MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2014; 20: 1389-1394
DOI: 10.12659/MSM.890627

Received: 2014.03.04
Accepted: 2014.03.23
Published: 2014.08.07

Evaluation of Influence of Chronic Kidney Disease and Sodium Disturbances on Clinical Course of Acute and Sub-Acute Stage First-Ever Ischemic Stroke

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Source of support: Departmental sources

Background: Chronic kidney disease (CKD) is an independent risk factor for cardiovascular morbidity and mortality. Hyponatremia is the most common electrolyte disturbance encountered in the neurological and neurosurgical intensive care units, and can exacerbate existing neurological deficits. The objective of this study was to observe the influences of chronic kidney disease and sodium disturbances on the clinical course of acute and sub-acute stages of first-ever ischemic stroke.

Material/Methods: 464 patients with previously diagnosed chronic kidney disease (aged 70.42±11.49 years; 250 women) who had experienced their first-ever ischemic stroke were qualified. The following examinations were performed: serum levels of sodium, creatinine, lipids, estimated glomerular filtration rate (eGFR), neurological state on 1st day of stroke (according to National Institutes of Health Stroke Scale), functional state measured with the Rankin scale, (RS) and mortality rate at 1 month after stroke.

Results: The neurological state on 1st day of stroke was worse and the median RS (30 days after stroke) was higher in patients with eGFR ≤60 ml/ (min×1.73). Men with eGFR ≤60 ml had greater neurological deficits and increased mortality within 1 month. In patients with eGFR >60 ml/, male sex was more often associated with worse outcomes at 1 month after ischemic stroke. Hyponatremia was associated with a more severe state in both the acute and sub-acute stages of stroke, with higher incidence of death within 1 month after stroke. Men with hyponatremia had greater neurological deficits on the 1st day and increased mortality within 1 month.

Conclusions: Renal impairment and hyponatremia are associated with worse neurological outcomes in patients in the acute stage of their first-ever stroke and within 1 month after the event. Males with impaired kidney function and hyponatremia have a more severe course in their first-ever ischemic stroke, as well as having increased mortality.

Keywords: Hyponatremia • Kidney Failure, Chronic • Stroke

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/890627

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Background

Chronic kidney disease (CKD), the prevalence of which is estimated to be 8–16% worldwide, is an independent risk factor for morbidity and mortality in patients with cardiovascular disease [1]. Sodium is important in maintaining irritability and conduction of nerve and muscle tissues and assists in the regulation of acid-base balance. Hyponatremia is the most common electrolyte disorder encountered in patients in the neurological and neurosurgical Intensive Care Units and can worsen existing neurological deficits [2–4]. Neurological disorders that cause hyponatremia are diverse and include neurotrauma, subarachnoid hemorrhage, intracerebral hemorrhage, meningitis, and stroke [4–6]. One reason for the increased risk of cardiovascular disease in patients with chronic kidney disease is accelerated atherosclerosis. Advanced asymptomatic atherosclerosis in the carotid arteries is observed in patients during the early stages of CKD, with intima and media thickness increasing directly with a decline in glomerular filtration rate [7]. Concentric arterial calcification is associated with arterial stiffness, resulting in a high pulse pressure and increased characteristic aortic impedance. It has been observed that there is an association between intima calcification and increased incidence of ischemic stroke [8].

The aim of this study was to evaluate the influence of chronic kidney disease and sodium disturbances on the clinical course of acute and sub-acute stage of first-ever ischemic stroke.

Material and Methods

This prospective, non-randomized study, performed from January 2013 to July 2013, consisted of 464 patients aged 70.42±11.49 years (250 women) with previously diagnosed chronic kidney disease (according to KDIGO 2012 guidelines) [9] admitted to the Department of Neurology due to a first-ever ischemic stroke commensurate with the WHO criteria [10]. The study group consisted of patients in which computed tomography (CT) of the head, performed during the first 24 h of an ischemic event, did not reveal any abnormalities or only revealed early ischemic changes. Patients with both symptoms of transient ischemic attack (TIA) and intracranial hemorrhage, complicated by ischemic stroke due to vasospasm, were excluded from the study. Ethics committee approval was not required because the study was based on a routine laboratory tests performed in every patient with a stroke – no patient identification was recorded and thus the study did not fulfill the criterion of a medical experiment.

The patients were divided into 1 of 2 subgroups:

a. depending on the value eGFR: ≤60 ml/(min×1.73 m^2) and >60 ml/(min×1.73 m^2).
b. depending on the sodium concentration: ≤135mmol/l and >135mmol/l.

