



مقارنة تأثير المؤشرات الحيوية الإجهاد القلبي والإجهاد التأكسدي بين مرضى الشريان التاجي الحاد والمزمن

أمجد كريم علوان

قسم الكيمياء والكيمياء الحيوية/ كلية الطب، جامعة كربلاء كربلاء – العراق

الأستاذ الدكتور فاضل جواد الطعمة

أستاذ الكيمياء الحيوية الجزيئية والسريرية، قسم الكيمياء والكيمياء الحيوية، كلية الطب، جامعة كربلاء / كربلاء – العراق

الأستاذ الدكتور أحمد حسين الميالي

استشاري أمراض القلب / مركز قلب كربلاء.

amjadkaree@gmail.com

المستخلص:

مرض القلب الإقفاري، الذي يشار إليه أحيانًا باسم مرض الشريان التاجي، هو حالة لا تتلقى فيها عضلة القلب ما يكفي من تدفق الدم بسبب الشرايين التاجية المتضيق أو المسدودة، وعادة ما يكون ذلك نتيجة لتصلب الشرايين. يعتبر مرض الشريان التاجي المزمن أو المستقر ومرض الشريان التاجي الحاد أو غير المستقر حالتين مختلفتين. تعد متلازمة الشريان التاجي المزمنة، والتي تسمى غالبًا مرض القلب الإقفاري المستقر، تشخيصًا شائعًا للعديد من المرضى [2]. يحدث خلل البطاني وتصلب الشرايين في الشرايين التاجية بسبب دسليبيديا وعدم التوازن بين توليد أنواع الأكسجين التفاعلية (ROS) وأنظمة الدفاع المضادة للأكسدة، سواء الأنزيمية أو غير الأنزيمية. [3] أثبتت التحقيقات المتعددة أن مرضى مرض الشريان التاجي (CAD) لديهم خلل في التوازن بين مضادات الأكسدة ومضادات الأكسدة. حددت الأبحاث الحديثة الإجهاد التأكسدي كعامل خطر جديد لمرض الشريان التاجي (CAD)، والذي يؤثر على تشخيص المرضى، ونوعية الحياة، وفرص البقاء على قيد الحياة. يعد الإجهاد التأكسدي، الناجم عن نقص التروية، وخلل البطان الأيسر (LV)، وتنشيط الغدد الصم العصبية، سمة مميزة أخرى للعلاقة بين أمراض الأوعية الدموية وفشل القلب. من خلال توليد إشارات تضخمية، وموت الخلايا المبرمج، والنخر، تؤثر أنواع الأكسجين التفاعلية (ROS) بشدة على معالجة الكالسيوم في عضلة القلب، وتؤدي إلى عدم انتظام ضربات القلب، وتؤدي إلى تفاقم إعادة تشكيل القلب. يؤدي التنشيط العصبي الهرموني عبر SNS وRAAS، جنبًا إلى جنب مع زيادة التحميل المسبق واللاحق، إلى تعرض القلب لضغط تأكسدي أعلى. [5] تؤكد العديد من الدراسات على أهمية قيم الببتيد المدر للصوديوم في الدماغ (النوع B) في تحديد درجة فشل القلب ومدى تلف عضلة القلب. هنا أخذنا هذه العلامة الحيوية مع القدرة الكلية لمضادات الأكسدة (TAC) لشرح دورها في ACS [6] تؤدي سلاسة الخلايا العضلية إلى تخليق وإطلاق BNP، وهو ببتيد مكون من 32 حمضًا أمينيًا، معظمه من عضلة القلب البطينية. يبدو أن التأثيرات الفسيولوجية لـ BNP كلها إيجابية تقريبًا، تشبه تأثيرات الببتيد الأذيني المدر للصوديوم (ANP) وتشمل هذه التأثيرات توسع الأوعية المتوازن، وإدرار الصوديوم، وفتح الجهاز العصبي الودي ونظام الرينين أنجيوتنسين. -نظام المستقبلات الأدرينالية-أنجيوتنسين [7] (TAC). [يتناسب عكسيًا مع ACS، الذي يمثل أحد أنظمة الحماية ضد المؤكسدات. 8]. النتائج: تم زيادة المستوى المتوسط لـ BNP (pg/ml) وكان ذو دلالة إحصائية وانخفض TAC قيمة $P = 0.0001$ وذو دلالة إحصائية مقارنة بين المريض والسيطرة مع متوسط مستوى 15.56 ± 71.42 ، 0.46 ± 3.12 في ACS



