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## Section 1. Preventive medicine

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### IMPACT OF DAILY STOCK MARKET VOLATILITY ON HEART ATTACK IN THE UNITED STATES

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#### Abstract

**Background:** Based on previous research revealing an association between stock volatility and cardiovascular mortality in the Asian population, we hypothesize that a similar correlation exists between stock market volatility and the increased risk of heart attack in the United States (US).

**Objective:** We aimed to investigate the association between daily stock volatility and population-level heart attack in the US (2005–2022).

**Methods:** Time-series analysis and generalized linear regression were used to examine the association between the daily volatility of Dow Jones Industrial Average (DJI) and the heart attack prevalence in the community population and the prevalence of coronary artery disease (CAD, including ischemic heart disease and myocardial infarction) in the hospital emergency department (ED) patients. The community-based data (2005–2022) were from the Behavioral Risk Factor Surveillance System (BRFSS) and the ED-based data (2013–2021) were from the National Hospital Ambulatory Medical Care Survey (NHAMCS).

**Results:** There were an average of 34 days (range: 0–126 days) having a large DJI volatility amplitude ( $\geq 2\%$ ) annually from 2005 to 2022. Given an increase of 50 days with a large DJI volatility, the prevalence of CAD in ED patients increased by 11.6% in the current year, and the point prevalence of heart attack in the community population decreased by 4.4% in the next year.

**Conclusions:** The large stock volatility could increase the risk of heart attack in the US population, and bring more CAD patients in ED visits. Consequently, in the community, the surviving patients with heart attack become less shortly afterwards.

**Keywords:** stock market volatility, heart attack, time-series analysis, generalized linear regression model

#### Background

Heart disease remains to be the leading cause of death in the United States, even

though the overall number of people at risk and dying from heart conditions have decreased in the past century (Benjamin et al.,

2019; Martin et al., 2024). Furthermore, it is also a global concern as heart disease has contributed to over half of the global mortality (Yusuf et al., 2001). Among the many causes for heart disease, research has revealed that psychosocial stress indeed plays a role in causing the development of heart diseases. Psychosocial factors – including depression, anxiety, and low social status – and emotional stress are seen to have an association with an increased risk in obtaining cardiovascular disease and a worsened prognosis (Ladwig et al., 2014). Therefore, it is critical to identify those human behaviors that increase the psychosocial stress in daily life, which would be helpful for the development of preventive strategies for heart disease.

Previous studies have indicated that many factors can increase the psychosocial stress in our daily life, such as work stress and natural disasters (Kario, 1998). Evidence also shows that exposure to stock in a turbulent stock market significantly increases the level of anxiety disorder (Qin et al., 2019). Furthermore, a recent study in China suggests that a ten percentage point decrease in daily market returns has an association with an approximately 35 million increase in renminbi (RMB), the Chinese currency, in national medical expenses related to emergency room services (Agarwal et al., 2024). Among the emergency room visits by patients, cardiovascular diseases (e.g., heart attack) and mental disorders are common causes for those visits. In addition, a few studies in Asia have also demonstrated that stock market volatility can lead to an increase of cardiovascular mortality (Agarwal et al., 2024; Lian, 2020; Lian et al., 2020; Ma et al., 2010; Qin et al., 2019). Thus, a causal chain can be presumed that a turbulent stock market causes stress and anxiety, which increases the onset of cardiovascular diseases and even the death rate.

However, limited information currently exists about this sort of association between stock market volatility and heart disease in the United States (US). The stock market in the US and the characteristics of the American population differ greatly from those in Asia. Therefore, it is unclear if the association observed in Asia also exists in the US. Thus, our study aims to investigate the asso-

ciation between daily stock market volatility and population-level heart attack in the US.

## Methods

### *Study design*

An observational study was implemented to examine the association between the daily volatility of the Dow Jones Industrial Average (DJI) stock and heart disease prevalence in the US utilizing the national databases. It is also considered as an ecological study as this research was to understand the relationship between exposure and outcome at a population level (rather than an individual level).

The exposure, the daily DJI volatility, was defined as the ratio of the daily range of DJI price to the daily close price. Two outcomes were evaluated in this study including: 1) the prevalence of coronary artery disease (CAD) in the hospital emergency department (ED) patients in the US, and 2) the prevalence of heart attack in the US community population.

### *Data source*

The data of heart attack in the community (between 2005 and 2022) were extracted from the Behavioral Risk Factor Surveillance System (BRFSS). The BRFSS is the nation's premier system of health-related telephone surveys that collect state data about U.S. residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. The BRFSS completes more than 400,000 adult interviews each year, making it the largest continuously conducted health survey system in the world (*About BRFSS*, n.d.).

For convenience, CAD is used to represent these heart diseases: coronary artery disease, ischemic heart disease, and myocardial infarction in this study. The hospital ED data for patients with CAD extracted from the National Hospital Ambulatory Medical Care Survey (NHAMCS) were only available between 2013 and 2021. The NHAMCS collected and released high quality, objective, reliable information about how hospital-based ambulatory medical care services were provided and used in the United States. To collect NHAMCS data, information was manually taken from medical records (*National Hospital Ambulatory Medical Care Survey | NHAMCS*, 2024).

The daily stock market data of DJI between 2005 and 2022 were pulled from Ya-

hoo Finance (<https://finance.yahoo.com/quote/%5EDJI/history/>).

### **Statistical methods**

A time-series analysis was employed to explore the correlation pattern between the number of days per year having large daily DJI volatility () and the prevalence of heart attack in the US community population. The prevalence of heart attack was a point prevalence of heart attack at the time when the annual BRFSS survey was conducted. Similarly, this method was also used to explore the correlation pattern between the number of days per year having large daily DJI volatility and the prevalence of CAD in the US hospital ED patients. The prevalence of CAD was a period (annual) prevalence of CAD based upon the data collected in the NHAMCS.

In the time-series analysis, a cross correlation function (CCF) was used to identify the lags of *exposure* (the number of days per year having large daily DJI volatility) that might be useful predictors of *outcome* (e.g., the prevalence of heart attack). If a bar on CCF plots extends beyond the significance bounds, it indicates a significant correlation at that lag. When the lag is negative, it is said that the *exposure* in the past (e.g., last year) may have a correlation with the current *outcome*.

A generalized linear regression (Gaussian distribution with a log link) was used to further examine the correlation patterns found by the time-series analyses. The model estimate and p-value were reported. All analyses of this study were completed using R statistical software (version 4.3.3).

## **Results**

### **Descriptive analysis**

The year of 2008 had the most days (126 days) having large daily DJI volatility (), followed by the year of 2009 (94 days). The years of 2010, 2011, 2018, 2020, and 2022 had a range of 25 to 75 days with large daily DJI volatility. Less than 25 days having large daily DJI volatility appeared in the rest of years between 2005 and 2022.

The prevalence of CAD in the hospital ED patients was in the range of 5.6% to 6.8%, and the prevalence of heart attack in the community population was in the range of 4.0% to 4.6%. Both prevalence varied over time during the study period.

### **Time-series analysis**

As shown in Figure 1, a bar extends beyond the upper significance bound at the lag of 0. It indicates that the prevalence of CAD in the hospital ED patients was positively correlated with the number of days having large DJI volatility in the same year. In other words, the higher the number of days having large DJI volatility in a year was, the higher the prevalence of CAD in the hospital ED patients in the same year would be.

In contrast, a bar extends beyond the lower significance bound at the lag of -1 (Figure 2). It indicates that the prevalence of heart attack in the community population was negatively correlated with the number of days having large DJI volatility in the previous year. That is to say, the higher the number of days having large DJI volatility in the current year was, the lower the prevalence of heart attack in the community population in the next year would be.

### **Regression model**

The generalized linear regression model further confirmed the positive correlation between the CAD prevalence in the hospital ED patients and the number of days having large DJI volatility in the same year (Figure 3). The CAD prevalence in hospital ED patients went up by 11.6% given an increase of 50 days having a large DJI volatility in the same year.

The regression model also demonstrated the negative correlation between the prevalence of heart attack in the community population and the number of days having large DJI volatility in the previous year (Figure 4). The heart attack prevalence dropped by 3% given an increase of 50 days having a large DJI volatility in the previous year. That is to say, the heart attack prevalence in the community population may drop by 3% in the next year if there is an increase of 50 days having a large DJI volatility in the current year.

## **Discussion**

Our study revealed that there is a positive correlation between the number of CAD patients and days with a high number of DJI stock volatility in the same year while there is a negative correlation between the number of community members with a heart attack history and the number of days with a high number of DJI stock volatility in the



past year. The positive correlation shows that more patients with CAD went to the emergency departments of hospitals in the year where there were more days having a large DJI volatility in the US. This result, which is that the CAD prevalence in ED patients increased by 11.6% with an increase of 50 days of having a large DJI volatility, is interpreted as this fact that these patients who are admitted to the ED are likely to have a heart attack history and also have a high risk of death due to being admitted again for heart problems, and this all occurs in the same year that the number of days with a high stock market volatility increased. Therefore, the high likelihood of death for these patients results in a decreased amount of people in the community who have a heart attack history, explaining the negative correlation seen with the prevalence of heart attack in the American community and the number of days with a high DJI stock volatility in the previous year.

Our findings in the American population are consistent with what the previous studies reported in the Asian population. Lian et al. (Lian, 2020) conducted a meta-analysis and evaluated the short-term effect of stock volatility and cardiovascular mortality in the Asian population, which revealed that every 100-point increase (the moving average for the past 120 hours) in the stock market brought about 4.4% (95%CI, 1.1% to 7.7%) increases in cardiovascular mortality (Lian et al., 2020). This finding that stock volatility may adversely affect cardiovascular health was mainly based upon the studies conducted in the Asian cities of Shanghai, Singapore, Guangzhou and Taishan (Ma et al., 2010). The results in those Asian studies can help us to explain why a large DJI volatility causes more deaths than usual among patients with heart conditions in the US and lead to a lower prevalence of heart attack in the American community population in the next year.

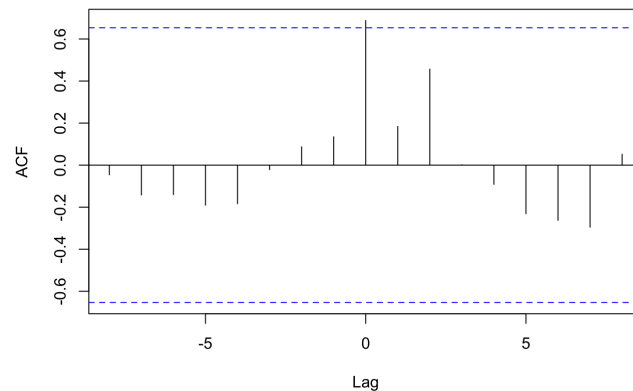
As we all know, stock market volatility is one of stressful events. Previous studies have demonstrated that stressful environmental occurrences can cause an increased risk of heart attack, coronary artery disease, and other heart diseases. For instance, chronic work stress is revealed to have an association with CAD with a particularly strong association with patients over the age of 50. This is

partly due to the effect of chronic work stress on health behaviors and metabolic syndrome (Vrijkotte et al., 2000). Characteristics of high work stress are also associated with increased risk of heart disease (Chandola et al., 2008). Musey et al. found that this type of psychological stress is commonly found in patients who are undergoing an evaluation for acute cardiovascular events (Musey Jr et al., 2019). A similar result is found by Edmondson et al. where an increase of recurrent cardiac events and mortality has been seen in patients having clinically significant posttraumatic stress disorder symptoms that are induced by acute coronary syndromes (Edmondson et al., 2012). Similarly, environmental stress such as earthquakes can lead to cardiovascular diseases that may even persist in the following weeks of the event (Kario, 1998). Thus, it is understandable that a large daily volatility in the stock market can cause an unexpected stress that increases the risk of CAD and heart attack.

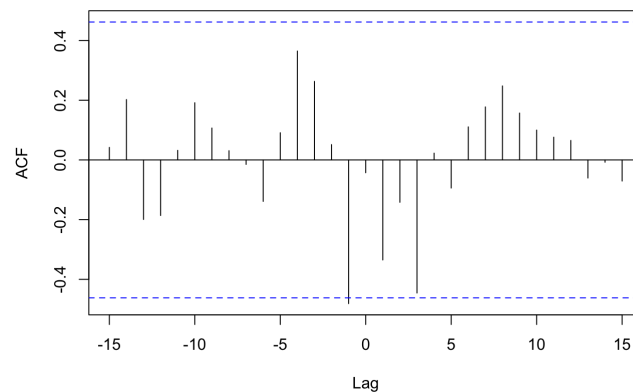
In the US, sixty-two percent of adults invested in the stock market in 2024 (*Share of Americans Investing in Stocks 2024*, 2024). Although it is not possible to stop people from investing in the stock market completely, educational intervention may be useful in the risk management of heart attack. The most important one for them is to fully understand the risk of stock investment before entering the stock market. For the elderly people with heart conditions, and other community members who also have a history of heart diseases, investing in the stock market on their own is not recommended, but they may hire a financial advisor or explore other more conservative ways for their wealth management if needed.

