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Acute cerebral infarction in non-diabetes patients: clinical pattern, stroke subtypes, and predictors of in-hospital mortality.

Junwu Zhang, Peiyu Li*

Department of Neurology, the Affiliated First Hospital of Jiamusi University, Jiamusi, Heilongjiang, PR China

Abstract

Purpose: Cerebral infarction is the most common type of ischemic stroke that is associated with early mortality and decrease functional capacity. Current study aims to compare prognostic characteristics and outcomes of acute cerebral infarction in diabetic and non-diabetic patients.
Methods: A total of 1283 with confirmed diagnosis of cerebral infarction were enrolled in the current study. The patients were followed-up up to 10 y to ascertain the clinical pattern, stroke subtypes and predictors of in-hospital mortality.
Results: The mean age of participants was 66.9 ± 5.3 y and majority 695 (54.1%) were male. Diabetes was diagnosed in one third of study population i.e. 403 (31.4%). Compared to diabetic patients, non-diabetic patients mostly presented with cardioembolic infarcts (28% *vs.* 17%) and infarcts of unknown cause (16.5% *vs.* 5.4%) while atherothrombotic (43% *vs.* 26%) and lacunar infarcts (36% *vs.* 22%) were more common among diabetics. A total of 210 (16%) cases of in hospital mortality were observed. There was no significant difference in mortality rates of both diabetic and non-diabetics (17.6% *vs.* 13.6%). Cardioembolic strokes, strokes of unknown cause and unusual etiology and Rankin score<3 were independently associated while age was inversely associated with cerebral infarction in non-diabetic patients. The predictors of mortality included female gender, atrial fibrillation, decreased consciousness, respiratory and cardiac complications.
Conclusion: Compared to diabetic patients, non-diabetic patients with cerebral infarction present with different disease pattern and prognosis. Clinical factors that indicate severity of stroke and predict early mortality might help physicians to assess prognosis of patients more effectively and provide adequate treatment.

Keywords: Cerebral infarction, Diabetic, Ischemic heart disease, Non-diabetic, Stroke, Mortality.

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Introduction

A stroke is defined as localized neurological sign or symptoms that appear due to blockage of blood supply to brain. It is the most frequent cause of mortality and one of the most common causes of disability world-wide [1]. Cerebral infarction is the most common type of ischemic stroke in many developed countries that results from blockage of blood vessels supplying to the brain. It causes focal brain necrosis and considered as a most severe type of ischemic stroke. The blockage of blood supply to the brain might be either atherothrombotic or embolic [1,2]. Diabetes Mellitus (DM) is a well-recognized risk factor of stroke where patients with diabetes experience 1.5 to 3 times higher risks of stroke as compared to non-diabetics [3]. In a largest population based case control study, after adjustment of all other potential risk factors, diabetic subjects were having 2.3 times increased risk of stroke [4]. Similarly, in the Framingham study, the incidence of cerebral infarction increases by 2.5 folds in diabetic male patients and 3.6 folds for diabetic women [5]. Apart from population based studies, many observational studies have also shown increased risk of stroke, particularly cerebral infarction, in diabetic patients [6,7].

Existing literature indicate that patients with diabetes mellitus are not only at increased risks of ischemic stroke but also portend significant mortality caused by stoke. Moreover, compared to non-diabetic subjects, the pattern of stroke is different in diabetic subjects. The data from European BIOMED stroke project showed that diabetic subjects are more susceptible to suffer from ischemic stroke than non-diabetic subjects (77% versus 72%) and less susceptible to suffer from hemorrhagic stroke (8.5% versus 11.5%) [8]. Similar results were reported by Copenhagen Stroke Study that augmented the fact by reporting that intra-cerebral hemorrhages are 6 times less frequent in diabetic subjects [9]. Tuttolomondo et al. conducted a study to evaluate the differences between stroke subtypes in diabetic and non-diabetic subjects and reported that diabetic subjects are more likely to have lacunar strokes as compared to non-diabetics [10].

Although there are number of clinical studies elaborating outcomes and prognosis of diabetic patients with cerebral infarction, however, very little is known about clinical patterns, outcomes and predictors of mortality after an acute cerebral infarction in non-diabetic subjects. Moreover, there is paucity of studies on local population of China. In this context, current study was conducted to improve knowledge of cerebral infarction in non-diabetic patients with following objectives: 1) to determine differences in demographic data, clinical variables and prognostic characteristics of acute cerebral infarction in diabetic and non-diabetic patients, and 2) to evaluate predictors of mortality during hospital stay and vitals at discharge in non-diabetic patients presenting with cerebral infarction. The purpose of current study is to gain more precise knowledge about the patterns of ischemic stroke among Chinese population (both diabetic and non-diabetics) presenting to the hospital with acute cerebral infarction, with intent of better understanding of disease management and patient`s care.