ومتوسط المستوى 30.85 والمزمن والمستوى المتوسط 0.34 ± 3.21 أب في CAD المزمن والمستوى المتوسط 18.21 ± 55.45 ب، 0.68 ± 3.47 في السيطرة على التوالي. خاصية تشغيل المستقبل (ROC) لمرضى BNP ذوي ACS الأبيض لديهم حساسية = 0.97، خصوصية = 0.98. كانت مجموعة مرضى TAC لديهم حساسية = 0.97، ونوعية = 0.013، بينما في المؤشرات الحيوية CAD المزمنة كان لديهم أقل حساسية ونوعية. كان الهدف من دراستنا هو مقارنة تأثير المؤشرات الحيوية للإجهاد القلبي والإجهاد التأكسدي (TAC) و (ANP) بين المرضى الذين يعانون من ACS والذين يعانون من Cronk CAD. في المجموع، تم تقسيم 120 موضوعًا حسب تصميم دراسة الحالات والشواهد إلى 60 مريضًا وتم تصنيفهم على أنهم ACS و CAD مستقر للمقارنة مع 60 مجموعة صحية ظاهريًا. كانت جميع الفئات العمرية للمشاركين ضمن (41-70) سنة. تم استخدام مجموعة مراقبة ذات توزيع مماثل للجنس للمقارنة. تم قياس مستويات BNP و TAC باستخدام تقنية مقايضة الامتصاص المناعي المرتبط بالإنزيم (ELISA). الاستنتاج: أثبتت الدراسة أن هناك تأثير سلبي لكل من المؤشرات الحيوية للإجهاد القلبي والإجهاد التأكسدي على ACS أكبر من التأثير السلبي على مرض الشريان التاجي المزمن. **الكلمات المفتاحية:** الببتيد الناتريوتريك من النوع B، إجمالي قدرة مضادات الأكسدة (TAC)، ACS و CAD المستقر

Comparison the Effect of Vital Indicators Cardiac Stress and Oxidative Stress Between Acute and chronic Coronary Artery Disease Patients

Amjed Kareem Alwan1

Department of Chemistry and Biochemistry, College of Medicine, University of
Kerbala Kerbala – Iraq \

Prof. Dr. Fadhil Jawad Al-Tu'ma

Professor of Molecular and Clinical Biochemistry, Department of Chemistry and
Biochemistry, College of Medicine, University of Kerbala / Kerbala – Iraq.

Prof. Dr. Ahmed Hussein AL-Mayali

Consultant cardiologist / kerbala heart center

Abstract:

Ischemic heart disease, sometimes referred to as coronary artery disease, is a condition in which the heart muscle does not receive enough blood flow because of constricted or blocked coronary arteries, typically as a result of atherosclerosis.[1]. Chronic, or stable, coronary artery disease and acute, or unstable, coronary artery disease are distinct conditions. Chronic coronary syndrome, often called stable ischemic heart disease, is a common diagnosis for many patients [2]. Endothelial dysfunction and atherosclerosis of the coronary arteries are caused by dyslipidemia



