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The Relationship Between Serum Polyunsaturated Fatty Acid Ratio and Functional Status in Patients with Stroke Induced Sarcopenia

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ABSTRACT

Though an optimal serum polyunsaturated fatty acid ratio has yet to be defined, the identification of serum polyunsaturated fatty acid ratio as a clinical biomarker may have important implications for stroke recovery. The purpose of this study was to quantify habitual serum polyunsaturated fatty acid ratio to determine their relationship with physical function in a cohort of chronic adult stroke survivors. Twenty chronic stroke survivors (age: 61±9 years; BMI: 29±8 kg/m2; mean ± SD) were assessed for two-minute walk distance (2MWD). Plasma lipid and glucose profiles were measured, and Hs-IR calculated. Serum polyunsaturated fatty acid ratio profiles were assessed by mass spectrometry. Results: Average serum omega-6 concentrations were 164+41 µg/d and serum omega-3 (EPA+DHA) concentrations were 163±26 µg/d, with an omega-6 (AA) to omega-3 (EPA+DHA) serum concentration ratio of 1.6±0.3. These data suggest that the concentration ratio of serum polyunsaturated fatty acid may be important indices of physical dysfunction in patients with stroke induced sarcopenia.

KEY WORDS: STROKE, SERUM POLYUNSATURATED FATTY ACID RATIO, PHYSICAL FUNCTION, SARCOPENIA.

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INTRODUCTION

Stroke is one of the leading causes of disability worldwide. Post-stroke declines in functional status is common and contribute to stroke being a leading cause of long-term disability (Feigin, V.L. 2019) Although sedentary activity is often implicated in these declines, less attention has been given to the role of dietary factors. A chronic a debilitating disease like stroke affects all the systems of human body. The long terms effects on the musculoskeletal system includes structural, metabolic and function loss, which is directly associated with the progression of disease and disability. The structural changes found in the effected muscles may be related to decreased synaptic communication leading to lesser motor unit (Scherbakov et al, 2013). In the long run these strokes induced changes in the muscle structure and its metabolic activities, leads to sarcopenia (Cruz-Jentoft et al, 2010), essentially a disease of old age, associated with poor quality of life and increased mortality rate in elderly population (Lathuilière et al, 2019).

In recent years, stroke related degenerative muscle changes have been found to be a leading cause of sarcopenia in this population. Studies to date implicate higher serum polyunsaturated fatty acid ratios in association with reduced physical functioning and elevated pro-inflammatory states in older adults and neurological deterioration following acute stroke. Despite being at elevated risk status of serum polyunsaturated fatty acid ratio of chronic stroke survivors is not well documented. Though an optimal ratio has yet to be defined, the identification of serum polyunsaturated fatty acid ratio as a clinical biomarker may have important implications for stroke recovery (Noguchi H et al, 2009). Therefore, the purpose of this study was to examine the relationship of serum polyunsaturated fatty acid ratio with physical function in patients with Stroke induced sarcopenia.

MATERIALS AND METHODS

Chronic stroke patients having a score of more than 21 on lower limb Fugl-Meyer Scale (Kwong et al, 2019) and capable of independently walking at least 200 meters without any aid were included for this study. Subjects having additional motor deficits including any vestibular or orthopedic disorders or bilateral cerebral lesions or aged above 70 years or having high risk cardiovascular disorder were excluded from the study. Based on the inclusion criteria twenty (20) subjects, who have been diagnosed with ischemic stroke of more than six-month duration, aged between 50–70 years were recruited from the Riyadh region. Informed consent was obtained from all the subjects before participating in this study. Participants were screened and their age, gender, height, weight and duration of onset of stroke were recorded. Severity of neurological impairment was determined by Fugl-Meyer scale (Sulliven et al, 2011).

Rivermead Mobility Index (RMI) (Collen et al,1991), which is a valid tool to asses functional mobility in the Stroke population and two-minutes' walk test a sub-maximal exercise test used to assess aerobic capacity and endurance, were used to assess the physical functioning (Hiengkaew et al,2012). Plasma lipid, and high sensitivity-C-reactive protein (hs-CRP) concentrations were determined by colorimetric method. Lipids were extracted from serum samples using a modified Bligh & Dyer lipid extraction protocol (Bligh EG, Dyer WJ, 2015). Targeted lipidomic assays were conducted on a QTRAP 5500 LC-MS/MS system to identify selective omega-3 and omega-6 lipid species by precursor ion scanning for the m/z values corresponding to the respective molecular weights. Statistical Analyses: All the data was tabulated, and descriptive statics was prepared using IBM SPSS (Version 22, Chicago, IL) software was used. Pearson correlation coefficients were used to determine relationships between serum polyunsaturated fatty acid ratio and physical functioning.

