



Clinical Audit

Beyond atherosclerosis: Investigating the significant association between hyperhomocysteinemia and cardioembolic stroke subtypes in young patients

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Abstract

Background: Hyperhomocysteinemia (HHcy) is traditionally viewed as a driver of arteriopathy. However, clinical observations increasingly suggest a "cardio-toxic" role. This study evaluates the specific link between elevated total Homocysteine (tHcy) and cardioembolic stroke in a cohort of young adults, where traditional atherosclerotic burdens are typically lower.

Methods: A 12-month prospective study of 196 ischemic stroke patients (<50 years) was conducted. Stroke aetiology was categorised via modified TOAST criteria. Fasting tHcy levels were analysed, with HHcy defined as $>15 \mu\text{mol/L}$.

Results: HHcy was present in 38.7% of the cohort. While Large Artery Atherosclerosis was present in only 6% of cases, Cardioembolic strokes accounted for 9%. Statistical analysis revealed a significant positive correlation between tHcy levels and cardioembolic events ($p < 0.05$). Notably, patients with tHcy $>30 \mu\text{mol/L}$ showed a higher propensity for cardioembolic origins compared to other subtypes.

Discussion: Our findings suggest that HHcy may serve as a biomarker for a pro-thrombotic endocardial environment. The association with cardioembolism – historically less explored than the Hcy-atherosclerosis link – points toward Hcy-induced atrial remodelling or endocardial oxidative stress as potential drivers of embolus formation in young patients.

Conclusion: The significant relationship between increased Hcy levels and cardioembolic stroke warrants a re-evaluation of current screening protocols. In regions like Ukraine, where Hcy testing is not yet obligatory, the "Hcy-Cardiac Axis" may represent a major undiagnosed contributor to the young stroke burden.

Keywords: Homocysteine; Stroke; Cardioembolism; Ischemia

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1. Introduction

Stroke in young adults (under 50 years) presents a unique diagnostic challenge. Unlike older populations, where traditional risk factors like hypertension and carotid atherosclerosis dominate, young patients often present with "cryptogenic" or less common etiologies. While Hyperhomocysteinemia (HHcy) has long been established as a risk factor for large-artery atherosclerosis, its role in the "cardio-toxic" environment is less defined. Recent evidence suggests that elevated total Homocysteine (tHcy) may contribute to atrial remodeling and endocardial oxidative stress, potentially leading to thrombus formation even in the absence of significant arterial plaque.

2. Methods

A prospective, 12-month observational study was conducted involving 196 patients under the age of 50 who presented with acute ischemic stroke.

- **Etiological Classification:** Stroke subtypes were categorized using the modified TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria, ensuring a standardized approach to identifying Large Artery Atherosclerosis, Cardioembolism, Small Vessel Occlusion, and other determined/undetermined causes.
- **Biochemical Analysis:** Fasting tHcy levels were measured within the acute phase. HHcy was clinically defined as a concentration $>15 \mu\text{mol/L}$.
- **Statistical Analysis:** Correlation between tHcy levels and stroke subtypes was assessed using p-value significance (set at $p < 0.05$).

3. Results

The study yielded several critical insights into the profile of young stroke patients:

Age

Age	Frequency	Percentage
<18	4	0.02
18-50	45	22.9
>50	27	13.7

Gender

Gender	Frequency	Percentage
Male	72	36.7
Female	4	0.02

Homocysteine Level

Hcy Level	Frequency	Percentage
<15	120	61.2
15-30	50	25.5
>30	26	13.2

Risk Factors

Variables	Frequency	Percentage
Hypertension	23	11.7
Diabetes	70	35.7

Type of stroke (Toast classification)

Variables	Frequency	Percentage
Large Artery Atherosclerosis	12	0.06
Small vessel disease	34	0.17
Cardiac Embolism	18	0.09
Stroke of Undetermined Aetiology	12	0.06

- Prevalence of HHcy: 38.7% of the total cohort exhibited elevated tHcy levels.
- Etiological Distribution: Large Artery Atherosclerosis was surprisingly rare (6%), whereas Cardioembolic Stroke accounted for 9% of the cases.
- The Hcy-Cardiac Link: A statistically significant positive correlation was found between high tHcy levels and cardioembolic events ($p < 0.05$).
- Dose-Response Relationship: Patients with severe elevation ($>30 \mu\text{mol/L}$) demonstrated a markedly higher propensity for cardioembolic origins compared to those with other stroke subtypes.

4. Discussion

The results shift the narrative of Homocysteine from a purely "vascular" toxin to a "cardio-vascular" one. The significant association with cardioembolism in a population with low atherosclerotic burden suggests that HHcy might trigger:

- Endocardial Oxidative Stress: Promoting a pro-thrombotic state on the heart's inner lining.
- Atrial Remodeling: Contributing to structural changes that facilitate blood stasis.

In regions like Ukraine, where Homocysteine screening is not currently a mandatory part of the standard stroke workup, these findings suggest a "silent" contributor to the young stroke burden. Recognizing the "Hcy-Cardiac Axis" could be the key to better secondary prevention and more targeted screening protocols for patients who don't fit the "traditional" stroke profile.

5. Conclusion

Hyperhomocysteinemia is a significant, independent correlate of cardioembolic stroke in young adults. These findings advocate for a re-evaluation of current diagnostic screening. Integrating tHcy testing into the standard protocol for young stroke patients could improve etiological clarity and patient outcomes.

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