

Abnormal ECG patterns during the acute phase of subarachnoid hemorrhage in patients without previous heart disease

Penka A. Atanassova^{1*}, Maria P. Tokmakova², Albena A. Djurkova¹,
Vulcho Naydenov¹, Nedka T. Chalakova¹, Borislav D. Dimitrov^{3†}

¹ *Stroke Unit, Department of Neurology, Medical University, 4000 Plovdiv, Bulgaria*

² *Department of Cardiology, Medical University, 4000 Plovdiv, Bulgaria*

³ *Information Services Section, Medical University Hospital 'St. George', 4000 Plovdiv, Bulgaria*

Received 9 December 2005; accepted 5 April 2006

Abstract: Subarachnoid hemorrhage (SAH) occurs primarily during early to mid-adulthood; approximately 30% of individuals with SAH die within 2 weeks, and mortality is 30% to 45%. SAH happens suddenly, without patients being aware of previous heart abnormalities. Here, we performed a pilot single cohort (historical) study to examine the hypothesis that early abnormal electrocardiographic (ECG) changes may reveal unknown but “silent” heart pathologies in SAH patients without previous heart disease (PHD). Data were collected retrospectively on 56 consecutive patients during the acute phase of SAH (29 men, 27 women; mean age 49.0 ± 6.2 years) with different degrees of neurologic deficit (Hunt-Hess scale assessment) in a 2-year period single-cohort study. Repolarization abnormalities were most frequent ($p < 0.05$) and were independent of a history of PHD, although it corresponded to a higher risk for such abnormalities (odds ratio $OR = 3.21$; $CI_{95\%} = 1.01-10.22$). ECG changes in patients without PHD were similar to those in PHD patients, confirming the hypothesis that SAH is associated with previously “silent” heart pathology. The increased frequency of ECG changes in PHD patients and their high incidence in no-PHD patients suggested a neurogenic form of myocardial dysfunction following SAH. Notably, repolarization changes were more frequent in patients with less severe deficit ($p < 0.05$), whereas rhythm and conductive abnormalities were more frequent in patients with more severe neurologic deficit. © Versita Warsaw and Springer-Verlag Berlin Heidelberg. All rights reserved.

Keywords: Subarachnoid hemorrhage, ECG changes, neurologic deficit, previous heart disease, Bulgaria

* E-mail: pp_atanassova@yahoo.com

† Dr Borislav D Dimitrov is currently with the Laboratory of Biostatistics at the Department of Renal Medicine, Mario Negri Institute for Pharmacological Research (Villa Camozzi, Ranica, Bergamo, Italy).

1 Introduction

Subarachnoid hemorrhage (SAH) is a severe vascular event that annually affects 30,000 people in the United States [1]. SAH occurs mainly during early to mid-adulthood, and approximately 30% of those affected die within two weeks of the initial event. Mortality rates for SAH are 30% to 45%, with a median age for death of 59 years. The most common cause of SAH is rupture of a congenital aneurysm in a blood vessel at the base of the brain. A less common source of hemorrhage is rupture of an aneurysm of traumatic or infectious origin or rupture of an arteriovenous malformation. The classical clinical signs and symptoms of SAH include abrupt onset of severe headache, nuchal rigidity, nausea, vomiting, and alteration in consciousness. Additionally, electrocardiographic (ECG) abnormalities often occur and include morphological waveform changes in the 12-lead electrocardiograms. Such cardiac manifestations can be associated with a wide variety of neurologic events, including cerebrovascular accident, head injury, meningitis, and tumors [1].