The following parameters were analyzed:

- age at which first-ever ischemic stroke occurred;
- prevalence of comorbidities, such as hypertension, persistent atrial fibrillation, diabetes mellitus (DM), and dyslipidemia. Diagnosis of hypertension was consistent with the recommendation of the Polish Society of Cardiology [11]; DM was diagnosed according to the criteria of the Polish Diabetes Association (2013) [12]; dyslipidemia was defined as total cholesterol serum level >200 mg/dl (>5.18 mmol/L); or LDL-cholesterol serum level >100 mg/dl (2.59 mmol/L), or HDL cholesterol serum level <35 mg/dl (0.91 mmol/L), or triglyceride serum level >135 mg/dL (1.53mmol/L);
- neurological condition during the first 24 h of the ischemic event using the NIHSS score (National Institutes of Health Stroke Scale) [13] (the neurological state was assessed as good or moderate: 0–12 points in NIHSS and severe >12 points in NIHSS respectively);
- mortality rate at 1 month after their first-ever stroke;
- the status of functioning at 1 month after first-ever stroke measured by modified Rankin scale (mRS) [14] during control medical examination in hospital (the functioning state after stroke was assessed as good when the patient did not require caregiver assistance (0–3 points in mRS) or severe when the patient was dependent on the caregiver or died (4–6 points in mRS).

The acute phase of stroke was defined as a period of 1–7 days. The subacute period was defined as 1–3 weeks.

All parameters were also analyzed after the respondents were divided by sex.

Laboratory tests

Laboratory tests were conducted in the Central Laboratory of the Upper Silesian Medical Centre in Katowice. Venous blood samples (20 ml), taken on admission, were withdrawn into plastic test tubes (Vacutainer system). The tubes were allowed to clot, and then centrifuged at room temperature (1000 × G) for 10 min.

The spectrophotometric method (Point Scientific Inc., Michigan, USA) was used to determine the serum level of sodium (Na), glucose, creatinine, and lipids. Estimated glomerular filtration rate (eGFR) was calculated according to the Chronic Kidney Disease Epidemiology Collaboration [14].

Statistical analysis

All parametric values were expressed as mean with standard deviations (SD). All statistical analyses were performed using the STATISTICA 8.0 PL software. The distribution was analyzed using the Kolmogorov-Smirnoff test. Because of the size of the

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Table 1. Patients' clinical characteristics (n,%).

Parameter	Patients with eGFR ≤60 ml/(min×1.73 m²) n=155		Patients with eGFR >60 ml/(min×1.73 m²) n=309		*p* (test Chi²)
Age	71.1±11.49		69.75±11.5		0.66*
Arterial hypertension	65	(41.9%)	136	(44.0%)	0.67
Atrial fibrillation	42	(27.1%)	105	(35.0%)	0.13
Lipid disorders	50	(32.3%)	82	(26.5%)	0.19
Diabetes	64	(41.3%)	120	(38.8%)	0.61

* t-student's test; eGFR – estimated glomerular filtration rate.

Table 2. Clinical state and mortality according to eGFR (mean ±SD).

Parameter	eGFR ≤60 ml/(min×1.73 m²) n=155	eGFR >60 ml/(min×1.73 m²) n=309	*p* (U Mann-Whitney)
NIHSS	6.85±6.55	5.74±6.12	0.0199
mRankin	3.10±1.91	2.43±2.01	0.0005

eGFR – estimated glomerular filtration rate; NIHSS – National Institutes of Health Stroke Scale on the 1st day of stroke; mRankin – modified Rankin scale on the 30th day after stroke.

control group, the subgroups, and the nonparametric distribution of some of the parameters, the Mann-Whitney U test was used to compare the study groups and for age we used the *t* test. For categorical variables, we used chi-square tests. P<0.05 was considered statistically significant.

Results

The age of patients with their first-ever stroke and the prevalence of selected comorbidities (hypertension, atrial fibrillation, dyslipidemia and diabetes mellitus) did not differ in subgroups of patients with decreased eGFR (≤60 *vs.* >60 mL/(min×1.73 m²) (Table 1).