and an imbalance between reactive oxygen species (ROS) generation and antioxidant defense systems, both enzymatic and nonenzymatic. [3] Multiple investigations have demonstrated that coronary artery disease (CAD) patients have an imbalance between antioxidants and prooxidants. Modern research has identified oxidative stress as a novel risk factor for coronary artery disease (CAD), which impacts patients' prognosis, quality of life, and chances of survival.[4] Oxidative stress, induced by ischemia, malfunction of the left ventricle (LV), and neuroendocrine activation, is another hallmark of the relationship between vascular disease and heart failure. By generating hypertrophic signaling, apoptosis, and necrosis, reactive oxygen species (ROS) severely impact myocardial calcium handling, lead to arrhythmias, and exacerbate cardiac remodeling. Neurohumoral activation via the SNS and RAAS, together with increased pre- and after-load, causes the heart to undergo higher oxidative stress. [5] Many studies emphasize the importance of Brain (B-type) natriuretic peptide values in determining the degree of heart failure and the extent of myocardial fibrosis Here we took this biomarker with the Total antioxidant capacity (TAC) to explain their role in ACS [6]. Myocyte strain triggers the synthesis and release of BNP, a 32-amino acid peptide, mostly from the ventricular myocardium. It appears that the physiological effects of BNP are nearly all positive, similar to those of atrial natriuretic peptide (ANP). These effects include balanced vasodilation, natriuresis, and suppression of the sympathetic nervous system and the renin-angiotensin system.-adrenoceptor-angiotensin system [7].(TAC) is inversely proportional to ACS, which represents one of the protection systems against oxidants[8]. Results: the mean level of BNP (pg/ml) was increased and statically significant and TAC was decreased (P-value=0.0001) and statically significant as compared between patient and control with mean level of 71.42 ± 15.56 , 3.12 ± 0.46 in ACS and mean level of 55.45 ± 18.21 b, 3.21 ± 0.34 ab in Chronic CAD and mean level of 30.85 ± 18.21 3.47 ± 0.68 in control respectively .

Receiver operating characteristic (ROC) for BNP patients white ACS had sensitivity= 0.97, Specificity =0.98 . TAC patients group had sensitivity= 0.97, Specificity =0.013, while in Chronic CAD Vital Indicators had the least Sensitivity and Specificity. The aim of our study was to compare the effect of vital indicators cardiac stress and oxidative stress ,TAC and (ANP) between patients with ACS and those with Cronk CAD. In total, 120 subjects as case -control study design were divided to 60 patients were categorized as ACS and stable CAD to compare with 60 apparently healthy group. All age range of participants was within (41-70) years old. A control group of similar sex distribution was used for comparison. Levels of BNP and TAC were measured using an enzyme linked immune sorbent assay (ELISA) technique. As conclusion: The study proved that there is a greater and



negative effect of both vital indicators of cardiac stress and oxidative stress on ACS than that of the negative effect on chronic CAD.

Keywords: B-type natriuretic peptide, Total antioxidant capacity (TAC) , ACS and stable CAD

Introduction

Statistically significant associations between oxidative stress and diseases affecting the cardiovascular system. Atherosclerosis, endothelial dysfunction, and ischemic heart disease are all conditions that have been the subject of substantial investigation into the potential involvement of oxidative stress. ACS comprises the largest proportion of cardiovascular diseases (CVDs) and accounts for more than one third of all mortalities worldwide [9]. Risk factors include hypertension, cigarette smoking, type 2 diabetes mellitus, increased cholesterol concentration and obesity [10].

Atherosclerosis is the primary cause of atherosclerotic coronary syndrome (ACS). It is accompanied by various pathological events, such as dysfunction of the endothelial cells, enhanced immunological responses (both innate and adaptive), vascular smooth muscle cell proliferation, and extracellular matrix remodeling [11].

Lipid peroxidation has the potential to cause damage, according to some reports. This is due to their capacity to form protein and DNA adducts through reactions with nucleophile chemicals, independent of metabolic activation by inflammation and vascular dysfunction mediators [12]. In contrast, enzymatic and non-enzymatic antioxidant systems are two broad categories of antioxidant mechanisms [13]. Enzymes such as catalase, glutathione peroxidase (GPx), superoxide dismutase (SOD), and glutathione reductase (GR) are antioxidants; non-enzymatic antioxidants include glutathione (GSH), vitamins A, E, and C, and uric acid [14]. Consequently, the ATC was used in this investigation because it is directly proportional to the displayed antioxidant values and inversely related to the antioxidants themselves. Acute coronary syndrome and coronary artery disease have the same risk factors. However, because ACS is so deadly, we will devote our attention to it. We will discuss its pathophysiology and mechanism, as well as compare and contrast risk factors, heart attack risk factors, and antioxidants in hard aquatic fish. In response to cardiac stress, the body releases pro-brain-type natriuretic peptide (pro-BNP), which causes fluid retention and vasodilation. Hormones are released in reaction to changes in heart pressure, which might be a useful signal for assessing heart-related health problems [15], particularly in individuals with acute coronary syndrome [16].]. This means that measuring the level of this hormone is crucial for making medical