Cardiac effects of intracranial hemorrhage were initially described in 1903 by Cushing; however, it was not until 1947 that Byer and collaborators described ECG changes in a patient with SAH. Indeed, some form of ECG changes was noted in almost all patients with SAH, and, currently, up to 10% of the patients with SAH are known to have potentially lethal arrhythmias, such as ventricular tachycardia and fibrillation [2]. Well-known ECG changes after SAH include disturbances corresponding to myocardial ischemia, kinetic disturbances of the left ventricular wall, myocytolysis, or arrhythmias [3]. ECG changes are also seen during the acute phase of SAH [4]. Of these, 25% indicate a myocardial ischemia [5] or, less frequently, myocardial infarction [6]. According to Calvo-Romero *et al* and Tung *et al* [6, 7], the ECG changes are established in patients with a previous myocardial damage or are a result of a severe neurological deficit during the SAH event. Khechinashvili & Asplund reported in 2002 the presence of ECG findings of ischemic type and/or elongation of the QT interval in 76% of the patients with SAH [8] independently of whether or not the patients had previously suffered from heart disease (HD).

These last results merit attention, and it was therefore of interest to compare the relationship between occurrence of ECG changes during the acute phase of SAH and the various degrees of neurological deficit and prevalence of previous HD. In the current study, we therefore retrospectively analyzed the relationship between ECG changes and the severity of neurological findings in a relatively large sample of SAH patients and used this information to explore the role of previous HD in SAH.

2 Material and methods

2.1 Study design, patients and procedures

We performed a single cohort (historical) study and collected data on 56 consecutive patients with SAH with different degrees of neurologic deficit over a period of 2 years. The

data were reviewed retrospectively for patients that had been recruited consecutively from all patients hospitalized and followed-up from 2001 to 2003 in the Ward of Cerebrovascular Diseases at the Clinic of Neurology in the Department of Neurology, St. George Medical University Hospital, Plovdiv, Bulgaria. Diagnosis of SAH had been confirmed by computer tomography and/or cerebrospinal fluid analysis. The review included 29 male and 27 female patients (mean age 49.0 ± 6.2 years).

The clinical examination data included the following: type of the SAH event (acute or subacute); cerebrovascular risk factors; physical examination, neurologic and mental status at hospitalization, and previous disease history. The extent of neurologic deficit was assessed using the Hunt-Hess scale [9]. All patients had a 12-lead electrocardiograms (ECGs) were evaluated twice by cardiologist: once at hospitalization and review at their inclusion in the study.

The study inclusion criteria were as follows: consecutive patients with a diagnosis of a first incident of SAH (i.e., no history of previous SAH), age 45 to 55 years, complete medical history of previous diseases, and complete clinical and laboratory data. The protocol was approved and the study was carried out according to the Helsinki Declaration guidelines.

2.2 Statistical analysis

Descriptive statistics and parametric and non-parametric tests were applied. In particular, frequency distribution tests, chi-square statistic, Fisher's exact test, Mantel-Haenzel summary tests, and related risk measures were used as appropriate. The calculations and comparisons of proportions/percentages and related confidence intervals were carried out using the critical ratio Z-test and method of rational approximation [10–12]. All *P* values were two-tailed and only significant values ($P < 0.05$) were indicated in the tables. Data were expressed as means and standard deviation or number and percentage (%) unless stated otherwise. All calculations were made using Excel and EpiCalc 2000 (ver. 1.02; J. Gilman & M. Myatt, Brixton Books, 1998).

Table 1 Distribution of patients according to the degree of neurological deficit and the presence of heart disease (HD) before the subarachnoid haemorrhage (SAH).

Neurological deficit [Hunt-Hess scale]	Patients without previous HD *			Patients with previous HD			Total **	
	N	%	% within degree	N	%	% within degree	N	%
I-II degree #	23	53.49	79.31	6	46.15	20.69	29	51.79
III degree ^	16	37.21	80.00	4	30.77	20.00	20	35.71
IV-V degree	4	9.30	57.14	3	23.08	42.86	7	12.50
Total	43	100.00	76.79	13	100.00	23.21	56	100.00

Note: Distribution differences within columns by chi-square test: * $p=0.0196$, ** $p=0.0219$; Percentage differences within degrees: # $p=0.00003$, ^ $p=0.0005$.

