Can we distinguish stroke and stroke mimics via red cell distribution width in young patients?

Recep Demir[1], Murat Saritemur[2], Omer Atis[3], Lutfi Ozel[1], İdris Kocaturk[1], Mucahit Emet[2], Hizir Ulvi[1]

[1]Department of Neurology, Medical School, Atatürk University, Erzurum, Turkey
[2]Department of Emergency Medicine, Medical School, Atatürk University, Erzurum, Turkey
[3]Department of Medical Biology, Medical School, Atatürk University, Erzurum, Turkey

Corresponding author:
Assist. Prof. Recep Demir
Department of Neurology
Medical School
Atatürk University
25420 Erzurum, Turkey
Phone: +905337785676
e-mail: demirnoro@gmail.com

Abstract

Introduction: Discrimination of stroke and stroke mimics is problematic in young patients. The aim of the study was to determine whether arterial ischemic stroke and stroke mimics can be differentiated via the red cell distribution width (RDW) value in young patients.
Material and methods: In this retrospective cross-sectional study, a total of 236 patients hospitalized at the neurology ward were investigated. The patients were divided into 3 groups: the 1st group included young stroke patients, the 2nd group included patients with epilepsy, and the 3rd group included patients with multiple sclerosis (MS). Complete blood count and computed tomographic brain imaging tests were performed in all patients, and magnetic resonance imaging was done when necessary.
Results: A total of 236 patients were included in this study. Ninety-five (40%) patients were young stroke patients, 71 (30%) had epilepsy and 70 (30%) had MS. The mean RDW values of young patients with stroke were significantly higher than patients with epilepsy or MS (14.9 ±1.2, 13.3 ±1.2, 13.4 ±0.6, $p < 0.0001$, respectively). The diagnostic power of RDW in the differentiation of patients with stroke is good (area under the curve (AUC) = 0.89). When an RDW cut-off value of 14.05% is accepted for differentiating young patients with stroke from other disorders, the sensitivity, specificity, positive predictive and negative predictive values were 73.7%, 87.9%, 6.1 and 0.043, respectively.
Conclusions: Red cell distribution width is a promising, rapid, easy and inexpensive parameter to distinguish young stroke from stroke mimics (such as epilepsy and MS) in young patients.

Key words: stroke, epilepsy, multiple sclerosis, diagnosis, red cell distribution width.

Introduction

Among all stroke cases, about 12% occur between 18 and 50 years of age, affecting approximately 2 million young people every year worldwide [1]. In young stroke patients with a life expectancy of decades, rapid diagnosis and treatment is extremely important with respect to quality of life [2]. There may not be any positive computed tomography (CT) findings in the early phases, and magnetic resonance imaging (MRI) may not be available on a 24 h/7 days basis at every center, so the diagnosis is mostly based on history and physical examination.

Disorders that mimic stroke are important for emergency physicians and neurologists. Approximately one third of stroke mimics have been shown to be misdiagnosed by physicians [3, 4]. Physicians must determine whether acute neurologic deficits represent a transient event or a potential stroke. The common stroke mimics are toxic-metabolic pathologies, seizure disorders, multiple sclerosis (MS), degenerative neurologic conditions, hemiplegic migraine, intracranial tumors and peripheral neuropathies [3, 5].

The red blood cell distribution width (RDW) reflects the presence of a difference of volume among red blood cells [6]. Red blood cell distribution width is an easy to perform test and a low-cost complete blood count (CBC) parameter. In a recent study by Kim et al. [7], a significant relationship was observed between a high RDW value and poor clinical outcome and mortality in patients with an acute cerebral infarct. A high RDW value was reported to be associated with stroke development in a study by Ani et al. [8].

In this study, we aimed to determine whether the RDW value was helpful in the differential diagnosis of young patients with arterial ischemic stroke and patients with epilepsy or MS, which mimic stroke.

Material and methods

Patients, setting and inclusion-exclusion criteria

In this retrospective cross-sectional study, a total of 236 patients hospitalized between 2010 and 2012 at the Department of Neurology were investigated. The patients were divided into 3 groups. The 1st group included young patients with stroke, and the other groups included patients with epilepsy and MS, which are stroke mimics.

The 1st group included 95 young stroke patients (between 18 and 48 years of age), hospitalized with a diagnosis of ischemic stroke, which had occurred suddenly and continued for more than 24 h, with a focal or global cerebral disturbance. The patients were taken into the study at the time they were admitted to the emergency department (ED). We did not include patients if the symptoms had already lasted more than 6 h.