Methodology

Ethical approval

Current study was approved by ethical committee of the Affiliated First Hospital of Jiamusi University Hospital. All the patients were asked to sign a consent form before participating in study. Identity of each patient was kept confidential and patients were anonymized during data analysis (RN: ERB/JUH/HRC/2016-4521).

Inclusion criteria

Between January 2003 and December 2014, data of all patients with first ever stroke due to cerebral infarction presented consecutively to Emergency department or Neurology department of the affiliated first Hospital of Jiamusi University were collected prospectively. All patients presented to Emergency department with characteristics of stroke such as vertigo, speech irregularities, hemiparesis (weakness of the right or left side of body), hemiplegia (complete paralysis of either half side of body), hemianopia (decreased vision or complete blindness), hemianaesthesia (loss of touch sensation on one side of body) with subsequent confirmation by CT scan are initially attended in the Emergency department and then transferred to the Neurology department for further evaluation and treatment. All patients presented to hospital within 48 hours of onset of symptoms (acute stroke) were included.

Exclusion criteria

All the patients who met below mentioned criteria were excluded from current study.

- Patients who had previously experienced a stroke or had experienced stroke after admission to hospital for any other condition other than stroke were excluded.
- Patients who were referred to other hospitals for patient personnel reasons and those with minor strokes were also excluded.
- All patients who were presented with onset of symptoms greater than 1 week were not deemed eligible for current study.
- Patients with previous history of head trauma, neurosurgery and intracranial tumors were also excluded.

Stroke sub-type

All patients with confirmed diagnosis of cerebral infarction participated in current study. According to Cerebrovascular Study Group of the Spanish Neurological Society, sub-types of stroke were classified [11]. These sub-types included lunar stroke, atherothrombotic stroke, transient ischemic attacks, cardioembolic infarction and infraction of unknown cause. Strokes due to other subtypes of classification such as intracerebral hemorrhage, subarachnoid hemorrhage, spontaneous epidural and subdural hematoma were excluded. Moreover, the classification also includes infarction due to unusual causes. None of the patient in our study was categorized in this group.

Baseline data

Data regarding patient demographics, laboratory profile including blood count, serum electrolytes, urinalysis, and biochemical tests were noted at baseline. Neurological examination was done on daily basis. A complete history of vascular risk factors, hypertension, cardiovascular disease such as congestive heart failure, angina, myocardial infarction, rheumatic heart disease, liver disease, Chronic Obstructive Pulmonary Disease (COPD), Chronic Kidney Disease (CKD) were noted at baseline. Moreover, patients were also inquired about smoking and alcohol use at the time of hospital admission. All patients underwent following diagnostic evaluations at baseline and after 48 h during first week of hospital admission: electrocardiography, echocardiography, carotid investigations and brain computed topography. At the time of discharge from hospital, outcome data was noted in terms of days of hospital stay, complications (infections, respiratory, cardiac). With respect to mortal cases, cause of death was noted from medical records. The extent of clinical disability was also noted at the time of discharge by using modified Rankin scale and Ad Hoc Committee recommended scale [12,13]. These scales categorized functional outcomes after stroke on the basis of a scoring system ranging from 1 to 6 where 1 signifies state of well-being where all usual every day activities can be performed while 6 represents death.

Definitions

For the purpose of current study, following definitions were used:

Cerebral infarction: Stroke with acute onset of localized neurological insufficiency that lasts longer than 24 h and CT scan excludes stroke causes other than cerebral infarction.

Thromboembolic infarction: Acute onset of localized neurological insufficiency with documented the site of

infarction on CT scan in either cerebral hemisphere or hind brain.

Cardiac embolic cerebral infarction: Acute onset of localized neurological insufficiency with documented site of infarction on CT scan in the presence of cardiovascular complication such as atrial fibrillation or myocardial infarction.

Current smoker: A person who smoked at least one cigarette per day for the past three months or more.

Ex-smoker: A person who smoked at least one cigarette per day for three months or more at some period during his/her life but has not smoked for the past three months or more.

