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Assessment the Potential Biomarkers before and after Coronary Intervention

A Thesis

Submitted to the Council of the College of Medicine / University of Kerbala in Partial Fulfillment of the Requirements for the Degree of Master in Clinical Chemistry

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صدق الله العلي العظيم

الشعراء : اية ٨٩

Supervisor Certification

We certify that this thesis **"Assessment the Potential Biomarkers before and after Coronary Intervention "** was prepared under our supervision at the Department of Biochemistry, College of Medicine /University of Kerbela, in a partial fulfillment of the requirement for the degree of Master in Clinical Chemistry.

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We, the examining committee, certify that we have read this thesis entitled **"Assessment the Potential Biomarkers before and after Coronary Intervention "** and have examined the student (**Rasha Mohammed Sharmookh**) in its contents. In our opinion, it meets the standards for the award of the degree of "higher master" in the science of clinical chemistry.

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Dedication

To the one who is near me at all times, Fatima Al-Zahra.

To the dearest to my heart, my father, may God have mercy on him, the man who raised me well.

To my mother, who came forward thanks to her prayers.

To my dear brothers and sisters and their children.

To My supportive brother, Riyadh.

I Dedicate this work with my love and gratitude..

Rasha

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Rasha

Summary

Background: The etiology of periprocedural myocardial injury and type 4a myocardial infarction (type 4a MI) are multifactorial and may result from percutaneous coronary intervention (PCI) related events or complications. Reperfusion following myocardial ischemia may lead to accelerated myocardial injury and worsening clinical outcomes. One of the most important pathological mechanisms in reperfusion injury is oxidative stress, which is the imbalance between the antioxidant system and the excessive production of reactive oxygen species (ROS), leading to the toxic accumulation of ROS. Ischemia modified albumin (IMA) has also been shown to be elevated in patients after PCI as a result of ischemia-reperfusion injury. The aims are to study the role of biomarkers IMA and Chitenase 3 like protein 1 (CHI3L1) in the complications and consequences after PCI in the coronary artery disease.

Methods: A case control study was carried out at the Karbala Center for Heart Diseases and Surgery and Imam Al – Hassan Al Mujtaba teaching hospital in Kerbala city. The present study involved 120 participants, ranging in age from (29- 84) years. (72) of them underwent elective PCI and (48) underwent diagnostic catheter angiography (CA) serving as a control group. Serum biomarkers level was measured, IMA and CHI3L1 levels were measured using ELISA technique.; Measurement of Lipid profile levels in Human serum was performed using Spectrophotometric Technique.

Results: Results showed that there was a trend of increasing average post-procedure IMA levels with higher Angiographic Lesion Complexity Scores. In Score 0 (absent of complexity) the mean IMA level was (172.1±122.3), Score 1 was (138.0±66.0), Score 2 was (214.4±119.1) and in Score 3 (most complex) IMA level was (530.7±246.6). Post- procedure IMA has a higher sensitivity (84.6%) compared to Pre- procedure IMA (58.6%). This means

post- procedure IMA is better at correctly identifying patients who have complex PCI. Both lesion length groups showed an increase in IMA levels following PCI. Lesion length < 30mm: Pre-procedure mean was (167.8±63.2), post- procedure level mean was (251.1±117.9), while Lesion length ≥ 30mm: Pre-procedure mean was (175.7±58.9), post-procedure mean was (296.3±129.1), the increase appears to be greater for longer lesions (≥ 30mm). In contrast to IMA, the trend for CHI3L1 was opposite., Pre-procedure IMA levels in case of Single vessel was (169.5±63.6), and the post-procedure level was (273.4±124.3) While in Single vessel with bifurcation, the Pre- procedure IMA level was (154.5±60.2), and post-procedure IMA was (335.5±166.2). The increase appears to be larger in the group with bifurcation, while might be reflect the degree of the complexity. For CHI3L1 the trend shown that in both groups it was decrease after PCI.

In the case of Multi-vessel with bifurcation, the pre- procedure IMA was (190.8±11.8), and the Post- procedure IMA was (332.7±83.4). The increase appears to be similar in both groups, despite the presence of a bifurcation. IMA levels were shown significant Differences when compared to the Pre & Post procedure level in multi-vessel PCI, and a significant difference when compared the Pre & Post procedure level in multi-vessel with bifurcation. The trend for CHI3L1 was markedly different between the two groups and showed a general decreased. Both Pre- procedure IMA and Post- procedure IMA have AUC values around 60%, indicating a moderate ability to distinguish between simple and complex PCI cases.

Conclusion: IMA, along with other clinical factors, could be used to refine risk stratification for patients undergoing procedures, particularly those with complexity expected. The relationship between angiographic lesion complexity, lesion length, number of vessels with bifurcation, and these biomarkers, researchers can develop better strategies to manage ischemia during procedures and potentially improve patient care. IMA levels

could be used as a marker to assess the degree of ischemia experienced during PCI, particularly in patients with bifurcations.

List of Abbreviations	
Abbreviations	Definition
AC index	Atherogenic Coefficient Index
ACS	Acute Coronary Syndrome
AIP	Atherogenic Index of Plasma
AMI	Acute Myocardial Infarction
BMI	Body Mass Index
CA	Catheter Angiography
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
cCAD	Complex Coronary Artery Disease
CCS	Chronic Coronary Syndrome
CHI3L1	Chitinase-3 Like-Protein-1
C-index	Cholesterol Index
CLPs	Chitinase-Like Proteins
cTn	Cardiac Troponin
CTO	Chronic Total Occlusion
DAP	Dose Area Product
DAPT	Dual Antiplatelet Therapy
DM	Diabetes Mellitus
ECG	Electrocardiogram
EF	Ejection Fraction
ESC/ACCF/AHA/ WHF	Comprising the European Society of Cardiology, American College of Cardiology Foundation, American Heart Association, and World Heart Foundation
HDL	High-Density Lipoprotein
HF	Heart Failure
HSA	Human Serum Albumin

hs-cTn	High Sensitive Cardiac Troponin
IHD	Ischemic Heart Disease
IMA	Ischemia Modified Albumin
K	Kerma
LAD	Left Anterior Descending
LBBB	Left Bundle Branch Block
LDL	Low-Density Lipoprotein
MACE	Majer Adverce Cardiac Event
MB	Main Branches
MI	Myocardial Infarction
MPG	Myocardial Perfusion Grade
NSTEMI	Non-ST-Segment Elevation Myocardial Infarction
NTS	N-Terminal Sequence
PCI	Percutaneous Coronary Intervention
PTCA	Percutaneous Transluminal Coronary Angioplasty
ROC	Receiver Operating Curve
ROS	Reactive Oxygen Species
SB	Side Branch
SD	Standard Deviation
STEMI	ST-Segment Elevation Myocardial Infarction
TG	Triglycerides
TIMI	Thrombolysis In Myocardial Infraction
Total K	Total Kerma
Type 4a MI	Type 4a Myocardial Infarction
UA	Unstable Angina
UPLMT	Unprotected Left Main Trunk

Chapter One

Introduction

&

Literature Review

1. Introduction & Literature Review

1.1. Introduction

1.1.1 Ischemic heart disease

Ischemic heart disease (IHD) is a leading cause of death and disability worldwide. In 2017, IHD affected around 126 million people globally (1655 per 100,000), which was estimated to be 1.72% of the world's population.(Khan et al., 2020)

IHD may also be called cardiac ischemia or ischemic cardiomyopathy. Ischemia is defined as inadequate blood supply (circulation) to a local area due to blockage of the blood vessels supplying the area. Ischemic means that an organ (e.g., the heart) is not getting enough blood and oxygen. IHD, also called coronary heart disease or coronary artery disease (CAD), is the term given to heart problems caused by narrowed heart (coronary) arteries that supply blood to the heart muscle. Although the narrowing can be caused by a blood clot or by constriction of the blood vessel, most often it is caused by buildup of plaque, called atherosclerosis.(Alisherovich, 2024)

In this context, the "modern" cardiology focuses much of its attention on the study of epicardial atheromatous plaque, its etiology, its prevention and its diagnostic and therapeutic interpretation. (Severino et al., 2020b) As early as the 1970s, the effects of progressive narrowing, due to a stenosis, on coronary flow, at rest and at maximum levels, have been described. In fact, a reduction in the diameter of a coronary artery ≥50% limits its maximum vasodilatory capacity, while a reduction ≥85% determines a reduction in flow, even at rest. (Fedele et al., 2013)

Currently, basic, translational, and clinical data have provided a massive amount of information about the etiology of myocardial ischemia, it is

necessary to overcome the concept that IHD is always an atherosclerotic disease synonym. (Severino et al., 2020a)

In the coronary tree, the proximal section is represented by epicardial coronary arteries, with diameters ranging from 250 μm to 2–5 mm(Fedele et al., 2013). These vessels have a capacitance function and offer merely a tiny contribution to coronary vascular resistance under normal conditions. Epicardial arteries are responsive to flow dependent dilatation and are subjected to shear stress that vary every heartbeat, during the phasicity of coronary blood flow .(Severino et al., 2020a)

When an atherosclerotic plaque obstructs over 70% of the luminal cross-sectional area with 50% coronary diameter reduction, it increases the proximal resistance significantly and decreases distal coronary perfusion pressure. In this situation, autoregulation is able to maintain basal coronary blood flow, but the dilator reserve is compromised(Severino et al., 2020a). This may lead to a non-symptomatic condition at rest, but insufficient flow at high metabolic demands, for example, during physical exercise .(Duncker and Bache, 2008)