The 2nd group included 71 patients with epilepsy (between 18 and 55 years of age), who had generalized tonic-clonic seizures. Patients with a diagnosis of epilepsy for a minimum of 1 year, who had at least one seizure in the last 6 months, were included in this study. Other forms of epilepsy were excluded, and also patients with epilepsy directly due to tumors, metabolic disorders or an acute infection were excluded.

The 3rd group included 70 patients (between 23 and 50 years of age) with MS of relapsing-remitting type. Other types of MS were not included in this study.

Stroke mimics are defined as disorders suggestive of acute focal brain dysfunction but turning out to be non-vascular in origin, such as epilepsy, MS, migraine, brain tumors, metabolic disorders, and conversion disorder.

Patients with transient ischemic attack, subarachnoid hemorrhage, subdural hemorrhage, intracerebral bleeding, venous sinus thrombosis and head trauma were not included in this study. Also, patients with anemia (as it affects RDW) and thalassemia (because of presence of erythrocyte shape abnormalities) were excluded.

Laboratory methods

Samples of peripheral venous blood of patients were taken at admission at the emergency department for CBC (in the initial 6 h after symptom onset). The samples were put into tubes containing EDTA, and plasma was separated by centrifuging at 3000 g at +4°C for 10 min. Red blood cell distribution width and other CBC parameters such as hemoglobin (Hb), hematocrit (Hct), platelets (Plt), lymphocytes, polymorphonuclear leukocytes (PMNL) and mean corpuscular volume (MCV) were measured using a Beckman Coulter Automated CBC Analyzer (Beckman Coulter, Inc, Fullerton, Miami). The normal reference values for RDW in the laboratory of our hospital are between 11% and 14%. According to the definition of the World Health Organization, anemia was defined as a hemoglobin level < 13 g/dl for males and < 12 g/dl for females.

Imaging

Brain CT (Toshiba Aguilion-16 model multislice) was performed in the patients on admission at the emergency department, and if indicated, MRI (Siemens Medical Systems 1.5 T) studies were done after hospitalization. The patients were classified in 4 subgroups of ischemic stroke, as in the Oxfordshire Community Stroke Project (OCSP), according to clinical findings, and brain CT and MRI results were also obtained at the 1st and 3rd days [9].

Statistical analysis

The data were presented as number, percent, mean and standard deviation. Comparisons between young patients with stroke and with stroke symptoms were made using one-way analysis of variance (ANOVA) techniques for continuous variables. Post hoc analysis were done using Turkey's honest significant difference (HSD) test. Receiver operating characteristic (ROC) curve analyses were performed to identify the optimal cut-off

point of RDW for the prediction of young stroke among patients with stroke mimics. In the analysis of the data, SPSS 20.0 (SPSS, Inc., Chicago, Illinois) software was used. Statistical hypotheses were tested using $p < 0.05$ as the level of statistical significance.

Results

A total of 236 patients were included in this study. Ninety-five (40%) of these were young patients with stroke, 71 (30%) had epilepsy and 70 (30%) had MS (Table I). There were no significant differences in comparisons of demographic characteristics between these three groups (Table I).

Among the 95 young stroke patients included in this study (group 1), 26 (27.4%) had a right-sided hemiparesis, 39 (41%) left-sided hemiparesis, 22 (23%) right-sided hemihypoesthesia, 38 (40%) left-sided hemihypoesthesia, and 44 (46%) had a speech disturbance, 19 (20%) vomiting, 17 (18%) vertigo, 14 (15%) headache, 7 (7.5%) blurred vision and 3 (3%) seizures.

Of the patients in the 1st group, 46 (48%) had partial anterior cerebral artery infarcts (PACI), 24 (25%) total anterior cerebral artery infarcts (TACI), 17 (18%) posterior cerebral artery infarcts (POCI) and 8 (9%) lacunar cerebral infarcts (LACI). There was no significant difference between the TACI, PACI, POCI and LACI groups in terms of mean RDW values (14.8 ±1.2; 15.0 ±1.3; 15.0 ±1.3; 14.9 ±1.2, respectively; $p > 0.05$). On the initial CT in the ED, 19 of the patients (19%) had early ischemic signs: loss of the gray-white interface in the basal ganglia and lentiform nucleus ($n = 6$), loss of insular ribbon ($n = 5$), hypoattenuation of the brain parenchyma ($n = 3$), focal and diffuse swelling of the cerebral parenchyma ($n = 3$), and hyperdense middle cerebral artery sign ($n = 2$). None of the patients with POCI and LACI had early ischemic signs on CT. Mean RDW values did not change between stroke

patients with early CT signs and patients with normal CT (14.8 ±1.2 and 14.9 ±1.2, $p = 0.720$, respectively).

