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Serum Levels of YKL-40 in Acute Ischemic Stroke Patients, and Its Relationship to Infarct Volume

Akut İskemik İnme Hastalarında Serum YKL-40 Düzeyleri ve Bunun Enfarktüs Hacmi ile İlişkisi

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ABSTRACT

Background: YKL-40, a novel inflammatory factor and has been shown to be involved in angiogenesis, tissue fibrosis, inflammation, and oxidative tissue injury. YKL-40 was reported to be implicated in the development of ischemic stroke. The aim of this study was to investigate of the levels of YKL-40 in serum from patients with acute ischemic stroke (aIS), and its relationship to infarct volume.

Methods: A total of 90 subjects, including 50 patients with aIS and 40 healthy controls were enrolled in study. Acute cerebral infarction was defined as area of increase signal intensity on the diffusion weighted images (DWI). To classify acute ischemic stroke according to etiologic subtype, used the Trials of Org 10172 in Acute Stroke Treatment. Serum YKL-40 levels was measured by ELISA. Volume of the cerebral infarction on DWI was measured by a separate investigator by Scion image software.

Results: The patient group consisted of 28 males and 22 females with a mean age of 60.4±7.9 years, while the control group comprised 21 males and 19 females with a mean age of 59.2±6.8 years. Serum YKL-40 levels of aIS patients were significantly higher than controls. Serum YKL-40 levels were 227.28±78.23 ng/mL in aIS patients and 74.78±13.94 ng/mL in controls (P<.001). There were significantly positively correlated with between serum YKL-40 levels and infarct volume in patients with aIS (r=0.931, P<.001).

Conclusion: Our study showed that serum YKL-40 levels increased in aIS patients, and the presence of a positive the relationship between the serum YKL-40 level and cerebral infarct volume. Further studies should clearly establish the effect of YKL-40 on the pathophysiology of acute-subacute cerebral ischemia and aim to predict the risk of stroke recurrence and post-stroke prognosis.

Keywords: YKL-40, ischemic stroke, infarct volume.

ÖZ

Amaç: YKL-40, yeni bir inflamatuvar glikoproteindir ve anjiyogenez, doku fibrozu, inflamasyon ve oksidatif doku hasarıyla ilişkilidir. YKL-40'ın iskemik inme gelişiminde rol oynadığı bildirilmiştir. Bu çalışmanın amacı, akut iskemik inmeli (aİİ) hastaların serumlarında YKL-40 düzeylerini ve bunun enfarktüs hacmi ile olan ilişkisini araştırmaktır.

Yöntemler: Çalışmaya 50 aİİ hastası ve 40 sağlıklı kontrol olmak üzere toplam 90 kişi dahil edildi. Akut serebral enfarktüs, difüzyon ağırlıklı görüntülerde (DAG) artmış sinyal yoğunluğuna sahip bir alan olarak tanımlandı. Akut iskemik inmeyi etiyolojik alt tipe göre sınıflandırmak için Trials of Org 10172 in Acute Stroke Treatment kullanıldı. Serum YKL-40 düzeyi ELISA ile ölçüldü. DAG üzerindeki serebral infarktüs hacmi, ayrı bir araştırmacı tarafından Scion Image yazılımı kullanılarak ölçüldü.

Bulgular: Hasta grubu 28 erkek ve 22 kadından (ortalama yaş 60.4±7.9 yıl), kontrol grubu ise 21 erkek ve 19 kadın (ortalama yaş 59.2±6.8 yıl) bireyden oluşmaktaydı. aİİ hastalarının serum YKL-40 düzeyleri anlamlı derecede yüksekti. Serum YKL-40 düzeyleri aİİ hastalarında 227.28±78.23 ng/mL ve kontrollerde 74.78±13.94 ng/mL idi (P<.001). aİİ hastalarında serum YKL-40 düzeyleri ile enfarkt hacmi arasında anlamlı pozitif korelasyon vardı (r=0.931, P<.001).