IHD occurs as the result of multiple altered regulating vascular pathways that include severe atherosclerosis just in some cases. IHD pathophysiology is complex and multifaceted. A large percentage of patients with IHD have minimal or no epicardial coronary vascular disease. In fact, the atherosclerotic point of view has been revised by a number of trials and studies. They suggest that microvascular disease plays an important role in the etiology of IHD, by regulating blood flow and oxygen and energetic substrates delivery, in the microcirculation–myocardium interaction. (Severino et al., 2020a)

1.1.2 Etiology

CAD is a multifactorial phenomenon. Etiologic factors can be broadly categorized into non-modifiable and modifiable factors. Non-modifiable factors include gender, age, family history, and genetics. Modifiable risk factors include smoking, obesity, lipid levels, and psychosocial variables. In the Western world, a faster-paced lifestyle has led people to eat more fast foods and unhealthy meals which has led to an increased prevalence of IHD.(Komilovich, 2023)

1.1.3 Pathophysiology

The hallmark of the pathophysiology of CAD is the development of atherosclerotic plaque. Plaque is a build-up of fatty material that narrows the vessel lumen and impedes the blood flow. The first step in the process is the formation of a "fatty streak." Fatty streak is formed by subendothelial deposition of lipid-laden macrophages, also called foam cells. When a vascular insult occurs, the intima layer breaks, and monocytes migrate into the subendothelial space where they become macrophages. These macrophages take up oxidized low density lipoprotein (LDL) particles, and foam cells are formed. T cells get activated, which releases cytokines only to aid in the pathologic process. Growth factors released activate smooth muscles, which also take up oxidized LDL particles and collagen and deposit along with activated macrophages and increase the population of foam cells. This process leads to the formation of subendothelial plaque. Over time, this plaque could grow in size or become stable if no further insult occurs to the endothelium. If it becomes stable, a fibrous cap will form, and the lesion will become calcified over time. As time passes, the lesion can become hemodynamically significant enough that not enough blood would reach the myocardial tissue at the time of increased

demands, and angina symptoms would occur. However, symptoms would abate at rest as the oxygen requirement comes down. For a lesion to cause angina at rest, it must be at least 90% stenosed. Some plaques can rupture and lead to exposure of tissue factor, which culminates in thrombosis. This thrombosis could cause subtotal or total occlusion of the lumen and could result in the development of acute coronary syndrome (ACS) in the form of unstable angina (UA), Non-ST segment elevation myocardial-infarction (NSTEMI), or ST-segment elevation myocardial-infarction (STEMI), depending on the level of insult.(Komilovich, 2023)

1.1.4 Classification of CAD

1.1.4.1 Chronic coronary syndrome (CCS)

Stable IHD presents as stable angina. Stable angina typically presents as substernal chest pain or pressure that worsens with exertion or emotional stress and gets relieved with rest or nitroglycerin and is of 2 months duration(Komilovich, 2023)

To reflect the dynamic nature of the syndrome, the term “chronic coronary syndrome” (CCS) was introduced to replace the previous terms “stable coronary artery disease” or “stable angina”. The change in nomenclature emphasizes the fact that CAD is a continuous and dynamic atherosclerotic process involving intravascular plaque accumulation, whether obstructive or non-obstructive. The natural pathogenesis of CAD gives us some insight into why this disease is never really "stable". The term "stable" is usually used to describe characteristics of plaque disease, however some patients with CAD do not have plaque disease, with the etiology of their CAD being epicardial coronary artery spasm or microvascular dysfunction.

CCS encompass clinical scenarios in subjects with suspected or established CCS (Figure 1.1), including the following 6 entities:

1. Patients with stable chest pain with/without dyspnea and suspected CAD.
2. New-onset heart failure (HF) with or without reduced ejection fraction (EF) in patients with suspected CAD .
3. Patients with stabilized symptoms after an initial ACS diagnosis or Percutaneous Coronary Intervention (PCI).
4. Patients with vasospastic angina (variant angina).
5. Patients with microvascular dysfunction.
6. Asymptomatic patients in whom screening detects CAD.

Hence, CCS can better reflect the heterogeneous pathophysiology of the coronary circulation. (Ueng et al., 2023)

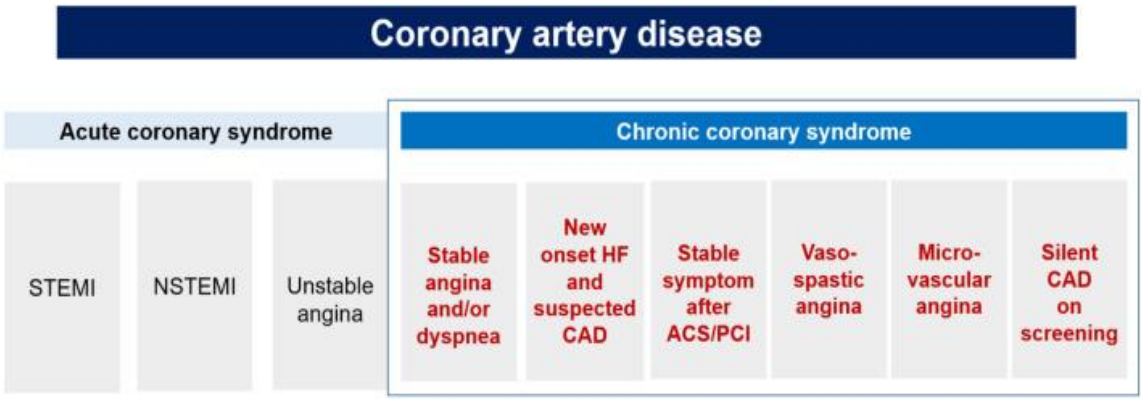

Figure [1.1] Terminology and definition of CCS.

ACS, acute coronary syndrome; CAD, coronary artery disease; HF, heart failure; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction. (Ueng et al., 2023)

1.1.4.2 Acute coronary syndrome (ACS)

ACS are a comprehensive disease concept characterized by acute myocardial ischemia caused by disruption of coronary artery plaque and consequent

thrombosis-induced severe coronary artery stenosis or occlusion, (Kimura et al., 2019) . ACS encompass a spectrum of conditions that include patients presenting with recent changes in clinical symptoms or signs, with or without changes on electrocardiogram (ECG) and with or without acute elevations in cardiac troponin (cTn) concentrations . Patients presenting with suspected ACS may eventually receive a diagnosis of acute myocardial infarction (AMI) or UA. ACS are associated with a broad range of clinical presentations, from patients who are symptom free at presentation to patients with ongoing chest discomfort/symptoms and patients with cardiac arrest, electrical/haemodynamic instability, or cardiogenic shock. (Byrne et al., 2024)

1.1.5 Myocardial infarction

Myocardial infarction (MI) is the outcome of IHD, including coronary artery stenosis and thrombogenesis, which causes a cascade of cardiac wound healing following myocardial cell necrosis, stimulated inflammation, and leukocyte influx (Chapman et al., 2020)

MI is defined by clinical presentation, new ischemic ECG changes, and cardiac biomarkers elevation. The cause of MI is acute myocardial injury. Prolonged ischemia (a restriction in tissue blood supply, causing a deficiency of oxygen) can lead to myocardial necrosis and cell death. (Kibel et al., 2020) AMI results from acute obstruction of the coronary arteries, leading to myocardial ischemia . Oxidative stress along with the inflammatory response plays a critical role in the acute phase of MI (Ong et al., 2018) . Under ischemic conditions, excessive accumulation of reactive oxygen species (ROS) induces DNA damage and cytochrome C release from mitochondria, leading to intrinsic apoptosis (Del Re et al., 2019). In contrast, chronic MI is a term widely used in the literature to refer to the protracted

pathophysiological processes following the ischemic insult which is characterized by cardiac fibrosis and cardiac remodeling (Larroza et al., 2017).

Based on the ECG supervised classification technique, MI is categorized into two types:

1. NSTEMI: revealing incomplete or sporadic obstruction in blood vessel.
2. STEMI: usually produced through comprehensive in addition to continuing obstruction in blood vessel. (Fathima, 2021)

The joint European Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Foundation (ESC/ACCF/AHA/WHF) Task Force for the Redefinition of MI subdivided MI into five main categories according to etiology, with their most recent criteria for each MI type published in 2018 (Figure 1.2). Types 1 and 2 are spontaneous etiologies of MI, while type 3 is by definition fatal and type 4 and type 5 are procedure-related. (Thygesen et al., 2019)

