Total Serum Cholesterol Level and Prognosis of Acute Cerebral Ischemic Stroke

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Abstract

Background & purpose: Although Cholesterol is a potential risk factor for stroke, there are some studies showed a reversal positive effect of cholesterol level on survival after ischemic stroke. The aim of this study was to demonstrate relationship between serum Total Cholesterol (TC) level and prognosis of acute ischemic stroke in Iranian patients with ischemic stroke

Material & methods: In this cross sectional descriptive & analytic study (2010-2012), 140 patients with diagnosis of acute ischemic stroke at emergency ward of 5th Azar hospital in Gorgan, in north of Iran, were included via systematic random sampling. TC level was extracted from clinical record of patients and the normal reference was less than 200 mg/dl. Barthel Index (BI) was used to assess general functional status in which scores range between 0-100 and greater scores indicate more independency and better functional status. Data were analyzed by SPSS version 16, descriptive statistics, and statistical tests (Spearman Correlation and Mann-Whitney U-test).

Results: 53.6% of patients were women. Mean age of them was 66.17 ± 12.78 years. Mean TC level was 204.29±49.55 mg/dl. The mean rank score of functional status by BI among two groups of TC <200 mg/dl and TC≥ 200 mg/dl was 63.34 and 76.53, respectively (P = 0.05). Spearman correlation did not show the significant relationship between total serum cholesterol level and function score (r= 0.16, P = 0.057).

Conclusion: High TC in patients with acute ischemic stroke is associated with better prognosis and higher general functional status according to BI. Therefore, evaluation of mechanisms leading to this relationship could be focus of future studies.

Key words: Total Cholesterol, Stroke, Prognosis, Barthel Index

Introduction

Stoke is a costly and debilitating disease in worldwide (1). It remains as one of the top causes of mortality and disability-adjusted life-years (DALYs) loss (2) that accounts for approximately 5.5 million deaths annually and 44 million disabilities (3).

The annual incidence of stroke for various ages ranged from 23 to 103 per 100, 000 population in Iran but is lower than developed countries (4). According to some studies, history of hypertension, waist-to-hip ratio, high risk diet, diabetes mellitus, current smoking, alcohol intake and substance abuse, psychosocial stress and depression, cardiac causes and defects, pregnancy, ratio of Apo-lipoproteins B to A1, and migraine headache are conditions which associated with ischemic stroke (5-7).

In a cohort study on predictors of stroke-associated mortality in the elderly, no significant effect of cholesterol was found (8). Firstly, in Dyker et al. research, the influence of the serum TC level on survival after stroke was studied and higher serum TC level associated with reduced long term mortality after stroke (9). Recent studies also indicated similar findings and lower risk of death or poor functional outcome in the first month after ischemic stroke was seen in patients with a high TC concentration (10-12). Moreover, Olsen et al. found relationship between high TC level and less stroke severity and lower long term mortality, too (13) and high cholesterol was not a risk factor for mortality (14).

As the global burden of stroke is high (2) and the 28-day case fatality rate has been reported about to 19-31%, in Iran (4) and due to the high prevalence of stroke and importance of patients` recovery and
better surveillance system, the aim of this study was to demonstrate the relationship between serum TC level and prognosis of acute cerebral ischemic stroke for the first time in Iranian patients.

**Materials and methods**

In this cross sectional descriptive analytic study, 140 patients with acute ischemic stroke recruited from emergency ward of 5th Azar hospital affiliated to Golestan University of Medical Sciences (Gorgan, North of Iran) via systematic random sampling during Aug 2010 to Feb 2012.

In this study, the sample size was estimated based on a pilot study and finally 140 patients with acute ischemic stroke were included.

Patients with definite diagnosis of acute cerebral ischemic stroke based on clinical findings and after confirmation on CT scan during 24 hours after admission enrolled in the study. Exclusion criteria for this study were patients with transient ischemic attack or hemorrhagic stroke, and patients with symptoms of aphasia which is not assessed by BI.

Following variables were included in the analysis; age, sex, chief complaint, past medical history of Diabetes Mellitus (DM), Ischemic Heart Disease (IHD), Hypertension (HTN), stroke, hyperlipidemia, smoking and substance abuse, findings of CT scan at admission, laboratory findings of Blood Sugar (BS), Triglycerides (TG), TC, Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL) levels, and general functional status level according to BI at first 48 hours and 1st month after admission. All of variables extracted from the clinical record of hospitalized patients except general function status at 1st month after admission which is asked by telephone contact to patients and their family.