Neurological condition in the acute stage of a first-ever stroke, evaluated using the NIHSS score, was worse, and the average score in mRS (indicative of a greater degree of disability within 30 days after stroke) was higher in patients with eGFR ≤60 ml/(min×1.73 m²) (Table 2). The mortality rate within 1 month did not differ in patients when divided according to eGFR (7% *vs.* 5%; p=0.4). Men with eGFR ≤60 ml/(min×1.73 m²) were characterized by greater neurological deficits on the first day of stroke and increased mortality within 1 month after neurological event compared to women. In patients with eGFR >60 ml/(min×1.73 m²), male sex was more often associated with worse outcome at 1 month after stroke (Table 3).

The mean serum sodium concentration ranged from 127 to 152 mmol/l. Hyponatremia was associated with a more severe condition of the patients in both the acute and subacute stages of stroke and higher incidence of death within 1 month (13.6% *vs.* 4%; Na ≤135 mmol/l *vs.* Na ≥135 mmol/l, respectively) (Table 4). Men with hyponatremia were characterized by greater neurological deficits on the first day of stroke and increased mortality within 1 month after. A greater level of disability was observed in men with a normal serum sodium level (Table 5).

Discussion

CKD is a major risk factor for cardiovascular disease, including stroke [15–17]. Available data indicate an increased risk of cerebral infarction and intracerebral hemorrhage in patients with CKD (40–46% and 39%, respectively) [18–20]. The factors that increase the incidence of stroke in the course of kidney disease include accelerated atherosclerosis, calcification of the cerebral arteries, hemodynamic disturbances, anemia, and anticoagulation therapy [17,20]. Patients with impaired renal function often develop lobar hemorrhages with extensive damage to brain structures, characterized by a more severe clinical course [21]. Chronic kidney failure worsens the early (the course of the acute stage of stroke), as well as the late prognosis (in terms of mobility and survival), and increases

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Table 3. Clinical state and mortality in female and male according to eGFR (n,%).

	eGFR ≤60 ml/min (n,%)			eGFR >60 ml/min (n,%)		
	Female n=64	Male n=91	*p* (Chi²)	Female n=150	Male n=159	*p* (Chi²)
NIHSS 0–12	57 (89.1%)	65 (71.4%)	0.0083	127 (84.7%)	131 (82.4%)	0.5900
NIHSS >12	7 (10.9%)	26 (28.6%)		23 (15.3%)	28 (17.6%)	
mRankin 0–3	35 (54.7%)	39 (42.9%)	0.1466	106 (70.7%)	92 (57.9%)	0.0190
mRankin 4–6	29 (45.3%)	52 (57.1%)		44 (29.3%)	67 (42.1%)	
1 month mortality	1 (1.6%)	10 (11.0%)	0.0244	5 (3.3%)	11 (6.9%)	0.1552

eGFR – estimated glomerular filtration rate; NIHSS – National Institutes of Health Stroke Scale.

Table 4. Clinical state, mortality according to serum sodium concentration (mean ±SD).

Parameter	Na ≤135 mmol/l n=88	Na >135 mmol/l n=376	*p* (U Mann-Whitney)
NIHSS	8.22±6.58	5.62±6.11	0.0001
mRankin	3.83±1.78	2.38±1.96	0.0000

NIHSS – National Instytutes of Health Stroke Scale; mRankin – modified Rankin scale.

Table 5. Clinical state, mortality in female i male according to serum sodium concentration.

	Na ≤135 mmol/l (n,%)			Na >135 mmol/l (n,%)		
	Female n=39	Male N=49	*p* (test Chi²)	Female n=175	Male N=201	*p* (test Chi²)
NIHSS 0–12	32 (82.1%)	30 (61.2%)	0.0334	152 (86.9%)	166 (82.6%)	0.2529
NIHSS >12	7 (17.9%)	19 (38.8%)		23 (13.1%)	35 (17.4%)	
mRankin 0–3	15 (38.5%)	16 (32.7%)	0.5710	126 (72%)	115 (57.2%)	0.0029
mRankin 4–6	24 (61.5%)	33 (67.3%)		49 (28%)	86 (42.8%)	
1 month mortality	2 (5.1%)	10 (20.4%)	0.0380	4 (2.3%)	11 (5.5%)	0.1153

NIHSS – National Institutes of Health Stroke Scale; mRankin – modified Rankin scale.