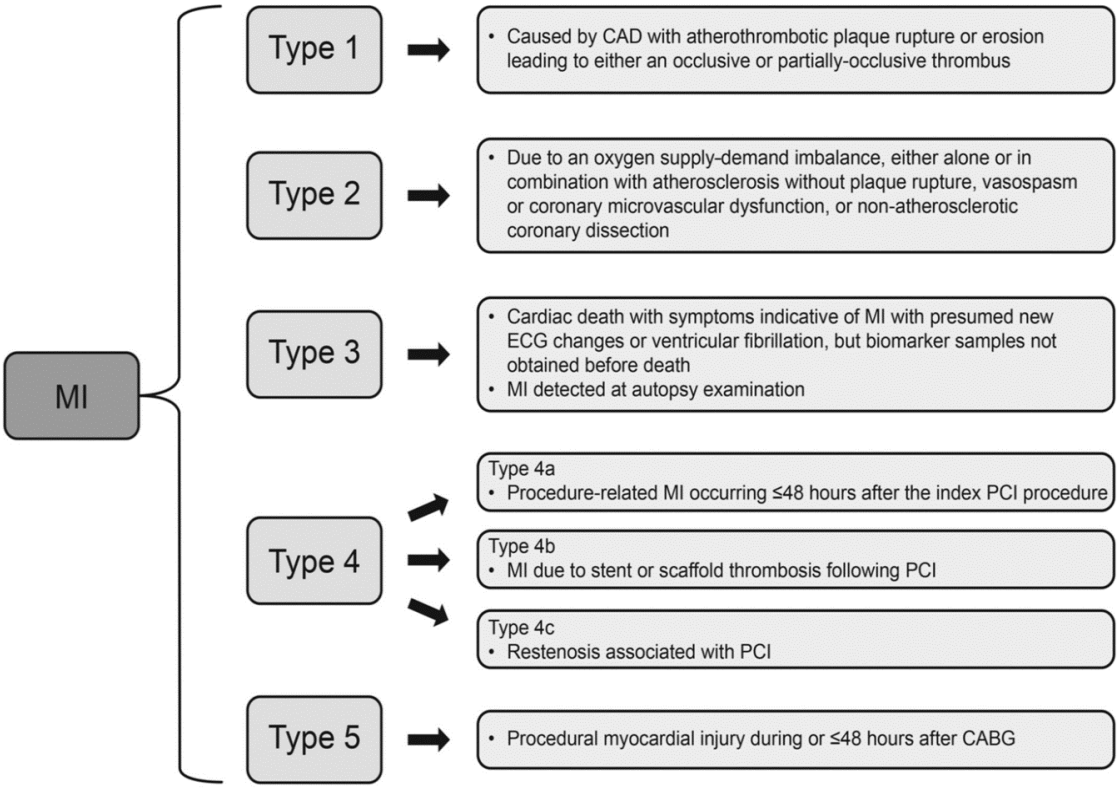

Figure [1.2] : Classification of MI based on the fourth universal definition. CABG, coronary artery bypass grafting; CAD, coronary artery disease; ECG, electrocardiogram; MI, myocardial infarction; PCI, percutaneous coronary intervention (Cohen and Visveswaran, 2020)

1.1.6 MI associated with PCI (type 4a myocardial infarction)

Stand-alone postprocedural increases of cTn values are sufficient to establish a diagnosis of procedural myocardial injury but not for the diagnosis of type 4a myocardial infarction (type 4a MI). Type 4a MI requires an elevation of cTn values >5 times the 99th percentile URL in patients with normal baseline values or, in patients with elevated preprocedure cTn in whom the cTn levels are stable (≤20% variation) or falling, the postprocedure cTn must rise >20% to an absolute value >5 times the 99th percentile URL. In addition, there should be evidence of new myocardial ischemia, either from ECG changes, imaging evidence, or from procedure-related complications associated with reduced coronary blood flow such as coronary dissection, occlusion of a

major epicardial artery or a side branch (SB) occlusion/thrombus, disruption of collateral flow, slow flow or no-reflow, or distal embolization.

Other criteria that meet the definition of type 4a MI, regardless of high sensitive cardiac troponin (hs-cTn) or cTn values, are the development of new pathological Q waves or autopsy evidence of recent procedure-related thrombus in the culprit artery. (Thygesen et al., 2019)

The diagnosis of a periprocedural myocardial injury requires:

increase in cardiac biomarkers (cTn) level, when initially patient presents normal values or; and increase in cardiac biomarkers (> 20%), when initially patient shows its values above the 99th percentile URL. (Domienik-Karłowicz et al., 2021)

In term of ECG which is one of the most commonly used non-invasive diagnostic tools for recording the physiological activities of the heart over a period of time (Hong et al., 2020), and compared with a pre-procedural ECG, new ischaemic ECG changes such as new ST-elevation at the J-point or new horizontal or downsloping ST-depression in two contiguous leads or new pathological Q waves are one of the requirements to define type 4a MI according to the 4th Universal Definition of MI . It should be noted that isolated post-PCI development of new pathological Q waves meets the type 4a MI criteria even if cTn values are elevated and rising but ≤5× 99th percentile URL. The presence of pre-existing left bundle branch block (LBBB) makes the diagnosis of new ischaemic changes challenging. However, in patients with LBBB, ST-elevation ≥1 mm concordant with the QRS complex in any lead may be an indicator of acute myocardial ischaemia. (Thygesen et al., 2019)

In summary, new ischaemic ST-segment changes and/or pathological Q waves on ECG are one of the key criteria for defining type 4a MI in CCS patients undergoing PCI.(Bulluck et al., 2021)

1.1.7 Percutaneous coronary intervention (PCI)

PCI is a non-surgical, invasive procedure with the goal of relieving the narrowing or occlusion of the coronary artery and improve blood supply to the ischemic tissue. This is usually achieved by different methods, the most common being ballooning the narrow segment or deploying a stent to keep the artery open (Figure 1.3).(Ahmad et al., 2020) Revascularization in the treatment of CAD aims to improve symptoms and/or prognosis.(Khan and Ludman, 2022) . In 2020, >100,000 PCI procedures were performed in the UK, with >5 times more people treated by PCI than by CABG.(Khan and Ludman, 2022)

In a substantial number of PCI cases for ACS and CCS, periprocedural myocardial injury and infarction occur, the actual incidences of which depend on the cardiac biomarker measured and the definitions used (Galassi et al., 2024).

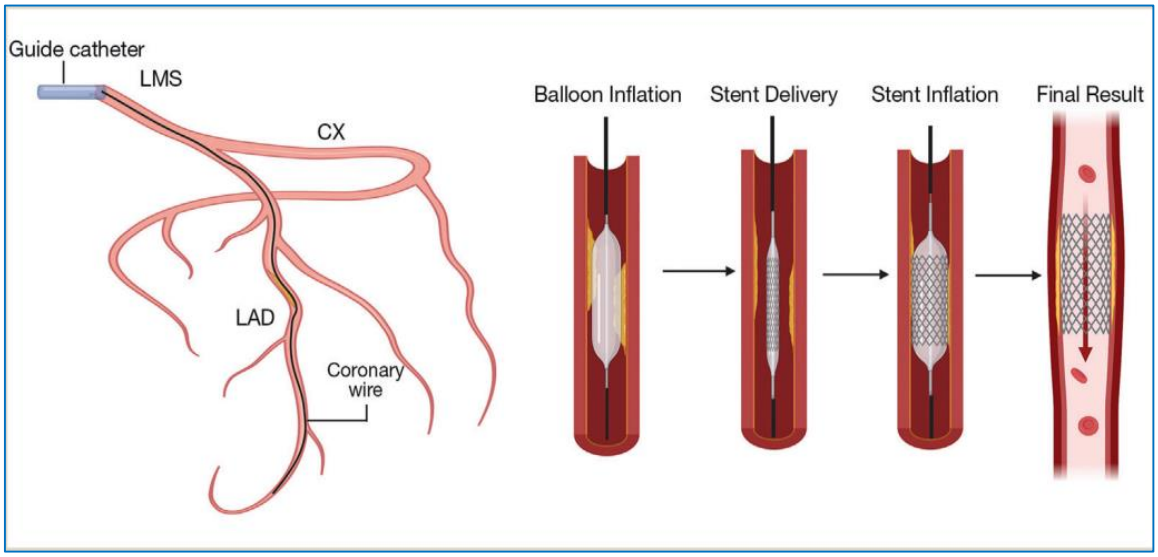

Figure [1.3] Percutaneous coronary intervention

CX, circumflex; LAD, left anterior descending; LMS, left main stem.(Khan and Ludman, 2022)

1.1.7.1 Indication of coronary catheterization in chronic coronary syndrome

The indications for revascularization in patients with stable angina or silent ischaemia for prognosis:

Left main disease with stenosis >50%, proximal LAD stenosis >50%, two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%), large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR, single remaining patent coronary artery with stenosis >50%.

For symptoms:

Haemodynamically significant coronary stenosis in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy.(Neumann et al., 2019)

1.1.7.2 Access type: femoral vs. radial access

Coronary arteries can be accessed for angiogram through a radial or femoral approach. In general, radial artery approach is preferred to reduce the risk of access site bleeding because the radial artery can be easily compressed against the radial bone, as compared to the femoral artery. However, access to the radial artery requires experience and expertise because of its small size.

Before access through the radial artery, palmar arch circulation should be assessed to avoid ischemia of the hand from complications during the procedure.(Ahmad et al., 2020)

1.1.7.3 Complication of PCI

It is of paramount importance that interventional cardiologists are equipped with the knowledge and skills required to rapidly recognize complications,

and have strategies to overcome them, thereby minimising the risk of injury to their patients. (Kandan and Johnson, 2019)

1.1.7.3.1 Catheter-related complications

1.1.7.3.1.1 Traumatic coronary dissection

Coronary dissection is a pathological separation of the layers of the vessel. Traumatic coronary dissection can be induced by the guide catheter, wire manipulation, equipment in the coronary artery (imaging probes, 'mother-and-child catheters') or excessive balloon and stent expansion. (Kandan and Johnson, 2019)

1.1.7.3.1.2 Iatrogenic coronary thrombosis

Iatrogenic coronary thrombosis can arise from thrombus injected from the guiding catheter, thrombus formation in situ because of suboptimal antithrombotic therapy and disturbed haemorrheology from intracoronary instruments or accidental thrombus migration from one vessel to another (aspiration thrombectomy). (Kandan and Johnson, 2019)

1.1.7.3.2 Procedural complications

1.1.7.3.2.1 Coronary perforation

perforation can be caused by disruption of the vessel wall secondary to instrumentation, for example, balloon angioplasty, stenting or atherectomy, or can occur distally secondary to coronary guidewire exit. The clinical consequences of a coronary perforation are clearly dependent on the location and extent of the disruption. (Kandan and Johnson, 2019)