Sonuç: Çalışmamız, aİİ hastalarında serum YKL-40 düzeylerinin artmış olduğunu ve serum YKL-40 düzeyi ile serebral enfarktüs hacmi arasında pozitif bir ilişki olduğunu göstermiştir. Daha ileri çalışmalar, YKL-40'ın akut-subakut serebral iskemi patofizyolojisi üzerindeki etkisini açıkça ortaya koymalı ve inme nüksü riskini ve inme sonrası prognozu öngörmeyi amaçlamalıdır.

Anahtar Kelimeler: YKL-40, iskemik inme, infarkt hacmi.

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INTRODUCTION

Stroke constitutes a complex and multifactorial disorder that constitutes a leading cause of mortality globally.[1] It is a significant contributor to long-term disability. Ischemic stroke comprises approximately 80-85% of cerebrovascular diseases.[2] Recent research has unequivocally demonstrated the pivotal role of systemic and local inflammatory processes in the pathophysiology of ischemic stroke .[3,4]

YKL-40, also known as Chitinase 3-like protein 1 (CHI3L1), is a novel inflammatory glycoprotein that interacts with chitin and heparin in a non-enzymatic manner. It is encoded by the CHI3L1 gene located on chromosome 1. YKL-40 has been implicated in inflammatory processes and atherosclerosis. While the precise physiological functions of YKL-40 remain to be fully elucidated, previous research suggests potential involvement in apoptosis, cell proliferation, oxidative stress, angiogenesis, and tissue remodeling.[5] Mainly generated and secreted by neutrophils. Other cells from which it is secreted are activated macrophages (such as astrocytes) endothelial cells, tumour cells and smooth muscle cells.[6] Elevated YKL-40 levels have been documented in a diverse range of pathologies, including cardiovascular diseases, solid tumors, inflammatory bowel disease, sarcoidosis, respiratory disorders (interstitial pneumonia, asthma), and arthritis.[7-8] Findings from studies investigating these conditions have consistently demonstrated that serum YKL-40 levels can significantly influence both disease prognosis and severity.

Despite extensive research into YKL-40 as an inflammatory biomarker across various neurological conditions over the past decade, its physiological roles within the central and peripheral nervous systems remain inadequately understood. Notably, elevated YKL-40 levels have been documented in a spectrum of neurological disorders, encompassing neurodegenerative diseases, multiple sclerosis, neuromyelitis optica, migraine, encephalitis, amyotrophic lateral sclerosis, and stroke.[9-15] A limited number of observational studies have reported a significant association between elevated YKL-40 levels and ischemic cerebrovascular disease.[15] However, the relationship between serum YKL-40 levels and clinical status, infarct size, and post-infarction prognosis remains inadequately clarified. This study aimed to investigate serum YKL-40 levels and their association with infarct volume in patients with acute ischemic stroke (aIS).

MAIN POINTS

- Inflammatory response is getting more and more attention for its critical role in the pathological process of acute ischemic stroke (AIS).
- YKL-40 is a novel inflammatory biomarker and plays a potential role in the formation of atherosclerotic plaques and development of stroke.
- Serum levels of YKL-40 is useful for the neurologists in the prognosis of AIS patients in the clinical practice

MATERIAL AND METHODS

Study Design and Ethical Consideration

This prospective study was conducted at the Department of Neurology, Recep Tayyip Erdoğan University Faculty of Medicine, between September 2012 and March 2013. All patients diagnosed with acute ischemic stroke (AIS) were consecutively recruited during the study period. The study protocol was reviewed and approved by the Ethics Committee of Recep Tayyip Erdoğan University Faculty of Medicine (Date: September 7, 2012; Decision No: 2012/125). Prior to participation, written informed consent was obtained from all patients and control subjects after providing detailed information about the purpose and procedures of the study. All procedures were performed in accordance with the ethical standards of the revised 2008 Declaration of Helsinki.