decisions to save patients when symptoms of ACS emerge [17]. A patient's probable left ventricular dysfunction could be better diagnosed with the use of BNP level estimation in human blood [18].

Aims:

The present study Aims to compare the effect of vital indicators cardiac stress and oxidative stress ,TAC ANP and) CK-MB relative index between patients with ACS and those with stable CAD.

Materials and Methods:

Sixty patients were classified as ACS to compare with sixty individuals who appeared to be in a healthy group out of a total of 120 subjects in this case-control study. The age range of the participants was from forty-one to seventy. To ensure fair comparison, a control group with a similar distribution of sexes was utilized. An enzyme-linked immune sorbent assay (ELISA) method was used to determine the levels of BNP and TAC.

Results:

Table 1 demonstrates a significant increase in the mean level of BNP (pg/ml) and a significant decrease in TAC when comparing patients to controls. The mean levels were 71.42 ± 15.56 and 3.12 ± 0.46 in ACS, 55.45 ± 18.21 and 3.21 ± 0.34 in Chronic CAD, and 30.85 ± 18.21 and 3.47 ± 0.68 in controls, respectively.

Receiver operating characteristic (ROC) for BNP patients white ACS had (AUC = 0.997, 95%CI = 0.991-1.000, sensitivity= 0.97, Specificity =0.98, Cut-off point =42.22) while TAC patients group had (AUC = 0.322, 95%CI = 0.214-0.430, sensitivity= 0.97, Specificity =0.013, Cut-off point =2.74) while Receiver operating characteristic (ROC) in Chronic CAD had the least Sensitivity and Specificity.



Table (1): Comparison mean level of BNP and TAC between patient and control

Groups	BNP (pg/ml)	TAC (U/ml)	P-value
ACS	71.42±15.56 a	3.12±0.46 a	0.0001[S]
Chronic CAD	55.45 ±18.21 b	3.21±0.34 ab	0.0001[S]
control	30.85±18.21 c	3.47±0.68 b	0.011[S]
Using the Post Hoc test means having the different letters in the same column differed significantly. ** (P≤0.01).			