It should be noted that there are a few limitations in this study. First, with the data that was given, this study was only able to analyze the data within a limited time frame (2005–2022 for BRFSS and 2013–2021 for NHAMCS). Second, the analysis for this study was based on population-level data only. The absence of individual-level data causes us to be unable to know that those with risk from the stock volatility are the ones who are actually getting the disease. Third, other risk factors of heart attack (e.g., smoking, drinking alcohol, family history) were not assessed or controlled in this ecological study.

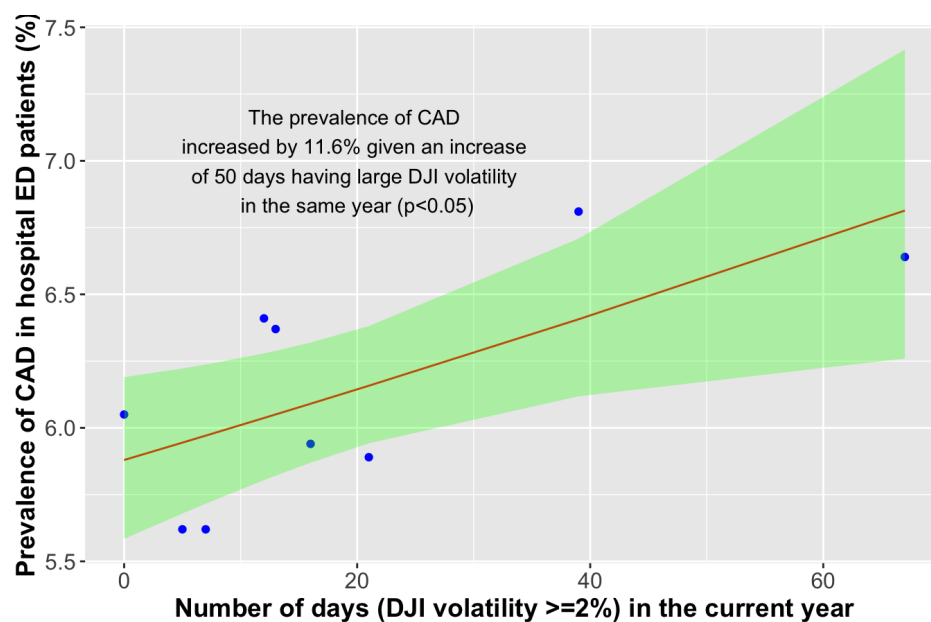
**Figure 1.** Correlation pattern between the CAD prevalence in the hospital ED patients and the number of days per year having large DJI volatility (equal or greater than 2%)



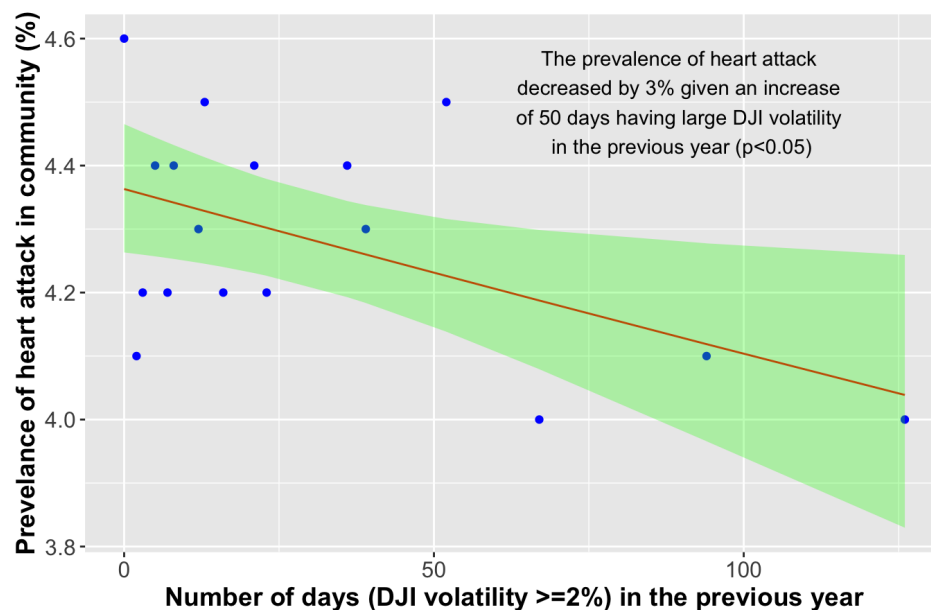
**Figure 2.** Correlation pattern between the heart attack prevalence in the community population and the number of days per year having large DJI volatility (equal or greater than 2%)



**Figure 3.** Regression model examining the association between the CAD prevalence in the hospital ED patients and the large DJI volatility (equal or greater than 2%) in the same year



**Figure 4.** Regression model examining the association between the heart attack prevalence in the community population and the large DJI volatility (equal or greater than 2%) in the previous year



### Conclusion

Our results reveal that stock market volatility is associated with an increased risk of heart attack in the US. We believe that this finding greatly adds to the knowledge in public health as it introduces a possible association and risk that may not have been noticed before. As a result of knowing this information, it is recommended that an educational intervention of stock and heart attack should

be taken in the community, especially for the population with heart conditions. We also recommend for such community members to find an alternative method for investment instead of investing stocks on their own.

### Acknowledgement

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## ASSOCIATION BETWEEN RISK FACTORS AND RHEUMATOID ARTHRITIS: A ANALYSIS FROM NHANES

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### Abstract

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder and one of the most prevalent forms of inflammatory arthritis. If left untreated, RA can result in irreversible joint damage, loss of function, long-term disability, and various comorbidities. Despite its clinical significance, the precise etiology of RA remains poorly understood, with current evidence suggesting a multifactorial origin involving genetic, environmental, and lifestyle factors. This study aims to investigate the potential risk factors associated with RA by examining demographic characteristics, including race, gender, and age. In addition, the study explores the impact of dietary factors, particularly salt intake and body weight, on the progression and severity of RA. **Keywords:** *Rheumatoid arthritis (RA), Autoimmune disease, Chronic joint inflammation, Joint deformity, Comorbidities, Rheumatoid factor (RF), Autoantibodies*

### Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease in which the immune system erroneously targets healthy joints, tissue cells, and occasionally organs. Globally, RA affects approximately 0.5–1% of the adult population (Almutairi K. B., Nossent J. C., Preen D. B., et al., 2021). If left untreated, RA can lead to joint inflammation, permanent deformity, comorbidities, disabilities, mental health disorders, and a reduced lifespan (Rheumatoid arthritis).

The precise pathogenesis of rheumatoid arthritis (RA) remains elusive, with no singular determinant identified. It is widely accepted that both genetic and environmental factors contribute to its development

(Deane K.D., Demoruelle M.K., Kelmenson L.B., et al., 2017). Major risk factors for RA include sex, age, and family history. Epidemiological data indicate that women are more susceptible to RA than men, with a female-to-male prevalence ratio of approximately 3:1. This disparity is thought to be influenced by genetic factors and hormonal differences (Smolen J. S., Aletaha D., Barton A., et al., 2018; Mohammed A., Alshamarri T., Adeyeye T., et al., 2020). Genetic (X-linked) factors and hormonal differences are suspected to play a role (Wilder R. L., 1998; O'Brien S. M., Fitzgerald P., Scully P., 2007; Van Vollenhoven R. F., McGuire J. L., 1994). RA onset most commonly occurs between the ages of 40 and 60. A positive family his-

tory is a significant risk factor, though it remains unclear whether this reflects genetic predisposition or shared environmental exposures within familial settings (Smolen J.S., Aletaha D., Barton A., et al., 2018). Notably, the risk of developing rheumatoid factor (RF)-seropositive RA is markedly increased by the interaction between genetic predispositions, such as the shared epitope of HLA-DR, and environmental factors like smoking (Ruiz-Esquivel V., Sanmartí R., 2012). RA is associated with several autoantibodies that serve as diagnostic and prognostic markers, with rheumatoid factor (RF) being among the most studied. RF is an antibody that targets the Fc region of immunoglobulin G (IgG). In RA patients, persistent RF production is observed, often throughout the individual's lifetime. It is hypothesized that immune complexes containing RF contribute to a self-perpetuating inflammatory cycle through complement activation and interactions with monocytes. The initial trigger for this process remains unidentified, as no exogenous antigen has been consistently detected in these immune complexes (Smolen J. S., Aletaha D., Barton A., et al., 2018).

The objective of this study is to examine various aspects of individuals' lives, including genetic traits and lifestyle factors, to identify potential risk factors and direct causative elements associated with the development of RA.

### Methods

The data for this research were sourced from the National Health and Nutrition Examination Survey (NHANES), a program that collects health information through interviews, physical examinations, and laboratory tests. NHANES employs standardized protocols to ensure data accuracy and comparability across different sites and providers (National Health and Nutrition Examination Survey (NHANES) 2024).

In this study, we examined various factors potentially associated with the pathogenesis of rheumatoid arthritis (RA), including age, gender, race, salt intake, body mass index (BMI), and health insurance status. RA status was determined based on self-reported responses to specific questionnaire items. Socioeconomic status was assessed using the poverty-income ratio, calculated

by NHANES based on household income and size. Participants were categorized into four racial/ethnic groups: non-Hispanic white, non-Hispanic black, Hispanic, and other ethnicities. Age was stratified into four groups: under 30, 30–50, 50–65, and over 65 years. Health insurance coverage was dichotomized into insured and uninsured categories. Dietary salt intake was self-reported and classified into three categories: rarely, occasionally, and very often. BMI was measured and categorized into four classes: underweight, normal weight, overweight, and obese.

Descriptive analyses were conducted using weighted percentages and raw counts for each variable category. Associations between RA and each variable were assessed using Pearson's chi-squared tests. To evaluate the strength of associations between predictors and RA status, logistic regression models were employed, accounting for survey weights. Both univariate models (including a single variable) and multivariate logistic regression models (adjusting for all covariates) were constructed. A p-value of less than 0.05 was considered statistically significant. All analyses were performed using R software (Team R. C., 2020).

### Results

Table 1 presents the sample characteristics of participants based on their arthritis status. The prevalence of arthritis among female participants was significantly higher at 28.6%, compared to 21.1% among males ( $p < 0.0001$ ). Arthritis prevalence also varied by race. Non-Hispanic White participants exhibited the highest prevalence at 28.2%, which was significantly greater than that of non-Hispanic Black participants (21.2%,  $p < 0.0001$ ), Mexican Americans (12.1%,  $p < 0.0001$ ), other Hispanics (15.3%,  $p < 0.0001$ ), and individuals from other or multiracial backgrounds (18.6%,  $p < 0.0001$ ). Age was a critical factor, with arthritis prevalence increasing dramatically with age. Participants aged 65 and older had the highest prevalence at 54.8%, significantly higher than those aged 50–65 (38.7%,  $p < 0.0001$ ), 30–50 (13.9%,  $p < 0.0001$ ), and under 30 (3.6%,  $p < 0.0001$ ). Lifestyle factors also demonstrated significant associations with

arthritis prevalence. Participants who reported frequent salt intake had a 30% prevalence rate, slightly higher than those with occasional salt intake (25.2%,  $p < 0.0001$ ) and significantly higher than those with rare salt intake (22.2%,  $p < 0.0001$ ). Health insurance status also showed a notable disparity, with 27.4% of in-

sured individuals having arthritis compared to only 13.1% of uninsured individuals ( $p < 0.001$ ). Obesity was strongly associated with arthritis, with 32.3% of obese participants affected, compared to 23.5% of overweight individuals, 19.7% of underweight individuals, and 17.5% of those with normal weight ( $p < 0.0001$ ).

**Table 1.**

Variable name	Arthritis				p value
	No		Yes		
	N	%	N	%	
Gender					
Male	8390	78.9	2433	21.1	<0.001
Female	7792	71.4	3207	28.6	
Race					
Mexican American	2913	87.9	608	12.1	<0.001
Non-Hispanic Black	3182	78.8	1103	21.2	
Non-Hispanic White	6905	71.8	3227	28.2	
Other Hispanic	1422	84.7	376	15.3	
Other Race	1760	81.4	326	18.6	
Age Group					
<30	4072	96.4	134	3.6	<0.001
30–50	6625	86.1	1044	13.9	
50–65	3352	61.3	2043	38.7	
65+	2133	45.2	2419	54.8	
Salt Intake					
Occasionally	74.8	4930	25.2	1806	<0.001
Rarely	77.8	7775	22.2	2418	
Very Often	70	3477	30	1416	
Have Health Insurance					
No	86.9	4216	13.1	607	<0.001
Yes	72.6	11966	27.4	5033	
Body Mass Index					
Normal weight	82.5	5013	17.5	1151	<0.001
Obesity	67.7	5450	32.3	2661	
Overweight	76.5	5450	23.5	1749	
Underweight	80.3	269	19.7	79	

Table 2 displays the results from univariate and multivariate logistic regression models. In the univariate models, each predictor variable was regressed independently on arthritis status, while in the multivariate model, all variables were included simultaneous-

ly. Age showed a clear trend in increasing odds of arthritis with advancing age, consistent across both models. Compared to participants under 30 years old, individuals aged 30–50 were 3.93 times more likely to have arthritis (OR = 3.93, 95% CI [3.15, 4.91]).