Out of 70 patients with MS included in this study, 18 (25%) had hemihypoesthesia, 15 (21%) hemiparesis, 15 (21%) headache, 13 (18%) blurred vision, 12 (17%) vertigo, 7 (10%) cerebellar disorder, 2 (2%) paraparesis, and 1 (1.4%) tetraparesis.

The mean RDW value of young patients with stroke was significantly higher than patients with epilepsy and MS (14.9 ±1.2, 13.3 ±1.2, and 13.4 ±0.6, $p < 0.0001$, respectively). Polymorphonuclear leukocytes values were also significantly higher (6.5 ±1.8, 4.5 ±1.2, 5.0 ±1.5, $p < 0.0001$, respectively) (Table II), although area under the curve (AUC) of PMNL was markedly lower than that of RDW (AUC for PMNL and RDW were 0.79 and 0.89, respectively). The diagnostic value of RDW in the differentiation of young patients with stroke and stroke mimics was found to be "good" (Figure 1). The most appropriate cut-off value of RDW in differentiating young patients with stroke from stroke mimics is 14.05% (Table III).

Discussion

The most important result of our study is to show that RDW is a parameter that may help in the differentiation of young patients with stroke symptoms from patients with conditions or disorders which mimic stroke. Red blood cell distribution width values of young patients with ischemic stroke were found to be significantly higher than those with conditions such as epilepsy and MS. There are two reasons for including young patients in this study. First, we believe that stroke is misdiagnosed in the young population as MS or epilepsy is frequently seen in this population. Second, it has proven that RDW increases with advanced age due to illnesses such as chronic heart failure, pulmonary embolism and acute myocar-

Table I. Demographic and laboratory features of young stroke and stroke mimics

Feature	Stroke (95% CI) ($n = 95$)	Epilepsy (95% CI) ($n = 71$)	MS (95% CI) ($n = 70$)	Value of p
Age [years]	37.6 ±6.7 (36.2–39)	34.7 ±9.0 (35–37.1)	35.5 ±9.3 (33.2–37.7)	0.064
Female (%)	60	62.9	62	0.927
MCV [fl]	87.7 ±3.6 (86.9–88.4)	88.6 ±3.9 (87.6–89.5)	87.3 ±4.2 (86.3–88.3)	0.161
Plt [×10³ µl]	271.3 ±82.2 (254.5–288)	256.9 ±57.8 (243.2–270.6)	278.6 ±69.2 (262.1–295.1)	0.187
RDW (%)	14.9 ±1.2 (14.7–15.2)	13.3 ±1.2 (13.1–13.5)	13.4 ±0.6 (13.2–13.5)	0.0001
PMNL [× 10³ µl]	6.5 ±1.8 (6–6.8)	4.5 ±1.2 (4.2–4.7)	5.0 ±1.5 (4.7–5.4)	0.0001
Lymphocyte [× 10³ µl]	2.1 ±0.7 (2–2.2)	2.0 ±0.6 (1.9–2.2)	2.1 ±0.6 (2–2.3)	0.694
Hb [g/dl]	14.2 ±1.6 (13.9–14.5)	14.0 ±1 (13.8–14.2)	14.2 ±1.2 (13.9–14.5)	0.692
Htc (%)	43.5 ±3.9 (42.7–44.3)	43.3 ±2.9 (42.4–44.1)	43.6 ±2.9 (43–44.3)	0.844

Table II. Areas under the ROC curves for stroke for diagnostic parameters in patients with stroke symptoms

Parameter	Diseases	AUC	SE	95% CI	Value of p
RDW (%)	Stroke vs. epilepsy	0.882	0.025	0.833–0.932	< 0.0001
RDW (%)	Stroke vs. MS	0.887	0.026	0.836–0.938	< 0.0001
RDW (%)	Stroke vs. 'epilepsy + MS'	0.885	0.022	0.843–0.927	< 0.0001

AUC – Area under the curve, SE – std. error; 95% CI – 95% confidence interval.

dial infarction [10]. However, in our study group these conditions that may lead to false positive results are very rare. Repeating this study in older stroke patients may lead to different results.