To assess the general functional status, BI was used (15) during 48 hours and 1 month after admission (16). The 15-item version of BI was used and score range for individual items is feeding 0–10 (3 functional descriptions, unable, needs some help, independent, score as 0, 5, or 10), moving from wheel chair to bed/return 0–15, personal hygiene 0–5, toileting 0–10, bathing 0–5, walking on level surface 0–15, ascend/descend stairs 0–10, dressing 0–10, controlling bowels 0–10, and controlling bladder 0–10 and total score range was from 0 to 100 and higher scores indicate greater independency and better general functional status (17).

In the present study, laboratory findings were reported based on the analysis of venous blood samples (5cc) obtained from patients at admission time. In laboratory, blood samples centrifuged by Auto-analyser model Biotecnica BT 3500 (Biotecnica, Rome, Italy). Serum levels of TC were measured by Pars Azmoon kit (and Pars Azmoon Inc., Tehran, Iran) with a normal reference less than 200 mg/dl.

Data analysis was carried out by SPSS software version 16. For statistical analysis, the level of TC categorized into two groups of TC < 200 mg/dl and TC ≥ 200 mg/dl. Moreover, the general function score of patients was calculated by subtracting admission scores (48 hours) from follow up scores (1 month). The more this subtraction, the better 1st month functional status of the patients. Descriptive statistics including frequency, mean and standard deviation (SD) was used to describe data. To compare the mean of general functional status in both groups and due to not normal distribution and ordinal type of TC level variable, Mann-Whitney U-test, a non-parametric statistical test, was used. Spearman correlation coefficient was used to assess the relationship between TC level and general functional status of patients. P value less than 0.05 was considered statistically significant.

**Results**

Overall, 140 patients with definite diagnosis of acute ischemic stroke with mean age of 78/12±17/66 years were studied. 53.6 % of patients were women. Majority of patients (50.7 %) were hospitalized due to right hemiplegia and chief complaint in 49.3 % of patients were left hemiplegia.

Table 1 shows frequency distribution of past medical history of patients. Hypertension was the most common past medical history among population studied (Table 1). Mean and standard deviation (SD) of laboratory findings and general functional status score is shown in Table 2. The mean ± SD of TC level was 204.29±49.55 mg/ dl (Table 2). In addition, results of CT scan at 24 hours after stroke showed right middle cerebral artery (RMCA) (37.2%), left middle cerebral artery (LMCA) (29.3%) and Lacunar (26.5%) were frequent involved artery, respectively (Table 3).
In this study, 45.7% of patients had TC<200 mg/dl and 54.3% of them had TC≥200 mg/dl. Moreover, the mean rank score of general functional status in both groups were 63.34 and 76.53 (p=0.05). Spearman correlation coefficient did not show significant relationship between TC level and general functional status score (P=0.057; r=0.16) (Graph 1).

47.7% of men and 60% of women had TC≥200 mg/dl. The mean rank score of general functional status had statistical difference among men (p=0.047), while no significant different was seen among women (Table 4).

Table 1. Frequency distribution of past medical history of patients

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency (n)</td>
<td>Percent (%)</td>
</tr>
<tr>
<td>DM</td>
<td>65</td>
<td>46.4</td>
</tr>
<tr>
<td>IHD</td>
<td>24</td>
<td>17.1</td>
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<tr>
<td>HTN</td>
<td>93</td>
<td>66.4</td>
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<tr>
<td>Stroke</td>
<td>36</td>
<td>25.7</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>43</td>
<td>30.7</td>
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<tr>
<td>Smoking</td>
<td>24</td>
<td>17.1</td>
</tr>
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<td>Substance abuse</td>
<td>29</td>
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</table>

Table 2. Mean and SD of laboratory findings and general functional status score

<table>
<thead>
<tr>
<th>Laboratory Findings</th>
<th>Mean</th>
<th>SD</th>
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<tbody>
<tr>
<td>BS (mg/dl)</td>
<td>154.76</td>
<td>86.42</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>136.88</td>
<td>78.4</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>204.29</td>
<td>49.55</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>114.05</td>
<td>27.39</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>64.1</td>
<td>17.76</td>
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<table>
<thead>
<tr>
<th>General functional Status (score)</th>
<th>48 Hours</th>
<th>1 month</th>
</tr>
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<tbody>
<tr>
<td>Mean rank score</td>
<td>34.93</td>
<td>55.54</td>
</tr>
<tr>
<td>SD</td>
<td>26.27</td>
<td>33.23</td>
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</table>

