in patients with hemorrhagic stroke and 8% in patients with ischemic stroke (p<0.01).



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	END OF ISCHAEMIC STROKE			Έ	HAEMORRHAGIC STRO				
	TREATMENT	Ν	Mean±SD	Р	Ν	Mean±SD	Р		
creatinine > 7 days of	total	216	1,1±0,58		47	1,3±1,2			
hospitalisation	survived	186	1,1±0,5	NS	34	1,3±1,4	0,057		
(mg/dl)	dead	30	1,3±0,8		13	$1,4\pm0,7$			
eGFR by	total	216	67,6±23,3		47	67,5±30,8			
CKD-EPI > 7 days of	survived	186	69,1±22,2	< 0.05	34	72,4±31,2			
hospitalisation	dead	30	58,0±28,2	-0,00	13	54,6±26,7	<0,05		
(ml/min/1,73m <sup>2</sup> )									

**Table 6.** Kidney function after 7 days of hospitalisation in patients with haemorrhagic and ischaemic stroke with regard to outcome

The eGFR (by CKD-EPI) measured more than 7 days (the last before discharge) of the study population was  $67,57\pm24,77$  ml/min/ $1,73m^2$ . The mean serum creatinine (the last before discharge) in patients with hemorrhagic stroke who survived was  $1.3\pm1.4$  mg/dl (0,5-8,2 mg/dL), and in patients who died was  $1.4\pm0.7$  (p = 0.057). There were significant differences in eGFR (using the CKD-EPI equation) measured more than 7 days in patients with ischaemic and haemorrhagic stroke, depending on the outcome (p < 0.05 vs p < 0.05) (Table 6).

31,7% of patients with ischemic stroke who survived and 56,7% who died, had the eGFR < 60 mL/min/1.73 m2 (using the CKD-EPI equation) measured more than 7 days. On the other hand, GFR  $\ge$  60ml/min/1,73m<sup>2</sup> in patients with ischemic stroke was observed significantly more frequently among those who survived (p <0.05).

#### Logistic regression analysis

In full model of multivariate regression analysis the following parameters were included: age, gender, systolic, diastolic blood pressure, HDL, LDL, cholesterol, triglycerides, glucose, creatinine, eGFR, presence of hypertension, diabetes, coronary artery disease or prior myocardial infarction. Stepwise logistic regression analysis was performed, including only variables with p<0.1 in the full model. Multivariate analysis showed that independent predictors of mortality in patients with ischemic stroke were: ischemic heart disease or myocardial infarction in the past (p = 0.034; OR = 1.905), diabetes (p = 0.009; OR = 0.282), admission glucose (p <0.001; OR = 1.009), and eGFR on admission (p <0.001; OR = 0.968). Multivariate analysis, the CKD-EPI equations, showed that independent predictors of mortality in patients with haemorrhagic stroke were: age (p = 0.011; OR = 1.060) and admission glucose (p = 0.001; OR = 1.031). (Table 7).

#### Discussion

In our study we found that 18,6% of patients with ischaemic stroke and 9,4% of patients with haemorrhagic stroke had a high proportion of elevated serum creatinine at admission. The mean serum creatinine at admission was significantly higher among patients who died in both types of stroke. Previous studies showed lower proportion of elevated serum creatinine at admission [10-12]. Wannamethee et al. [10] reported that cardiovascular mortality risk increased with decreasing levels of eGFR, particularly among men with eGFR <60 mL/min per 1.73 m<sup>2</sup> even after adjustment for established risk factors. Fierd et al. [11] confirmed that an elevated creatinine level (creatinine level > or =1.5 mg/dl in men or > or =1.3 mg/dl in women) was associated with increased risk of stroke compared to patients with normal level of creatinine (21,1% vs 11,9%). Ikram et al. [12] identified risk factors affecting mortality during the first three months after stroke. They found that serum creatinine >115µmol/L was associated with increased risk of cardiovascular mortality. Renal function is mostly assessed