Participants

A total of 90 subjects, including 50 with aIS patients (28 males and 22 females, mean age 60.4±7.9 years) and 40 healthy controls (21 males, 19 females, mean age of 59.2±6.8 years) were enrolled in study. The diagnose of aIS by a clinical neurological examination and diffusion weighted images (DWI) imaging results with in <24hours. All MRI examinations were performed on a 1.5-T MR scanner (Siemens AG, Germany, 16-channel head coil). The MRI standard stroke protocol included high-resolution DWI. Volume of the cerebral infarction on DWI was measured by a separate investigator by Scion image software. To classify acute ischemic strokes according to etiology, we used the Trials of Org 10172 in Acute Stroke Treatment (TOAST) criteria. The TOAST classification was developed to categorize the causes of acute ischemic stroke, and five major subtype described: large artery atherosclerosis, cardioembolic, small vessel occlusion, other determined aetiology and undetermined aetiology.[16]

Exclusion criteria were transient ischaemic attacks, presence of cerebral venous thrombosis, intracerebral and subarachnoid hemorrhage, renal and hepatic failure, malignancies and systemic autoimmune diseases (such as system lupus erythematosus, rheumatoid arthritis, Behcet's syndrome).

Measuremet of YKL-40

Peripheral venous blood samples were collected from aIS patients with in 48 hours of hospital admission, and healthy controls after overnight fasting. The blood samples were immediately centrifuged (3000 g for 10 minutes at 4°C), and serum was collected and stored at -80°C until analysis. The ELISA kits (Cat No: ab355786, Abcam biological reagents) were used to analysis serum levels of YKL-40 according to the manufacturer's protocol. The intra-assay and inter-assay precision coefficients of variation were 6.7% and 6.9%, respectively. The sensitivity was calculated to be 15.6 ng/ml.

Statistical Analysis

All data were analyzed with Statistical Package for the Social Sciences version 22.0. (IBM SPSS Corp.; Armonk, NY, USA)Continuous variables, when distributed normally, were expressed as mean ± standard deviation (SD), while the categorical data were analysed as percentages. Non-parametric variables were compared using Mann-Whitney U test. The baseline characteristics of the two groups were compared with Student's t test and the Chi square test. The normality of the distribution for all variables was assessed by the Kolmogorov-Smirnov test. Pearson test was used to detect correlations. Values of P<.05 were considered as statistically significant.

RESULTS

Baseline characteristic

The demographic data and clinical parameters in with all participants were summarized in Table 1. No statistically significant differences were present patients with aIS and healthy controls in the aspects of sex and age.

Vascular risk factors and stroke subtypes according to TOAST classification in patients with aIS were shown in Table 2.

Table 1. Demographic data and study parameters

Variables	aIS patients (n=50)	Controls (n=40)	P
Males, n	28	21	.756
Females, n	22	19	.918
Age (years, mean±SD)	60.4±7.9	59.2±6.8	.634
Infarct volume (cm3)	15.2±6.8	-	-
Serum YKL-40 levels (ng/ml)*	227.28±78.23	74.78±13.94	.001

aIS, acute ischemic stroke; *P<.05.

Table 2. Vascular risk factors and stroke subtypes according to TOAST classification in with acute ischemic stroke (aIS) patients

Variables	aIS patients(n=50)	Serum YKL-40 levels (ng/ml)	P
Vascular risk factors, n (%)			
Hypertension	32 (64%)		
Diabetes mellitus	21 (42%)		
Dyslipidemia	16 (32%)		
Hyperhomocysteinemia	7 (14%)		
Obesity	10 (20%)		
Active smoker	43 (86%)		
Alcohol use	8 (16%)		
Stroke subtypes			
Large artery atherosclerosis	14 (28%)	196.28 ± 28.1	.001
Cardioembolic	18 (36%)	107.32 ± 19.46	.046
Small vessel occlusion	7 (14%)	63.71 ± 13.72	.382
Other determined aetiology	7 (14%)	42.68 ± 33.51	.749
Undetermined aetiology	4 (8%)	54.44 ± 37.34	.893

Active smoker, if they were current smokers and had smoked at least one cigarette per day or one cigar a week for the past year. Alcohol use, 1-15 drinks a week. aIS: acute ischemic stroke , *P<.05.