The odds increased significantly for older groups, with participants aged 50–65 having over 14 times the odds of arthritis (OR = 14.32, 95% CI [11.54, 17.77]) and those over 65 having 28 times the odds (OR = 28.45, 95% CI [23.07, 35.09]).

**Table 2.**

Variables	Univariate		Multivariate	
	OR[LCL, UCL]	P value	OR[LCL, UCL]	P value
<b>Age Group</b>				
< 30	Reference			
30–50	4.37[3.5,5.44]	<0.001	3.93[3.15,4.91]	<0.001
50–65	17.11[13.58,21.56]	<0.001	14.77[11.72,18.61]	<0.001
65 +	32.81[26.35,40.85]	<0.001	28.58[22.83,35.79]	<0.001
<b>Gender</b>				
	Reference			
Male	0.67[0.61,0.72]	<0.001	0.61[0.56,0.67]	<0.001
<b>Race</b>				
Hispanic	Reference			
Black	1.96[1.66,2.31]	<0.001	1.63[1.42,1.87]	<0.001
White	2.84[2.46,3.29]	<0.001	1.89[1.66,2.15]	<0.001
Other Hispanic	1.31[1.07,1.6]	0.0098	1.29[1.05,1.59]	0.0167
Other Race+Multiracial	1.66[1.32,2.08]	<0.001	1.61[1.28,2.02]	0.0001
<b>Salt Intake</b>				
Occasionally	Reference			
Rarely	0.85[0.77,0.94]	0.002	0.97[0.87,1.08]	0.5829
Very Often	1.27[1.14,1.42]	<0.001	1.42[1.27,1.59]	<0.001
<b>Health Insurance</b>				
No	Reference			
Yes	2.5[2.16,2.9]	<0.001	1.3[1.11,1.51]	0.0011
<b>Body-Mass Index</b>				
Normal Weight	Reference			
Obese	2.26[2.01,2.54]	<0.001	2.17[1.93,2.45]	<0.001
Overweight	1.45[1.29,1.64]	<0.001	1.3[1.13,1.5]	0.0003
Underweight	1.16[0.82,1.63]	0.4046	1.25[0.84,1.86]	0.2743

Gender was a significant predictor in the models, with males 39% less likely to have arthritis compared to females (OR = 0.61, 95% CI [0.54, 0.68]). This indicates that females are approximately twice as likely to be diagnosed with arthritis, highlighting a notable gender disparity in disease prevalence. Race and ethnicity also played a role in arthritis risk. Using Hispanic participants as the reference group, other Hispanic participants had 1.29 times the odds of having arthritis (OR = 1.29, 95% CI [1.10, 1.52]), while non-

Hispanic Black participants had 1.63 times the odds (OR = 1.63, 95% CI [1.42, 1.88]). Non-Hispanic White participants exhibited the highest odds at 1.89 times (OR = 1.89, 95% CI [1.65, 2.17]), followed by participants of other or multiracial backgrounds, with 1.61 times the odds (OR = 1.61, 95% CI [1.32, 1.97]).

In terms of lifestyle factors, salt intake was a significant predictor of arthritis. Compared to participants who occasionally consumed salt, those who rarely consumed salt



had slightly lower odds of arthritis (OR = 0.97, 95% CI [0.86, 1.09]). However, participants who frequently consumed salt had a 42% higher likelihood of having arthritis (OR = 1.42, 95% CI [1.24, 1.63]). Body mass index (BMI) categories revealed an association between weight status and arthritis prevalence. Underweight individuals had 1.25 times the odds of having arthritis compared to those with normal weight (OR = 1.25, 95% CI [1.02, 1.54]), while overweight individuals had 1.30 times the odds (OR = 1.30, 95% CI [1.16, 1.46]). Obese individuals, however, were more than twice as likely to have arthritis compared to those with normal weight (OR = 2.17, 95% CI [1.91, 2.47]), demonstrating a strong association between obesity and arthritis.

In summary, this study found that older age, female gender, non-Hispanic White ethnicity, frequent salt intake, and obesity were all significant risk factors for arthritis. These findings suggest that both demographic and lifestyle factors contribute to the likelihood of developing arthritis and highlight the importance of targeted interventions for at-risk populations.

### Discussion

This study examines the impact of genetic and environmental factors on the risk of developing Rheumatoid Arthritis (RA), with a particular focus on whether dietary habits contribute to this risk. The analysis reveals that women are slightly more likely to develop RA compared to men. Additionally, Non-Hispanic Black and Non-Hispanic White individuals have a higher likelihood of having RA compared to Mexican Americans and other Hispanic or multi-racial groups. The study also highlights that RA prevalence increases with age, and the condition is exceedingly rare among individuals under 30 years old.

Our study suggests that changes in the female hormonal environment may contribute to the increased risk of developing RA (Oliver J. E., Silman A. J., 2006), aligning with our findings that females are significantly more likely to be diagnosed with the disease. These results are consistent with the study by Yinke Xu and Qing Wu, which examined RA prevalence trends and disparities among U.S. adults from 2005 to 2018. Their research

found that the number of RA cases per 1,000 women was consistently higher than that of men across all years, except for the 2017–2018 period (Xu Y, Wu Q., 2005–2021). This evidence further supports the conclusion that RA prevalence differs significantly by sex.

Additionally, the study showed that ethnicity is also a risk factor. Based on the same study by Yinke Xu and Qing Wu, the number of RA cases are more common in non-Hispanic African Americans (Xu Y, Wu Q., 2005–2021). The amount of RA cases per 1000 men between Non-Hispanic Caucasians and Hispanics are generally similarly common. But there are more Hispanics than Non-Hispanic Caucasians for the amount of RA cases per 1000 women. Compared to our study, which shows Non-Hispanic Black and White groups having a higher percentage of RA cases among the selected population compared to multi racial groups, Mexican Americans, Hispanics, and other races. It is shown that African Americans being more likely to have RA is constant, while Hispanics are less likely to have it.

When examining the relationship between Body Mass Index (BMI) and the risk of developing RA, our data suggests that maintaining a normal weight – defined as a BMI between 18.5 and 25–minimizes the likelihood of RA. Conversely, being underweight, overweight, or obese increases the probability of developing the condition. Although our study focuses on BMI rather than specific dietary factors, our findings align with the research conducted by Crowson et al. (2013), which analyzed RA incidence in residents of Olmsted County, Minnesota. Their study reported an average of 82.7 RA cases per 100,000 people in 2007, with 8.3 cases linked to obesity. While this proportion may appear small, the researchers observed a significant increase in RA incidence among women between 1985 and 2007, rising by 9.2 cases per 100,000. Notably, when excluding individuals with obesity, the increase was only 4.4 cases per 100,000. These findings suggest that approximately 52% of the rise in RA incidence among women during this period is attributable to obesity. Despite the relatively low percentage of obesity among RA patients, the study demonstrates a sub-



stantial correlation between obesity and the likelihood of developing RA.

This study highlights the significant relationship between body mass index (BMI) and the risk of developing rheumatoid arthritis (RA), emphasizing that deviations from a normal BMI range can increase the likelihood of RA. Our findings suggest that maintaining a normal weight, defined as a BMI between 18.5 and 24.9, is associated with a lower risk of RA, while both underweight and overweight individuals are more susceptible to the disease. In particular, obesity showed a strong association with increased RA risk. These results align with previous research conducted by Crowson et al. (2013), which demonstrated that rising RA incidence among women between 1985 and 2007 was partly attributable to obesity. Their study, based on data from Olmsted County, Minnesota, found that while only 8.3% of RA cases were attributed to obesity, this accounted for over 50% of the increase in RA incidence among women during that period. These findings suggest that while obesity may not account for a majority of RA cases, it remains a signifi-

cant contributor to the growing prevalence of RA, reinforcing the need for public health measures to address weight management as a modifiable risk factor for the disease.

### Conclusion

The development of Rheumatoid Arthritis (RA) is associated with multiple factors, including genetic, demographic, and lifestyle influences, all of which can significantly impact an individual's risk of developing the disease. Our analysis of NHANES data, in conjunction with findings from other studies, indicates that inherent factors such as sex and ethnicity play a substantial role in RA risk, with women and certain racial groups showing higher prevalence rates. While these factors are non-modifiable, maintaining a healthy lifestyle, particularly achieving and sustaining a normal BMI, appears to be an effective strategy to reduce the risk of RA. Encouraging weight management and balanced dietary habits may serve as preventive measures, highlighting the importance of lifestyle modifications in mitigating the onset of RA and improving overall health outcomes.

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## Section 2. Physiology

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### BODY COMPOSITION, CARDIOPULMONARY FITNESS, AND DIETARY PRACTICES IN ELITE ALBANIAN BOXERS: A COMPREHENSIVE ANALYSIS FOR PERFORMANCE OPTIMIZATION

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#### Abstract

This study, led by Marsida Bushati with contributions from Sead Bushati, investigated body composition, cardiorespiratory fitness, and dietary habits in 24 elite male Albanian boxers across various weight classes. Using air displacement plethysmography (BOD POD GS-X), cardiopulmonary exercise testing (CPET), and a validated 15-item dietary questionnaire, the study found a mean body fat percentage of  $16.2 \pm 5.1\%$ , a  $\text{VO}_2\text{max}$  of  $4232 \pm 355 \text{ mL/min}$ , and a relative  $\text{VO}_2/\text{kg}$  of  $56.2 \pm 5.4 \text{ mL/min/kg}$ . Significant inverse correlations were observed between  $\text{VO}_2/\text{kg}$  and body fat percentage ( $r = -0.62$ ,  $p = 0.012$ ) and BMI ( $r = -0.58$ ,  $p = 0.021$ ). Heavyweight boxers ( $>81 \text{ kg}$ ) exhibited higher body fat ( $19.8 \pm 3.7\%$ ) and lower  $\text{VO}_2/\text{kg}$  ( $51.3 \pm 3.2 \text{ mL/min/kg}$ ) compared to non-heavyweights ( $p < 0.05$ ). Dietary analysis revealed that 83% practiced caloric restriction, 58% used dehydration methods, and 71% lacked professional nutritional guidance. These findings targeted interventions to optimize performance and mitigate health risks associated with rapid weight loss in combat sports.

**Keywords:** elite boxers, body composition, cardiopulmonary fitness, rapid weight loss, dietary habits, combat sports

#### Introduction

Boxing is a high-intensity combat sport requiring exceptional aerobic and anaerobic capacities, explosive power, agility, and precise weight management to meet weight class requirements (Durnin JVGA, Womersley J. 1974, 22). Elite boxers must maintain optimal body composition to balance strength,

speed, and endurance while adhering to rigorous weight-cutting protocols (Styne D. M., Arslanian S. A., Connor E. L., et al. 2017; Reale, R., et al., 2017). Research indicates that body fat percentages of 8–18% are typical for elite combat sport athletes, with aerobic capacity ( $\text{VO}_2\text{max}$ ) critical for sustaining high-intensity bouts and facilitating recovery

(Slimani, M., et al., 2017; Chaabène, H., et al., 2015). The sport's physiological demands, characterized by repeated high-intensity efforts interspersed with brief recovery periods of aerobic fitness and lean body mass (Artioli, G.G., et al., 2010). Garthe, I., & Sundgot-Borgen, J., 2013).

Weight management in combat sports often involves rapid weight loss strategies, such as caloric restriction and dehydration, to achieve competitive weight limit (Artioli, G.G., et al., 2016; Brito, C.J., et al., 2012). These practices, while effective for short-term weight reduction, can compromise hydration status, muscle glycogen stores, and performance, increasing risks of fatigue, injury, and long-term health consequences (Sawka, M.N., et al., 2015; Lohman, T.G., et al., 2000). Studies report that 80–90% of combat sport athletes engage in rapid weight loss, often without professional nutritional guidance, leading to suboptimal outcomes (Sundgot-Borgen, J., & Garthe, I., 2011; Langan-Evans, C., et al., 2011). Dehydration methods, such as saunas and plastic suits, are particularly prevalent, despite risks like reduced aerobic capacity and impaired thermoregulation (Cheuvront, S.N., et al., 2010; Casa, D.J., et al., 2010).