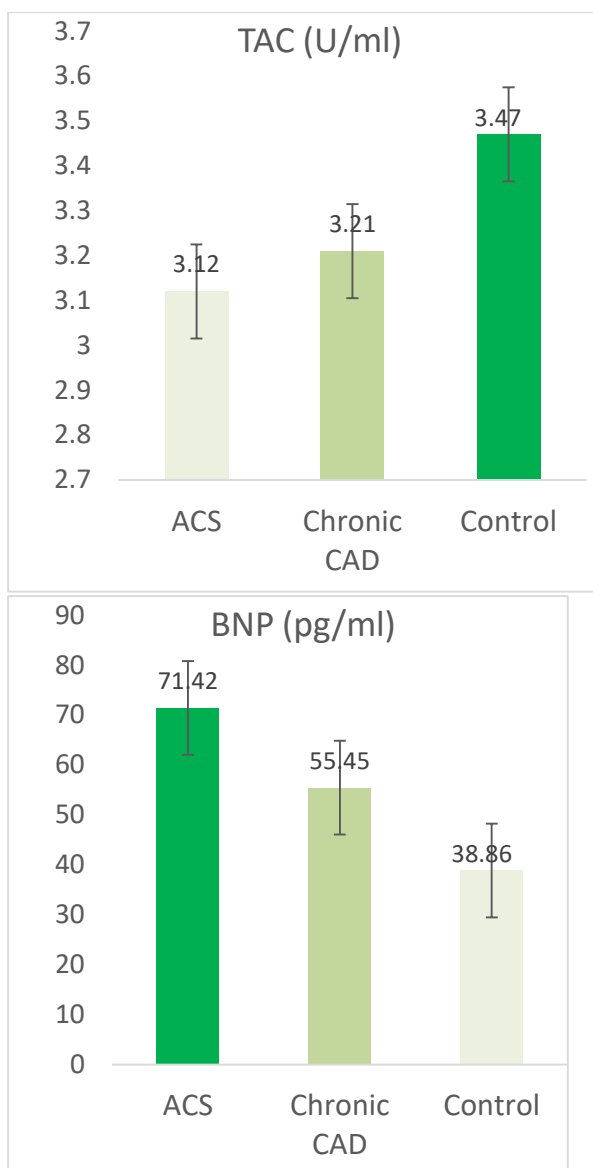


Fig.1: Comparison mean level of BNP and TAC between patient and control

The CK-MB relative index used to confirm the degree of myocardial damage or not, and the severity of this index, if it reflects the extent of myocardial damage. CK-MB relative index was highest at the age of 60-70 among other age groups and lowest at the age of 40-50 age group 60 -70 among the CAD was higher than that of the ACS, and all of them had significant statistical significance with a P-Value of 0.001. Figure 2 CK-MB relative index was highest at the obese patients among other BMI group and lowest at the normal weight group and all of them had significant statistical significance with a P-Value of 0.001 Figure 3

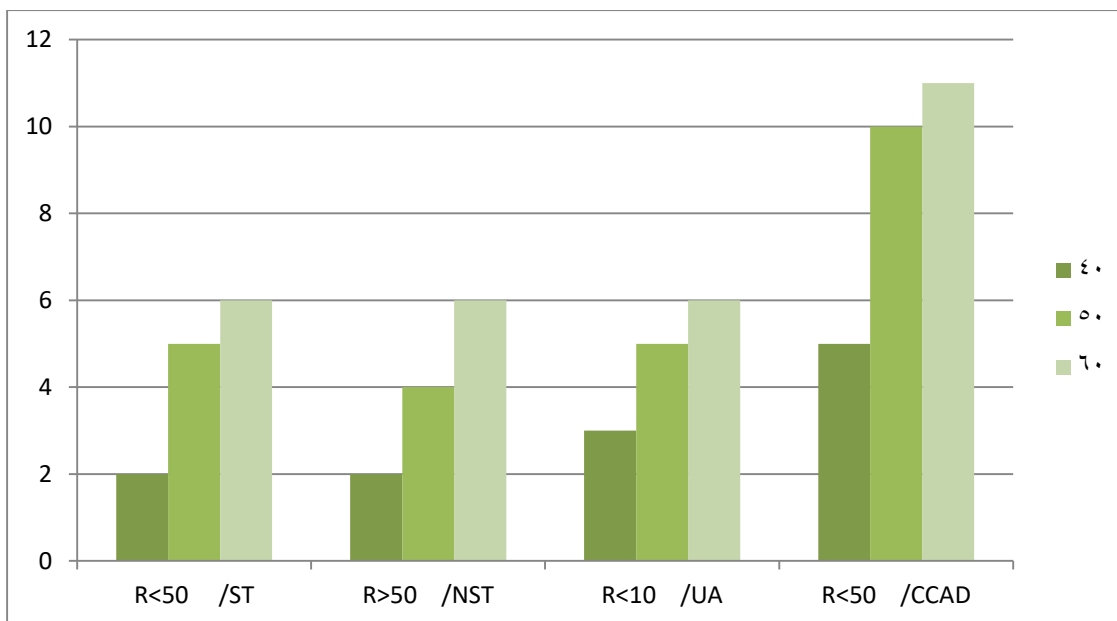


Fig.2: Comparison mean level of CK-MB relative index patient in deferent age groups