Serum Levels of YKL-40 in all participants

Serum YKL-40 levels in patients with aIS were significantly higher than healthy controls. Serum YKL-40 levels were 227.28±78.23 ng/mL in aIS patients and 74.78±13.94 ng/mL in healthy controls (P<.001) (Figure 1). Serum YKL-40 levels were especially elevated in large artery (carotid) atherosclerosis patients.

Infarct volume was 15.2±6.8 cm^3 in patients with aIS. Serum YKL-40 levels were significantly correlated infarct volume (r=0.931, P<.001) (Figure 2).

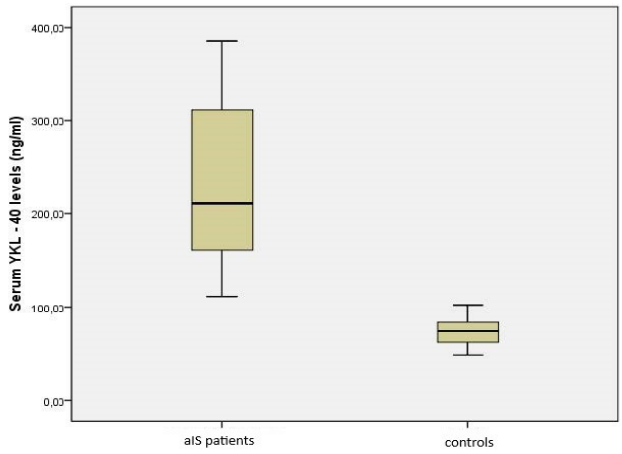

Figure 1. Serum YKL-40 levels in patients with acute ischemic stroke (aIS) and controls.

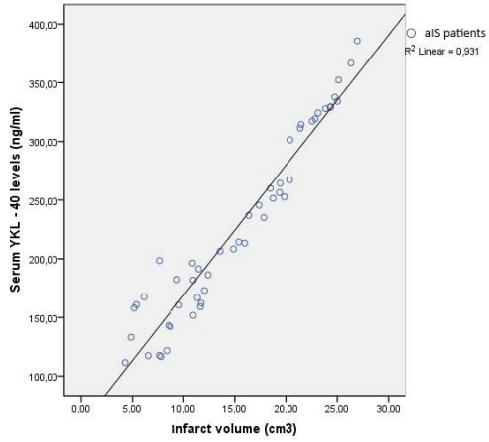

Figure 2. The corelation with between serum YKL-40 levels and infarct volume in patients with acute ischemic stroke (aIS) (P<.001).

DISCUSSION

This prospective study demonstrated statistically significant elevations in serum YKL-40 levels in patients with acute ischemic stroke (AIS), exhibiting a positive correlation with cerebral infarct volume. Furthermore, serum YKL-40 concentrations were significantly higher in patients with large artery (carotid) atherosclerosis according to the (TOAST) etiologic classification.

