INVESTIGATE THE RELATIONSHIP BETWEEN PLASMA GGT WITH METABOLIC SYNDROME IN MIDDLE-AGED PATIENTS WITH ISCHEMIC STROKE

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ABSTRACT: *A prospective study, cross-sectional description of 205 middle-aged patients including 106 outpatients without cerebral stroke and 99 patients with ischemic stroke at Cerebral Stroke center - 108 Military Central Hospital from January 1, 2018 to December 30, 2020.*

Results: *Metabolic Syndrome (MS) and high blood pressure were correlated with increased risk of cerebral stroke with OR: 4.511, 95%CI: 2.454-8.291, p = 0.000 and OR: 5.078, 95%CI: 4.579-12.579, p = 0.000, respectively. The risk of cerebral stroke was significantly elevated with increased GGT levels, with OR: 3.6, 95%CI: 1.638-7.911, p = 0.001. The patients were men, with increased blood pressure and round the waist leading to suffer from Metabolic syndrome with OR: 7.05, 95%CI: 2.71-18.34, p = 0.000, OR: 5.714, 95%CI: 1.891-17.264, p = 0.001 and OR: 2.779, 95%CI: 1.226-6.302, p = 0.016, respectively. Increased blood glucose, triglyceride, GGT levels were highly associated with the risk of Metabolic Syndrome with OR: 6.857, 95%CI: 2.551-18.435, p = 0.000, OR: 5.374, 95%CI: 4.724-24.896, p = 0.000 and OR: 3.912, 95%CI: 1.413-10.831, p = 0.007, respectively.*

Conclusion: *Elevated GGT levels were associated with the risk of Metabolic Syndrome in middle-aged patients with cerebral infarction, with OR: 3.912, 95%CI: 1.413-10.831, p = 0.007.*

Keywords: Metabolic syndrome, GGT, ischemic stroke, 108 Military Central Hospital

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1. INTRODUCTION.

Cerebral stroke including cerebral hemorrhage and cerebral infarction is a public health problem of worldwide concern. The multi-center studies of the World Health Organization which were conducted in 12 countries showed that the annual incidence of cerebral stroke occurred in 0.2-2.5‰ of the population. It is also the leading cause of disability and the fourth leading cause of death globally. Death from cerebral stroke accounted for 10-12% of the total number of deaths due to diseases in developed countries [1].

The levels of Gamma-Glutamyltransferase (GGT) increased often indicating the disease of liver and alcohol intoxication (beer, alcohol, etc.). Recently, some studies have shown an association between persistently elevated GGT levels and important risk factors for cerebral infarction stroke (such as diabetes mellitus, hypertension, cardiovascular disease, metabolic syndrome) [2], [3]. Up to now in Vietnam, the assessment of the relationship between the above risk factors and GGT levels in patients with cerebral infarction and its application in diagnosis and treatment has not yet received adequate attention from clinicians.

To contribute to the clarification of the above issues, we carried out this study to investigate the relationship between plasma GGT levels and metabolic syndrome in patients with cerebral infarction stroke at 108 Military Central Hospital.

2. SUBJECTS AND METHODS OF THE STUDY.

2.1. Subjects of the study:

A study was conducted in 205 patients aged from 45 to 65, including two groups:

- Group 1 (group of patients with cerebral infarction): 99 patients with cerebral infarction stroke, treated at Cerebral Stroke Center, 108 Military Central Hospital, from January 1, 2018 to December 30, 2020.

- Group 2 (group of patients without cerebral infarction): 106 outpatients without cerebral infarction, treated at 108 Military Central Hospital.

2.2. Methods of the study:

- Study design: a prospective study, cross-sectional description.

- Sample size: selection of convenient sample. Collect samples according to sampling procedures of laboratory ISO 15189:2012.

- Test method: photometric.

- Steps to carry out the study: the patients were clinically examined, tested, and collected information.

- Criteria for diagnosis of the patients with cerebral infarction:

+ Clinically (according to the definition of cerebral stroke by the World Health Organization, 1970): focal (or general) *cerebral* dysfunction developed rapidly, extended more than 24 hours or lead to death, there was no obvious cause besides vascular origin [1].