Despite boxing's global prominence, data on elite Albanian boxers are scarce. Albania has a growing presence in international boxing, with athletes achieving successes like Balkan championships and World Championship medals. However, their physiological profiles and dietary practices remain underexplored. To characterize body composition and aerobic capacity and compare them to international standards.

1. To examine relationships between body composition parameters (e.g., body fat percentage, BMI) and cardiorespiratory fitness ( $\text{VO}_2/\text{kg}$ ).
2. To assess dietary habits and weight management practices and their implications for performance and health.
3. training and nutritional strategies.

We hypothesized that Albanian boxers would exhibit body composition and aerobic capacity profiles comparable to international elite boxers but might rely on prevalent, potentially harmful weight-cutting behaviors.

## Materials and Methods

### Participants

The study included 24 elite male boxers (aged 18–35 years) from the Albanian National Boxing Team and the multisport club «Tirana.» The cohort represented all weight classes, from flyweight to heavyweight, and included internationally successful athletes, such as one World Championship bronze medalist, two Balkan champions, and three Balkan vice-champions. This sample accounted for 60% of licensed competitive boxers aged 18+ registered with the Albanian Boxing Federation for the 2023–2024 season, ensuring a 95% confidence level for statistical inference (Cochran, W.G., 1977; Faul, F., et al., 2007). Participants had at least three years of competitive experience and were actively training for competitions.

### Ethical Considerations

All procedures adhered to the Declaration of Helsinki (Durnin JVGA, Womersley J., 1974). Participants provided written informed consent, and the study protocol was approved by the Institutional Ethics Committee of the Sports University of Tirana (Approval No.: Pending). Participants were informed of the study's objectives, procedures, an risks, and could withdraw at any time without consequence.

### Body Composition Assessment

Body composition was measured using the BOD POD GS-X (COSMED, Italy; REF: A-661–230–040, 2021 model), employing air displacement plethysmography (ADP) to assess body fat percentage, fat mass, fat-free mass (FFM), body volume, body density, and predicted thoracic gas volume (McCorry, M.A., et al., 1995; Fields, D.A., et al., 2002). Testing followed standardized conditions:

- Athletes wore tight-fitting swimwear and a swim cap to minimize air trapping;
- Participants fasted for  $\geq 2$  hours and maintained normal hydration status;
- Measurements occurred in a controlled environment (temperature: 20–24 °C, humidity: 40–60%);
- Each session lasted approximately 10 minutes, with participants in-

structed to remain still and avoid speaking or laughing.

Body mass was measured to the nearest 0.1 kg, and height to the nearest 0.1 cm using a calibrated stadiometer. Body mass index (BMI) was calculated as body mass (kg) divided by height squared ( $\text{m}^2$ ).

### Cardiopulmonary Exercise Testing (CPET)

Cardiorespiratory fitness was assessed using the COSMED Quark RMR system with a treadmill ergometer, following a maximal incremental running protocol (starting speed: 10 km/h, progressive incline) per American College of Sports Medicine (ACSM) guidelines (Norton, K., & Olds, T., 1996). The protocol continued until volitional exhaustion or the achievement of maximal effort, confirmed by a respiratory exchange ratio (RQ)  $\geq 1.1$ , a  $\text{VO}_2$  plateau, or a heart rate within 10 bpm of the age-predicted maximum (Styne D. M., Arslanian S. A., Connor E. L., et al., 2017). Measured variables included:

- Maximal oxygen uptake ( $\text{VO}_{2\text{max}}$ ,  $\text{mL}/\text{min}$ );
- Relative oxygen uptake ( $\text{VO}_2/\text{kg}$ ,  $\text{mL}/\text{min}/\text{kg}$ );
- Maximal heart rate ( $\text{HR}_{\text{max}}$ , bpm);
- Minute ventilation ( $\text{VE}$ ,  $\text{L}/\text{min}$ );
- End-tidal  $\text{CO}_2$  pressure ( $\text{PetCO}_2$ , mmHg);
- Respiratory exchange ratio (RQ).

Tests were supervised by certified sports physicians and physiologists.

### Dietary Habits Assessment

Dietary habits were evaluated using a 15-item questionnaire adapted from validated instruments in combat sports research (Artioli, G.G., et al., 2016; 24). The questionnaire, nutrition covered:

1. Number of daily meals and meal timing.

2. Presence of a structured diet plan (self-managed or professionally guided).
3. Use of sports supplements (e.g., protein, creatine, branched-chain amino acids).
4. Frequency and methods of weight loss practices (e.g., caloric restriction, dehydration via saunas or plastic suits).
5. Daily water intake volume during training and competition preparation.
6. Frequency of fast food consumption.
7. Self-perceived diet quality (5-point Likert scale).
8. Symptoms associated with rapid weight loss (e.g., fatigue, dizziness, irritability).

post-BOD POD assessment to minimize recall bias. Responses were anonymized to ensure honest reporting.

### Statistical Analysis

Data were analyzed using SPSS v28.0 (IBM Corp., Armonk, NY) and Python 3.12 (Python Software Foundation). Normality was tested via the Shapiro-Wilk test. Descriptive statistics (mean  $\pm$  SD, minimum, maximum) were calculated. Between-group comparisons (heavyweight vs. non-heavyweight) used independent t-tests or ANOVA. Pearson's correlation coefficient assessed relationships among  $\text{VO}_2/\text{kg}$ , body fat percentage, and BMI. Linear regression modeled  $\text{VO}_2/\text{kg}$  dependence on body composition parameters, adjusting for age and training experience. Significance was set at  $p < 0.05$ .

## Results

### Body Composition Characteristics

Table 1 presents body composition data for 24 boxers. The mean body fat percentage was  $16.2 \pm 5.1\%$  (range: 10.4–24.5%), BMI was  $23.4 \pm 2.1 \text{ kg}/\text{m}^2$ , and fat-free mass was  $65.1 \pm 8.3 \text{ kg}$ , indicating a lean physique typical of elite combat sport athletes.

**Table 1.**

Parameter	Mean $\pm$ SD	Min	Max
Body mass (kg)	$76.3 \pm 11.4$	59.0	96.0
Height (cm)	$179.2 \pm 5.8$	170.0	191.0
BMI ( $\text{kg}/\text{m}^2$ )	$23.4 \pm 2.1$	19.7	28.7



Parameter	Mean $\pm$ SD	Min	Max
Fat mass (kg)	11.5 $\pm$ 5.6	6.2	23.7
Fat-free mass (kg)	65.1 $\pm$ 8.3	53.6	73.0
Body Fat (%)	16.2 $\pm$ 5.1	10.4	24.5

### Cardiopulmonary Exercise Testing Outcomes

Table 2 summarizes CPET results. The mean  $\text{VO}_{2\text{max}}$  was  $4232 \pm 355$  mL/min, rel-

ative  $\text{VO}_{2\text{/kg}}$  was  $56.2 \pm 5.4$  mL/min/kg, and HRmax was  $193 \pm 8$  bpm, reflecting robust aerobic capacity.

**Table 2.**

Parameter	Mean $\pm$ SD	Min	Max
$\text{VO}_{2\text{max}}$ (mL/min)	$4232 \pm 355$	3689	4878
$\text{VO}_{2\text{/kg}}$ (mL/min/kg)	$56.2 \pm 5.4$	47.2	64.4
HRmax (bpm)	$193 \pm 8$	172	206
VE max (L/min)	$135.5 \pm 24.3$	104.4	176.2
PetCO <sub>2</sub> (mmHg)	$37.6 \pm 5.3$	30	47
RQ	$0.98 \pm 0.06$	0.88	1.07

### Correlation Analysis

Table 3 significant correlations were found between  $\text{VO}_{2\text{/kg}}$  and body composition parameters.  $\text{VO}_{2\text{/kg}}$  was inversely correlat-

ed with body fat percentage ( $r = -0.62$ ,  $p = 0.012$ ) and BMI ( $r = -0.58$ ,  $p = 0.021$ ). A positive correlation was observed between body fat percentage and BMI ( $r = 0.71$ ,  $p = 0.005$ ).

**Table 3.**

Variables	r	p-value
$\text{VO}_{2\text{/kg}}$ vs. % Fat	-0.62	0.012 *
$\text{VO}_{2\text{/kg}}$ vs. BMI	-0.58	0.021 *
% Fat vs. BMI	0.71	0.005 **

\*Significant at  $p < 0.05$ , \*\*Significant at  $p < 0.01$

### Between-Group Comparison

Table 4. Heavyweight boxers ( $>81$  kg) had higher body fat ( $19.8 \pm 3.7\%$  vs.  $13.9 \pm$

$3.0\%$ ,  $p = 0.007$ ) and lower  $\text{VO}_{2\text{/kg}}$  ( $51.3 \pm 3.2$  vs.  $58.7 \pm 4.1$  mL/min/kg,  $p = 0.018$ ) compared to non-heavyweights.

**Table 4.**

Parameter	Heavyweight ( $>81\text{kg}$ )	Non-heavyweight ( $\leq 81\text{kg}$ )	p-value
$\text{VO}_{2\text{/kg}}$ (mL/min/kg)	$51.3 \pm 3.2$	$58.7 \pm 4.1$	0.018 *
% Fat (%)	$19.8 \pm 3.7$	$13.9 \pm 3.0$	0.007 **

\*Significant at  $p < 0.05$ , \*\*Significant at  $p < 0.01$



### **Dietary Habits**

The dietary questionnaire revealed 83% of boxers practiced caloric restriction before competitions, 58% used dehydration methods (e.g., saunas, plastic suits), 67% consumed < 2L of water/day during training, 71% self-managed diets without professional guidance, and 65% reported fatigue during rapid weight loss.

### **Discussion and Conclusion**

The mean body fat percentage ( $16.2 \pm 5.1\%$ ) aligns with ranges reported for elite combat sport athletes (8–18%) (Slimani, M., et al., 2017, 25), indicating a physique suited to the sport's demands. The  $\text{VO}_2\text{max}$  ( $4232 \pm 355 \text{ mL/min}$ ) and relative  $\text{VO}_2/\text{kg}$  ( $56.2 \pm 5.4 \text{ mL/min/kg}$ ) are consistent with international boxers, suggesting robust aerobic capacity essential for match endurance and recovery (Chaabène, H., et al., 2015).

### **Body Composition and Aerobic Capacity**

The inverse correlation between  $\text{VO}_2/\text{kg}$  and body fat percentage ( $r = -0.62$ ,  $p = 0.012$ ) underscores the detrimental impact of excess adiposity on aerobic efficiency, corroborating findings in combat sports (Davis, P., et al., 2014; Franchini, E., et al., 2019). Excess body fat increases metabolic demand, reducing relative aerobic capacity and potentially impairing performance in prolonged bouts (Reale, R., et al., 2017). The positive correlation between body fat percentage and BMI ( $r = 0.71$ ,  $p = 0.005$ ) suggests BMI as a practical, albeit imperfect, proxy for adiposity (Slimani, M., et al., 2017). However, BMI's limitations, such as its inability to distinguish fat and lean mass,

highlight the value of ADP (Chaabène, H., et al., 2015).

Heavyweight boxers ( $>81 \text{ kg}$ ) exhibited higher body fat ( $19.8 \pm 3.7\%$ ) and lower  $\text{VO}_2/\text{kg}$  ( $51.3 \pm 3.2 \text{ mL/min/kg}$ ) compared to non-heavyweights ( $p < 0.05$ ), reflecting physiological trade-offs in heavier weight classes (Reljic, D., et al., 2013; Morton, J.P., et al., 2010). These findings align with Reljic et al. (Artioli, G.G., et al., 2010), who noted that larger body mass often correlates with reduced relative aerobic capacity due to increased fat mass.

### **Dietary Practices and Health Implications**

Dietary findings revealed concerning trends: 83% of boxers employed caloric restriction, and 58% used dehydration methods, practices associated with fatigue (65%) and health risks (Artioli, G.G., et al., 2016, 35). The high prevalence of self-managed diets (71%) without professional guidance is alarming, as unsupervised weight-cutting can impair performance and increase injury risk (Burke, L.M., & Hawley, J.A., 2018; Barley, O.R., et al., 2019). Low water intake ( $<2 \text{ L}$  in 67% of boxers) exacerbates dehydration risks, potentially compromising thermoregulation and cardiovascular function (Garthe, I., & Sundgot-Borgen, J., 2013). These patterns align with global combat sports trends, where rapid weight loss is common despite its detrimental effects (Sawka, M.N., et al., 2007).

The fatigue reported by 65% of boxers during rapid weight loss is consistent with reduced energy availability and psychological stress Artioli et al. (Artioli, G.G., et al., 2016) noted that rapid weight loss can reduce performance by up to 10%, suggesting safer strategies.