In recent years, neuro-inflammation plays a key role in pathophysiology both acute and chronic ischemic cerebrovascular diseases. Acute ischemic stroke (aIS) is associated with a variety of pathological changes affecting both glial and neuronal brain tissue. These changes are mirrored in the release of proteins into the cerebrospinal fluid (CSF) and to lesser extent into the blood. Experimental studies have found that cerebral ischemia promotes changes of cytoskeleton and activation of apoptosis-related genes, resulting in morphological reactions of neurons, astrocytes, oligodendrocytes, and microglia.[17] Microglia exhibit rapid responses to ischemic injury during cerebral ischemia-reperfusion, initiating an immune inflammatory cascade. In the acute phase of cerebral ischemia, the M1 phenotype of microglia is believed to secrete pro-inflammatory cytokines (TNF-α, IL-6, and IL-1β) and chemokines, attracting peripheral immune cells to the

brain and exacerbating ischemic damage through the amplification of post-stroke neuroinflammation. Conversely, the M2 phenotype of microglia produces anti-inflammatory cytokines (such as IL-4 and IL-13), mitigating ischemic brain damage and promoting the restoration of cerebral tissue [17]. During the acute phase of ischemic stroke, microglia release pro-inflammatory cytokines that, in combination with peripheral pro-inflammatory cytokines, activate macrophages. Activated macrophages then release specific biomarkers of neuroinflammation, including YKL-40, which contribute to the pathophysiology and clinical severity of stroke.[18]

Serum YKL-40 levels were reported in a few studies, in patients with cerebrovascular disease. Both Hao et al.[13] and Shi et al.[14] reported a significant increase in serum YKL-40 levels from the initial assessment in their respective clinical studies on aIS patients. These findings indicate that elevated YKL-40 may be a prognostic marker for unfavorable outcomes. Kjaergaard and colleagues, in their investigation of the Danish general population, suggested that increased plasma YKL-40 concentrations could be a predictive factor for a higher risk of developing ischemic stroke.[19] Wang et al. investigated the association between plasma YKL-40 levels and two-year stroke-specific mortality in acute ischemic stroke patients, stratified by drinking status and alcohol consumption. The study found that elevated YKL-40 levels were associated with an increased risk of stroke-specific death within two years in patients who consumed alcohol.[20] Jia et al. analyzed data from 6931 acute ischemic stroke patients (mean age 62.3±11.3 years) and 15 biomarkers to investigate the association between multiple biomarkers and modified Rankin Scale score change. They found that WBC, hs-CRP, IL-6, IL-1, and YKL-40 were significantly associated with worse outcomes in acute ischemic stroke patients, and all inflammatory biomarkers except YKL-40 were independent predictors of worse outcomes at 3 months.[21] Our knowledge, there is a study reported in the literature on the relationship between serum YKL-40 levels and cerebral infarction volume.[22] Park HY reported that YKL-40 and C-reactive protein (CRP) levels in aIS patients increased rapidly from baseline, blunting with infarct volume, and were associated with poor functional impairment.

YKL-40 is recently regarded as a pro-inflammatory cytokine involved in the pathological process of atherosclerosis and lipid metabolism. Focal inflammation and atherosclerosis play a pivotal role in the pathophysiology of large artery atherosclerosis.[23] Cerebral infarcts exceeding 15-20 mm in size typically arise from large vessel disease, a consequence of atherosclerosis affecting the cervical carotid or proximal intracranial arteries. This constitutes a substantial cause of acute stroke, encompassing 30% to 40% of cases.[24] The circulating profile of YKL-40 in patients with different TOAST subtypes has been less extensively studied. Our study revealed significantly elevated serum YKL-40 levels specifically in patients with carotid atherosclerosis among the etiological causes of stroke. Activated macrophages within early atherosclerotic plaques and smooth muscle cells within the endothelium have been demonstrated to express very high levels of YKL-40.[25] YKL-40 exerts its effect in atherosclerosis by promoting chemotaxis, cell migration and differentiation and tissue remodeling in response to endothelial damage. There are several studies reported on the relationship between serum YKL-40 levels and atherosclerotic carotid lesion. In the study conducted by Michelsen et al., YKL-40 may be a potential marker of plaque instability, macrophage activation and matrix disruption in patients with symptomatic carotid atherosclerosis.[25] In their study, Xu et al. found that genetically determined high plasma YKL-40 levels were causal associated with increased risks of large artery stroke.[26] Conversely, Wu et al. demonstrated that elevated serum YKL-40 levels in patients with carotid atherosclerosis complicated by Helicobacter pylori infection were associated with increased plaque instability and more severe clinical manifestations [27] However, the precise role of YKL-40 in mediating plaque instability. in patients with carotid atherosclerosis remains elusive.