1.1.7.3.2.2 No-reflow

In the setting of PCI, no-reflow is characterised by chest pain, persistent or new ST segment change, and thrombolysis in myocardial infarction (TIMI) flow <3 , or in the case of TIMI 3 flow when myocardial blush grade is 0 or 1. (Kandan and Johnson, 2019)

1.1.7.3.2.3 Side branch occlusion

Side branch (SB) occlusion is a potentially serious complication associated with PCI of bifurcation lesions.(Kandan and Johnson, 2019)

1.1.7.4 Medina classification

Although several classifications of Coronary bifurcation lesions exist, the Medina classification (Figure 1.4) , endorsed by major bodies such as the European Bifurcation Club, is the most widely used.(Ludwig et al., 2021, Riley et al., 2020) This classification assigns a binary value (0 or 1) to the proximal and distal main branches (MBs) as well as the SB, in that respective order, based on the presence (1) or absence (0) of significant plaque burden (≥50% stenosis) in that vascular segment.(Medina et al., 2006) Furthermore, Coronary bifurcation lesions can be classified into true bifurcation lesions, if both the MB and SB have significant stenosis, and nontrue bifurcation lesions if either the MB or SB is not significantly stenosed.(Mohamed et al., 2022)

Medina classification (0,1,1)/(1,1,1) were significantly associated with periprocedural myocardial infarction in contemporary elective PCI.(Mizuno et al., 2020)

Mohamed et al. findings demonstrate that the most prevalent coronary bifurcation lesion subtypes are Medina 1.1.1 (35.5%) and 1.1.0 (26.8%), whereas the least prevalent is Medina 0.0.1 (3.5%).(Mohamed et al., 2022)

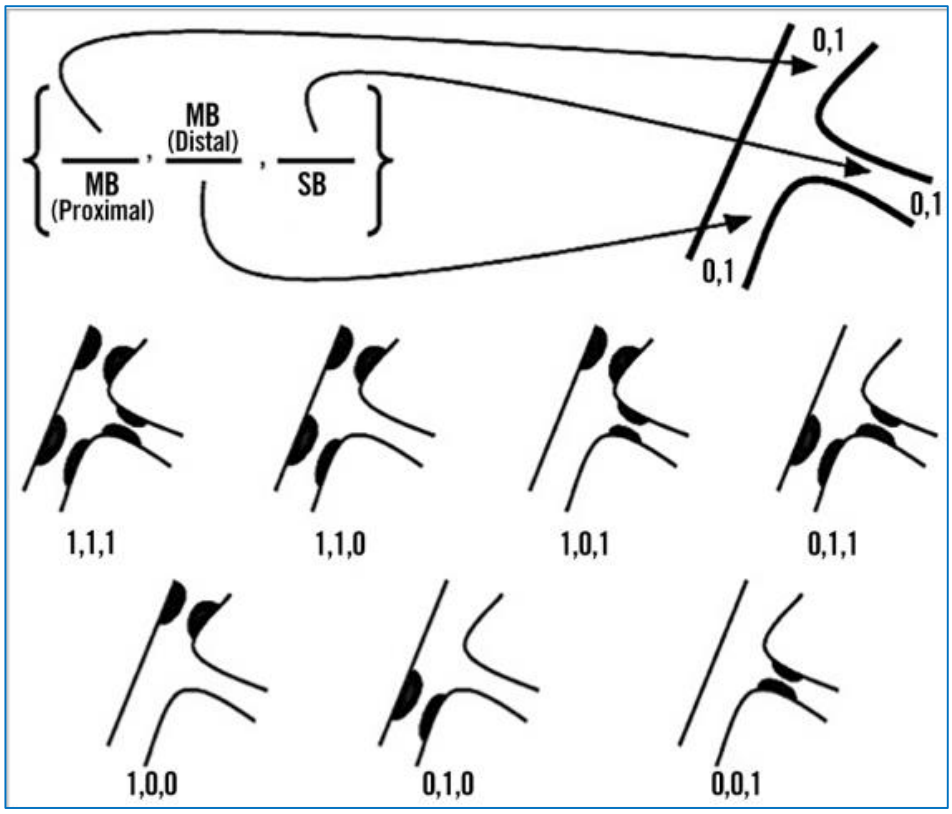

Figure [1.4] Medina's classification.(Louvard and Medina, 2015)

1.1.8 An etiology of periprocedural myocardial injury and type 4a MI

The etiology of periprocedural myocardial injury and type 4a MI is multifactorial and may result from PCI-related events or complications, alone or in combination (figure*1.5*). (Bulluck et al., 2021) SB occlusion is considered to be the most common cause of type 4a MI in CCS patients undergoing PCI,(Ganesha Babu et al., 2011) but it is likely that its impact on outcome depends on the size of the occluded side branches. The incidence of SB occlusion may be associated with the choice of stent type, but also with the type of procedure [such as chronic total occlusion (CTO), rotational atherectomy, etc.] and the target segment, with the mid left anterior

descending (LAD) coronary artery having the highest density of side branches(Ishibashi et al., 2015).Distal coronary embolization of intracoronary thrombus and atheromatous material can result in no-reflow/slow-flow during PCI in CCS patients. Embolization may not be preventable, despite current anticoagulant and antiplatelet adjunctive therapy and use of aspiration or protection devices(Bulluck et al., 2021). PCI -related factors, such as pre-dilation, partially occlusive devices (such as catheter extension devices, retrograde CTO procedures, atherectomy devices), which are needed for optimal stent placement, can result in prolonged total vessel occlusion times and induce periprocedural myocardial injury. Abrupt vessel closure during PCI is usually caused by dissection proximal or distal to the stent or acute stent thrombosis. Other potential rare periprocedural causes of myocardial injury include coronary artery wire perforation, air embolization, and arrhythmias.(Bulluck et al., 2021) Even transient occlusions of the coronary artery during balloon angioplasty inflations have been reported to increase cTn values during PCI in CCS patients.(Árnadóttir et al., 2021)

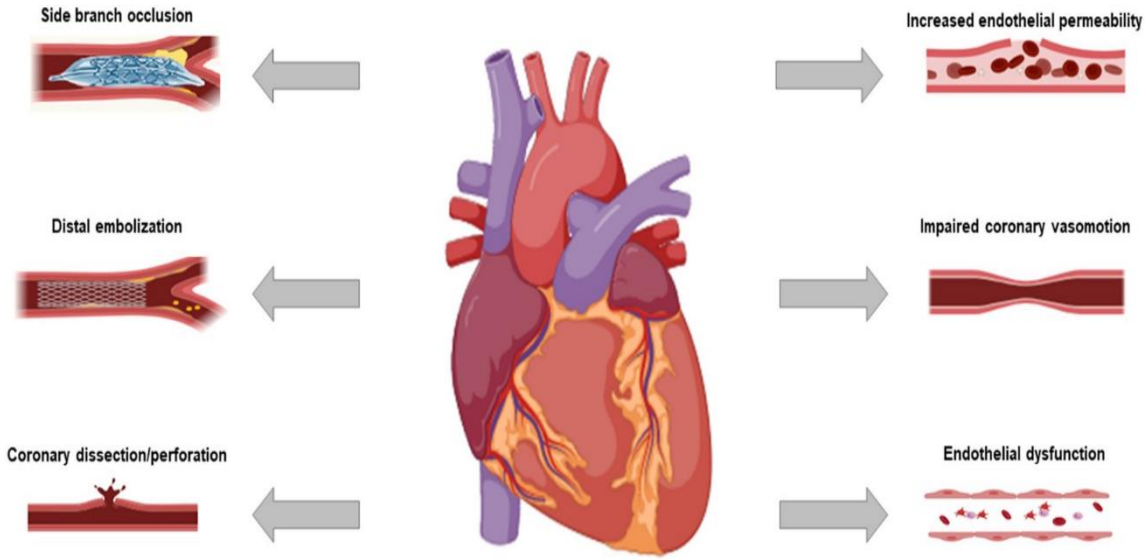

Figure [1.5] Aetiology of periprocedural myocardial injury and type 4a MI.(Bulluck et al., 2021)

1.1.9 Risk factors of PCI complexity

A variety of patient features, lesion characteristics, and periprocedural factors have been shown to be independent predictors of periprocedural myocardial injury, type 4a MI in CCS patients undergoing PCI .(Bulluck et al., 2021)

1.1.9.1 Patient risk factors

the concept of complex PCI and higher-risk indicated population for revascularization has recently been proposed (Kirtane et al., 2016). Briefly, the following 9 factors were defined as clinical risk factors: age ≥75 years, diabetes, hypertension, current smoking, peripheral artery disease, prior stroke, prior PCI or coronary artery bypass grafting, history of heart failure, and renal dysfunction (estimated glomerular filtration rate < 60 mL/minute per 1.73 m2).(Kang et al., 2021)

1.1.9.2 Lesion characteristics and complications

Complex Coronary artery disease (cCAD) is defined by anatomical features of the coronary tree that include American College of Cardiology/American Heart Association (ACC/AHA) type C lesions and includes bifurcation/ trifurcation disease, ostial lesion, severe calcification/ fibrocalcific or undilatable lesions, total occlusion, left main disease, stenoses of tortuous vessels, degenerated saphenous vein graft lesions, and thrombotic lesions. (Werner et al., 2018)

patients with more comorbidities and/or lesions that are more complex are now treated with PCI. However, certain patients and lesion subsets present unique challenges to the interventional cardiologist and are still associated with technical difficulties, periprocedural complications and high rates of restenosis. Currently, approximately 30% of PCIs are considered complex