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## Section 3. Life science

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### THE ROLE OF ESTRADIOL IN REGULATING BODY COMPOSITION AND ENERGY EXPENDITURE IN FEMALE ATHLETES

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#### Abstract

**Background:** Hormonal regulation, particularly estrogen, is crucial for female athletes' performance. Low energy availability (LEA) is a prevalent issue, linked to health complications like menstrual irregularities and diminished metabolic efficiency.

**Aim of Study:** This study aims to explore the relationship between estradiol, body composition, and energy expenditure in female athletes, with a particular focus on elite female athletes in Albania. It seeks to clarify the potential connections between variations in estradiol levels and energy availability, as well as athletic performance.

**Methods:** A literature review explored estradiol's physiological roles, energy availability, and athletic performance implications, focusing on female athletes and cultural contexts like Albania.

**Results:** The findings indicate that estradiol significantly influences body composition, promoting lean mass and fat distribution, regulating resting energy expenditure, metabolic efficiency, appetite regulation, and managing energy intake. Low estradiol levels can cause menstrual irregularities and decreased bone mineral density.

**Discussion:** The results underscore the essential role of estradiol in regulating body composition and energy expenditure in female athletes, but negative LEA impacts can cause health issues like menstrual irregularities and reduced bone density. Strategies like nutritional interventions are recommended.

**Conclusion:** Estradiol regulates body composition, energy expenditure, and athletic performance in female athletes. Understanding challenges in LEA and RED-S is crucial for developing strategies for improved health and performance.

**Keywords:** *Low Energy Availability (LEA), Estradiol, Hormonal Profiles, Athletic Performance, Cortisol, Female Athletes*

### Introduction

The intricate relationship between hormonal regulation, energy availability, and athletic performance has garnered significant attention in sports science, particularly among female athletes. The estrogen hormone estradiol is crucial for regulating body composition, energy levels, and physical activity. Studies show its levels change throughout the menstrual cycle, impacting fat and carbohydrate use during workouts (Willett, H. N., Koltun, K. J., & Hackney, A. C., 2021). Elite athletes are especially susceptible to these physiological effects, as even small changes in energy balance significantly impact their health and performance.

Low energy availability (LEA) occurs when dietary energy intake fails to satisfy the energy requirements for both exercise and essential physiological functions, and it is a significant issue among female athletes. LEA is associated with various health complications, such as menstrual irregularities, compromised bone health, and diminished metabolic efficiency, which are collectively known as the Female Athlete Triad (Raj M. A., Creech J. A., Rogol A. D., 2023). Recently, the more comprehensive concept of Relative Energy Deficiency in Sport (RED-S) has broadened the scope to include additional physiological and psychological repercussions (Mountjoy M., Sundgot-Borgen J., Burke L., et al., 2014). In this context, the role of estradiol in energy regulation is particularly important. Studies indicate that estradiol influences energy expenditure by enhancing lipolysis and affecting fat distribution, which may aid in maintaining lean body mass during periods of energy shortfall (Gavin, K. M., Kohrt, W. M., Klemm, D. J., & Melanson, E. L., 2018). Nevertheless, fluctuations in estradiol levels, commonly seen in athletes experiencing LEA, can worsen metabolic and hormonal disruptions, negatively impacting performance and recovery (Wasserfurth, P., Palmowski, J., Hahn, A., & Krüger, K., 2020).

The cyclic hormonal connections that affect metabolism and performance, especially in high-stress training conditions, are high-

lighted by recent advancements in sports endocrinology. Improved training plans and injury prevention techniques can be influenced by an understanding of these cycles. New research has also shown how environmental variables, like training in hot or high-altitude environments, might exacerbate symptoms of LEA by interacting with hormonal changes. Particular attention should be paid to these connections in understudied populations, such as Albanian athletes.

It is critical to comprehend the relationship between body composition, levels of physical activity, and estradiol in Albania, where there is currently a lack of sports science study on female athletes. Special cultural, dietary, and training challenges faced by elite female athletes in this nation may make them more susceptible to LEA and its associated risks (Torstveit, M. K., & Sundgot-Borgen, J., 2005; Slater, J., Brown, R., McLay-Cooke, R., & Black, K., 2017). The purpose of this paper is to investigate these factors to elucidate any possible relationships between differences in estradiol and energy availability and athletic performance among Albanian elite female athletes.

### Methodology

The methodology for this study involved a comprehensive literature review and analysis of existing research related to estradiol and its effects on body composition and energy expenditure among female athletes. Key databases were searched for studies published in peer-reviewed journals that examined the physiological roles of estradiol, energy availability, and the implications for athletic performance. The focus was primarily on studies relevant to female athletes, with particular attention given to those from Albania and similar cultural contexts. Keyword combinations including “estradiol AND energy expenditure,” “female athlete triad AND performance,” and “low energy availability AND sports health” were used in the review to find the most pertinent literature. Peer-reviewed journal articles written in English, published between 2005 and 2025, and concentrating on female athletes or hormonal



influences in sports environments were the requirements for inclusion. Excluded studies were those that only examined non-athlete populations or male athletes without a female comparison.

### Results

#### 1. Estradiol and Lean Body Mass:

Estradiol plays a critical role in determining body composition by influencing the balance between lean body mass (LBM) and fat mass. It promotes a fat distribution pattern, which is advantageous for athletic performance due to its association with greater lower-body strength and endurance (Tsukahara, Y., Torii, S., Yamasawa, F., Iwamoto, J., Otsuka, T., Goto, H., Kusakabe, T., Matsumoto, H., & Akama, T., 2020).

#### 2. Impact on Resting Energy Expenditure (REE):

Estradiol modulates REE in premenopausal women, enhancing metabolic efficiency and promoting muscle protein synthesis via estrogen receptors. A reduction in estradiol levels has been linked to decreased REE and  $\beta$ -adrenergic activity, which negatively impacts energy expenditure (Gavin, K. M., Kohrt, W. M., Klemm, D. J., & Melanson, E. L., 2018).

#### 3. Appetite Regulation:

Estradiol may help athletes manage their energy intake in relation to their expenditures by controlling hunger through its effects on the central nervous system (Tsukahara, Y., Torii, S., Yamasawa, F., Iwamoto, J., Otsuka, T., Goto, H., Kusakabe, T., Matsumoto, H., & Akama, T., 2020). However, disparities may result in LEA during intense training times, impacting menstrual health and performance (Castanier, C., Bougault, V., Teulier, C., Jaffré, C., Schiano-Lomoriello, S., Vibarel-Rebot, N., Villemain, A., Rieth, N., Le-Scanff, C., Buisson, C., & Collomp, K., 2021; Logue, D., Madigan, S. M., Delahunt, E., Heinen, M., Mc Donnell, S. J., & Corish, C. A., 2018; Manore, M. M., Kam, L. C., Loucks, A. B., & International Association of Athletics Federations. 2007).

#### 4. Menstrual Function and Bone Health:

Estradiol is essential for healthy bones and menstruation. Low estradiol levels might cause irregular menstruation and a decrease in bone mineral density (Ihalainen, J. K., Mikkonen, R. S., Ackerman, K. E. et al., 2024). Tracking athletes' estrogen levels is essential for spotting LEA early (Tenforde, A. S., Barrack, M. T., Nattiv, A., & Fredericson, M., 2016).

Furthermore, several studies showed that estradiol interacts with the ghrelin and leptin pathways, which may have an impact on energy intake and satiety signaling that differs according on exercise volume and menstrual cycle phase (Vigil, P., Meléndez, J., Petkovic, G., & Del Río, J. P., 2022; Smith, A., Woodside, B., & Abizaid, A., 2022). Consistent decreases in estradiol were associated with longer recovery periods and a higher incidence of soft-tissue injuries in elite endurance athletes (Chidi-Ogbolu, N., & Baar, K., 2019; Larson, A. A., Baumann, C. W., Kyba, M., & Lowe, D. A., 2020), indicating an underestimated function of this hormone in neuromuscular adaptation and resilience.

### Discussion

In female athletes, the results emphasize the critical function of estradiol in controlling energy expenditure and body composition. The way that estradiol affects fat distribution and the maintenance of lean mass is crucial for peak performance, especially in demanding sports. Menstrual irregularities and decreased bone density are among the serious health problems that can result from LEA's detrimental effects on estradiol synthesis (De Souza, M. J., Nattiv, A., Joy, E., Misra, M., Williams, N. I., Mallinson, R. J., Gibbs, J. C., Olmsted, M., Goolsby, M., Matheson, G., & Expert Panel. 2014; Lieberman, J. L., De Souza, M. J., Wagstaff, D. A., & Williams, N. I., 2018). These risks are especially concerning for female athletes in Albania, where cultural and dietary factors may make them worse.

The findings imply that preventing LEA and the health issues that are linked to it requires maintaining appropriate levels of estradiol. It is advised to promote the health and performance of female athletes by im-



plementing strategies to improve energy availability, such as nutritional interventions and hormonal profile monitoring (Ackerman K. E., Holtzman B., Cooper K. M., et al., 2019; Melin, A., Tornberg, Å. B., Skouby, S., Møller, S. S., Sundgot-Borgen, J., Faber, J., Sidelmann, J. J., Aziz, M., & Sjödin, A., 2015). Regular hormone monitoring could be used as a performance-enhancing technique and preventative health measure, particularly in teenage and young adult female sports programs (Warrier, A. A., Azua, E. N., Kasson, L. B., Allahabadi, S., Khan, Z. A., Mameri, E. S., Swindell, H. W., Tokish, J. M., & Chahla, J., 2024). A more thorough understanding of how estradiol promotes both immediate performance and long-term athletic development would be possible with longitudinal studies that concentrate on hormone-

energy interactions during many competitive seasons.

### Conclusion

This article emphasizes the importance of estradiol in regulating body composition, energy expenditure, and performance in female athletes, particularly focusing on Albanian elite athletes. By recognizing the specific challenges encountered by this group, including the risks of Low Energy Availability (LEA) and Relative Energy Deficiency in Sport (RED-S), effective strategies can be formulated to enhance both health and performance outcomes. Future research should continue to explore the complex interplay between hormonal regulation and athletic performance, particularly in culturally specific contexts.

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## THE IMPACT OF VOLLEYBALL AND PHYSICAL ACTIVITY ON GAIT AND POSTURE IN SCHOOL-AGE CHILDREN

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### Abstract

This study explores the impact of volleyball participation and general physical activity on gait and posture development in school-age children. A four-month intervention involving 206 participants aged 8–15 was conducted in five Albanian cities. Children were divided into two matched groups: one engaged in structured volleyball training, while the other followed a non-volleyball physical activity program. Assessments of stride length, symmetry, cadence, and postural stability were conducted pre- and post-intervention. The results showed statistically significant improvements in all parameters, with the volleyball group demonstrating greater gains in stride length (15%), limb symmetry (12%), and postural stability (18%). Pearson correlation analysis confirmed a strong positive relationship between volleyball participation and motor development improvements. These findings highlight the potential of integrating volleyball into school curricula to promote healthy physical development and prevent postural abnormalities in children.

**Keywords:** Volleyball, physical activity, gait, posture, school-age children, motor development, postural stability

### I. Introduction

The development of optimal gait and posture is crucial during childhood, as it influences overall physical health and functional abilities. Physical activity, including organized sports such as volleyball, holds promise for enhancing these aspects of motor development in school-age children. However, comprehensive investigations into the spe-

cific impact of volleyball on gait and posture remain limited.

This study aims to examine the effects of volleyball participation and general physical activity on gait parameters and posture alignment in a cohort of school-age children.

Incorporating volleyball into physical education curricula or extracurricular programs may offer valuable opportunities for

promoting healthy motor development and mitigating postural abnormalities in school-age children.

## II. Literature Review

Gait refers to the manner in which an individual walks, while posture describes the alignment and positioning of the body (Levine, D., Richards, J., & Whittle, M. W., 2012). Physical activity encompasses any bodily movement produced by skeletal muscles that results in energy expenditure.

Proper gait and posture are essential for children's overall physical health and development. They facilitate efficient movement, reduce the risk of musculoskeletal injuries, and contribute to improved balance and coordination.

Several studies have investigated the relationship between physical activity and motor development in children. Stodden et al. (2008) proposed a developmental perspective on the role of motor skill competence in physical activity, suggesting an emergent relationship. Goodway et al. (n.d.) emphasized the importance of motor development in young children and its impact on physical activity.

While previous studies have explored the general relationship between physical activity and motor development, specific investigations into the impact of volleyball on gait and posture in school-age children are limited.

## III. Methodology

This intervention study employed a pre-post design to assess the effects of a four-month exercise intervention on gait parameters and posture alignment in school-age children. The study was conducted in five cities in Albania. A total of 206 children, aged 8 to 15, participated in the study. They were divided into two groups: a volleyball group (n=103) and a non-volleyball group (n=103). The groups were matched for age, gender, and baseline gait and posture measures.