Several limitations of this study warrant consideration. Firstly, a comparative analysis of serum YKL-40 levels with other established neuroinflammatory markers, such as IL-6 and CRP, would have enriched the findings. Secondly, the temporal relationship between stroke severity, as assessed by the National Institutes of Health Stroke Scale (NIHSS), and serum YKL-40 levels could not be explored within this study. Thirdly, given that serum YKL-40 levels were measured solely at baseline in aIS patients, without subsequent follow-up measurements, any potential association with long-term prognosis remains undetermined. Furthermore, the relatively small sample size of this cohort necessitates cautious interpretation of the results. Therefore, it is premature to consider serum YKL-40 as an independent risk factor for aIS.

CONCLUSION

In conclusion, this study demonstrated a significant association between elevated serum YKL-40 levels and cerebral infarct volume in aIS patients. Future research endeavors should comprehensively investigate the impact of YKL-40 on the pathophysiology of acute-subacute cerebral ischemia, with a specific focus on elucidating its potential role in predicting stroke recurrence and post-stroke prognosis, particularly in patients with symptomatic or asymptomatic carotid atherosclerosis.

Ethics Committee Approval: The study was approved by the Recep Tayyip Erdoğan University Faculty of Medicine (Date: September 7, 2012; Decision No: 2012/125)

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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REFERENCES

1. Feske SK. Ischemic Stroke. Am J Med. 2021;134(12):1457-1464. [CrossRef]
2. Ajoolabady A, Wang S, Kroemer G, et al. Targeting autophagy in ischemic stroke: From molecular mechanisms to clinical therapeutics. *Pharmacol Ther.* 2021;225: 107848. [CrossRef]
3. Simats A, Liesz A. Systemic inflammation after stroke: Implications for post-stroke comorbidities. *EMBO Mol Med.* 2022;14(9):e16269. [CrossRef]
4. Zhu H, Hu S, Li Y, et al. Interleukins and Ischemic Stroke. *Front Immunol.* 2022;13:828447. [CrossRef]
5. Chen XL, Li Q, Huang WS, et al. Serum YKL-40, a prognostic marker in patients with large-artery atherosclerotic stroke. *Acta Neurol Scand.* 2017;136(2):97-102. [CrossRef]