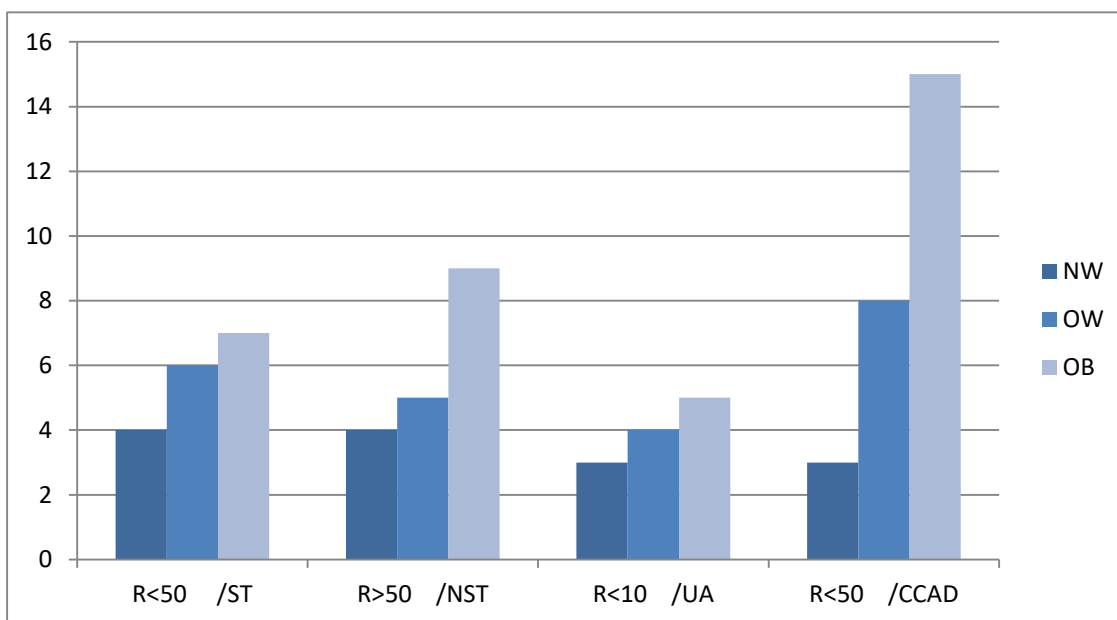


Fig.3: Comparison mean level of CK-MB relative index patient in deferent BMI group



Table2: AUC, optimal threshold, sensitivity, and specificity of BNP and TAC obtained by ROC curve in patients with ACS.

	Parameter s	Cut- off	Sensitivit y	Specificit y	AUC	P- value	95% CL	
ACS	BNP(pg/ml)	42.2 2	0.97	0.98	0.99 7	0.000 1	0.99 1	1.00 0
	TAC (U/ml)	2.74	0.94	0.13	0.32 2	0.004	0.21 4	0.43 0
Chronic CAD	BNP(pg/ml)	41.0 6	0.98	0.65	0.89 6	0.000 1	0.82 4	0.96 4
	TAC (U/ml)	2.96	0.96	0.24	0.35 8	0.038	0.24 4	0.47 3