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parameters		Full n	nodel		М	odel after	eliminat	ion
	OR	95% CI		р	OR	95% CI		р
ischaemic								
age	1,023	0,986	1,060	0,224				
gender (female vs male)	1,004	0,537	1,879	0,990				
hypertension	0,785	0,303	2,033	0,618				
coronary artery disease or myocardial infarction	1,794	0,978	3,289	0,059	1,905	1,050	3,455	0,034
diabetes	0,290	0,110	0,765	0,012	0,282	0,109	0,732	0,009
glucose at admission (mg/dl)	1,009	1,004	1,013	<0,001	1,009	1,004	1,013	<0,002
eGFR by CKD-EPI *	0,971	0,952	0,990	0,003	0,968	0,956	0,981	<0,002
creatinine at admission (mg/dl)	1,011	0,679	1,505	0,959				
haemorrhagic								
age	1,069	1,009	1,134	0,024	1,060	1,014	1,108	0,011
gender (female vs male)	0,477	0,129	1,759	0,266				
hypertension	20,573	0,192	2,207	0,205				
coronary artery disease or myocardial infarction	0,261	0,043	1,581	0,144				
diabetes	1,351	0,226	8,068	0,741				
glucose at admission (mg/dl)	1,033	1,015	1,052	<0,001	1,031	1,013	1,048	0,001
eGFR by CKD-EPI *	1,001	0,963	1,040	0,970				
creatinine at admission (mg/dl)	1,140	0,526	2,471	0,740				
* eGFR by CKD-EPI at admission (m	l/min/1,7	73m <sup>2</sup> ); OR	- odds ra	tio, CI coe	efficient i	nterval.		

at admission to the hospital [1]. In our study, serum creatinine was analysed on admission and during hospitalisation: within 48 hours and more than 7 days after admission i.e. before discharge. We would like to stress that patients with haemorrhagic as well as ischaemic stroke who died, had a significant rise in serum creatinine within 48 hours, fulfilling the criteria of acute kidney injury. The best indicator of renal function is estimated GFR rather than creatinine [13]. However, as eGFR cames from mathemathical formula based on serum creatinine, age and gender, thus in a case of unequal distribution of age and gender between groups studied, eGFR might differ while serum creatinine might be similar between groups studied. In our case there was significant difference in age for both population of stroke patients studied (mean age in ischaemic stroke was 72 years while in haemorrhagic stroke was 65 years), while gender did not differ significantly (52,1% of males in ischaemic vs 46.5% in haemorrhagic stroke). As in our case the relatively high SD for the "survived" group is of borderline significant difference from the "dead" group is due to an outlier creatinine value (8.2 mg/dL) in the relatively small "dead" group leading to a large standard deviation.

In many studies, reduced glomerular filtration rate and/or albuminuria independently and significantly increased the risk for stroke [2,7,14-16]. Lee et al. [17] in meta-analysis of 21 articles derived from 33 prospective studies, found that patients with a baseline eGFR of <60 ml/min/1.73 m<sup>2</sup> had a risk of future stroke that was 43% greater than those with a normal baseline eGFR [17]. Sweileh et al. [16], identified in stroke patients, three predictors of inhospital mortality: creatinine clearance (p = 0.004), number of post-stroke complications (p= 0.001), and type of stroke (p = 0.034). In our study, CKD (defined as eGFR <60 mL/min/1.73  $m^2$  by KDIGO) occurred in 31.1% - 34.9% patients with stroke (depending on the equation MDRD or CKD-EPI), similarly to the study of Ovbiagele et al. [18]. In the study by Lin et al. [19] on 934 patients with acute first-ever ischaemic stroke, 28.3% had a reduced eGFR, but serum creatinine levels were obtained within 3 days of acute stroke onset. In contrast, Xu et al. [20] found the presence of CKD in 47.7% patients with incident cerebrovascular lesions. In the recent interim report of the Korean Stroke Cohort for Functioning and Rehabilitation, the prevalence of CKD was much lower and accounted for 12.7% of the population studied [21]. It may be due to the fact, that younger patients were included in the study (mean age was 65.5 ±12.4 years) with higher proportion of males (63%). In logistic regression,