Never smoker: A person who does not qualify the criteria for a current smoker or ex-smoker.

Ever-drinker/never drinker: A subject who has ever/never drank alcohol in whole lifetime.

Statistical analysis

The normality of data was tested by using Kolmogorov-Smirnov test. Continuous data were presented as mean (standard deviation). Categorical data were presented as frequency (proportion) for which frequency served as numerator and total number of patients served as denominator. Relevant denominator was stated before proportion, where it varied. Chi-Square test (if at least 80 percent of cells have expected frequencies of 5 or more) or Fisher's Exact test (if less than 80 percent of cells have expected frequencies of 5 or more) were used to compare categorical variables between two groups. Comparison of continuous variables was done by a Student's t-test when comparing two groups and by ANOVA when comparing more than two groups [14,15]. Logistic regression models were built to identify variables independently associated with ischemic stroke. Following variables were included in regression analysis models both independently and combined (Demographic variables, vascular risk factors, stroke sub-type and localization of cerebral infarction). Significant variables in univariate analysis were subjected to multi-variate analysis with forward stepwise selection. Results were presented in Odds ratio along with 95% confidence interval calculated from beta coefficients and standard errors. Goodness of fit χ^2 test was used to test the hypothesis that logistic model adequately fits data [16]. Cox-proportional hazard models were used to determine Relative Risk (RR) of mortality. For all analysis a p-value of <0.05 was considered statistically significant. All categorical data were entered by coding 0 indicating absence/no while 1 showing presence/yes. Data were analysed by using SPSS 20.0.0.

Results

The baseline demographics and clinical characteristics of entire patient population are shown in Table 1. A total of 1283 patients with mean age of 66.9 ± 5.3 y were included in current study. More than half (54.1%) of the study population were males while females constituted approximately 46% of entire cohort. At the time of hospital admission, hypertension 755 (59%) was the most observed cardiovascular risk factor. Other cardiovascular risk factors included hyperlipidaemia (19%), ischemic heart disease (16%) while the least observed cardiovascular risk factors were valvular heart disease (7.5%) and peripheral vascular disease (8.4%). With respect to frequency of stroke subtype, atherothrombotic stroke was the most prevalent stroke presenting in 406 (31.6%) patients. Lacunar infarcts (26.7%) and cardioembolic strokes (24.8%) were the second most common stroke subtypes in our cohort. The stroke of unknown cause (13%) and unknown etiology (5%) were the least observed stroke sub-types in our cohort. Lastly, according to localization of cerebral infarcts, majority of infarcts (25%) were localized to temporal region while only few only 6.5% cases were localized to Pons region.

At baseline, 403 (31.4%) patients were diabetics. The differences in baseline characteristics of diabetics with cerebral infarction and non-diabetics with cerebral infarction are summarized in Table 1. The distribution of age and gender was similar in both groups. Compared to non-diabetics, diabetic patients with cerebral infarction were having higher prevalence of all cardiovascular risk factors except vulvular heart disease. Vulvular heart disease was the only cardiovascular risk factor more prevalent among non-diabetics (8.6% versus 5.2%). Moreover, diabetic patients tend to have more lacunar (36% versus 22%) and atherothrombotic (43% versus 26%) strokes while non-diabetic patients had increase prevalence of cardioembolic strokes (28% versus 17%) and strokes of unknown (16.5% versus 5.4%) and unusual etiology (7% versus 1%). There were no differences in the medication used, hospital stay and mortality in both groups.

A total of 210 (16%) cases of in hospital mortality were observed in entire study cohort. Although, there were more cases of mortality among non-diabetic patients (17.6% versus 13.6%) but this difference was statistically insignificant (p-value: 0.415). Rankin score that was used to categorize patients on the basis of functional ability after stroke showed that more non-diabetic (56% versus 41%) patients had <3 score that signifies better functional ability while score of 4-5 showing more difficulty in everyday functional activities was more in diabetic patients (45 versus 26%).