Ischemic stroke in young adults accounts for > 10% of all first ischemic strokes [11]. The etiology of young stroke is heterogeneous, and it has a serious socioeconomic affect, including functional deficits, financial costs, inability to work, and inability to plan or have a family [2]. A major aim is to diagnose and treat early, while the thrombolytic indication is still valid. It was found that 8% of young adults are not given thrombolytics due to delays in diagnosis, and 10% of patients with conditions mimicking stroke are inadvertently given thrombolytic treatment [12]. In a recent study analyzing 8187 patients, 30% had a stroke mimic. Patients with a stroke mimic were younger, and the proportion of patients with a stroke mimic was higher among women, patients without any risk factors, those seen as a code stroke or who arrived at the emergency department via a personal vehicle, and those in whom symptoms occurred during hospitalization [13].

Many investigations have been carried out for early diagnosis of young patients with stroke [14, 15]. Computed tomography and MRI are the most valuable tools for the diagnosis of stroke. Computed tomography has some disadvantages. The involved area of the brain does not appear abnormal for the first several hours after the onset of stroke. Also, the stroke region may be too small to be seen on a CT scan, or areas such as the brain stem or cerebellum infarcts cannot be visualized well [16]. Magnetic resonance imaging has high sensitivity and specificity, but it is expensive, it takes longer to perform and it is not available at all ED on a 24-hour basis. Thrombolytic therapy is planned in the first 4.5 h, when imaging cannot obtain clear-cut
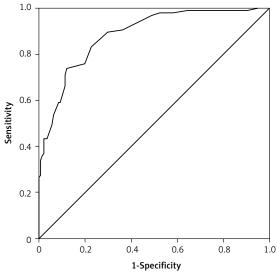

Figure 1. Receiver-operating characteristic (ROC) curves for red cell distribution width (RDW) value in prediction of stroke among patients with stroke symptoms (AUC = 0.89)

information [12]. Our study showed that RDW levels were significantly raised compared to stroke mimics in young ischemic stroke patients who have normal CT brain imaging initially.

Neuroimaging has become one of the most powerful tools for diagnosing stroke. Sensitivity of head CT without contrast for ischemic stroke ranges between 64% and 85% within the first three hours of stroke. After 6 h, the sensitivity falls to 47–80% [17]. Magnetic resonance imaging is more sensitive than CT for ischemic stroke in the first 24 h of symptoms. Sensitivity of brain MRI is found to be 65% 6 h after symptom onset. In 122 patients who underwent diffusion-weighted imaging (DWI) within 6 h of stroke, diffusion-weighted MRI was 97.3% sensitive and 100% specific and had much higher accuracy than CT and

Table III. Diagnostic value of the cut-off value of RDW for young stroke in patients with stroke symptoms

Cut-off value of RDW as a prognostic marker	Sensitivity (%)	Specificity (%)	LR+	LR–
14.05	73.7	87.9	6.1	0.043
14.75	43.2	96.5	12.1	0.046
15.05	35.8	98.6	25.2	0.025
15.15	33.7	99.3	47.5	0.014

conventional MRI [18]. However, the occurrence of false-negative DWI in stroke was as high as 63% in a cohort of 27 patients with acute stroke-like symptoms and negative initial DWI [19]. For patients with unknown time of symptom onset, a recent large multicenter observational study showed that DWI-FLAIR mismatch can be used to identify patients within 4.5 h of symptom onset with 78% specificity and 83% positive predictive value [20]. In our study, sensitivity and specificity of RDW in defining stroke were 74% and 88%, respectively. It is a fact that the RDW itself may not lead to considering making the treatment decision, while a combination of RDW and imaging (CT or MR) may give a better outcome. Thus, RDW would better be used as a tool that shows which patients need further evaluation with imaging modalities. Another possible use of RDW is for patients with high RDW levels and normal non-contrast CT findings. For these patients, RDW may aid in considering MRI or PET to diagnose or rule out stroke.

Other tests are needed for both the early diagnosis of ischemic stroke and discrimination among the disorders mimicking ischemic stroke. Selected biochemical markers were investigated for this reason. Two of the biomarkers studied to differentiate stroke from its mimics are S100 calcium binding protein B (S100B) and neuron-specific enolase (NSE). However, it has been found that they are not specific to cerebral infarction [21]. Levels are raised in other neuropathologies including traumatic brain injury, extracranial malignancies including schwannoma, melanoma and neuroblastoma [22]. Dassan *et al.* [23] found that S100B is not a valuable biomarker for diagnosing acute ischemic stroke, as its levels rise late. Koch *et al.* [24] found that plasma NSE levels were inversely related to disability and progression in patients with MS. The RDW values were not found to be significantly increased in the groups of patients with MS and epilepsy.