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proteinuria, hyperglycemia and anemia were independent predictors for risk of sequelae at 30 days for both ischaemic and non-ischaemic cerebrovascular lesions. Many studies have demonstrated an association between stroke and CKD. However, in many papers the stroke was not differentiated by subtype [4,6,17] and renal function was assessed only in ischaemic [15,16] or haemorrhagic stroke [15,10,22]. The Rotterdam Study has found that decreased GFR is a strong risk factor for haemorrhagic, but not ischaemic stroke [22]. Similarly, in the pooled analyses of 4 prospective community-based cohorts, including Atherosclerosis Risk in Communities Study (ARIC), the Cardiovascular Heart Study (CHS), the Multi-Ethnic Study of Atherosclerosis (MESA) and the Prevention of Renal and Vascular End-stage Disease (PREVEND) Study, the low eGFR was significantly associated with increased risk of ischaemic, but not haemorrhagic, stroke risk, while high albumin/creatinine ratio was associated with both stroke types [8]. Moreover, Lin et al. [19] found that reduced eGFR during the acute stroke stage was associated with increased risk of 3-year mortality. Furthermore, the risk of acute complications and poor functional outcomes following discharge was significantly higher in patients with a reduced eGFR [19].

However, renal function is not considered as a stroke risk factors in the current recommendations of the Expert Group of the National Cardiovascular Disease Prevention and Treatment Programme POLKARD [23]. Decreased renal function in stroke patients with CKD is associated with coexistence and accumulation of traditional and new (associated with chronic kidney disease) cardiovascular risk factors [24]. In our study the most common comorbidity was hypertension, followed by coronary artery disease.

In the present study, multivariate analysis showed that independent predictors of mortality in patients with ischaemic stroke were: ischaemic heart disease or myocardial infarction in the past, diabetes, glucose at admission, and eGFR on admission, while in patients with haemorrhagic stroke were: age and glucose at admission. Mac Walter et al. [25] reported that after acute stroke, patients with reduced calculated creatinine clearance at admission and raised serum creatinine had a higher mortality risk (follow-up was up to 7 years) similar to the study of Lin et al. [26]. In another study on patients with ischaemic stroke it was found that the reduction in GFR was associated with higher mortality [27].

In many countries rapid and correct diagnosis of stroke and access to a high quality stroke unit is effective in reducing in-hospital fatality rates and the length of hospital stays. Our study showed that the mean duration of hospitalization was  $16.31 \pm 14.97$  days. The length of hospitalization and in-hospital mortality was significantly longer in patients with haemorrhagic stroke than patients with ischaemic one. The recent study of Mohamed et al. [28] showed that presence of CKD was associated with longer length of stay, which is the most predictive factor in determining in-patient costs.

The strength of our study is the fairly large population of patients with two types of stroke, prospective collection of data, though retrospectively analysed. We would like to stress that in our study creatinine was assessed not only once, but at admission, and during hospitalisation: within 48 hours and more than 7 days after admission before discharge. As creatinine is not routinely measured during hospitalisation in stroke patients, we undertook this study also to assess the role of kidney function in stroke outcome and prevalence of acute kidney injury in this population. High prevalence of acute kidney injury in haemorrhagic stroke may contribute to worse outcomes. This is the first study in Poland to report the incidence of acute kidney injury in patients with stroke (20% in patients with haemorrhagic stroke and 8% in patients with ischaemic stroke). In Romania prevalence of acute kidney injury in stroke patients was 14.5% [29]. We focused also relation between mortality and type of stroke and found that the in-hospital mortality was particularly high in haemorrhagic stroke. It is envisioned that kidney function assessment is of paramount importance for the outcome of stroke patients, in particular in ischaemic stroke. A limitation might be that this study was a single-center with short follow-up, but with the same pattern of care. It is acknowledged that our results, although of clear and statistical significance, will need to be validated on a larger population.





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#### Conclusion

Patients with haemorrhagic stroke experienced worsening of renal function during hospitalisation and had significantly worse outcomes than patients with ischaemic stroke. Ischaemic heart disease, diabetes, glucose level and renal function were risk factors for mortality in ischaemic stroke, while age and glucose level at admission in haemorrhagic stroke. The assessment of kidney function is prerequisite to employ the necessary measures to decrease the risk of in-hospital mortality among patients with acute stroke. However, waiting for a baseline serum-creatinine is an unnecessary delay to emergency reperfusion treatment [30]. Furthermore, appropriate approach to deal with patients with renal dysfunction (i.e. adequate hydration, avoidance of nephrotoxic drugs, drug dose adjustment etc) should be considered as preventive and therapeutic strategies of acute stroke.

#### **Disclosure Statement**

The authors declare that they have no competing interests.

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