the risk of recurrent stroke [22–26]. CKD was 1 of the 9 most important risk factors for recurrent stroke within 1 year of diagnosis of the previous incident, according to the Fukuoka Stroke Registry Study (FSR) [27]. We found that in the acute stage of stroke, patients with a decreased glomerular filtration rate (eGFR <60 ml / min) have a greater degree of neurological damage. These patients often remain dependent on help for daily activities within 1 month after the stroke. The results obtained allow us to conclude that hyponatremia influences the course of the acute and sub-acute stroke periods. The mean age of onset of stroke and the incidence of other diseases likely affect its course, and did not differ significantly for the 2 subgroups. We did not observe that a reduced glomerular filtration rate increased the mortality during the month of follow-up. However, it must be noted that male sex had a negative impact on neurological condition in the acute stage of stroke and survival rate within 1 month of the onset of cerebral ischemia. The age and sex differences in the incidence and course of stroke in men and women have already been demonstrated, but the reason for that phenomenon remains unclear. The impact of sex on the incidence, course, and outcome of stroke is analyzed with respect to the hormonal profile. Risk factor profiles are different, with men having a higher incidence of coronary artery disease, dyslipidemia, diabetes, carotid stenosis, and tobacco smoking, while women had a higher incidence of atrial fibrillation and hypertension. When compared to men, women were older and more significantly impacted by acute stroke. Some authors demonstrated significantly worse functional outcomes for women compared to men at 1 and 5 years after stroke [28–31]. Other authors have observed that hemorrhagic transformation in acute ischemic stroke and increased mortality during hospitalization were more common

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in patients with CKD [32]. Hirano et al. demonstrated that patients with renal impairment receive less benefit from thrombolytic therapy in the acute stage of stroke [33]. In addition, the same authors demonstrated a higher incidence of iatrogenic bleeding into intracranial structures, causing a high degree of post-stroke morbidity and increased mortality in this group of patients. It has also been demonstrated that chronic kidney disease has a negative effect on the course of other cardiovascular diseases, including coronary heart disease, and a worse prognosis after angioplasty [34–42]. Patients with chronic kidney disease have a higher incidence of occult stroke and microhemorrhages, regardless of incidents of acute cerebral ischemia [16,17]. Imaging studies in patients on hemodialysis (conducted both pre and post mortem) demonstrate the presence of small-vessel infarcts and cerebral atrophy [16,41]. Hyponatremia is another factor that may affect the course and prognosis of patients after stroke. It is the most common electrolyte disorder in hospitalized patients in various clinical settings [42]. Even a small reduction in the serum sodium level is associated with a worse prognosis, regardless of the disease. These observations have also been made in patients with myocardial infarction, pulmonary hypertension, and subarachnoid hemorrhage [43,44]. Additionally, Wannamethee et al. recognized hyponatremia as a potential risk factor for stroke [45]. The relationship between hyponatremia and clinical outcomes after stroke is not completely understood. The worse outcomes in patients with hyponatremia may possibly be explained by osmotic changes (decreased plasma osmolality) resulting in cerebral edema and secondarily increased intracranial pressure. Osmotic changes within neurocytes could also be responsible for cellular damage and their premature death. In the present study, hyponatremia was associated with a more severe condition of the patients in the acute and subacute phases of their first-ever stroke and a higher incidence of mortality within 1 month of the onset of their first-ever stroke. Therefore, hyponatremia observed in patients with their first-ever stroke could be regarded as an essential risk factor for increased mortality and worse prognosis. Interestingly, in the present study, the effect of hyponatremia on both neurologic condition during the first 24 h after stroke and increased mortality rate was significantly higher in men. Other authors obtained similar results. Rodriguez et al. found hyponatremia to be an independent predictor of long-term cumulative mortality rates at 3 and 12 months after stroke and a worse condition at discharge from hospital. It is important to note that no difference has been found when comparing stroke etiologies (ischemic *vs.* hemorrhagic) in patients with hyponatremia [46]. Huang et al. demonstrated that decreased sodium level (<135 mmol/l) was a predictor of 3-year mortality in patients with their first-ever acute stroke, independent of other clinical predictors of adverse outcome [47]. This study is one of the few that evaluated the effect of kidney function and sodium disturbances on the course and clinical outcomes in patients after their first-ever stroke during short-term observation. It is not known whether adequate correction of sodium level in patients with acute stroke will improve prognosis and reduce the risk of death. It would be interesting to discover why men with impaired renal function had a more unfavorable course of stroke and higher post-stroke mortality. These findings require further investigation.

Conclusions

Renal impairment and hyponatremia are associated with worse neurological condition in patients in the acute stage of their first-ever stroke and worse outcomes within 1 month after a neurological event. Male patients with impaired kidney function and hyponatremia have a more severe course of a first-ever stroke and greater short-term mortality compared to females.