Table 1. *Baseline demographic and clinical characteristics of study participants and comparison between diabetic and non-diabetic subjects with Univariate analysis.*

Variable	Overall (N=1283)	Diabetics (N=403)	Non-diabetics (N=880)	p-value
Male	695 (54.1%)	213 (52.8%)	482 (54.7%)	0.453
Females	588 (45.8%)	190 (47.1%)	398 (45.2%)	0.642

Age (years)	66.9 ± 5.3	66.5 ± 4.7	67.3 ± 5.9	0.183
CV risk factors				
Vulvular heart disease	97 (7.5%)	21 (5.2%)	76 (8.6%)	0.032
Ischemic heart disease	205 (15.9%)	81 (20%)	124 (14%)	0.041
Hyperlipidaemia	243 (18.9%)	92 (22.8%)	151 (17.1%)	0.032
Hypertension	755 (58.8%)	298 (73.9%)	457 (51.9%)	0.001
Peripheral vascular disease	108 (8.4%)	42 (10.4%)	66 (7.5%)	0.073
Localization of C. I				
C. P involvement	129 (10%)	62 (15.3%)	67 (7.6%)	0.013
Pons	84 (6.5%)	35 (8.6%)	49 (5.5%)	0.065
Thalamus	92 (7.1%)	48 (11.9%)	44 (5.0%)	0.089
Temporal	322 (25.0%)	82 (20.3%)	240 (27.2%)	0.024
Parietal	300 (23.3%)	78 (19.3%)	222 (25.2%)	0.075
Subtypes				
Atherothrombotic	406 (31.6%)	175 (43.4%)	231 (26.2%)	0.004
Cardioembolic	319 (24.8%)	70 (17.3%)	249 (28.2%)	0.002
Lacunar infarct	343 (26.7%)	145 (36.0%)	198 (22.6%)	0.037
Unknown cause	168 (13.0%)	22 (5.4%)	146 (16.5%)	<0.000
Unusual etiology	65 (5.0%)	5 (1.2%)	60 (6.8%)	<0.000
Medications				
Antibiotic therapy	178 (13.8%)	64 (15.8%)	114 (12.9%)	0.624
Anti-platelets	1085 (84.5%)	346 (85.8%)	739 (83.9%)	0.527
Anti-coagulants	206 (16.0%)	72 (17.8%)	134 (15.2%)	0.009
*Other medications	1238 (96.4%)	394 (97.7%)	844 (95.9%)	0.274
Rankin score				
<3	659 (51.3%)	166 (41.1%)	493 (56.0%)	0.014
4-5	414 (32.2%)	182 (45.1%)	232 (26.3%)	0.002
6	168 (13.0%)	55 (13.6%)	155 (17.6%)	0.415
Outcomes				
Symptom free at hospital discharge	284 (22.1%)	87 (21.5%)	197 (22.3%)	0.925
Duration of hospital stay	11.5 (7-22)	12 (7-22)	11 (7-22)	0.631
Mortality during hospital stay	210 (16.3%)	55 (13.6%)	155 (17.6%)	0.415

CV: Cardiovascular; CI: Cerebral Infarction; CP: Cerebral Posterior

Logistic regression models were run to determine variables independently associated with cerebral infarction in non-diabetic patients. All the significant variables for non-diabetic patients in Table 1 were run into different models in multivariate analysis (Table 2). Cardioembolic strokes, strokes of unknown cause and unusual etiology and Rankin score<3 were independently associated, while age was inversely associated with cerebral infarction in non-diabetic patients.

The characteristics of non-diabetic patients with cerebral infarction according to their vital status at discharge are summarized in Table 3. Out of total 880 non-diabetic patients with cerebral infarction, 725 (82.4%) survived while 155 (17.6%) patients died during their hospital stay. With respect to demographic characteristics, patients who died had increased age and were females while males tend to survive. Compared to patients who remained alive at discharge from hospital,

patients who died had statistically significant higher prevalence of all cardiovascular risk factors except chronic nephropathies, cardiac, respiratory and infectious complications. Moreover, except seizures and sensory symptoms, all other clinical findings such as limb weakness, decreased consciousness and hemianopia were statistically more prevalent among died patients.

Table 2. *Factors associated with cerebral infarction in non-diabetic patients.*

Logistic regression models	β	S.E	Odds ratio (95% CI)
Demographic and vascular risk factors			
Age>70 y	-0.326	0.175	0.62 (0.43-0.94)
Valvular heart disease	0.426	0.194	1.63 (1.07-1.89)
Demographic, vascular risk factors, stroke sub-types			
Age>70 y	-0.382	0.186	0.60 (0.39-0.91)
Cardioembolic	1.938	0.276	6.82 (3.41-9.74)
Unknown cause	1.864	0.248	3.45 (2.68-6.71)
Unusual etiology	1.830	0.245	3.27 (2.49-6.97)
Demographic, Vascular risk factors, stroke sub-type, localization of cerebral infarction			
Age>70 y	-0.372	0.174	0.59 (0.46-0.95)
Cardioembolic	1.956	0.278	6.95 (3.48-9.82)
Unknown cause	1.869	0.251	3.49 (2.71-6.75)
Unusual etiology	1.834	0.246	3.29 (2.50-7.01)
Temporal	0.957	0.201	1.71 (1.04-2.49)
Rankin score<3	1.562	0.276	1.48 (1.56-2.48)