Table 2 Distribution of ECG findings by the presence or absence of heart disease (HD) before the subarachnoid haemorrhage (SAH).

ECG findings	Cases without previous HD			Cases with previous HD*			Total	
	N	%	% within findings	N	%	% within findings	N	%
Repolarization changes **	9	31.03	40.91	13	59.09	59.09	22	43.14
Heart rhythm disturbances *	4	13.79	50.00	4	18.18	50.00	8	15.69
Conductive disturbances *	7	24.14	63.64	4	18.18	36.36	11	21.57
Left-ventricular hypertrophy ^***#	9	31.03	90.00	1	4.55	10.00	10	19.61
Total	29	100.00	56.86	22	100.00	43.14	51	100.00

Note: *Distribution differences within columns by chi-square or Fisher's exact test: *p=0.0273, ^p=0.00077; Percentage (proportion) differences between cases with HD versus without previous HD: **p=0.045, ***p=0.018; Percentage differences within various ECG findings: #p=0.0017.

3 Results and discussion

Analysis of disease characteristics revealed that three-quarters (75.0%; n=42) of the patients had typical acute onset of SAH, whereas 14.3% (n=8) and 10.7% (n=6) had acute but atypical onset of SAH (e.g., chest pain, back pain, hyperacusis, vertigo, ataxia) or subacute onset of SAH, respectively ($P<0.05$). More than three-quarters of the patients (85.7%; n=48; $P<0.05$) had reported severe headache (together with nausea and vomiting) at the onset of SAH. At the same time, according to a history of previous and/or concomitant diseases, arterial hypertension was found in more than two-thirds (67.8%; n=38; $P<0.05$) of the patients. Previous HD was established in 13 patients (23.2%; 95% confidence interval (CI_{95%})=13.4%–36.7%). Overall, during the acute phase, 12.5% (3 men and 4 women) died from complications of SAH.

Using the Hunt-Hess scale, we evaluated and classified the SAH patients into three main categories. We found the following distribution: approximately one-half of the patients (51.8%; n=29) had first- to second-degree neurologic deficits; 35.7% (n=20) had third-degree deficits; and 12.5% (n=7) had fourth- to fifth-degree deficits ($P=0.0219$) (Table 1). Thus, we further stratified the SAH patients according to their degree of neurological deficit and presence/absence of previous HD (Table 1). This significant difference in the above distribution is likely due to the fact that, within the sub-group of patients without previous HD, the patients with first- and second-degree neurologic deficits (n=23; 53.5%) were more than those with third- (37.2%) or fourth/fifth-degree (9.3%) deficits ($P=0.0196$). Within the group of patients with previous HD, the highest prevalence was found for first- through second-degree deficits (46.2%), although the difference was not statistically significant ($P>0.05$). Furthermore, most patients without previous HD were