+ Subclinically: The results of Cranial computed tomography (CT) Scan or Magnetic resonance imaging MRI showed that the image of cerebral infarction was consistent with clinical injuries.

- The diagnostic standard for the metabolic syndrome (as defined by the International Diabetes Federation - IDF for Asian people [3]): The patient had at least three of the following criteria:

+ Waist: men ≥ 90 cm, women ≥ 80 cm.

+ Increased triglycerides ≥ 1.69 mmol/l (150 mg/dl).

+ Decreased HDL (High Density Lipoprotein): male ≤ 1.03 mmol/l (40 mg/dl); female ≤ 1.29 mmol/l (50 mg/dl).

+ Blood pressure ≥ 130/85 mmHg.

+ Blood glucose ≥ 6.1 mmol/l (≥ 100 mg/dl).

- Criteria to exclude patients from the study: patients with stroke, cerebral hemorrhage, having malignant diseases, thyroid disease, cirrhosis, hepatitis, kidney failure...; The patient was taking certain medications that affected the criteria in the study (such as carbamazepine, estrogen, ethanol, niacin, lovastatin, oral contraceptives, phenobarbital, pravastatin, simvastatin, androgens, beta-blockers, diuretics, progestins), estrogen, lovastatin, thyroxine...); Patients or family members did not agree to participate in the study.

- Study criteria: age, sex, waist circumference, systolic blood pressure (SBP), diastolic blood pressure (DBP); blood glucose (Glu), triglyceride (TG), HDL-cholesterol (HDL), LDL-cholesterol (LDL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), plasma GGT.

The biochemical indexes were analyzed on an automatic biochemical analyzer AU5800 (Beckman Coulter, USA). The reference range of GGT < 61 U/l (according to the manufacturer's procedure provided for GGT testing methods, equipment, and chemicals for GGT analysis.

Data processing: according to the medical statistical algorithm (Chi-square test) on SPSS 20.00 software (IBM Co., Armonk, NY, USA).

3. RESULTS OF THE STUDY.

Table 1. The relationship between sex and laboratory indicators in the studied patients.

Characteristics		Patients		p; OR 95%CI (min-max)
		Cerebral infarction	Without cerebral infarction	
Sex	Male	67 (67.7%)	64 (60.4%)	0.311; 1.374 (0.774-2.438)
	Female	32 (32.3%)	42 (39.6%)	
suffered Metabolic syndrome		55 (55.6%)	23 (21.7%)	0.000; 4.511 (2.454-8.291)
Increase blood pressure		68 (68.7%)	31 (29.2%)	0.000; 5.078 (4.579-12.579)
Increase waist		52 (52.5%)	43 (40.5%)	0.052; 2.559 (1.444-4.535)
Increase blood glucose		70 (70.7%)	70 (66.0%)	0.548; 1.241 (0.688-2.241)
Increase triglycerides		65 (65.6%)	78 (73.6%)	0.018; 0.449 (0.25-0.806)
Decreased HDL		38 (38.4%)	49 (46.2%)	0,262; 0,725 (0,415-1,264)
Increase LDL		41 (41.4%)	42 (39.6%)	0.887-1.077 (0.616-1.882)
Increase AST		12 (12.1%)	9 (8.5%)	0.267; 4.25 (1.889-9.564)
Increase ALT		13 (13.1%)	7 (6.6%)	0.157; 2.138 (0.816-5.601)
Increase GGT		27 (27.3%)	10 (9.4%)	0.001; 3.6 (1.638-7.911)

Increased metabolic syndrome and blood pressure leaded to increase the risk of developing cerebral infarction, with OR: 4.511, 95%CI: 2.454-8.291, p = 0.000 and OR: 5.078, 95%CI: 4.579-12,579, p = 0.000, respectively. Increasing GGT concentration increases the possibility of cerebral

infarction with OR: 3.6, 95%CI: 1.638-7.911, p = 0.001.

Table 2. The relationship between sex and laboratory indicators with metabolic syndrome in patients with cerebral infarction.