Table 3. *Characteristics of 880 non-diabetic patients according to vital status at discharge.*

Variables	Patient alive (n=725)	Patient died (n=155)	p-value
Gender			
Male	413 (56.9%)	60 (38.7%)	0.024
Females	312 (43.0%)	95 (61.2%)	0.029
Age	74.5 ± 6.4	79.5 ± 9.7	0.001
Clinical findings			
Seizures	7 (0.96%)	4 (2.5%)	0.064
Decreased consciousness	73 (10.0%)	105 (67.7%)	0
Limb weakness	505 (69.6%)	142 (91.6%)	0.002
Sensory symptoms	306 (42.2%)	92 (59.3%)	0.072
Lacunar syndrome	210 (28.9%)	0	-------
Hemianopia	87 (12.0%)	47 (30.3%)	0.001
Cardiovascular risk factors			
Atrial fibrillation	211 (29.1%)	90 (58.0%)	0
Congestive heart disease	42 (5.7%)	21 (13.5%)	0.035
Chronic nephropathy	19 (2.6%)	10 (6.4%)	0.384
Complications			
Respiratory	42 (5.7%)	66 (42.5%)	<0.000
Cardiac	29 (4.0%)	54 (34.8%)	0.001
Urinary	32 (20.6%)	50 (6.8%)	0.095
Infectious	58 (8.0%)	37 (23.8%)	0.001

The predictors of mortality in non-diabetic patients presenting with cerebral infarction by using Cox-proportional hazard model is shown in Table 4. Female gender, atrial fibrillation, decreased consciousness, respiratory and cardiac complications were statistically significantly associated with adverse outcome of mortality in non –diabetic patients with cerebral infarction.

Table 4. *Relative risk of in hospital mortality in non-diabetic patients with cerebral infarction.*

Models to evaluate predictors of death	HR (95% CI)	p-value
Demographic and vascular risk factors model		
Age	1.03 (1.24-1.97)	0.067
Female gender	1.05 (1.12-1.86)	0.042

Atrial fibrillation	2.02 (1.44-2.75)	0.002
Congestive heart disease	1.09 (1.83-2.47)	0.075
Demographic, vascular risk factors, clinical variables model		
Female gender	1.04 (1.10-1.80)	0.035
Atrial fibrillation	1.94 (1.39-1.48)	0.000
Decreased consciousness	2.32 (1.10-1.57)	0.002
Limb weakness	1.32 (1.35-1.96)	0.085
Hemianopia	1.27 (1.18-2.270	0.04
Demographic, vascular risk factors, clinical variables, complications model		
Female gender	1.02 (1.10-1.57)	0.030
Atrial fibrillation	1.72 (1.12-1.73)	0.001
Decreased consciousness	2.14 (1.45-2.49)	0.000
Hemianopia	1.01 (1.37-2.89)	0.072
Respiratory complications	1.58 (1.02-1.94)	0.002
Cardiac complications	2.74 (1.89-2.43)	0.001
Infectious	1.09 (1.75-3.47)	0.094

Discussion

Current study is a hospital based study conducted on 1283 consecutive patients with acute cerebral infarction over a period of 10 y. The prevalence of diabetes in our cohort was about 31% that is somewhat higher to other studies conducted by Megherbi et al. and Arboix et al. where authors have reported the prevalence of diabetes as 21% [8,17]. This higher prevalence in our study might be explained by stronger disposition to stroke in diabetic patients, as previous data indicate the higher incidence of cerebrovascular risk factors and progressive atherogenesis in diabetic patients that are independent determinants of stroke. Diabetic patients in our cohort also had higher incidence of cerebrovascular risk factors such as hyperlipidaemia and ischemic heart disease and these findings are in concordance with the previous literature [18,19]. In last two decades, many studies demonstrating the association between ischemic strokes and diabetes have been published. Olsson et al. conducted a prospective study by including 121 diabetic ischemic heart patients with follow-up of 10 years in order to elaborate their outcomes and survival patterns [20]. Moreover, apart from single center hospital based studies, many multi-centered and community based data have addressed this issue in an elaborative way [8,9,21]. Nevertheless, the growing body of literature on diabetic patients resulted in scarcity of data on non-diabetic patients with ischemic stroke, particularly with cerebral infarction. Therefore current study was aimed to elucidate the outcomes and characteristics of non-diabetic patients with cerebral infarction.