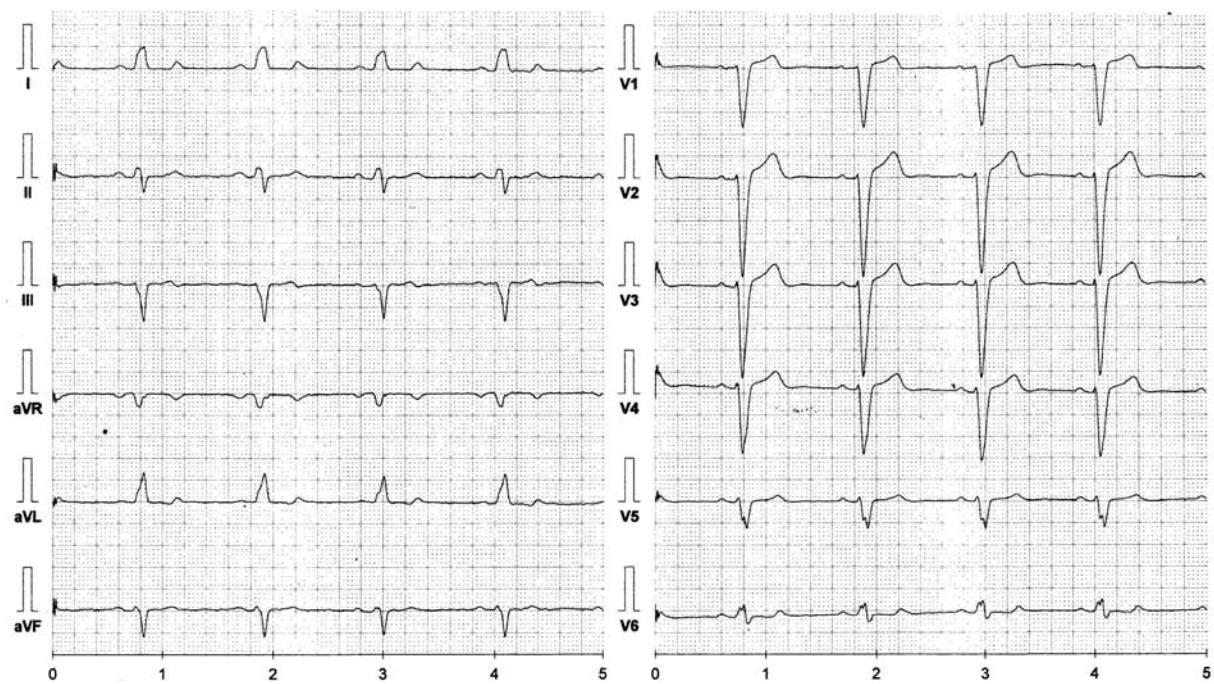


Fig. 1 Left bundle branch block in a 52-year old man without previous HD. At admission, the patient had a neurologic deficit (second degree by Hunt-Hess scale) with a recent, 6-month history of untreated arterial hypertension.