PCIs. Despite this shift in expanding the applicability of PCI, the underlying determinants and impact of PCI complexity on clinical outcomes remain poorly characterised.(Wykrzykowska and Kerkmeijer, 2020)

1.1.9.2.1 Lesion complexity risk score

A complex lesion was defined as a treated lesion possessing at least one of the following high-risk angiographic lesion characteristics: bifurcation, CTO, Type C, unprotected left main trunk (UPLMT), and thrombus formation. The operator determined the presence of these characteristics at the time of the catheter angiography (CA). Patients were stratified both by absolute complex lesion status (yes/no), and by the total number of the five complex lesion criteria that were present (score 0: no complex lesion, score 1: one complex lesion, score 2: two complex lesions, score 3: three complex lesions, score 4: four complex lesions, and score 5: all complex lesions).(Endo et al., 2015)

1.1.9.3 Complex PCI procedure

cCAD often but not necessarily results in a complex PCI procedure. cCAD may result in longer procedure times, more complex interventional strategies than usual, higher amount of contrast dye, and higher risk for procedural complications—all characteristics of complex PCI procedures. The main issue is that the aforementioned factors are highly operator dependent and the definition of complex PCI is strongly associated to the skills level of the operator. (Werner et al., 2018)

Although there is no universal definition (Table 1.1), complex PCI usually includes bifurcation with 2 stents implanted, ≥ 3 stents implanted, ≥ 3 lesions treated, total stent length > 60 mm or treatment of a CTO (Byrne et al., 2018). Other procedural characteristics, such as left main (LM) or proximal LAD artery location, vein bypass graft PCI, bifurcation lesion with SB ≥ 2.5 mm, lesion length ≥ 30 mm, thrombus containing lesion, or rotational

atherectomy use for severely calcified lesions, have been used to characterize a complex PCI as well (Figure 1.6) (Généreux et al., 2018).

Table [1.1] Definition of complex PCI (Benetou et al., 2020)

Study	Complex-PCI definition
ESC focused update on (Dual antiplatelet therapy)DAPT (Byrne et al., 2018)	≥ 3 stents implanted, ≥ 3 lesions treated, bifurcation PCI with 2 stents, stent length > 60 mm or chronic total occlusion
Giustino et al. (Giustino et al., 2016)	3 vessels treated, ≥ 3 stents implanted, ≥ 3 lesions treated, bifurcation PCI with 2 stents, stent length > 60 mm or chronic total occlusion
Yeh et al. (Yeh et al., 2017)	Unprotected left main, > 2 lesions/vessel, length ≥ 30 mm, bifurcation with SB ≥ 2.5 mm, vein bypass graft or thrombus-containing lesion
Généreux et al. (Généreux et al., 2018)	≥ 3 stents implanted, bifurcation PCI with 2 stents, rotational atherectomy for severely calcified lesions, left main or saphenous vein graft PCI
Serruys et al. (Serruys et al., 2019)	Multivessel PCI, ≥ 3 stents implanted, ≥ 3 lesions treated, bifurcation PCI with ≥ 2 stents or total stent length > 60 mm
Costa et al. (Costa et al., 2019)	≥ 3 stents implanted, ≥ 3 lesions treated, bifurcation stenting, stent length > 60 mm or CTO revascularization
Dangas et al. (Dangas et al., 2020)	3 vessels treated, ≥ 3 lesions treated, stent length > 60 mm, bifurcation with 2 stents implanted, atherectomy device use, left main PCI, bypass graft, or CTO intervention

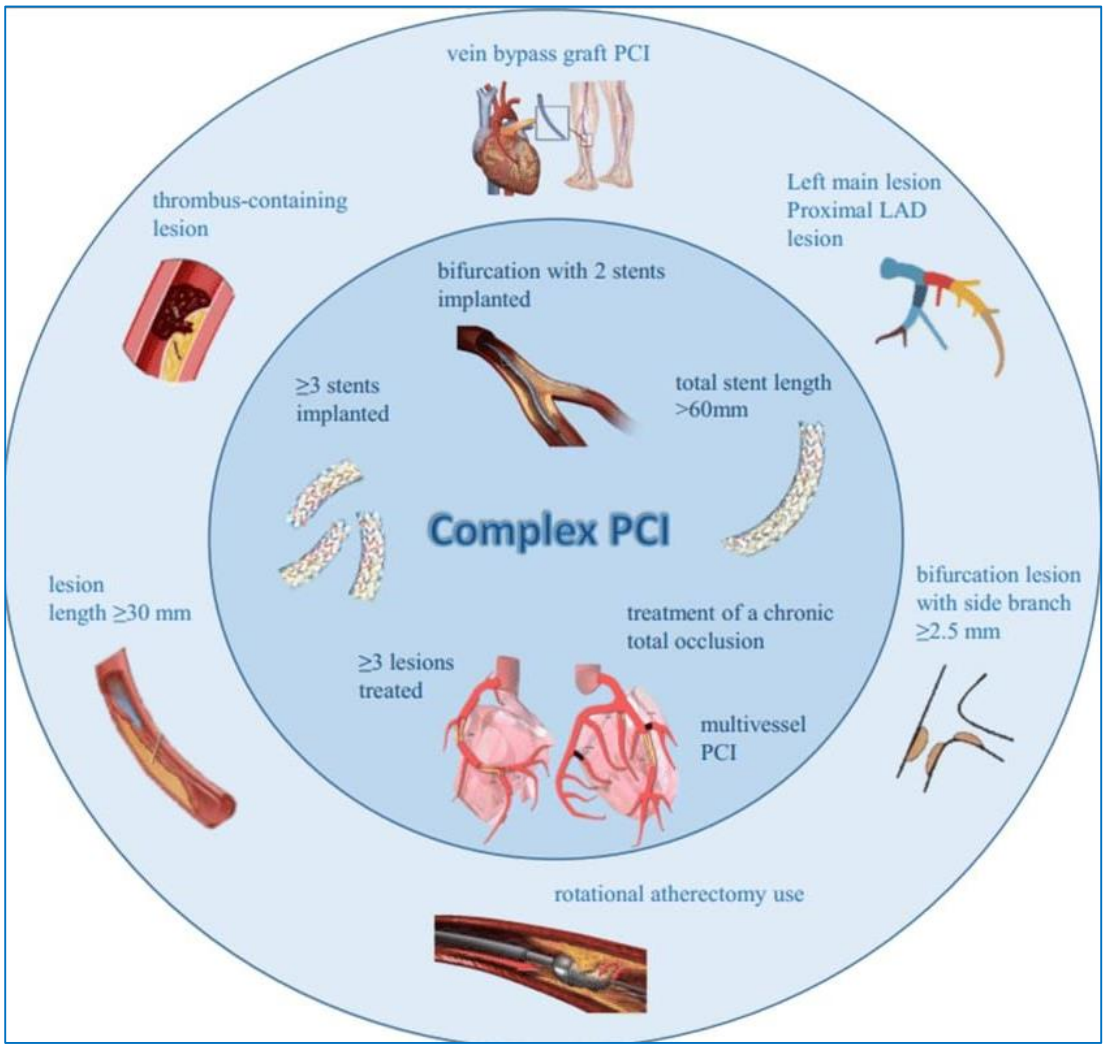

Figure [1.6] Features of complexity used in complex PCI definitions.(Benetou et al., 2020)

Definition reported in ESC focused update on DAPT is presented within the inner circle (Byrne et al., 2018)

Jin et al was define complex PCI as PCI with at least 1 of the following characteristics: 1) 3 vessels treated; 2) ≥3 lesions treated;3) ≥3 stents implanted; 4) total stent length >60 mm;5) bifurcation with 2 stents implanted; 6) left main PCI; and 7) chronic total occlusion PCI.(Jin et al., 2024)

In general, complex PCI procedures are often characterized by difficult wire crossing of the lesions (e.g. in calcified, tourtous, occluded vessels), the need for extensive lesion preparation (e.g. the usage of rotational atherectomy,

thrombectomy, cutting/scoring balloon angioplasty), difficulty to deliver balloons and stents (e.g. in diffusely calcified, tourtous vessels), and a higher proportion of procedural complications (e.g. acute vessel occlusion, dissection, perforation, and hemodynamic compromise)(Kirtane et al., 2016) Complex PCI goes along with complex lesions, significant comorbidities of the patient and in a lot of cases with impairment of the left ventricular ejection fraction. Patient treated are often octogenerians and/or surgical turn-downs in whom the Heart Team or the patient voted for an interventional strategy. Personal skills and experience of the operator influences the perception of the complexity of the interventional procedure (figure1.7).(Werner et al., 2018)

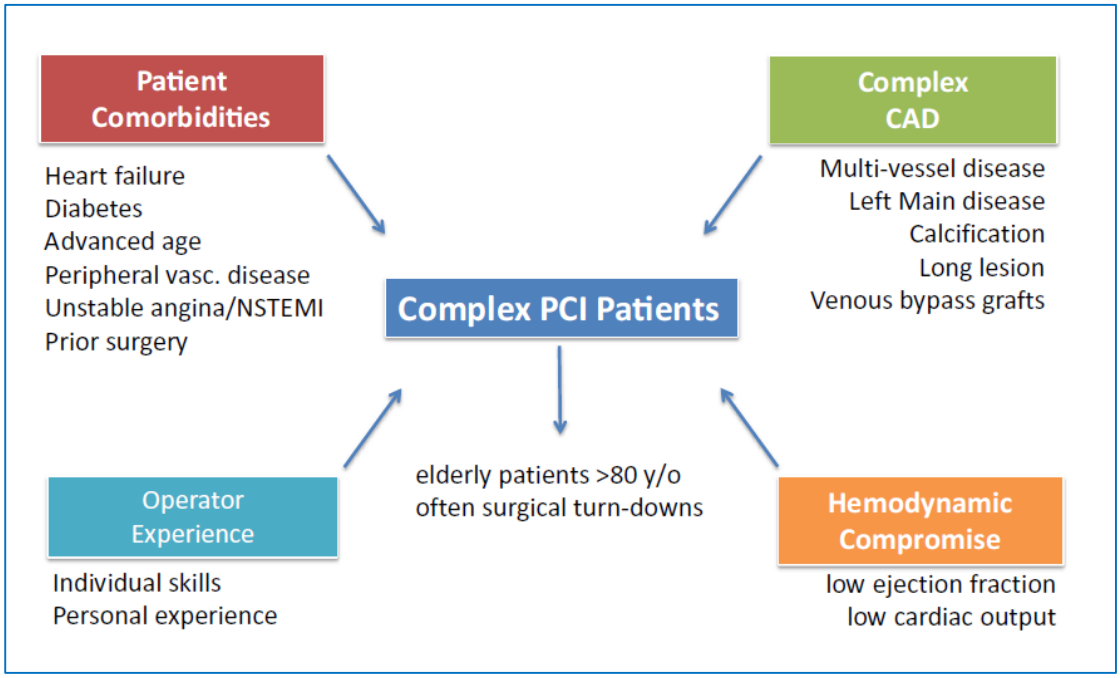

Figure [1.7] The complex PCI patient.