Our data indicate the higher prevalence of cardioembolic strokes in non-diabetic patients while diabetic patients tend to have more atherothrombotic and lacunar infarcts. These findings are consistent with previous studies reporting the higher prevalence of atherothrombotic and lacunar infarcts in non-diabetic patients, possibly due to diabetes associated atherogenesis and small vessel arteriolopathy especially in retina and brain [8,21]. The most effected regions of arteriolopathy in brain are thalamus and pons [22,23]. In current study, non-diabetic patients had localization of their infarcts in pons and thalamus region of brain showing small vessel arteriolopathy induced by diabetes. Similar findings have been reported by Alex et al. where small vessel associated cerebral infarcts were 2.5 times more common among diabetics [24]. On the other hand, non-diabetic patients had shown increased prevalence of cerebral infarcts in temporal and parietal region of the brain. This is another interesting clinical manifestation that distinguishes cerebral infarcts pattern between diabetic and non-diabetic patients.

Current study has demonstrated no difference in the mortality rate of both diabetics and non-diabetics. Although it is presumed that diabetic patients will have better survival and functional recovery after ischemic strokes since lacunar infarcts are more common in diabetics that are associated with favorable outcomes [22,23]. However, such difference was not observed in present study and it might be attributed to the reason that we have just noted in-hospital mortality or more accurately early mortality, since the patients were admitted to the hospital for maximum of 22 d. Therefore, it is cautiously suggested that there is no difference in early mortality of both diabetic and non-diabetics patients with cerebral infarction. However, long term survival should be monitored. In a population based study Sacco et al. reported better prognosis of patients with lacunar infarcts compared to those with non-lacunar infarcts and patients with non-lacunar infarcts had higher prevalence of vascular events [25].

Independent predictors of death in our cohort were female gender, atrial fibrillation, decreased consciousness, cardiac and respiratory complications. A higher prevalence of stroke mortality cases is observed in female gender across the globe. It is estimated that approximately 62% of all strokes related death in United States are in female gender [26,27]. It is assumed that gender related differences in stroke associated mortality and functional disability are attributed to limited access of female gender to diagnostic facilities and genetic predisposition of higher risk of thromboembolism [26,28]. In agreement with the results of previous studies, decreased consciousness was also an independent determinant of early mortality [29,30]. Although the study conducted by Hamidon and Raymond was among diabetic patients, but authors showed that patients with poor consciousness were more likely die during hospital stay compared to conscious patients [29]. Atrial fibrillation was another aggravating predictor of early mortality among non-diabetic patients. This finding is similar to other studies where presence of cardiovascular disease such as atrial fibrillation and congestive heart failure were reported as significant prognostic markers of mortality [30,31]. Patients with atrial fibrillation are reported to have larger infarcts that are one of the reasons of early mortality. Moreover, atrial

fibrillation also causes severe sensory and motor deficit that also explains low consciousness among these patients [32].

Although current study is a single-center study but it has the advantage of complete case ascertainment and large sample size. Moreover, our cohort comprised of both diabetics and non-diabetics, therefore this study gives insight about disease prognosis in both high risk (diabetics) and low risk patients (non-diabetics).

Conclusion

In the current series of prospective patients with cerebral infarction from a single-center hospital based records, the clinical picture of non-diabetic patients was characterized by more frequent cardioembolic infarcts, mostly localized in temporal region of brain, and a Rankin score of less than 3. Mortality during hospital stay is associated with demographic factors such as female gender and other clinical factors such as atrial fibrillation and organ complications. In order to increase life expectancy of such patients adequate care should be given to concomitant respiratory and cardiac comorbidities which would be translated to increased quality of life and decreased early mortality among these patients.

Conflict of Interest

All authors declare no conflict of interest

Author's Contribution

PL contributed in the conception of the work, conducting the study, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. JZ contributed in the conception of the work, drafting and revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work.

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*Correspondence to

Peiyu Li

Department of Neurology

The Affiliated First Hospital of Jiamusi University

PR China