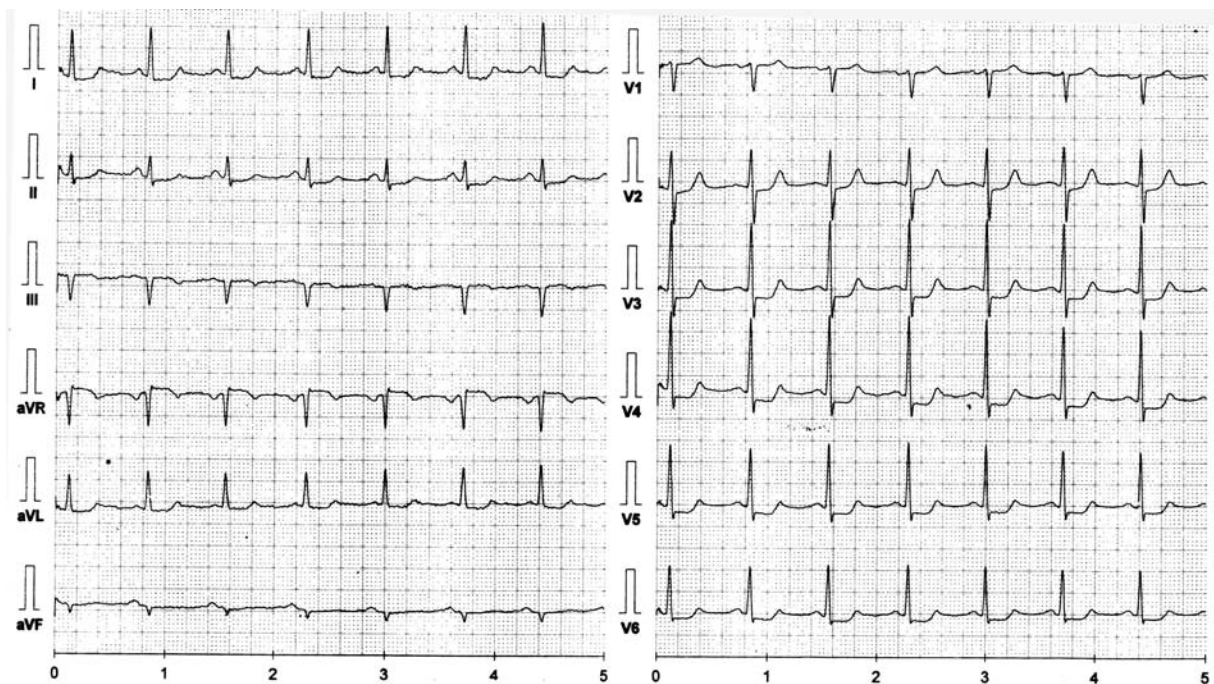


Fig. 2 Repolarization changes in 48-year old woman without previous HD. At admission, the patient had a neurologic deficit (first degree by Hunt-Hess scale), with a 3-year history of arterial hypertension and occasional headaches during episodes of increased blood pressure.

found in the first- through second-degree (79.3% without vs. 20.7% with previous HD) and third-degree deficits (80.0% without vs. 20.0% with previous HD) (Table 1).

Abnormal ECG findings were revealed in 80.4% (n=45) of the 56 patients. The 51 abnormal ECG findings were distributed as follows (Table 2): 43.1% (n=22 cases) showed repolarization changes, 21.6% (n=11) - conductive disturbances, 19.6% (n=10) - left ventricular hypertrophy (LVH), 15.69% (n=8) - heart rhythm disturbances. The findings were equally distributed according to the presence or absence of previous HD (43.1% vs. 56.9%, respectively; $P=0.235$). Significant distribution differences (by Fisher's exact test) were found only in the cases of patients with previous HD (e.g., only one case with LVH was found among the cases of patients with previous HD [$P=0.00077$]; see Table 2 for the P values for other comparisons). A higher percentage of repolarization changes was seen in cases of patients with than without previous HD (59.1% vs. 31.0%, respectively; $P=0.045$), whereas a higher percentage of LVH was found in cases of patients without than without previous HD (31.0% vs. 4.55%, $P<0.05$, respectively). When the above findings were controlled and compared for the type of ECG findings, there was a statistically lower percentage of cases of patients with previous HD only for LVH (10.0% vs. 90.0%, respectively; $P=0.0017$), which indicates that, most likely, the other two types of ECG changes were equally frequent between the two subgroups. In other words, although the statistical significance was marginal, the presence of a previous HD was associated with a 3-fold higher risk of repolarization changes (OR=3.21; CI_{95%}=1.01–10.22) in patients with SAH.

These differences in the distribution of previous HD according to neurologic deficit combined with the type of ECG findings raised the question of why previous HD is a risk factor with the appearance of ECG changes according to the degree of neurological deficit (Table 3). Notably, the abnormal ECG findings are more prevalent in the patients without than with previous HD (56.86% vs. 43.14%), although the difference was not statistically significant. Moreover, in the patients without previous HD (n=29 cases), the repolarization changes and LVH prevail with a total of 62.06% (CI_{95%}=42.35%–78.69%). At a low severity of neurologic deficit (first- to second-degree), these changes account for 88.89% of the studied population (CI_{95%}=63.93%–98.05%; $P=0.00014$; 50.00% and 38.89%, respectively). By our lowest conservative estimation, at least 64% of SAH patients may have had such early heart abnormalities, even presenting with less severe neurological deficit at SAH. These patients may have been hypertensive, but they may have never known of their existing, previously “silent” HD.

Table 3 Comparison of ECG findings according to the degree of neurological deficit and the presence of heart disease (HD) before the subarachnoid haemorrhage (SAH).