6. Deng Y, Li G, Chang D, et al. YKL-40 as a novel biomarker in cardio-metabolic disorders and inflammatory diseases. *Clin Chim Acta.* 2020;511:40-46. [CrossRef]
7. Song M, Zhang G, Shi H, et al. Serum YKL-40 in coronary heart disease: linkage with inflammatory cytokines, artery stenosis, and optimal cut-off value for estimating major adverse cardiovascular events. *Front Cardiovasc Med.* 2023;10:1242339. [CrossRef]
8. Rusak A, Jabłońska K, Dzięgiel P. The role of YKL-40 in a cancerous process. Postepy Hig Med Dosw (Online). 2016;70(0):1286-1299.
9. Shi G, Ke D, Gong P, et al. Serum YKL-40 levels and white matter hyperintensities in patients with acute ischemic stroke. *J Inflamm Res.* 2023;16:311-319. [CrossRef]
10. Dündar A, Cafer V, Aslanhan H, et al. Increased visinin-like protein-1, YKL-40, lipocalin-2, and IL-23 levels in patients with migraine. *Neurol Res.* 2023;45(2):97-102.[CrossRef]
11. Qi Y, Chou LS, Zhang LJ, et al. Increased cerebrospinal fluid YKL-40 levels are associated with disease severity of neuromyelitis optica spectrum disorders. *Mult Scler Relat Disord.* 2020;45:102395. [CrossRef]
12. Li J, Wang Y, Xia R, et al. Elevated cerebrospinal fluid YKL-40 levels in patients with anti-gamma-aminobutyric-acid-B receptor encephalitis. *J Neuroimmunol.* 2023;381:578119. [CrossRef]
13. Hao G, Sun J, Zhong T, et al. Association of serum YKL-40 change with prognosis in acute ischemic stroke patients complicated with diabetes mellitus. *Biomark Med.* 2023;17(5):253-263. [CrossRef]
14. S hi G, Li M, E Y, et al. Prognostic performance of serum YKL-40 for one-year clinical outcomes in acute ischemic stroke. *Aging (Albany NY).* 2023;15(4):1199-1209. [CrossRef]
15. Xu X, Ma H, Xu J, et al. Elevation in circulating YKL-40 concentration in patients with cerebrovascular disease. *Bosn J Basic Med Sci.* 2014;14(3):120-124. [CrossRef]
16. Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke.* 1993;24(1):35-41. [CrossRef]
17. Im JH, Yeo IJ, Park PH, et al. Deletion of Chitinase-3-like 1 accelerates stroke development through enhancement of Neuroinflammation by STAT6-dependent M2 microglial inactivation in Chitinase-3-like 1 knockout mice. *Exp Neurol.* 2020;323:113082. [CrossRef]
18. Ormstad H, Aass HC, Lund-Sørensen N, et al. Serum levels of cytokines and C-reactive protein in acute ischemic stroke patients, and their relationship to stroke lateralization, type, and infarct volume. *J Neurol.* 2010;258(4):677-685. [CrossRef]
19. Kjaerqaard AD, Bojesen SE, Johonsen JS, et al. Elevated plasma YKL-40 levels and ischemic stroke in the general population. *Ann Neurol.* 2010;68(5):672-680. [CrossRef]
20. Wang Z, Zhang K, Zhong C, et al. Alcohol drinking modified the effect of plasma YKL-40 levels on stroke-specific mortality of acute ischemic stroke. *Neuroscience.* 2024;552:152-158. [CrossRef]
21. Jia WL, Jiang YY, Jiang Y, et al. Associations between admission levels of multiple biomarkers and subsequent worse outcomes in acute ischemic stroke patients. *J Cereb Blood Flow Metab.* 2024;44(5):742-756. [CrossRef]
22. Park HY, Jun CD, Jeon SJ, et al. Serum YKL-40 levels correlate with infarct volume, stroke severity, and functional outcome in acute ischemic stroke. *PLoS One.* 2012;7(12):e51722. [CrossRef]
23. Boot RG, van Achterberg TA, van Aken BE, et al. Strong induction of members of the chitinase family of proteins in atherosclerosis: chitotriosidase and human cartilage gp-39 expressed in lesion macrophages. *Arterioscler Thromb Vasc Biol.* 1999;19(3):687-694. [CrossRef]
24. Hauck EF, Natarajan SK, Ohta H, et al. Emergent endovascular recanalization for cervical internal carotid artery occlusion in patients presenting with acute stroke. *Neurosurgery.* 2011;69(4):899-907. [CrossRef]
25. Michelsen AE, Rathcke CN, Skjelland M, et al. Increased YKL-40 expression in patients with carotid atherosclerosis. *Atherosclerosis.* 2010;211(2):589-595. [CrossRef]
26. Xu Q, Sun L, Wang Y, et al. Causal effects of YKL-40 on ischemic stroke and its subtypes: A 2-sample mendelian randomization study. *J Am Heart Assoc.* 2023;12(17):e029000. [CrossRef]
27. Wu Y, Tao Z, Song C, et al. Overexpression of YKL-40 predicts plaque instability in carotid atherosclerosis with CagA-positive Helicobacter pylori infection. *PLoS One.* 2013;8(4):e59996. [CrossRef]