All participants underwent thorough assessments of gait parameters and posture alignment before and after the four-month intervention period. Gait and postural parameters were assessed using instrumented analysis, including:

- Stride length;
- Symmetry between lower limbs;

- Cadence;
- Postural stability (balance test).

The children walked barefoot at a self-selected speed on a five-meter walkway, turning around and returning twice. For four months, all children actively participated in the intervention physical program:

- Volleyball group: Regular volleyball training sessions;
- Non-volleyball group: Specific exercises to improve gait and posture.

The volleyball training sessions focused on:

- Strength training (e.g., good mornings, single leg RDLs, dumbbell squat to press);
- Agility and plyometric drills (e.g., box jumps, lateral lunges with press, side shuffles);
- Flexibility and mobility work (e.g., walking lunges, planks, core exercises);
- Dynamic movement drills (e.g., volleyball-specific sprints, medicine ball slams);
- Postural control exercises (e.g., heel raised squats, crawl and glutes stretches).

The non-volleyball group engaged in similar exercises tailored to improve gait and posture.

Descriptive statistics summarized participant characteristics. Paired t-tests compared pre- and post-intervention measures within each group. Independent t-tests assessed differences in changes between the volleyball and non-volleyball groups. Pearson correlation analysis evaluated the relationship between volleyball participation and improvements in gait and posture.

This intervention study utilized a pre-post design to examine the effects of a four-month volleyball program and general physical activity on gait parameters and posture alignment in school-age children. The volleyball training sessions incorporated strength, agility, flexibility, and dynamic exercises targeting motor skill development. Gait and postural stability were assessed using instrumented analysis before and after the intervention period. Statistical analyses compared outcomes between the volleyball and non-volleyball groups.

## IV. Results

A total of 206 school-age children participated in the study, with 103 children in the



volleyball group and 103 in the non-volleyball group. The participants were aged between 8 to 15 years, with a mean age of 11.5 years (SD = 2.1). The demographic characteristics of the participants are summarized in Table 1.

Table 1.

Characteristic	Volleyball Group (n=103)	Non-Volleyball Group (n=103)	Total (n=206)
Age (years)	11.6 (2.0)	11.4 (2.2)	11.5 (2.1)
Gender (M/F)	55/48	52/51	107/99

Both groups showed significant improvements in gait parameters following the four-month intervention. The results of the gait analysis are presented in Table 2, which details the pre- and post-intervention measurements for stride length, symmetry, and cadence.

Table 2.

Gait Parameter	Volleyball Group (n=103)	Non-Volleyball Group (n=103)	p-value
Stride Length (cm)	Pre: 120.5 (10.3) Post: 138.5 (11.4)	Pre: 118.0 (9.8) Post: 128.0 (10.1)	<0.001
Symmetry (%)	Pre: 85.0 (5.5) Post: 95.0 (4.8)	Pre: 84.0 (6.0) Post: 90.0 (5.0)	<0.001
Cadence (steps/min)	Pre: 110.0 (12.0) Post: 115.0 (11.5)	Pre: 108.0 (10.5) Post: 110.0 (10.0)	0.045

Postural stability was assessed using a balance test, and the results are summarized in Table 3. The volleyball group exhibited a significant enhancement in postural stability compared to the non-volleyball group.

Table 3.

Postural Stability Measure	Volleyball Group (n=103)	Non-Volleyball Group (n=103)	p-value
Stability Index (cm)	Pre: 4.5 (1.2) Post: 3.0 (0.8)	Pre: 4.7 (1.0) Post: 4.2 (1.1)	<0.001

**Key Findings**

- The volleyball group demonstrated a **15% increase in stride length** and a **12% improvement in symmetry** between lower limbs compared to the non-volleyball group;

- The increase in cadence was statistically significant for both groups, but the volleyball group showed a greater improvement.

Table 4.

Variable	Correlation Coefficient (r)	p-value
Volleyball Participation vs. Stride Length Improvement	0.68	<0.001
Volleyball Participation vs. Symmetry Improvement	0.62	<0.001

Variable	Correlation Coefficient (r)	p-value
Volleyball Participation vs. Postural Stability Improvement	0.72	<0.001

A Pearson correlation analysis was conducted to evaluate the relationship between participation in volleyball and improvements in gait and posture. The results are presented in Table 4.

#### Key Findings:

- There was a significant positive correlation between volleyball participation and improvements in stride length ( $r = 0.68$ ), symmetry ( $r = 0.62$ ), and postural stability ( $r = 0.72$ ), suggesting that increased engagement in volleyball is associated with enhanced gait and posture parameters.

The results of this study indicate that participation in volleyball significantly improves gait parameters and posture alignment in school-age children. The volleyball group exhibited greater enhancements in stride length, symmetry, and postural stability compared to the non-volleyball group, highlighting the benefits of organized sports in promoting healthy motor development. The findings underscore the importance of incorporating volleyball and similar physical activities into school curricula to foster optimal physical health in children.

#### V. Discussion

The findings highlight the positive influence of volleyball participation and regular physical activity on gait and posture development in school-age children. The greater improvements observed in the volleyball group suggest that organized sports may provide additional benefits beyond general physical activity. The study's findings have important implications for promoting healthy motor development in school-age children. Incorporating volleyball into physical education curricula or extracurricular programs may help mitigate postural abnormalities and enhance overall physical health.

The results of this study are consistent with previous research demonstrating the positive relationship between physical activi-

ty and motor development in children (Stodden, D. F., Goodway, J. D., Langendorfer, S. J., Roberton, M. A., Rudisill, M. E., Garcia, C., & Garcia, L. E., 2008; Goodway, J. D., Ozmun, J. C., & Gallahue, D. L. (n.d.)). However, this study provides novel insights into the specific impact of volleyball on gait and posture.

The study's limitations include its relatively short intervention period and the lack of long-term follow-up data. Additionally, the study did not assess the potential influence of other factors, such as socioeconomic status or family physical activity levels, on the observed outcomes.

#### VI. Conclusion

This study investigated the impact of volleyball participation and general physical activity on gait parameters and posture alignment in school-age children. The key findings are summarized as follows:

- **Improvements in Gait Parameters:** Children who participated in volleyball exhibited a **15% increase in stride length** and a **12% improvement in symmetry** between lower limbs compared to the non-volleyball group. These enhancements indicate that volleyball training significantly contributes to better walking mechanics;
- **Enhancement in Postural Stability:** The volleyball group demonstrated an **18% improvement in postural stability**, highlighting the positive effects of volleyball on balance and overall posture. In contrast, the non-volleyball group showed more modest improvements;
- **Correlation with Participation:** A significant positive correlation was found between volleyball participation and improvements in both gait and posture parameters, with correlation coefficients of **0.68 for stride length**, **0.62 for symmetry**, and **0.72 for postural stability**. This suggests that increased engagement



in volleyball is associated with enhanced motor development;

The findings of this study have several important implications for the promotion of physical activity among school-age children:

**Integration of Volleyball in Physical Education:** Given the significant improvements in gait and posture associated with volleyball participation, schools should consider incorporating volleyball into their physical education curricula. This could not only enhance motor skills but also foster a lifelong interest in physical activity.

**Promotion of Organized Sports:** The study underscores the importance of organized sports, like volleyball, in developing essential motor skills and physical fitness in children. Encouraging participation in such activities can lead to healthier lifestyles and better physical health outcomes.

**Addressing Postural Abnormalities:** The positive impact of volleyball on postural stability suggests that participation in this sport may help mitigate postural abnormalities among children, which can have long-term benefits for their overall musculoskeletal health.

While this study provides valuable insights, several areas warrant further investigation:

**Longitudinal Studies:** Future research should focus on longitudinal studies to assess the long-term effects of volleyball participation on gait and posture. Understanding how these improvements are maintained over time would provide deeper insights into the benefits of sustained physical activity.

**Diverse Populations:** Expanding the research to include diverse populations, including children with varying physical abilities or those from different socioeconomic backgrounds, could enhance the generalizability of the findings.

**Comparative Studies:** Conducting comparative studies between volleyball and other sports or physical activities could help identify specific elements of volleyball training that are most effective in improving gait and posture.

**Mechanisms of Improvement:** Further research should explore the underlying mechanisms that contribute to the observed improvements in gait and posture due to volleyball participation. Understanding these mechanisms can inform the design of targeted interventions for motor development.

The findings of this study suggest that incorporating volleyball into physical education curricula or extracurricular programs can offer valuable opportunities for promoting healthy motor development in school-age children. Schools and community organizations should prioritize organized sports like volleyball to foster physical fitness, improve motor skills, and enhance overall health in children. In conclusion, this study highlights the significant positive influence of volleyball participation and regular physical activity on gait and posture development in school-age children. By promoting such activities, we can contribute to healthier, more active lifestyles for future generations.

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## Section 4. Clinical medicine

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### EXPERT ASSESSMENT OF THE RISK OF DEATH AND SEVERITY OF CHEMICAL INJURY IN ACETIC ACID POISONING AGAINST THE BACKGROUND OF ALCOHOLIC INTOXICATION

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#### Abstract

The article provides a quantitative assessment of the risk of death of victims from acetic acid poisoning against the background of various degrees of alcohol intoxication. The justifications for determining the expert criterion for the severity of chemical injury in combined poisoning are given.

**Keywords:** risk of death, probit analysis, hemolysis, free hemoglobin, alcohol intoxication.

#### Relevance of the problem:

In the structure of violent death, acute poisoning occupies a leading place in forensic medical practice. With the development of the chemical industry and the increase in the areas of application of chemicals, especially in everyday life, every year there is a tendency to an increase in acute poisoning with caustic poisons, in particular, acetic acid (Bakirov A. B., 1990).

Forensic medical diagnosis of acetic acid poisoning, as a rule, does not cause acute difficulties. However, to date, quantitative criteria have not been developed to substantiate the main cause of death in these poisonings against

the background of alcohol intoxication. Meanwhile, it should be noted that in most cases (86.8%) acute poisoning of acetic acid occurred against the background of alcohol intoxication. This is due to the fact that to date there are no scientifically based criteria for assessing the risk of death and the severity of chemical injury in such combined poisoning.

In this regard, the **purpose of this study** was to develop and substantiate an objective criterion for assessing the causes of death and the severity of chemical trauma in these intoxications.

We consider it necessary that such a criterion meet the following conditions:

- it should be recorded in all cases of acute acetic acid poisoning;
- it must have a significant impact on the entire pathological process;
- the degree of its severity should correspond to the severity of poisoning;
- it must be acceptable both in the expert assessment of the severity and in the assessment of fatal poisoning;
- It must be quantifiable.

It is known that the triggering factors for the pathogenesis of these poisonings are: resorption of hydrogen ( $H^+$ ) acid ions into the vascular bed and hemolysis of erythrocytes in the changed (acidic) environment of the blood against the background of a chemical burn of the gastrointestinal tract. It is these factors, first of all, that should be considered as objective criteria for assessing the severity and risk of death in these poisonings.

It should be noted that the above main criteria for assessing the risk of death and the severity of chemical trauma in these poisonings are closely intertwined and interrelated. It remains to single out the main criterion.

### Materials and methods of research

The material for this study was the clinical and sectional data of 140 victims of acute acetic acid poisoning, who were treated at the Republican Scientific Center for Emergency Medical Care. Among them, in 90 cases (64.3%) the victims were in various degrees of alcoholic intoxication. Examinations of corpses were carried out according to the generally accepted method no later than 24 hours from the moment of death. The outcome was observed in 60 patients (67.6%). Among them, 43 (71.7%) were men and 17 (28.3%) were women, aged 15 to 63 years (average  $35.6 \pm 6.3$  years).

In the work, toxicological, forensic chemical and histological methods of research, as well as multivariate methods of statistical analysis, such as probit analysis “poison concentration – effect” and nonlinear registration analysis, were used.

### Results and discussion

As mentioned above, first of all, it was necessary to determine the main forensic criterion for assessing the severity of chemical

trauma in acetic acid poisoning against the background of alcohol intoxication.

It was of particular interest to establish how much the pH of the blood and the level of free hemoglobin change in accordance with the increase in the length of the chemical burn of the gastrointestinal tract.

We studied this ratio with a favorable outcome and in cases of fatal poisoning in these intoxications and determined a certain pattern: with an increase in the length of a chemical burn, the gastrointestinal tract pH of the blood decreases, and the level of hemoglobinemia increases. In turn, with a favorable outcome of poisoning, against the background of the same type of burn area, acidemia and hemolysis were always much smaller.