Characteristics	Patients with cerebral infarction		p; OR 95%CI (min-max)
	Metabolic syndrome (n = 55)	Without Met.syn (n = 44)	
Male	47 (85.5%)	20 (45.5%)	0.000; 7.05 (2.71-18.34)
Female	8 (14.5%)	24 (54.5%)	
Increase Blood pressure	50 (90.9%)	28 (63.6%)	0.001; 5.714 (1.891-17.264)
Increase waist	35 (63.6%)	17 (38.6%)	0.016; 2.779 (1.226-6.302)
Increase blood glucose	48 (87.3%)	22 (50.0%)	0.000; 6.857 (2.551-18.435)
Increase triglyceride	45 (81.8%)	20 (45.4%)	0.000; 5.374 (4.724-24.896)
Decreased HDL	25 (45.5%)	13 (29.5%)	0.145; 1.987 (0.86-4.591)
Increase LDL	22 (40.0%)	19 (43.2%)	0.838; 0.877 (0.392-1.961)
Increase AST	13 (23.6%)	15 (34.1%)	0.27; 0.598 (0.248-1.444)
Increase ALT	9 (16.4%)	4 (9.1%)	0.375; 1.957 (0.56-6.841)
Increase GGT	21 (38.2%)	6 (13.6%)	0.007; 3.912 (1.413-10.831)

Male characteristics, increased blood pressure and waist circumference leaded to increase the possibility of metabolic syndrome in patients with cerebral infarction stroke, respectively with OR: 7.05, 95%CI: 2.71-18.34, p = 0.000; OR: 5.714, 95%CI: 1.891-17.264, p = 0.001 and OR: 2.779; 95%CI: 1.226-6.302, p = 0.016.

The characteristics of increased blood glucose levels, triglyceride and GGT leaded to increase the possibility of metabolic syndrome in patients with cerebral infarction stroke,respectively with OR: 6,857, 95%CI: 2,551-18,435, p = 0.000; OR: 5,374; 95%CI: 4.724-24.896, p = 0.000; OR: 3,912; 95%CI: 1.413-10.831: p = 0.007.

4. DISCUSSION.

The study was conducted in middle-aged patients (from 45-65 years old), the results (Table 1) showed that the male patients in the group without cerebral infarction and the group with cerebral infarction stroke was higher than the female patients (60.4% and 67.7% versus 39.6% and 32.3%). The patients suffering from metabolic syndrome, increased blood pressure, increased waist circumference, increased AST levels increased plasma GGT levels led to an increase in the possibility of cerebral infarction stroke, with p < 0.05.

A study on the relationship between sex and some laboratory indicators of patients suffering from cerebral infarction stroke with metabolic syndrome (Table 2) showed that in the group of patients with cerebral infarction, the proportion of males with metabolic syndrome was higher than that of females, the difference was statistically significant with p < 0.001; increased blood pressure, increased waist circumference, increased blood glucose levels, increased triglyceride and increased GGT led to increasing the risk of metabolic syndrome in patients with cerebral infarction stroke, the difference with p < 0.05.

Currently, metabolic syndrome is becoming a global health problem. The prevalence of metabolic syndrome depended on age, sex, insulin resistance, and obesity [3]. This rate varied by sex at each age, being more common in middle-aged men, but higher in postmenopausal women [4]. This difference can be explained by biological characteristics, psychology, nutrition, and living habits. The prevalence of metabolic syndrome varied by sex due to changes in female hormones during the menopause stage and lifestyle changes in each age group [4].

The metabolic syndrome was thought to be closely associated with inflammation, insulin resistance, endothelial dysfunction, renal and hepatic dysfunction, and oxidative stress. Therefore, some biological indicators, such as white blood cell count (WBC), CRP-hs, insulin resistance index - HOMA-IR (homeostasis model assessment insulin resistance index), homocysteine, uric acid, cystatin C, ALT, GGT was considered to be a risk factor for metabolic syndrome [5]. According to author Lee et al., GGT was associated with risk factors for cardiovascular diseases, metabolic syndrome, especially increasing with age, male, dyslipidemia, hypertension, increased blood glucose, and smoking. Compared with the factors such as age, sex, alcohol consumption, CRP, etc., GGT had the strongest relationship with the risk of metabolic syndrome [6]. Thus, our study results were also consistent with previous publications, the distribution of metabolic syndrome was higher in

middle-aged men and there was a close relationship between metabolic syndrome and increased blood glucose, triglycerides levels. GGT, increased waist circumference, increased blood pressure.