Stroke mimics constitute 15–20% of all cases presenting to the ED, prominent among them being seizures, hypoglycemia, somatoform disorders, tumors, migraines, encephalitis and posterior reversible leukoencephalopathy. The two most common stroke mimics in the young adult population are MS and epilepsy [25]. Norris and Hachinski [26] found that the initial diagnosis of stroke was incorrect in 13% of patients. The most common misdiagnosis resulted from unwitnessed or unrecognized seizures, with the postictal state being misdiagnosed as stroke in 5% of the study group. Most of these patients had postictal confusion or stupor, but transient focal neurological signs were observed in about half of the patients including hemiparesis (Todd's paralysis), monoparesis, abnormalities of extraocular movements,

or hemisensory deficits. In the ED, where establishing a diagnosis in minutes is a vital necessity, RDW levels in CBC results may aid the physicians in further evaluation.

Red blood cell distribution width is a hematological parameter routinely measured as part of the standard full blood count tests, reflecting the variability of red blood cell volume [6]. Red blood cell distribution width levels may increase in anemia of iron deficiency, malnutrition, vitamin B_{12} and folate deficiency, erythropoietin resistance, hemolysis and after blood transfusions [27]. An elevated RDW level was a strong independent predictor of outcome in patients with chronic heart failure, pulmonary embolism, acute myocardial infarction and end-stage renal failure [28]. High RDW is also found to be associated with risk of carotid artery atherosclerosis in patients with hypertension.

The association between stroke and RDW levels is not yet fully established. Ani *et al.* [8] found that high RDW levels contribute to stroke development. Also, high RDW levels were reported to be a strong predictor of mortality in patients with cardiovascular disease or stroke. Elevated RDW in patients with acute cerebral infarction was associated with poor functional outcome and mortality. It has been shown that RDW may be used as a biomarker for the prediction of long-term outcomes in patients with acute cerebral infarction [7].

We report here for the first time that RDW may be a good test with high specificity in differentiating young patients with ischemic stroke from patients with conditions mimicking stroke.

In conclusion, RDW seems to be a good test to differentiate stroke among young patients with stroke symptoms. It seems to be an easy, inexpensive and fast laboratory parameter which may provide guidance to physicians in ED and neurology outpatient clinics.

This is a retrospective study carried out in only one center. Many conditions that increase RDW such as malignancy, coronary artery disease, and pulmonary embolism are rarely seen in young patients. The differences in RDW between the groups may decrease in studies done with a larger sample of patients having such diseases. Inclusion of only patients with MS or epilepsy in the stroke mimic groups is another limitation. On the other hand, other stroke mimics apart from these two common disorders are rare and they are easily diagnosed. For example, a bedside blood glucose test is sufficient to detect hypoglycemia. Focal neurological deficits due to migraine are very rare (1/20 000), and no patient with this condition could be found. Patients with conversion are primarily diagnosed at the emergency department and treated at the same place. The number of patients hospitalized

and treated at our department with a diagnosis of conversion is very low, and these could not be included in this study. As it is possible to diagnose intracranial masses with a brain CT in patients admitted at the ED, these were not considered as stroke mimics.

Conflict of interest

The authors declare no conflict of interest.