SAH cases with ECG findings	Neurological deficit [Hunt-Hess scale]	Previous HD				Total	
		Without		With			
		n1 [m1,m2] (%)	% within rows	n2 [m1,m2] (%)	% within rows	N (M1,M2) (%)	
Repolarization changes*	I-II degree**	9 (31.03)	40.91	13 (59.09)	59.09	22 (43.14)	
	III-IV-V degree	0 (0.00)	0.00	2 (20.00)	100.00	2 (9.52)	
Left-ventricular hypertrophy***^	I-II degree****#	7 (38.89)	87.50	1 (8.33)	12.50	8 (26.67)	
	III-IV-V degree	2 (18.18)	100.00	0 (0.00)	0.00	2 (9.52)	
Heart rhythm disturbances	I-II degree	2 (11.11)	100.00	0 (0.00)	0.00	2 (6.67)	
	III-IV-V degree	2 (18.18)	33.33	4 (40.00)	66.67	6 (28.57)	
Conductive disturbances	I-II degree	0 (0.00)	0.00	0 (0.00)	0.00	0 (0.00)	
	III-IV-V degree	7 (63.64)	63.64	4 (40.00)	36.36	11 (52.38)	
Total	Total (I-II degree)	18 (100.00)	60.00	12 (100.00)	40.00	30 (100.00)	
	Total (III-IV-V degree)	11 (100.00)	52.38	10 (100.00)	47.62	21 (100.00)	

Note: Percentage (proportion) differences between cases with HD versus without previous HD: *p=0.0451, **p=0.017, ***p=0.0183, ****marginal p=0.063; Percentage differences within various ECG findings: ^p=0.0017, #p=0.012. See text for additional sub-group comparisons.

Our clinical and ECG study of patients in the acute phase of SAH did not find the expected significant difference between the frequency of registered ECG changes in the patients with previous HD and those without such a history (Table 2). On the other hand, a higher frequency of ECG abnormalities in the patients with more severe neurologic deficit (according to the Hunt-Hess scale) was also not observed. The most striking finding of our study, however, is that there was increased frequency of abnormal ECG patterns in the patients without previous heart pathology and/or a low level of neurologic deficit. Although our results were different from those that we originally expected based on the previous literature, they do not contradict the previous reports; instead, they extend the current paradigm and support the recently established connection between SAH and accompanying ECG changes [13, 14].

Furthermore, our results support the hypothesis of Macmillan and collaborators [14], that a neurogenic form of myocardial dysfunction may appear during the acute phase of SAH. The acute reversible heart impairment consists of a large number of subclinical injuries (e.g., hypokinesias) prior to the catastrophic heart insufficiency. It is very likely that the increased frequency of ECG changes in the patients with previous HD and the large variety and high frequency of such changes in those without such history are a consequence of brain damage. According to these authors [13, 14], the massive quantities of plasma catecholamines that are released during the hypothalamic stress might provoke specific myocardial lesions.

We found that 43.3% of the patients had repolarization changes, which is very close to the 41% reported by Sommargren and colleagues [4]. The authors had also reported that 14% had LVH independently of the previous history of HD, which is very similar to our finding of 19.6%. It is possible that the higher percentage in our study was due to an increased number of patients that had not suspected or had neglected their arterial hypertension.

Interestingly, independent of previous HD, many more of the repolarization changes were observed in the subgroup of patients with less severe than more severe neurologic deficit (66.67% vs. 9.52%, respectively). Likewise, more rhythm and conductive disturbances were found in the subgroup of patients with more than less severe deficit (80.95% vs. 6.67%, respectively). Most likely, the link between the severity of the neurologic deficit and ECG changes with respect to the history of previous HD could be correctly assessed not only according to the absolute frequency of such changes but, even more, by their specific type. The findings of our study, still and all, support the hypothesis that early abnormal specific changes may serve as a marker for SAH in patients without previously diagnosed HD. Further prospective trials are needed, however, to more thoroughly investigate the potential relationships between the occurrence of SAH, neurological deficit, and the history of previous, even “silent” cardiovascular pathologies such as hypertension and HD.