RESULTS AND DISCUSSION

A total of 20 subjects, including 11male and 9 females with a mean age of 61.4+4.1 and with mean onset of stroke of 9.7+5.3 months, have participated in the study. Out of twenty, twelve participants were affected on left side and remaining eight suffered from right sided stroke Participants undergoing treatment for hypertension and dyslipidaemia occurred in 78% and 84%, respectively. Despite 38% being treated for diabetes, all participants had elevated fasting plasma glucose (≥100 mg/dL) and elevated hs-CRP (>3 mg/L) was observed in 18% of the participants. Serum Fatty Acid Profiles: Average serum omega-6 concentrations were 164+41 µg/d and serum omega-3 (EPA+DHA) concentrations were 163±26 µg/d, with an omega-6 (AA) to

omega-3 (EPA+DHA) serum concentration ratio of 1.6±0.3. Higher serum polyunsaturated fatty acid ratio were associated with lower two-minute walk test, higher HOMA-IR and increased serum hs-CRP concentration (P's<0.05). Additionally, a higher serum polyunsaturated fatty acid ratio was associated with higher fasting glucose and insulin concentrations, while higher serum polyunsaturated fatty acid ratio were associated with lower aerobic capacity and endurance (P's<0.05).

DISCUSSION

Many studies have documented the decline in quality of life associated with stroke related derangement in muscle metabolism and functions. Despite it, prevention of muscle loss is not considered as essential in most of the clinical and rehabilitation guidelines for managing stroke (Quinn et al, 2009). In this regards our study will pave way by establishing a relationship between the long chain poly unsaturated fatty acid ratio and it's the physical and metabolic functions in this population (Garbagnati et al 2009). Previous studies have suggested beneficial effects of the nutritional supplement provided immediately after stroke, on body composition (Ha et al, 2010). In contrast to this, our study shows that, greater serum polyunsaturated fatty acid ratio may adversely influence physical function and a decline in the distance walking ability. This may be due the fact that the study by Ha et al used caloric rich fatty acid supplements which may have a utilized the protective effects of essential amino acids in stabilizing the muscle metabolism. This study supports data from non-stroke populations suggesting that higher systemic concentrations of omega-3, compared to omega-6s, protect against accelerated age and disease-associated decline of physical performance (Reinders I. et al, 2015). Despite studies identifying an association between acute post-stroke plasma fatty acid profiles and stroke recurrence, (Galan et al, 2010) there is further need to design studies to establish the beneficial effects of these fatty acids in improving muscle health and function.

Although our data are limited in this regard, a higher omega-3 membrane concentration may explain the associations between higher serum polyunsaturated fatty acid ratio profiles and physical dysfunction in stroke by altering cell membrane fluidity, enhancing nitric oxide-mediated vasodilation, and attenuating platelet aggregation (Zanetti M. et al, 2015) Further, there is some suggestion that the neuroprotective mechanism of action of omega-3s may occur through their effects on inflammation and oxidative stress; omega-6s produce eicosanoid products, which are more potent mediators of thrombosis and inflammation than similar products derived from omega-3s (Gutierrez et al, 2013). Although the exact mechanisms are unclear, these findings suggest that serum omega-3s might be important indicators to help attenuate and monitor the progression of stroke disability (Reinders et al, 2015).

Table 1. Participant characteristics and physical and metabolic functioning data

N=20	Mean SD
Gender (male/female) n	12/8
Age, years	61.4+4.1
Stroke Onset, months	9.7+5.3
BMI (kg/m2)	29±5.3
Fugl-Meyer scores (Lower extremity)	28+5.3
Rivermead Mobility Index score	4.3+3.8
Six Minute Walk Distance (m)	112+28
Total Cholesterol (mg/dl)	139+47
Triglycerides (mg/dl)	67+23
LDL Cholesterol (mg/dl)	88+35
HDL Cholesterol (mg/dl)	51+22
hs-CRP (mg/L)	4.9+3.6
Eicosapentaenoic Acid (µg/dL)	61+18
Docosahexaenoic Acid (µg/dL)	102+33
Arachidonic Acid (µg/dL)	164+41

Table 2. Relationships of Omega-6/Omega-3 Dietary Serum Concentrations with Physical Function and metabolic risk factors

Pearson Coefficients	RMI	2MWD (m)	Glucose (mg/dL)	Insulin (µU/mL)	hs-CRP (mg/L)
Serum Polyunsaturated Fatty Acid Ratio	-0.32*	-0.35*	0.21	0.31	0.42**

*P<0.05; **P<0.01. Key: RMI: Rivermead Mobility Index, 2MWD: Two-Minute Walk Test

Limitation: The results from this cross-sectional study were obtained from a small group of subjects; therefore, the results must be interpreted with caution. In addition, this study did not examine the effect of dietary poly unsaturated fatty acids and thus failed to determine a potential mechanism for the effectiveness of physical and metabolic function.

CONCLUSIONS

These data suggest that the concentration ratio of serum polyunsaturated fatty acid may be important indices of physical dysfunction in patients with stroke induced sarcopenia.

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