References

1. Rutten-Jacops LC, Arntz RM, Maaijwee NA, et al. Long-term mortality after stroke among adults aged 18 to 50 years. JAMA 2013; 309: 1136-44.
2. Rutten-Jacobs LC, Maaijwee NA, Arntz RM, et al. Risk factors and prognosis of young stroke. The future study: a prospective cohort study. Study rationale and protocol. BMC Neurol 2011; 11: 109.
3. Magauran BG Jr, Nitka M. Stroke mimics. Emerg Med Clin North Am 2012; 30: 795-804.
4. Karliński M, Gluszkiewicz M, Członkowska A. The accuracy of prehospital diagnosis of acute cerebrovascular accidents: an observational study. Arch Med Sci 2015; 11: 530-5.
5. Ng CL. Diagnostic challenge is this really a stroke? Aust Fam Physician 2006; 35: 805-8.
6. Abbate A, Bonanno E, Mauriello A, et al. Widespread myocardial inflammation and infarct-related artery patency. Circulation 2004; 110: 46-50.
7. Kim J, Kim YD, Song TJ, et al. Red blood cell distribution width is associated with poor clinical outcome in acute cerebral infarction. Thromb Haemost 2012; 108: 349-56.
8. Ani C, Ovbiagele B. Elevated red blood cell distribution width predicts mortality in persons with known stroke. J Neurol Sci 2009; 277: 103-8.
9. Paci M, Nannetti L, D'Ippolito P, Lombardi B. Outcomes from ischemic stroke subtypes classified by the Oxfordshire Community Stroke Project: a systematic review. Eur J Phys Rehabil Med 2011; 47: 19-23.
10. Demir R, Saritemur M, Ozel L, Ozdemir G, Emet M, Ulvi H. Red cell distribution width identifies cerebral venous sinus thrombosis in patients with headache. Clin Appl Thromb Hemost 2015; 21: 354-8.
11. Varona JF. Diagnostic work up and etiology in ischemic stroke in young adults: before and now. J Neurol Neurophysiol 2012; 3: 133.
12. Giraldo EA, Khalid A, Zand R. Safety of intravenous thrombolysis within 4.5 h of symptom onset in patients with negative post-treatment stroke imaging for cerebral infarction. Neurocrit Care 2011; 15: 76-9.
13. Merino JG, Luby M, Benson RT, et al. Predictors of acute stroke mimics in 8187 patients referred to a stroke service. J Stroke Cerebrovasc Dis 2013; 13: 1052-7.
14. Varona JF, Guerra JM, Bermejo F, et al. Causes of ischemic stroke in young adults, and evolution of the etiological diagnosis over the long term. Eur Neurol 2007; 57: 212-8.
15. Siebert J, Gutknecht P, Molisz A, Trzeciak B, Nyka W. Hemodynamic findings in patients with brain stroke. Arch Med Sci 2012; 8: 371-4.
16. Srinivasan A, Goyal M, Al Azri F, Lum C. State of the art imaging of acute stroke. Radiographics 2006; 26: 75-95.
17. Biola H, Crowell K, Grover F Jr. Clinical inquiries. Which imaging modality is best for suspected stroke? J Fam Pract 2005; 54: 538-9.
18. Mullins ME, Schaefer PW, Sorensen AG, et al. CT and conventional and diffusion-weighted MR imaging in acute stroke: study in 691 patients at presentation to the emergency department. Radiology 2002; 224: 353-60.
19. Ay H, Buonanno FS, Rordorf G, et al. Normal diffusion-weighted MRI during stroke-like deficits. Neurology 1999; 52: 1784-92.
20. Thomalla G, Cheng B, Ebinger M, et al. DWI-FLAIR mismatch for the identification of patients with acute ischaemic stroke within 4.5 h of symptom onset (PREFLAIR): a multicentre observational study. Lancet Neurol 2011; 10: 978-86.
21. González-García S, González-Quevedo A, Peña-Sánchez M, et al. Serum neuron-specific enolase and S100 calcium binding protein B biomarker levels do not improve diagnosis of acute stroke. J R Coll Physicians Edinb 2012; 42: 199-204.
22. González-García S, González-Quevedo A, Fernández-Concepción O, et al. Short-term prognostic value of serum neuron specific enolase and S100B in acute stroke patients. Clin Biochem 2012; 45: 1302-7.
23. Dassan P, Keir G, Brown MM. Criteria for a clinically informative serum biomarker in acute ischaemic stroke: a review of S100B. Cerebrovasc Dis 2009; 27: 295-302.
24. Koch M, Mostert J, Heersema D, Teelken A, De Keyser J. Plasma S100beta and NSE levels and progression in multiple sclerosis. J Neurol Sci 2007; 252: 154-8.
25. Ferro JM, Massaro AR, Mas JL. Aetiological diagnosis of ischaemic stroke in young adults. Lancet Neurol 2010; 9: 1085-96.
26. Norris JW, Hachinski VC. Misdiagnosis of stroke. Lancet 1982; 1: 328-31.
27. Uyarel H, Ergelen M, Cicek G, et al. Red cell distribution width as a novel prognostic marker in patients undergoing primary angioplasty for acute myocardial infarction. Coron Artery Dis 2011; 22: 138-44.
28. Felker GM, Allen LA, Pocock SJ, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM program and the Duke Databank. J Am Coll Cardiol 2007; 50: 40-7.