Complex CAD often goes along with extensive comorbidities and hemodynamic impairment. Operator experience and skills influence decision-making and outcomes (Werner et al., 2018)

Patients who undergo complex percutaneous coronary revascularization procedures are at a substantially higher risk of ischemic events, in a graded fashion, with increased procedural complexity. (Giustino et al., 2016)

Compared with noncomplex PCI, PCI complexity was associated with a considerably higher risk of adverse ischemic events . The ischemic risk tended to be greater for progressively higher degrees of procedural complexity. (Wang et al., 2020a)

Recent evidence suggests that a one-stent strategy with provisional stenting is a more effective strategy than a two-stent strategy in the majority of cases when treating bifurcations (Behan et al., 2016) .

Post-complex PCI monitoring has not been evaluated systematically. In most cases, of complex PCI, patients remain stable and do not need special monitoring. However, a number of studies suggest that post-interventional troponin evaluation helps to estimate myocardial ischemia during the procedure which is in turn an important outcome measure (Feldman et al., 2011).

1.1.10 Oxidative stress

1.1.10.1 Oxidative stress and myocardial ischemia

Myocardial cell death is a fundamental process in both physiological and pathological conditions (Zhang et al., 2020). Somatic (physical) stress is associated with physicochemical tissue injury, often called systemic when considered on a larger scale – affecting whole organs or the whole body (Gonzalez et al., 2011).Oxidative or excitotoxic stress, which refer to physicochemical changes at the cellular and tissue level (subcategories of somatic stress)(Dimsdale, 2008)

Oxidative stress, characterized by an imbalance between the generation ROS and the capacity of the intrinsic antioxidant defense system, has been implicated in the pathogenesis of cardiovascular diseases (Juni et al., 2013). Infections, inflammatory processes- especially those that are chronic-ischemia, senescence, physical and psychological stress are the main factors involved in generating oxidative stress in the human body (Khansari et al., 2009)

It has been revealed that inflammation and ROS can cause the constriction of capillaries under ischemic conditions and participate in the phenomenon of myocardial no-reflow(Doll et al., 2020, Wang et al., 2020b)

Reperfusion following myocardial ischemia may lead to accelerated myocardial injury and worsening clinical outcomes. One of the most important pathological mechanisms in reperfusion injury is oxidative stress, which is the imbalance between the antioxidant system and the excessive production of ROS, leading to the toxic accumulation of reactive oxygen intermediates.(Xiang et al., 2021)

PCI , for example, percutaneous transluminal coronary angioplasty (PTCA)and stent deployment, induce pathophysiological levels of vascular ROS production (Kochiadakis et al., 2010), leading to post-procedural pathological changes, including restenosis, stent thrombosis, and endothelial dysfunction.

One of the important sources of ROS is electron leakage from the electron transport chain (ETC) in mitochondria . (Xiang et al., 2021)

1.1.10.2 Oxidative stress and atherosclerosis

Atherosclerosis is a multisystemic, progressive, chronic inflammatory disease characterized by the interaction of immune and endothelial cells that is mediated by adhesion molecules on the surface of the vascular endothelium leading to the release of numerous proinflammatory mediators (Sima et al., 2018). Specifically, it has been demonstrated that there is a close interaction between vascular endothelial inflammation and intense oxidative stress in triggering the atherosclerotic process (Malekmohammad et al., 2019) .Increased oxidative stress results to the formation of atherogenic oxidized LDL which is a major determinant of atherogenesis(Kattoor et al., 2019).

1.1.10.3 Oxidative stress and MI

Oxidative stress plays a significant role in a MI as they cause cardiac ischemia and reperfusion injuries (Fathima, 2021) . Under oxidative stress, ROS attacks biomolecules which leads to damage of nuclear and mitochondrial DNA; cross-linking of protein and lipid peroxidation ensues, resulting in protein denaturation and loss of enzyme and membrane pump function. Tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-6 production activated by ROS contribute to intracellular calcium dysregulation and an increase in its concentration. Myocardial cytosolic calcium overload leads to myofibrillar hyper contracture, cytoskeletal damage and myocardial cell disruption via activation of calcium dependent proteases and phospholipases. Mitochondrial calcium overload causes disorganized ATP synthesis and utilization, causing necrosis (Vichova and Motovska, 2013).

1.1.10.4 Cardiac oxidative stress markers

Oxidative stress markers may have a possible role in clinical practice, such as to refine the prognostic evaluation of patients with acute myocardial infarction, treatment monitoring, or a supportive antioxidant treatment to overcome negative effects of reperfusion injury and longer ischemic time.(Vichova et al., 2021)

1.1.10.4.1 Cardiac troponin

Troponins are structural proteins found in the troponin complex within skeletal and cardiac muscle thin filaments. The troponin complex consists of three subunits (I, T, and C) and along with calcium ions plays an important role in the regulation of muscle contraction (Kozinski et al., 2017). Each molecule has a specific role in the muscle contraction process: troponin T attaches the troponin complex to the actin filament, troponin C acts as the calcium binding site, and troponin I inhibits interaction with myosin heads in the absence of sufficient calcium ions (Garg et al., 2017). While troponin C is synthesised in both skeletal and cardiac muscles, troponin T and I are mainly localised in the myocardium, thus being referred to as cardiac troponin (cTnI and cTnT). Even if there are several contradictory studies indicating their presence in other sites, such as tunica media of the vena cava and pulmonary veins, aorta, trachea, gut, urinary bladder, or even the skeletal muscle, it is generally accepted that these biomarkers possess the greatest specificity in identifying myocardial injury (Chaulin, 2021). Increases in cTnI values have not been reported to occur following injury to non-cardiac tissues (Thygesen et al., 2019). hs-cTnI is more sensitive and specific and is now commonly recommended for the diagnosis of myocardial injury and MI(Khaled Elsayed Hamada 2024).

High-sensitivity troponin assays are used to detect troponins, but at a much lower concentration than classical assays. These assays offer several advantages, first of all being the fact that they are highly sensitive, thus providing faster recognition of AMI (rule-in/rule-out). The use of the new generation hs-cTn is now recommended by the international guidelines as a centerpiece in the diagnosis of myocardial infarction.(Lazar et al., 2022)
In CCS patients with normal baseline cTn levels, the post-PCI cTn elevation of ≥5x 99th percentile URL used to define type 4a MI, is associated with 1 year mortality, and could be used to detect "Major" procedural myocardial injury in the absence of procedural complications or evidence of new myocardial ischaemia.(Silvain et al., 2021)

1.1.10.4.2 Ischemia-modified albumin

Albumin is one of the most abundant proteins in the body of mammals: about 40% of its pool is located in the intravascular space and the remainder is found in the interstitial space. The content of this multifunctional protein in blood is about 60-65% of total plasma proteins. A decrease in its synthesis or changes of functional activity can destabilize oncotic blood pressure, cause a violation of transporting hormones, fatty acids, metals, and drugs. Albumin properties change under ischemic attacks associated with oxidative stress, production of ROS, and acidosis. (Shevtsova et al., 2021a) When there is ischemia, a change in the N-terminal occurs that reduces this binding capacity of metal ions such as copper, cobalt and nickel , with ROS probably being the causative agent of this change, giving rise to ischemia-modified albumin (IMA) (Figure 1.8).(Shevtsova et al., 2021b)

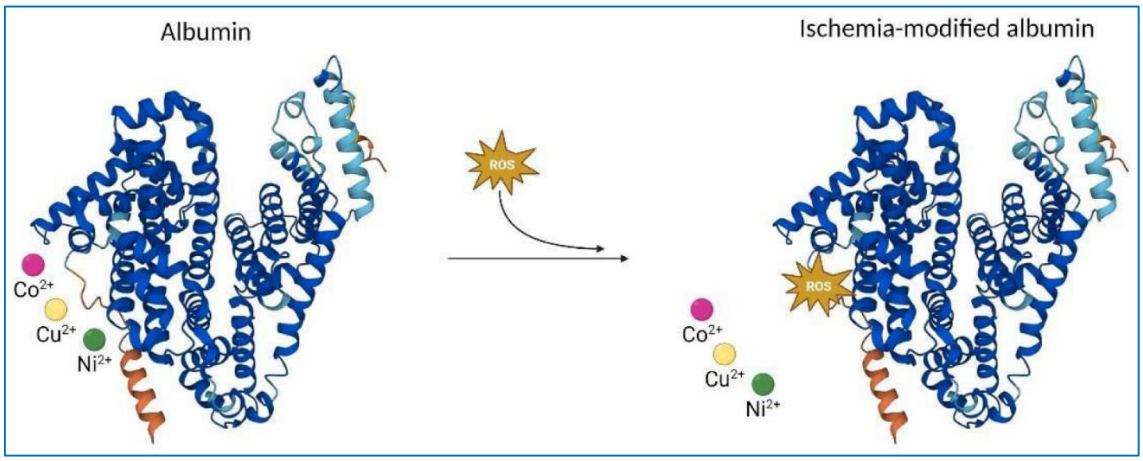

Figure [1.8] Structure of Human IMA.