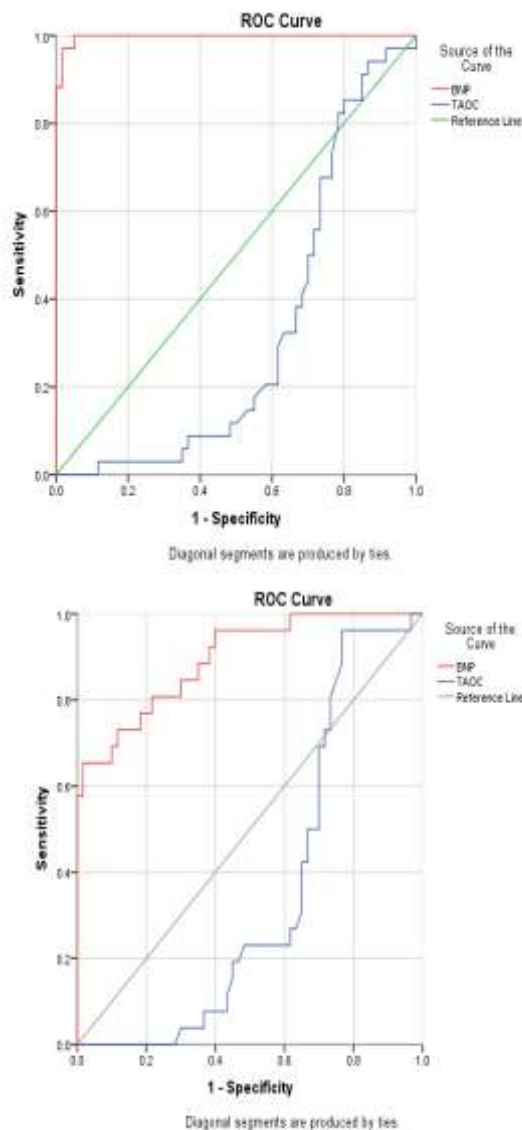


Figure (3): Receiver Operating Characteristic (ROC) curve of serum BNP and TAC levels as discriminators of patients with ACS.

Desiccation

The discussion focuses on the comparison of ACS with Control and Cronk CAD patients, highlighting the rise of BNP and the decline of TAC.

Comparison mean level of BNP and TAC between patient and control



The BNP concentration was remarkably higher (P-value=0.0001) in ACS patients(51.40 ± 12.97) than healthy group (30.85 ± 18.21) respectively.

A signal is generated when the heart is exercised after exposure to an ACS branch, as stated by Sawatani, Shirakabe et al. 2023. BNP Here is an analysis of the points made below:

BNP is released when the heart needs to work harder, leading to fluid retention and the widening of blood vessels. Thus, the hormonal response to changes in heart pressure, especially in patients with ACS, can serve as a valuable indicator for assessing heart-related health issues. [19].

The level of B-type natriuretic peptide (BNP) experiences a swift rise within the first 24 hours after a heart attack, and then tends to level off. It is important to mention that patients who have a significant infarct might go through a subsequent peak approximately 5 days later, which could potentially indicate the ongoing remodeling process. [20].

The study uncovered a decrease in antioxidant capacity and a decline in the functionality of the antioxidative systems when compared to the healthy control group. Therefore, the use of external antioxidants may offer therapeutic benefits in reducing oxidative stress in these individuals. However, it is important to conduct a thorough investigation into other important pathways involved in the development of atherosclerosis, particularly those associated with markers of inflammation. [21].

Given the significant correlation between GPx and TAC and their decreased levels in ACS diseases, because they have the same mechanism of action as antioxidants, they are included in the discussion here.

The results of the study show that individuals diagnosed with ACS exhibited decreased TAC activity. Based on a study conducted by Bastani, Rajabi et al., it was found that the levels of erythrocyte GPx decrease in comparison to those of healthy controls. The patient groups showed a connection between decreased erythrocyte GPx and TAC activity, and the occurrence of induced oxidative conditions. This led to a notable increase in oxidative stress and a greater susceptibility of the erythrocyte membrane to this oxidant state. [22].



Based on a previous study, it has been observed that the level of GPx may be increased in response to a modification in oxidative stress during ACS [23].

Comparison mean level of BNP and TAC among patient groups

This study seeks to offer insights into the relationship between B-type natriuretic peptide (BNP), total antioxidant capacity (TAC), and the oxidative status of affected patients. The results A study conducted on patients with coronary artery disease (CAD) indicates that the chronic form of the disease is more prone to oxidative stress when compared to the acute form. This discovery emphasizes the significance of managing oxidative stress in individuals diagnosed with acute coronary syndrome (ACS). There is a significant vulnerability of the erythrocyte membrane in both acute coronary syndrome (ACS) and chronic coronary artery disease (CAD) patients. [24]. Therefore, the use of external antioxidants may provide promising therapeutic benefits in reducing the level of oxidants in these individuals [25]. Thus, the utilization of external antioxidants may offer promising therapeutic advantages in decreasing the level of oxidants in these individuals. [26].]. However, it is important to thoroughly investigate other important pathways involved in the development of atherosclerosis, especially those associated with indicators of inflammation [27].