Table 3. Frequency distribution of involved arteries according to CT scan

<table>
<thead>
<tr>
<th>Involved Arteries</th>
<th>Frequency (n)</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Anterior Cerebral Artery (RACA)</td>
<td>2</td>
<td>1.4</td>
</tr>
<tr>
<td>Left Anterior Cerebral Artery (LACA)</td>
<td>2</td>
<td>1.4</td>
</tr>
<tr>
<td>Right Middle Cerebral Artery (RMCA)</td>
<td>52</td>
<td>37.2</td>
</tr>
<tr>
<td>Left Middle Cerebral Artery (LMCA)</td>
<td>41</td>
<td>29.3</td>
</tr>
<tr>
<td>Right Posterior Cerebral Artery (RPCA)</td>
<td>4</td>
<td>2.8</td>
</tr>
<tr>
<td>Left Posterior Cerebral Artery (LPCA)</td>
<td>2</td>
<td>1.4</td>
</tr>
<tr>
<td>Lacunar</td>
<td>37</td>
<td>26.5</td>
</tr>
<tr>
<td>Total</td>
<td>140</td>
<td>100</td>
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Table 4. Mean and SD of general function status according to sex

<table>
<thead>
<tr>
<th>Mean rank score</th>
<th>TC level</th>
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<tr>
<td></td>
<td>TC&lt;200 mg/dl</td>
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<tr>
<td>sex</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>28.57</td>
</tr>
<tr>
<td>Women</td>
<td>35.20</td>
</tr>
</tbody>
</table>

Graph 1. Scatter diagram of correlation between TC and general functional status
Discussion

According to our findings, patients with high level of TC had better general functional status.

We know that high TC level is a risk factor for cerebrovascular accidents. It has already been reported that lower TC level in acute ischemic stroke patients is associated with better outcome. Dyker et al. indicated significant association between higher serum cholesterol concentrations and reduced long term mortality after stroke and patients with lower serum cholesterol had poor stroke outcome (9). Zuliani et al. indicated that short-term mortality following ischemic stroke was higher in patients with low TC levels and (47.4% in patients with low TC levels versus 23.0% and 24.1% in those with normal and high TC levels, respectively) (12). In Vauthy. et al. investigation, better outcome in early phase after ischemic stroke was found among patients with higher levels of cholesterol and patients with high cholesterol levels had a 2.2 and 2.1 folds lower risk of death and poor functional outcome at 1st month, respectively (11). Li et al. indicated good prognosis following stroke among patients with high TC level (18). Findings of previous studied supports the positive effect of high TC on better stroke prognosis. In our study, although the mean of general function status in high TC level group was better in comparison to the group with lower TC level; however, no correlation was found between TC level and general functional status score. While, this relationship was border line and very near to significant level. Although the reversal relationship between prognosis after ischemic stroke and level of TC in comparison to the nature of TC as a risk factor for ischemic stroke seems somehow paradoxical but this relationship can be justified according to previous studied that cholesterol can act as a buffer and neutralize free radicals and oxidative stress (19-21).

Moreover, there are small studies about sex differences in stroke management and prognosis. According to systematic review on sex differences in stroke epidemiology in 2009, stroke was more common among men but more severe among women and 1 month case fatality rate among women was higher than men (24.7% versus 19.7%) (22). In Di Carlo, et al. study, female sex was reported as a predictor of disability. Although there were no major sex differences in stroke presentation or management, compared with men, women had a slightly worse functional status at 6 months after stroke (23). In Glader at al. research, quality of life among women was worse in female patients in comparison to men and they were more dependent to other persons (24). In our study, although the mean rank score of general functional status among men had significant difference between the two groups, among women was not significant. Therefore, further investigations are suggested.

This study had some limitations, firstly, small sample size due to time and financial support limitations. Thus, long lasting studies with large sample size is suggested. Another limitation was use of BI to assess the general functional status of patients with acute ischemic stroke. BI has not the ability to evaluate the symptoms of language problem so this was the second limitation of our study.

Conclusion

Findings of the present study indicated that high TC level in Iranian patients with acute ischemic stroke may be associated with a better prognosis and general functional status. Thus, further studies are suggested to assess this finding and mechanisms which lead to this relationship.

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References


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