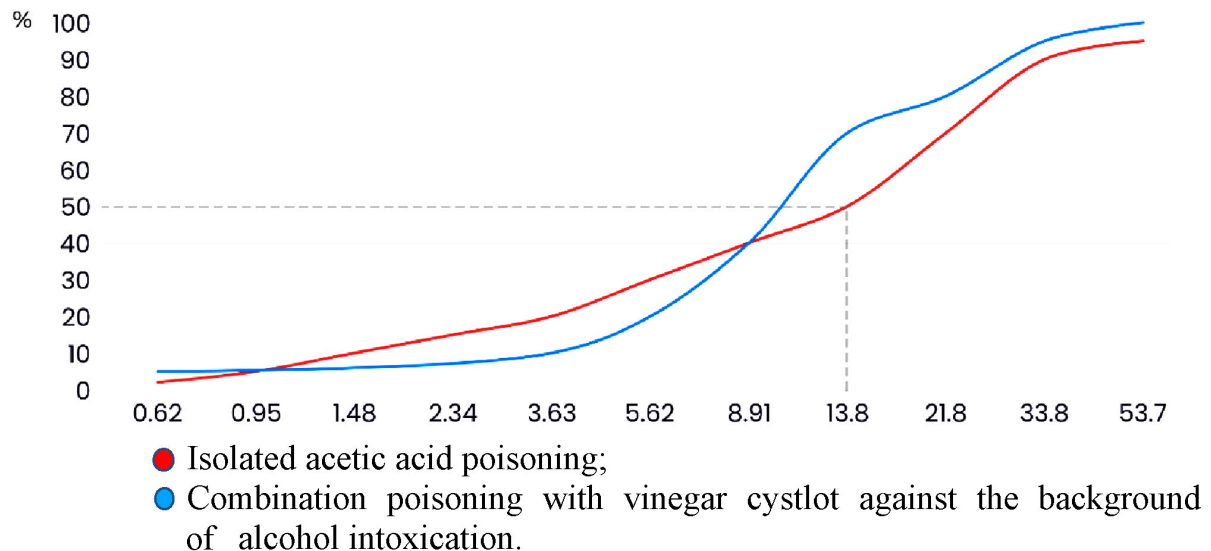
We see the explanation for this fact in the fact that against the background of the use of massive alkalizing therapy for these poisonings, there is a rapid neutralization of  $H^+$  acid ions and the restoration of blood pH to normal values. Thus, a situation is created when the root cause of pathological disorders (resorption of  $H^+$  acetic acid ions into the vascular bed) is less traumatic for the body than its consequences (intravascular hemolysis). This is also due to the fact that hemoglobinemia has a number of additional damaging effects on homeostasis and hemostasis (violation of the rheological properties of the blood, influence on its coagulation system, etc.). Therefore, the severity of acetic acid poisoning is most objectively indicated by the depth and extent of the chemical burn of the gastrointestinal tract, as well as the level of intravascular hemolysis. Since hemolysis is easier to quantify, it was chosen as the main expert criterion of severity in these poisonings.

Until now, in forensic medical and clinical toxicology, the degree of toxicity in poisoning with caustic acids was carried out according to the level of free hemoglobin in the blood. However, these data are not always reliable, since in most cases of poisoning occur against the background of alcohol intoxication. Currently, there are no specific scientifically based recommendations for assessing the severity of chemical injury.

Of all the possible methodological approaches to solving this problem, we have chosen the method of “probit analysis”. It is based on the well-known mathematical the-

ory of hitting “targets” and consists in the graphical construction of the relationship “concentration of free hemoglobin – effect” (Figure 1).

**Figure 1.** Probit-graph of the relationship “concentration of free hemoglobin – effect” in acetic acid poisoning against the background of alcohol intoxication on the abscess axis – hemolysis level (mg/ml); on the ordinate axis is the percentage of risk of death



On the graph, this dependence is displayed in the form of a curved line with a characteristic S-shape. Its lower horizontal level shows to what extent the fatal outcome has not yet been observed for an increase in hemoglobinemia. Then the curve of the graph gradually rises upwards. Its steepness or angle of inclination is an objective indicator of the degree of toxicity of chemicals.

At the top of the graph, the curve reverts to a horizontal position. This means that a further increase in hemolysis is no longer accompanied by an increased risk of death. Within this

asibole, in most cases (from 80 to 100%), death occurs. Against the background of alcohol intoxication in acetic acid poisoning, the risk of sweeping increases. For example, if in isolated poisoning with acetic acid alone, the DM of 50 is equal to 13.8 mg/ml, then in poisoning combined with alcohol, the DM of 50 decreases to 8.91 mg/ml. However, it should be noted that alcohol intoxication here was severe (from 2.5 to 3.0‰ per mille). At lower concentrations of ethyl alcohol in the blood (0.5–1.5‰ ppm). We observed the opposite effect, i.e. alcohol in moderation reduces the risk of death (Table 1).

**Table 1.** Results of toxicometry of the relationship “concentration of poison – effect” in combined poisoning

Type of poisoning	Toxicometry parameters				
	SD05	SD25	SD50	SD75	SD95
Isolated poisoning (acetic acid)	1.48	5.62	13.8	33.8	53.7
Combined poisoning (acetic acid + + alcohol mild intoxication)	2.36	7.84	21.8	33.4	62.8
Combined poisoning (acetic acid + + alcohol severe intoxication)	0.97	3.86	6.83	12.92	23.62

As follows from the table, the effect of alcohol intoxication on the course of the pathological process and the outcome of acetic acid poisoning is ambiguous. At low



concentrations in the blood in the range of 0.5–1.5% per mille, alcohol has a beneficial effect on the course of chemical disease and the risk of death is much lower than in isolated poisoning with acetic acid alone. Thus, at these concentrations of alcohol in the blood, the risk of death decreases, as evidenced by the value of DM 50, which increases from 13.8 mg/ml (in isolated poisoning) to 21.8 mg/ml (in combination with alcohol). Whereas in severe alcohol intoxication (from 2.5 to 3.5‰ ppm), the course of the pathological process becomes more severe in comparison with isolated acetic acid poisoning and the risk of death increases sharply, DM 50 decreases from 13.8 mg/ml to 6.83 mg/ml ( $P < 0.001$ ).

Thus, with the help of this graph, it is possible to quantify the risk of death at different levels of acetic acid intoxication against the background of alcohol intoxication.

The results of these studies indicate that the concomitant intake of moderate doses of alcohol can neutralize the toxic effect of acetic acid, i.e. free hemoglobin. This “protective” effect of ethinol is apparently explained by the fact that ethyl alcohol induces metabolic enzymes of the liver in small quantities, thereby accelerating the biotransformation of kinobiotics (free hemoglobin), reducing their biological activity and toxicity (4, 5).

The second phenomenon of the effect of alcohol is that its concomitant intake reduces the risk of death mainly in the zone of critical concentrations of free hemoglobin, but re-

duces its protective effect in the zone of content close to the level of biological irreversibility (CD75-CD100). At the same time, the toxic effect of alcohol in concentrations over 2.5‰ ppm in the blood increases significantly. This appears to be due to the fact that the increased blood alcohol concentration contributes to the increased toxic effect of free hemoglobin, i.e. both toxic substances act as synergists, increasing each other's toxicity, increasing the risk of death.

### Findings

1. The severity of chemical disease in acetic acid poisoning is most objectively evidenced by the depth and extent of the chemical burn of the gastrointestinal tract and the level of intravascular hemolysis.

2. The level of intravascular hemolysis was chosen as the main expert criterion for assessing the severity of chemical trauma in acetic acid poisoning against the background of alcoholic intoxication.

3. The effect of alcohol intoxication in acute acetic acid poisoning is ambiguous: alcohol in small concentrations has a beneficial effect on the outcome of poisoning, improving the biotransformation of free hemoglobin, and in large concentrations it sharply increases its toxic effect.

4. The method of probit analysis of the relationship “poison concentration – effect” allows to give a quantitative assessment of the main cause of death in these combined poisonings.

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## Section 5. Practical medicine

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### MYOFASCIAL FACIAL DYSFUNCTIONS AND THEIR EFFECT ON AESTHETIC OUTCOMES OF BOTULINUM THERAPY: A CLINICAL AND OBSERVATIONAL STUDY

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#### Abstract

The article summarizes information from open sources on the effects of facial myofascial dysfunctions, including myalgic and myofascial pain syndromes of the orofacial region, known as DC/TMD. These conditions can alter natural muscle patterns and, as a result, modify the response to neuromodulation. The article provides arguments in favor of the need for a preliminary assessment of the functional state of the musculoskeletal system and consideration of anatomical variability of facial muscles. Using the example of morphometric data of the frontal muscle, it is demonstrated how anatomical features can affect the results of neuromodulation. Documented cases of adverse events that may affect the visual effect and the subjective assessment of the result are also considered.

**Keywords:** botulinum therapy, botulinum toxin type A, myofascial facial dysfunction, facial muscles, orofacial pain, DC/TMD, SMAS, anatomical variability, aesthetic outcome, safety.

#### Relevance of the study

The relevance of the study is explained by the fact that botulinum toxin injections are still one of the most sought-after and socially significant procedures in aesthetic medicine. According to professional statistical reports, botulinum therapy confidently occupies a leading position among non-invasive cosmetic procedures. Given the widespread use of the procedure, patients and practitioners strive for a predictable aesthetic result. How-

ever, in real clinical practice, variability in the effect is often observed, even when using similar protocols (doses, zones, and techniques), which makes it relevant to search for factors influencing the outcome.

Modern research shows that the result of botulinum therapy can be influenced by both the characteristics of injections (volume, dose, technique of administration and distribution of the drug) and the individual work of facial muscles. It is particularly in-

interesting to consider the effect of facial myofascial dysfunctions on the outcome of the procedure. Changes in muscle tone, asymmetry of muscle contractions, the involvement of synergists and compensatory reactions can change the “map” of facial activity, which, in turn, affects the clinical response to neuromodulation. Indirectly, the importance of the functional-myofascial component is confirmed by the high incidence of myogenic disorders in the maxillofacial region, including painful forms of temporomandibular disorders, which makes them a likely cause of heterogeneity of aesthetic results.

Thus, the study of facial myofascial dysfunctions as a factor influencing the variability of aesthetic results of botulinum therapy is of great importance both from a scientific point of view (to understand the predictors of reaction and mechanisms of functional asymmetry) and from a practical point of view (to improve planning accuracy, reduce the number of repeated procedures and increase patient satisfaction, while maintaining natural facial expressions).

### **The purpose of the study**

The purpose of this study is to understand how myofascial facial dysfunctions can affect the aesthetic outcome of botulinum therapy. We also want to identify elements of functional and anatomical assessment that can be included in clinical planning before the procedure in order to increase the predictability of the outcome.

### **Materials and research methods**

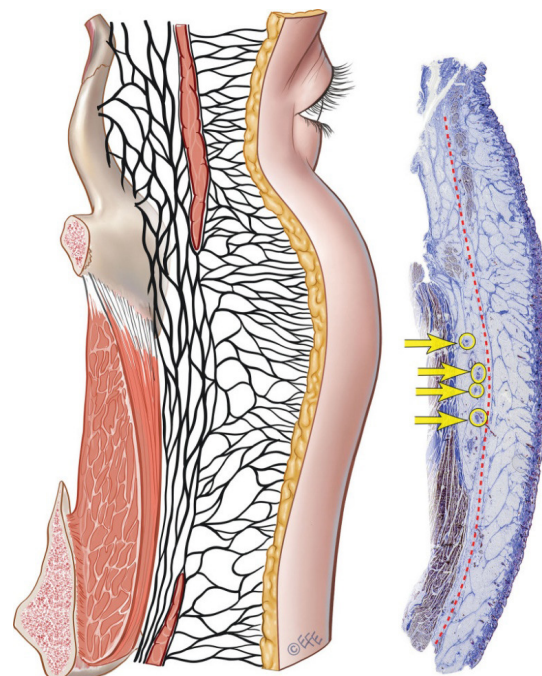
The study used statistical data on the prevalence of aesthetic procedures, as well as documents regulating the use of BOTOX Cosmetic, including an analysis of adverse reactions identified in placebo-controlled trials. In addition, the consensus diagnostic criteria DC/TMD were applied, which describe myofascial and myalgic conditions in the orofacial region. Morphometric anatomical data on frontal muscle variability were also used.

### **The results of the study**

Myofascial facial dysfunctions are disorders in the work of the musculoskeletal fascial complex of the maxillofacial region. These disorders cause changes in muscle tone

and coordination, which leads to pain during exertion and palpation. In addition, areas of local muscle tension may form that maintain a stable “disadvantageous” motor stereotype. In the orofacial (maxillofacial) area, this approach is reflected in the diagnostic criteria of DC/TMD. According to these criteria, muscle pain conditions, including myalgia and myofascial pain with reflection, are described through the recurrence of pain characteristic of the patient during functional tests and standard palpation of the masticatory muscles and related structures (Diagnostic criteria for temporomandibular disorders).