Albumin binds transport metal ions such as copper, cobalt and nickel in its N-terminal region. During an ischemic episode, an increase in the ROS occurs, modifying this region and giving rise to the IMA, which reduces the binding capacity of the ions. Co: cobalt; Cu: copper; Ni: nickel; ROS: reactive oxygen species.(Resano-Barrio et al., 2023)

1.1.10.4.2.1 Generation of ischemia-modified albumin

Some models were proposed to explain the IMA formation. (Shevtsova et al., 2021a) One of them is an autodegradation of N-terminal sequence (NTS), the scheme of which is shown in (Figure 1.9) According to this model, the α-amino group of Asp1 exhibits nucleophilic properties caused by the dissociation of a carboxyl group and the release of a proton. A nucleophilic attack of Asp1 amine nitrogen on the carbonyl of the peptide bond between Ala2 and His3 leads to its cleave and release of a cyclic dipeptide. As result, truncated albumin cannot bind transition metal ions (Chan et al., 1995).

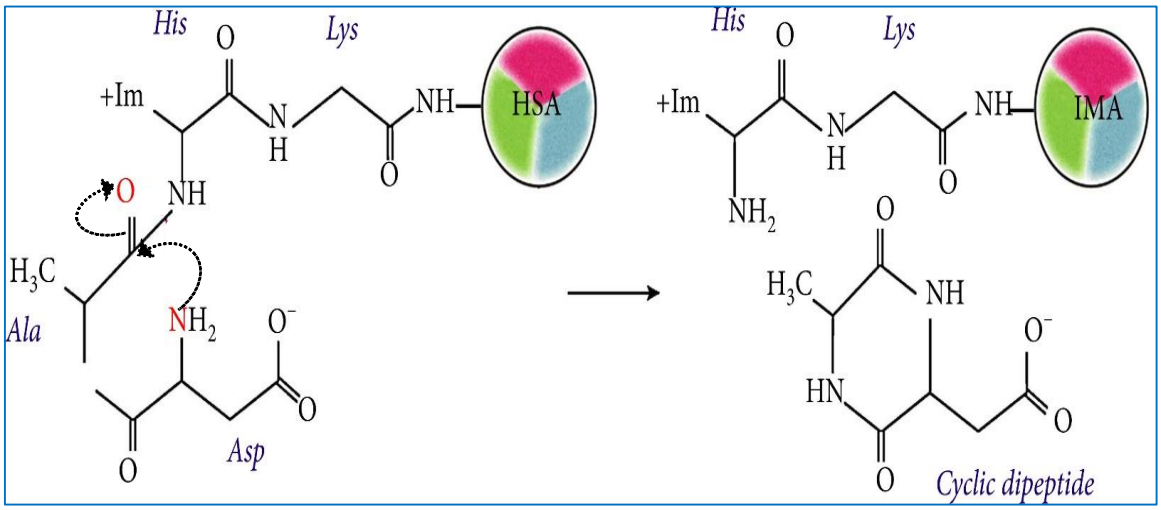

Figure [1.9] IMA formation through dipeptide cleavage. A nucleophilic attack by the α-amino nitrogen on the carbonyl of Ala2-His3 peptide bond cleaves and releases the cyclic dipeptide. The truncated NTS cannot bind transition metal ions (Chan et al., 1995)

Another model of IMA formation is based on the generation of ROS during the Fenton reaction. According to this model, ischemia results in the acidosis and release of Cu^{2+} from weak binding sites on circulating proteins and peptides. In the presence of reducing agents (for example, ascorbic acid), free Cu^{2+} is converted to Cu^{+}, which can then react with O^2 and generate superoxide radicals. During this reaction, Cu^{+} is oxidized to Cu^{2+}, and albumin N-terminus scavenges these ions. The superoxide radicals are converted to hydrogen peroxide (H_2O_2) by superoxide dismutase, and H_2O_2 is then degraded by catalase or converted to hydroxyl free radicals in the Fenton reaction. These radicals can damage human serum albumin (HSA), causing the removal of two or three N-terminal amino acids and releasing Cu^{2+}. The steps of the above-mentioned process are repeated in a chain reaction (Gaze, 2013), and IMA rises rapidly following an ischemic attack. The stages of IMA formation by this mechanism are presented in (Figure 1.10).(Shevtsova et al., 2021a)

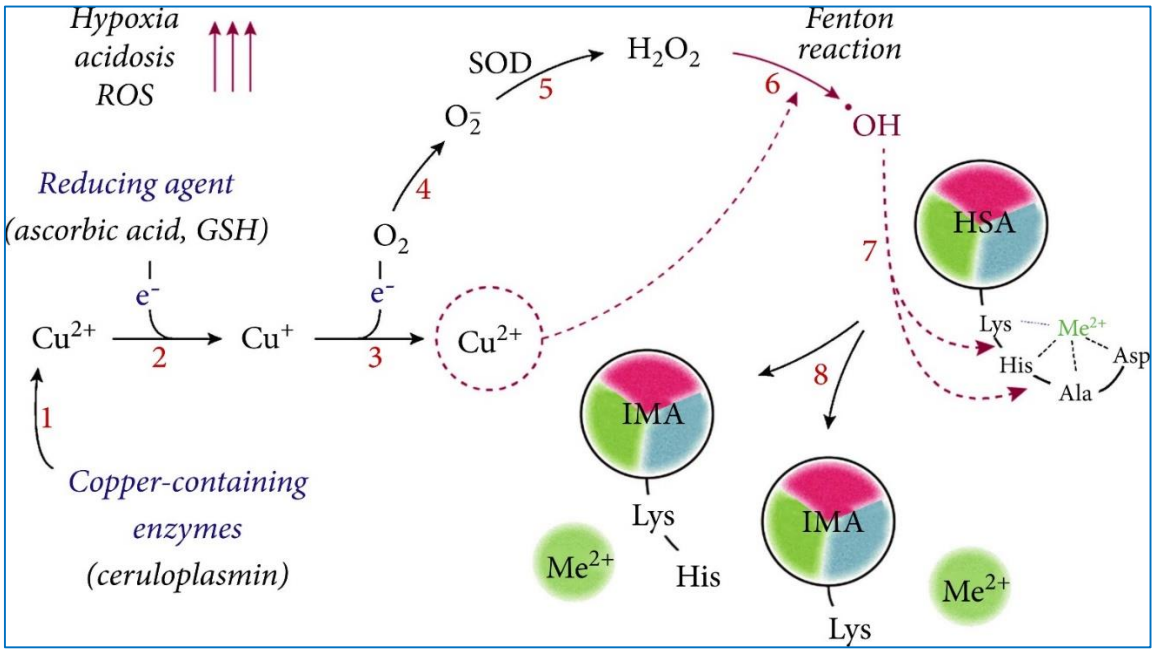

Figure [1.10] The mechanism of IMA formation driven by oxidative stress.Tissue hypoxia and activation of anaerobic glycolysis induce acidosis and release Cu^{2+} ions from copper-containing proteins, such as ceruloplasmin (1). In the presence of reducing agents, e.g., ascorbic acid, Cu^{2+} is reduced to Cu^{+} (2), followed by the formation of superoxide anion O^{-2} (3-4). Superoxide dismutase (SOD) catalyzes the dismutation of superoxide O−2 to hydrogen peroxide H_2O_2 (5), which, in the presence of Cu^{2+}, undergoes the Fenton reaction with the formation of hydroxyl radicals ·OH (6). These radicals contribute to the degradation of NTS (7) and IMA formation (8), which cannot bind Cu^{2+} and other metal ions.

(Shevtsova et al., 2021a)

1.1.10.4.2.2 Kinetic release of IMA

Studies on patients receiving angioplasty where ischemia is induced in a controlled manner, have indicated the kinetics of IMA production. There is rapid rise in IMA after balloon inflation with subsequent fall at 6 hours and return to normal values by 24 hours.(Sinha et al., 2006) The rise in IMA occurs earlier than rise in cTn and natriuretic peptides (figure1.11) The

magnitude of IMA elevation has been found correlated with the number and frequency of balloon inflations during PCI (Quiles et al., 2003) .