4 Conclusions

- (1) Different types and frequencies of ECG changes were found in patients with SAH. Most frequent were repolarization abnormalities, independent of the previous history of HD, although such disease might have increased the risk for their appearance (OR=3.21; CI_{95%} 1.01–10.22).
- (2) The frequency of all ECG changes was not statistically different between patients with and without a previous history of HD, supporting the hypothesis of a pathogenic association between SAH and a previously “silent” heart pathology.
- (3) The high percentage of ECG changes in the patients without previous HD as well as the relatively increased percentage of such changes in those with previous HD supports the hypothesis that a neurogenic form of myocardial dysfunction develops during and/or following SAH.
- (4) The severity of the neurologic deficit was most likely related to the type of ECG changes rather than to their frequency. The repolarization changes were more frequent in the patients with less severe deficits, whereas the rhythm and conductive heart abnormalities were more frequent in the patients with more severe neurologic deficits.

References

- [1] C.E. Sommargren: “Electrocardiographic abnormalities in patients with subarchnoid hemorrhage”, *Am. J. Crit. Care.*, Vol. 11(1), (2002), pp. 48–56.
- [2] S. Homma and C. Grahame-Clarke: “Myocardial Damage in Patients With Subarachnoid Hemorrhage”, *Stroke*, Vol. 35, (2004), p. 552.
- [3] J.J. De Oliveira and S.R. Silva: “Signs of myocardial ischemia associated with subarachnoid hemorrhage”, *Arq. Bras. Cardiol.*, Vol. 67(6), (1996), pp. 403–406.
- [4] C.E. Sommargren, J.C. Zaroff, N. Banki and B.J. Drew: “Electrocardiographic repolarization abnormalities in subarachnoid hemorrhage”, *J. Electrocardiol.*, Vol. 35, (2002), pp. 257–262.
- [5] J.G. Zaroff, G. Rordorf, J.B. Newell, C.S. Ogilvy and J.R. Levinson: “Cardiac outcome in patients with subarachnoid hemorrhage and electrocardiographic abnormalities”, *Neurosurgery*, Vol. 44(1), (1999), pp. 34–39.
- [6] J.M. Calvo-Romero, R. Fernandez De Soria-Pantoja, J.D. Arrebola-Garcia and M. Gil-Cubero: “Electrocardiographic abnormalities in subarachnoid hemorrhage”, *Rev. Neurol.*, Vol. 32(6), (2001), pp. 536–537.
- [7] P. Tung, A. Kopelnik, N. Banki, K. Ong, N. Ko, M.T. Lawton et al.: “Predictors of neurocardiogenic injury after subarachnoid hemorrhage”, *Stroke*, Vol. 35(2), (2004), pp. 548–551.
- [8] G. Khechinashvili and K. Asplund: “Electrocardiographic changes in patients with acute stroke: a systematic review”, *Cerebrovasc. Dis.*, Vol. 14(2), (2002), pp. 67–76.
- [9] A.A. Kothavale, N.M. Banki, A. Kopelnik et al.: “Predictors of left ventricular dys-

- function after subarachnoid hemorrhage”, *J. Am. Soc. Echocardiogr.*, Vol. 15, (2003), p. 530.
- [10] J.L. Fleiss: *Statistical Methods for Rates and Proportions*, 2nd ed., John Wiley & Sons, 1981, pp. 23–24, 29–30.
- [11] D. Cooke, A.H. Craven and G.M. Clarke: *Basic Statistical Computing*, 2nd ed., Edward Arnold, 1990, pp. 84–85.
- [12] K.J. Rothman *Modern Epidemiology*, Little brown and Company, 1986, pp. 131–176.
- [13] E. Kawahara, S. Ikeda, Y. Miyahara and S. Kohno: “Role of autonomic nervous disfunction in electrocardiographic abnormalities and cardiac injury in patients with acute subarachnoid hemorrhage”, *Circ. J.*, 67(9), (2003), pp. 753–756.
- [14] C.S. Macmillan, I.S. Grant and P.J. Andrews: “Pulmonary and cardiac sequelae of subarachnoid hemorrhage: time for active management?”, *Intensive Care Med.*, 28(8), (2002), pp. 1012–1023.