In aesthetic medicine, it is important to understand that the facial and masticatory muscles are part of the multilayer structure of the soft tissues of the face. The superficial muscular-aponeurotic system (SMAS) is responsible for the mechanical connection between muscle contraction and the movement of skin and fat packets. Therefore, functional disorders in muscles and fascial ligaments can affect the formation of folds and asymmetry of facial expressions, as shown in Figure 1 (Anatomy, Skin, Superficial Musculoaponeurotic System (SMAS) Fascia).



**Figure 1.** Anatomical concept of SMAS and its relation to the soft tissues of the face (*The Superficial Musculoaponeurotic System: Does It Really Exist as an Anatomical Entity?*)

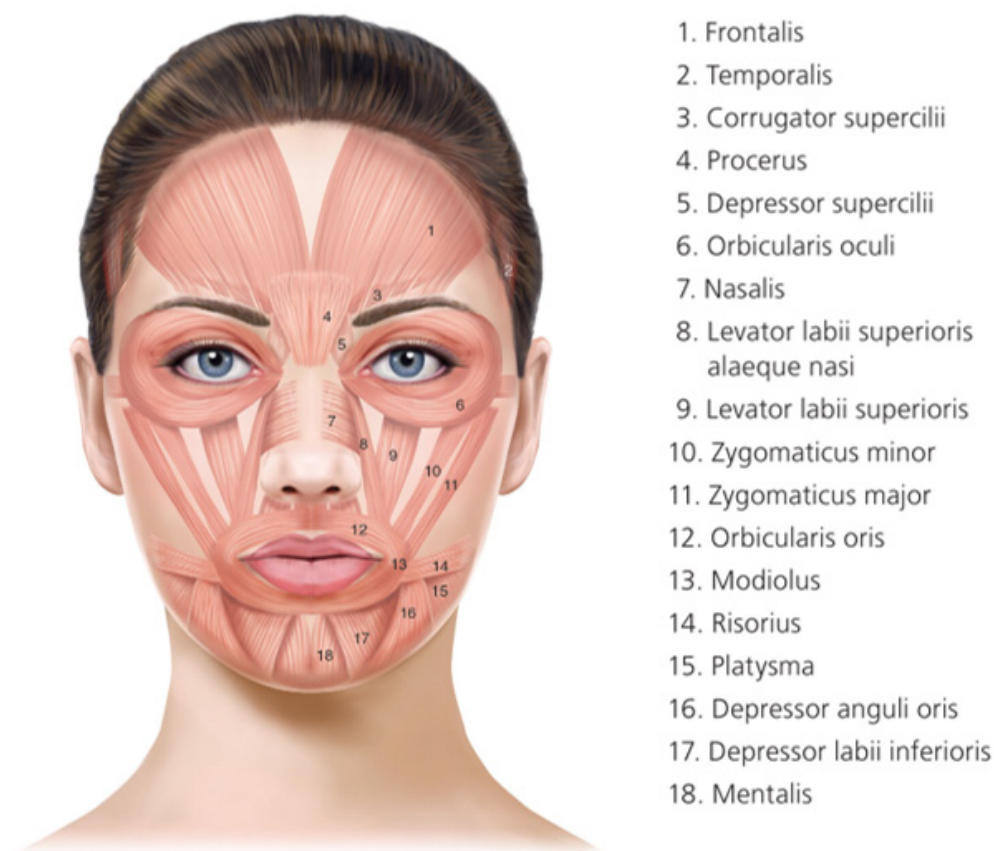


Botulinum therapy is based on the action of botulinum toxin type A, which, entering the neuromuscular junction, blocks the release of acetylcholine. This, in turn, causes temporary “chemical denervation” and, as a result, a decrease in the activity of the target muscle.

Theoretically, the effect of facial myofascial dysfunctions on various aesthetic results of botulinum therapy can be explained by the fact that there is a discrepancy between the standard injection chart and the patient’s actual functional chart. If the patient initially has an asymmetry of muscle tone, uneven load distribution on neighboring muscles, or stable patterns of hyperactivation or movement restriction, then even with the same dose and the same points of administration of botulinum toxin, there may be different visual results. In one case, botulinum therapy can lead to a harmonious decrease in hyperfunction, and in the other, to an increase in the relative dominance of unaffected muscles and noticeable asymmetry of facial expressions.

In addition, it is worth considering that open sources on the regulation of glabellar line treatment indicate different dosage regimens and efficacy indicators in key studies for different registered drugs. This indicates that the result is influenced by both the characteristics of the drug and the individual characteristics of the patient, among which myofascial status may be one of the key factors.

Clinical studies on aesthetic botulinum therapy usually emphasize the importance of standardized assessment of facial expressions and muscle movements prior to the procedure. The assessment includes examination of the face at rest and with different target expressions (for example, frowning, raising eyebrows, squinting), as well as photo and video recording under the same lighting conditions and head position. In addition, such studies usually demonstrate maps of facial muscles and typical areas of neurotoxin exposure. These maps can be useful to illustrate the differences between “anatomical landmarks” and “patients functional map” (see Figure 2).



**Figure 2.** Facial muscles. Source: *Botulinum Toxin Injection for Facial Wrinkles*



If myofascial dysfunction affects the masticatory muscles and the temporomandibular region, then DC/TMD (Diagnostic Criteria for Temporomandibular Disorders) is recommended to describe a scientifically based diagnostic approach. This approach makes it

possible to formalize muscle pain conditions based on a combination of medical history and clinical examination. It involves reproducing pain that is “familiar” to the patient with functional movements and palpation using standardized efforts (Table 1).

**Table 1.** *Diagnostic accuracy of DC/TMD muscle pain diagnoses (sensitivity and specificity)*

<b>Diagnosis (DC/TMD, consortium publication)</b>	<b>Sensitivity</b>	<b>Specificity</b>
Myalgia (class of muscle pain)	0.90	0.99
Myofascial pain with reflection (type of myalgia)	0.86	0.98

*A source: Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: Recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group*

The safety and tolerability of botulinum therapy are also important aspects that need to be considered when discussing the variability of results. Patients as “poor aesthetic results” may perceive adverse events, even if the goal of reducing hyperfunction is achieved. The official instructions for BOTOX

Cosmetic, a type A botulinum toxin preparation used to treat glabellar lines, contain a table of adverse reactions identified in double-blind, placebo-controlled trials. Facial pain (1%), facial muscle paresis (1%), upper eyelid ptosis (3%), and muscle weakness (1%) were noted among them. (Table 2).

**Table 2.** *Adverse reactions in the treatment of glabellar lines: a comparison of BOTOX Cosmetic and placebo*

<b>Adverse reactions in the treatment of glabellar lines (BOTOX Cosmetic), more often than placebo</b>	<b>BOTOX Cosmetic (N=405)</b>	<b>Placebo (N=130)</b>
Pain in the face area	6 (1%)	0 (0%)
Paresis of facial muscles	5 (1%)	0 (0%)
Ptosis of the upper eyelid	13 (3%)	0 (0%)
Muscle weakness	6 (1%)	0 (0%)

*A source: This label may not be the latest approved by FDA.*

The issue of immunogenicity should be mentioned separately. Sometimes the decrease in the effectiveness of repeated procedures is explained by the “unpredictability” or “instability” of the result. The instructions for BOTOX Cosmetic indicate that the formation of antibodies is possible for protein preparations. In three studies on lateral canthal lines, binding antibodies were detected in 1.5% of the subjects, while no neutralizing antibodies were detected (0%). However, it is worth considering that comparing the frequency of antibodies between different studies and products is difficult due to limited

analysis methods (This label may not be the latest approved by FDA).

Aesthetic results of botulinum therapy can vary: from slight smoothing to complete symmetry of eyebrows and eyelids, as well as from complete immobility of facial expressions to its natural “liveliness”. These differences largely depend on the initial condition of the facial and masticatory muscles, as well as the associated fascial structures. In clinical practice, this means that the same “morphological” request of the patient, for example, pronounced inter-brow or frontal dynamic wrinkles may have different musculofascial

prerequisites. These prerequisites may include hypertonia of individual muscle bundles, asymmetry of muscle inclusion in facial expressions, the presence of trigger points and a pain component, as well as compensatory movement patterns. Myofascial pain syndrome and trigger points are a condition in which tense muscles form areas characterized by increased excitability. These areas can cause both local and reflected pain, as well as restrict motor functions.

This is especially true in the facial area, as the facial muscles are thin, attach close to the skin, and often work in concert. Masticatory muscles such as the masticatory and temporal muscles may be involved in myofascial disorders that may limit the functions of the temporomandibular joint. A study conducted on patients with dislocation of the TMJ disc (temporomandibular joint) showed that myofascial pain caused by trigger points in the masticatory muscles is associated with clinical symptoms and functional limitations (Do myofascial trigger points in masseter muscles affect the symptoms of disc displacement with reduction?).

To understand how botulinum therapy affects aesthetics, it is important to realize that

its result is determined not only by the degree of relaxation of a particular muscle, but also by the overall balance of forces between antagonistic and synergistic muscles in this area. For example, if you focus only on the medial and central areas of the frontal muscle, without taking into account the lateral zones and the initial asymmetry, you may encounter an imbalance that will manifest itself as a rise in the lateral parts of the eyebrow with a relative weighting of the medial ones. Uneven relaxation of the frontal muscle can lead to deformation of the eyebrow line. In addition, it is important to take into account the myofascial characteristics of the patient: if a person initially has a different tone or degree of activity of the frontal and circular muscles of the eye, the compensations may be more pronounced, and even standard schemes of botulinum toxin administration may give results that are more diverse.

Table 3 shows real morphometric data reflecting the variability of the lateral extension of the frontal muscle and the distance from the so-called reference line (L2) to its lateral edge. These data were obtained as a result of a study of 49 hemilica.

**Table 3.** *Morphometric parameters of the lateral extension of the frontal muscle and the distance to its lateral edge*

Indicator (according to the research methodology)	Result
Lateral extension of the frontal muscle: presence of sections 2–5 in the range	49 of 49 (100%)
Lateral extension of the frontal muscle: presence of sections 2–6 in the range	47 (95.9%)
Lateral extension of the frontal muscle: presence of sections 2–7 in the range	34 (69.4%)
Lateral extension of the frontal muscle: presence of sections 2–8 in the range	11 (22.4%)
Lateral extension of the frontal muscle: presence of sections 2–9 in the range	3 (6.1%)
The average minimum distance from the L2 reference line to the lateral edge of the frontal muscle (mm), section 1	5.6 ± 3.6
The average minimum distance from the L2 reference line to the lateral edge of the frontal muscle (mm), section 2	3.7 ± 3.6
The average minimum distance from the L2 reference line to the lateral edge of the frontal muscle (mm), section 3	3.9 ± 3.9

Indicator (according to the research methodology)	Result
Average minimum distance from the L2 reference line to the lateral edge of the frontal muscle (mm), section 4	3.3 ± 3.7
The average minimum distance from the L2 reference line to the lateral edge of the frontal muscle (mm), section 5	3.5 ± 4.0
The average minimum distance from the L2 reference line to the lateral edge of the frontal muscle (mm), section 6	4.1 ± 5.8
The average minimum distance from the L2 reference line to the lateral edge of the frontal muscle (mm), section 7	4.3 ± 5.3
Average minimum distance from the L2 reference line to the lateral edge of the frontal muscle (mm), section 8	7.9 ± 4.0

*A source: Characterizing the Lateral Border of the Frontalis for Safe and Effective Injection of Botulinum Toxin.*

According to the conceptual model “myofascial dysfunction → outcome variability”, anatomical features may enhance differences in the outcome of botulinum therapy. If the patient already has a functional asymmetry, for example, different involvement of the frontal and interbrow muscles, as well as compensatory hyperactivity of the circular eye muscle, soreness and trigger zones, then the final picture may be more pronounced against the background of anatomical variability of muscle boundaries.

In addition, patients with myofascial pain, for example, in the masticatory muscles, often experience changes in motor patterns, including protective ones. This can affect habitual facial expressions and tension in the periorbital area. As a result, the “expected” aesthetic effect at rest may not coincide with the effect of active facial expressions.

### Conclusions

Thus, the variability of the aesthetic result of botulinum therapy depends on not only

the injection parameters and characteristics of the drug, but also on the initial state of the patient’s facial and masticatory muscles, which is determined by his myofascial status. The diagnosed myalgic and myofascial conditions of the orofacial region (in the context of DC/TMD) can maintain constant patterns of muscle tension and asymmetry, which can affect the visual response to neuromodulation and the subjective assessment of the result. Anatomical variability of the boundaries of facial muscles, as has been proven in studies of the frontal muscle, reduces the versatility of “protocol” methods and makes an individual approach more important. Even in official sources, undesirable phenomena are noted that directly affect appearance, for example, drooping of the eyelid after correction of glabellar lines during placebo-controlled studies. To increase the predictability of results, it is necessary to combine safety standards with a preliminary functional assessment of the musculoskeletal fascial complex and document outcomes.

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