Comparison mean level of CK-MB relative index among patient groups

According to the study, SEMI had the highest CK-MB relative index % of all heart disorders since it represents the most damage leading to elevated creatinine, which denotes the existence of a full infarction as shown by the ST wave. This was in line with other studies that addressed a greater creatinine rate during any given NSEMI. Because there was no absence of ischemia that resulted in these crises, rates of both stable and unstable angina were lower because there was no discernible loss of heart tissue. [28].

When the ratio between the two myocardial infarction sections was examined, it was shown that ST is more common than NSEMI. It was also discovered that, on average, males with SEMI are older—66 years old on average—than men with Non-ST, who are 60 years old on average.

This study findings indicate a correlation between longer duration and lower CK-MB relative index %. Interestingly, this study observed that several cases with normal CK levels exhibited a higher index, particularly in the SA and UA groups, suggesting a potential heightened sensitivity to AMI. An analysis was conducted on



the hospital course of consecutive patients who were admitted with suspected myocardial infarction. The aim was to investigate whether patients who had normal serum creatine kinase (CK) levels but elevated MB isoenzyme fractions had experienced clinically significant events. The study involved a total of 340 patients, divided into three groups. The first group consisted of 232 patients with normal CK levels (182 ± 44 IU) and normal MB percentages. The second group included 68 patients with elevated CK levels (1195 ± 178 IU) and corresponding elevated MB percentages (10.5 ± 0.6). The third group comprised 40 patients with normal CK levels (96 ± 7 IU) but elevated MB percentages (9.6 ± 0.5). Patients with macroinfarction tended to be older and had a higher incidence of congestive heart failure. Additionally, they experienced a higher rate of in-hospital mortality and required more extensive monitoring and treatment. Given the elevated risk associated with macroinfarction patients, it is imperative to provide them with proactive treatment and additional testing.. [29].

Several studies have examined the impact of neurohormonal activation on patients who have experienced a myocardial infarction (MI). Another peak, approximately five days later, may be observed in patients with a significant infarct, suggesting the occurrence of the remodeling process. When evaluated 1-7 days following MI, an elevated BNP level suggests a potential risk of left ventricular dysfunction in patients [30].

This study investigated BNP readings following a myocardial infarction after a few days, while our study only measured it after one day. Nevertheless, BNP values showed a greater increase in myocardial infarctions compared to angina, prompting us to conduct more extensive examinations and employ catheters. Accurate assessment of arterial damage through diagnostic testing It seems that this correlation is reinforced by conducting comprehensive studies on it, which involve monitoring other flip enzymes and observing the parameters over a longer period of time. STEMI exhibits elevated BNP levels and a greater kinase index compared to NSTEMI [31].

The study showed a professional observation of BNP-TAC inverse association. Modern study shows a substantial link between TAC and GPX. A shortage in antioxidants likely caused the heart's stress to address free radical oxidative stress and its effects on lipid peroxidation and endothelial dysfunction. Thus, stress-induced cardiac muscle injury releases BNP levels that reflect antioxidant depletion [32].

The CK-MB relative index also indicates myocardial destruction, with the severity of this index reflecting the extent of muscle damage in complete myocardial



infarction. A ROC curve was generated, showcasing exceptional sensitivity and privacy values. The calculation for the area under the curve for the BNP with the TAC was also performed. It is frequently used in research to predict or monitor the progress of patients with ACS.

Conclusion

The study compare the effect of vital indicators cardiac stress and oxidative stress , between patients with ACS and those with stable CAD ,the greater and negative effect of both vital indicators on ACS is greater than that of the negative effect on chronic CAD ,The CK-MB relative index reflects the extent of muscle destruction in complete myocardial infarction.

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