References:

1. Levey AS, Sarnak MJ: Chronic kidney disease as a risk factor for cardiovascular disease and all-cause mortality: a pooled analysis of community-based studies. J Am Soc Nephrol, 2004; 15: 1307–15
2. Palmer BF: Hyponatremia in patients with central nervous system disease: SIADH versus CSW. Trends Endocrinol Metab, 2003; 14: 182–87
3. Coenraad MJ, Meinders AE, Taal JC, Bolk JH: Hyponatremia in intracranial disorders. Neth J Med, 2001; 58: 123–27
4. Lath R: Hyponatremia in neurological diseases in ICU. Indian J Crit Care Med, 2005; 9: 47–51
5. Cole CD, Gottfried ON, Liu JK, Couldwell WT: Hyponatremia in the neurosurgical patient: Diagnosis and management. Neurosurg Focus, 2004; 16: E9
6. Casulari LA, Costa KN, Albuquerque RC et al: Differential diagnosis and treatment of hyponatremia following pituitary surgery. J Neurosurg Sci, 2004; 48: 11–18
7. Preston E, Ellis MR, Kulinskaya E et al: Association between carotid artery intima-media thickness and cardiovascular risk factors in CKD. Am J Kidney Dis, 2005; 46: 856–62
8. London GM: Arterial calcification: cardiovascular function and clinical outcome. Nefrologia, 2011; 31: 644–47
9. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International Supplements, 2013; 3: 5–14
10. The World Bank. World Development Report 1993. Investing in health. Oxford University Press, Oxford, 1993
11. Mancia G, De Backer G, Dominiczak A et al: Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J, 2007; 28: 1462–536
12. Standards of medical care in diabetes – 2013. American Diabetes Association. Diabetes Care, 2013; 36: 11–66
13. Young FB, Weir CJ, Lees KR: GAIN International Trial Steering Committee and Investigators. Comparison of the National Institutes of Health Stroke Scale with disability outcome measures in acute stroke trials. Stroke, 2005; 36: 2187–92
14. Weisscher N, Vermeulen M, Roos YB et al: What should be defined as good outcome in stroke trials; a modified Rankin score of 0–1 or 0–2? J Neurol, 2008; 255: 867–74
15. Eikelboom JW, Connolly SJ, Gao P et al: Stroke risk and efficancy of apixaban in atrial fibrillation patients with moderate chronic kidney disease. J Stroke Cerebrovasc Dis, 2012; 21: 429–35