Recently, the mechanism and role of GGT in metabolic syndrome had gradually been elucidated. Some authors suggested that GGT had a key role in the intracellular antioxidant defense system, as it supplied cysteine, which promoted the resynthesis of intracellular glutathione (G-SH). In addition, GGT participated in extracellular G-SH catabolism by cleaving gamma-glutamyl bonds, producing free glutamate and the dipeptide cysteinyl-glycine, the end products of which were glycine and cysteine. GGT was also involved in regulating the oxidation state of thiol proteins on the cell surface, generating oxidative radicals and hydrogen peroxide. On the other hand, GGT was considered a pro-inflammatory substance, because it mediated the conversion of the inflammatory leukotriene C4 to D4. Elevated plasma GGT concentrations were a reflection of increased oxidative stress and chronic inflammation, two processes closely related to the pathogenesis of metabolic syndrome [2].

Up to now, the role of metabolic syndrome with the risk of cerebral infarction and affecting the prognosis of patients with cerebral infarction stroke had been mentioned by several authors [7], [8]. In addition, studies also showed that metabolic syndrome increased the risk of recurrent cerebral infarction, and women were affected more than men [9], [10]. Furthermore, the author Whitfield et al. noted the relationship between GGT and increased oxidative stress. Increased oxidative stress led to increasing G-SH synthesis, this process was GGT-dependent and, therefore, increased GGT synthesis. Increased GGT had also been shown to be associated with inflammatory markers, such as C-reactive protein (CRP), another factor involved in the development of atherosclerosis, which played an important role in the pathogenesis of cerebral infarction [2]. An analysis of the Korean population had shown an association between increased GGT levels and the possibility of myocardial infarction, cerebral stroke and the risk of death from these diseases [11].

It can be said that the change of GGT concentration and the relationship with metabolic syndrome in patients with cerebral infarction stroke in our study were consistent with the publications of authors around the world. However, we did not see a relationship between lipid metabolism disorders and cerebral infarction, ALT levels and metabolic syndrome ($p > 0.05$). This difference may be due to the dissimilarity in sample size, race, life regime...of patients between studies.

Our study had some limitations that cannot compare GGT with other risk factors, such as CRP-hs, Cystatin C... and need to collect more information on family history, nutrition regime, exercise habits, drinking alcohol, smoking... because these were also factors that can affect GGT levels and were risk factors leading to suffering from metabolic syndrome and cerebral infarction stroke. Therefore, more large-scale studies were needed to fully evaluate the characteristics of biological indicators and the relationship with metabolic syndrome and cerebral infarction.

5. CONCLUSION.

A prospective study, cross-sectional description of 99 middle-aged patients with cerebral infarction stroke and 106 patients without cerebral infarction stroke, at the 108 Military Central Hospital, from January 1, 2018 to December 30, 2020, we concluded: Increasing GGT concentration leads to an increase the possibility of metabolic syndrome in middle-aged patients with cerebral infarction, with OR: 3.912, 95%CI: 1.413-10,831, p = 0.007.

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SURVEY THE RELATIONSHIP BETWEEN FECAL OCCULT BLOOD TEST WITH COLORECTAL POLYPS IN 510 WORKERS...

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- 53.5% of workers had the positive fecal occult blood test once and 46.5% of workers had positive fecal occult blood test twice. 212/510 workers (41,6%) had positive fecal occult blood tests and were detected colorectal polyps by colonoscopy.

- The workers with a positive fecal occult blood test twice were 9.22 times more likely to have colorectal polyps than those with a positive test result once; the difference was statistical significance with $p < 0.001$.

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