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16. Drew DA, Bhadelia R, Tighiouart H et al: Anatomic brain disease in hemodialysis patients: a cross-sectional study. Am J Kidney Dis, 2013; 61: 271–78
17. Toyoda K: Cerebrorenal interaction and stroke. Contrib Nephrol, 2013; 179: 1–6
18. Lee SH, Kim BJ, Ryu WS et al: White matter lesions and poor outcome after intracerebral hemorrhage: a nationwide cohort study. Neurology, 2010; 74: 1502–10
19. Perkovic V, Cass A: Glomerular filtration rate and the risk of stroke. BMJ, 2010; 341: 4390
20. Abramson JL, Jurkovitz CT, Vaccarino V et al: Chronic kidney disease, anemia, and incident stroke in a middle-aged, community-based population: the ARIC Study. Kidney Int, 2003; 64: 610–15
21. Molshatzki N, Orion D, Tsabari R et al: Chronic kidney disease in patients with acute intracerebral hemorrhage: association with large hematoma volume and poor outcome. Cerebrovasc Dis, 2011; 31: 271–77
22. Kumai Y, Kamouchi M, Hata J et al: FSR Investigators Proteinuria and clinical outcomes after ischemic stroke. Neurology, 2012; 78: 1909–15
23. Yahalom G, Schwartz R, Schwammenthal Y et al: Chronic kidney disease and clinical outcome in patients with acute stroke. Stroke, 2009; 40: 1296–303
24. MacWalter RS, Wong SY, Wong KY et al: Does renal dysfunction predict mortality after acute stroke? A 7-year follow-up study. Stroke, 2002; 33: 1630–35
25. Tsagalis G, Bakirtzi N, Spengos K et al: Long-term prognosis of combined chronic heart failure and chronic renal dysfunction after acute stroke. Eur J Heart Fail, 2010; 12: 849–54
26. Brzosko S, Szkolka T, Mysliwiec M: Kidney disease is a negative predictor of 30-day survival after acute ischaemic stroke. Nephron Clin Pract, 2009; 112: 79–85
27. Kamouchi M, Kumagai N, Okada Y et al: Risk score for predicting recurrence in patients with ischemic stroke: the Fukuoka stroke risk score for Japanese. Cerebrovasc Dis, 2012; 34: 351–57
28. Fukuda M, Kanda T, Kamide N et al: Gender differences in long-term functional outcome after first-ever ischemic stroke. Intern Med, 2009; 48: 967–73
29. Smith DB, Murphy P, Santos P et al: Gender differences in the Colorado Stroke Registry. Stroke, 2009; 40: 1078–81
30. Duan H, Cai Y, Sun X: Platelet glycoprotein IIb/IIIa polymorphism HPA-3 b/b is associated with increased risk of ischemic stroke in patients under 60 years of age. Med Sci Monit, 2012; 18(1): CR19–24
31. Xu SY, Pan SY: The failure of animal models of neuroprotection in acute ischemic stroke to translate to clinical efficacy. Med Sci Monit Basic Res, 2013; 19: 37–45
32. Sico JJ, Concato J, Wells CK et al: Anemia is associated with poor outcomes in patients with less severe ischemic stroke. J Stroke Cerebrovasc Dis, 2013; 22: 271–78
33. Hirano T: Thrombolysis and hyperacute reperfusion therapy for stroke in renal patients. Contrib Nephrol, 2013; 179: 110–18
34. Al Suwaidi J, Reddan DN, Williams K et al: Prognostic implications of abnormalities in renal function in patients with acute coronary syndromes. Circulation, 2002; 106: 974–80
35. Sadeghi HM, Stone GW, Grines CL et al: Impact of renal insufficiency in patients undergoing primary angioplasty for acute myocardial infarction. Circulation, 2003; 108: 2769–75
36. Manzano-Fernandez S, Marin F, Pastor-Perez FJ et al: Impact of chronic kidney disease on major bleeding complications and mortality in patients with indication for oral anticoagulation undergoing coronary stenting. Chest, 2009; 135: 983–90
37. Latif F, Kleiman NS, Cohen DJ et al: In-hospital and 1-year outcomes among percutaneous coronary intervention patients with chronic kidney disease in the era of drug-eluting stents: a report from the EVENT (Evaluation of Drug Eluting Stents and Ischemic Events) registry. JACC Cardiovasc Interv, 2009; 2: 37–45
38. Cooper WA, O'Brien SM, Thourani VH et al: Impact of renal dysfunction on outcomes of coronary artery bypass surgery: results from the Society of Thoracic Surgeons National Adult Cardiac Database. Circulation, 2006; 113: 1063–70
39. Charytan DM, Yang SS, McGurk S, Rawn J: Long and short-term outcomes following coronary artery bypass grafting in patients with and without chronic kidney disease. Nephrol Dial Transplant, 2010; 25: 3654–63
40. Zakeri R, Freemantle N, Barnett V et al: Relation between mild renal dysfunction and outcomes after coronary artery bypass grafting. Circulation, 2005; 112: 270–75
41. Steinicke R, Gaertner B, Grittner U et al: Kidney function and white matter disease in young stroke patients: analysis of the stroke in young Fabry patients study population. Stroke, 2012; 43: 2382–88
42. Anderson RJ, Chung HM, Kluge R, Schrier RW: Hyponatremia: a prospective analysis of its epidemiology and the pathogenetic role of vasopressin. Ann Intern Med, 1985; 102: 164–68
43. Goldberg A, Hammerman H, Petcherski S et al: Hyponatremia and long-term mortality in survivors of acute ST-elevation myocardial infarction. Arch Intern Med, 2006; 166: 781–86
44. Klein L, O'Connor CM, Leimberger JD et al: Lower serum sodium is associated with increased short-term mortality in hospitalized patients with worsening heart failure: results from the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) study. Circulation, 2005; 111: 2454–60
45. Wannamethee G, Whincup PH, Shaper AG, Lever AF: Serum sodium concentration and risk of stroke in middle-aged males. J Hypertens, 1994; 12: 971–79
46. Rodrigues B, Staff I, Fortunato G, McCullough LD: Hyponatremia in the Prognosis of Acute Ischemic Stroke. J Stroke Cerebrovasc Dis, 2013; pii: S1052-3057(13)00277-2
47. Huang WY, Weng WC, Peng TI et al: Association of hyponatremia in acute stroke stage with three-year mortality in patients with first-ever ischemic stroke. Cerebrovasc Dis, 2012; 34: 55–62

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