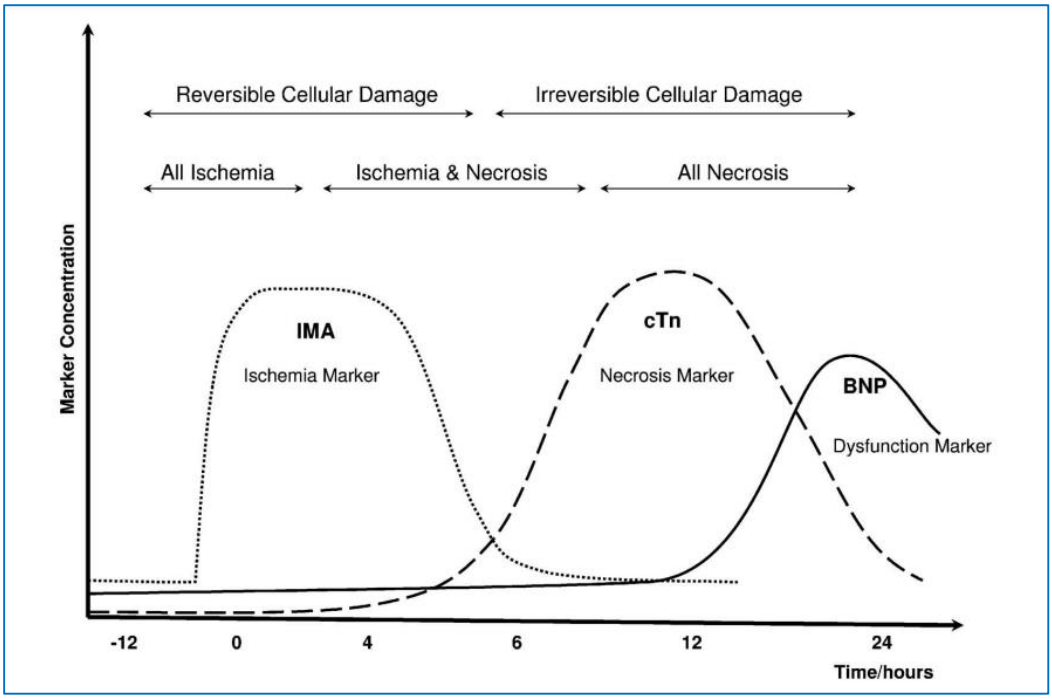

Figure [1.11] Release kinetics of IMA in relation to standard cardiac biomarkers of necrosis (cardiac troponin, cTn) and dysfunction (B type natriuretic peptide, BNP) (Gaze, 2009)

Elevation of markers in relation to concentration not to scale

IMA formation kinetics have been studied in patients with chronic stable angina undergoing PCI considered a clinical model of myocardial ischemia-reperfusion. According to the results of these studies, blood IMA increased within 6-10 minutes following PCI; it remained high for about 6-12 hours and returned to normal after 12-24 hours in patients with positive exercise stress test and CAD .(Sinha et al., 2006, Bar-Or et al., 2001)

IMA is a blood biomarker accepted by the Food and Drug Administration (FDA, USA) for the diagnosis of ACS in adults as a direct measurement of oxidative stress, an intermediate mechanism involved in the development of arteriosclerosis and cardiovascular disease. (Gaze, 2009)

IMA has been proposed as a marker for diseases that combine ischemia and oxidative stress.(Tampa et al., 2022)

IMA content also depends on the duration of ischemic events: its levels after prolonged ischemia (25-60 min) are much higher than levels observed after short-term (15-21 min) ischemia (Gaze, 2013)

the evaluation of its content may provide valuable information regarding the duration of diseases and possible complications, and it can be used in the differential diagnosis of certain pathological conditions. IMA's advantage as a biomarker over other markers is its ability to detect ischemic conditions at earlier stages.(Shevtsova et al., 2021a)

IMA holds promise as a potential marker for assessing IHD. Its ability to detect myocardial ischemia and its association with clinical outcomes make it a valuable addition to the diagnostic armamentarium (Tiwari, 2023). IMA was closely related to the occurrence and severity of ACS and might become a novel marker for diagnosis of ACS.(Yang et al., 2019a). Evaluation of serum IMA is recommended not only for early detection of myocardial ischemia but also as a prognostic indicator of the disease severity.(Shevtsova et al., 2021a) It is a sensitive marker of PCI induced ischemia in the PCI setting, and may have a role in clinical practice (Kandeel Fathi Kandeel et al., 2022) .IMA has also been shown to be elevated in patients after PCI as a result of ischemia reperfusion injury (Sinha et al., 2003).

1.1.10.4.3 Chitinase-3 like-protein-1

Glycoside hydrolase family 18 includes chitinases and nonenzymatic chitinase-like proteins (CLPs), both of which bind chitin, a polysaccharide chain composed of N-acetylglucosamine repeats and present in arthropods and other taxa as a major structural polymer. While chitinases cleave chitin,

CLPs do not possess this enzymatic activity. chitinase-3 like-protein-1 (CHI3L1), one of the CLPs (Zhao et al., 2020) . which is also called YKL-40, based on its three N-terminal amino acids, tyrosine (Y), lysine (K), and leucine (L), and its molecular weight of 40 kDa (Mazur et al., 2021). The murine homolog of CHI3L1, with a molecular weight of 39 kDa, was first discovered in breast cancer cells and therefore named breast regression protein 39 (BRP-39) (Mohanty et al., 2021) .

1.1.10.4.3.1 Structure of CHI3L1

CHI3L1 is comprised of two globular domains (Mohanty et al., 2021). The structures of human and mouse CHI3L1 are shown in (Figure 1.12) , respectively. The structure of CHI3L1 suggests that it acts as a sensor to modulate innate defenses and inflammatory responses (Zhao et al., 2020). The sugar-binding groove in CHI3L1 could be its potential binding site for receptors, ligands, and inhibitor drugs.(Li et al., 2023)

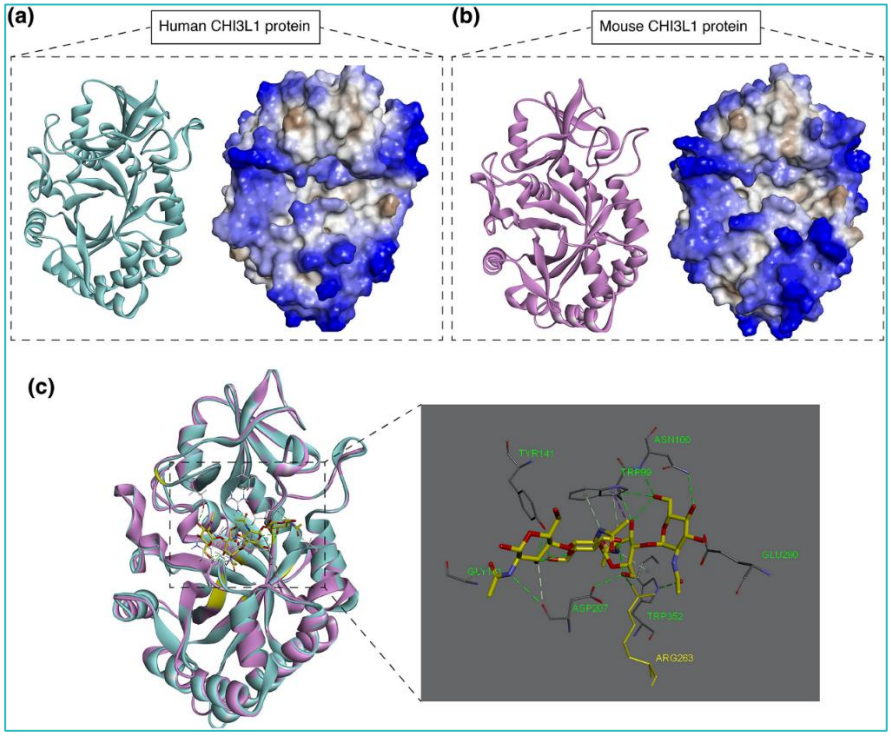

Figure [1.12] Crystal structure of CHI3L1 (Li et al., 2023)

Serum CHI3L1 is elevated in patients with CAD, and there was an association between serum CHI3L1 and the extent of CAD defined by the number of diseased vessels assessed by CA (Kucur et al., 2007). As one of the most investigated candidate biomarkers, CHI3L1 has been shown to contribute significantly to the progression of atherosclerosis since macrophages isolated from early atherosclerotic plaques express excessive CHI3L1, consequently suggesting that CHI3L1 could be identified as an emerging prognostic marker of atherosclerosis.(Deng et al., 2020)

It has been shown that serum CHI3L1 is closely associated with the early and late stages of the atherosclerotic process, and CHI3L1 induces monocytes to mature into macrophages, which are then secreted by macrophages and activated macrophages at a later stage of differentiation(Rehli et al., 2003).In addition, previous studies have shown that CHI3L1 levels are higher in patients with myocardial infarction(Fang et al., 2022b), stable CAD (Schroder et al., 2020), and HF (Chirinos et al., 2020). High levels of serum CHI3L1 are an independent predictor of major adverse cardiac events (MACE) after PCI in STEMI patients, and serum CHI3L1 can be used as a biomarker to predict the long-term prognosis of STEMI patients after PCI (Yang et al., 2019b, Hjort et al., 2021). Serum CHI3L1 levels predict postoperative myocardial reperfusion and in-hospital MACE in STEMI patients (Çetin et al., 2013).

CHI3L1 has been found to protect cardiomyocytes from apoptosis during ischemia-reperfusion injury(Harutyunyan et al., 2012). CHI3L1 could potentially be a new biomarker for myocardial ischemia, inflammation, remodelling and maybe a prognostic marker.(Wang et al., 2008)

1.2. The knowledge gap

The role of IMA has been previously confirmed to reflects the magnitude and duration of ischemia during PCI, and is not just a simple marker of free radical injury, the evaluation of its content may provide valuable information regarding the duration of diseases and possible complications, and it can be used in the differential diagnosis of certain pathological conditions. Since it has been reported before that IMA is a sensitive marker of PCI-induced ischemia in the PCI setting, and may have a role in clinical practice. (Shevtsova et al., 2021b, Kandeel Fathi Kandeel et al., 2022)

Myocardial cell death is a fundamental process in both physiological and pathological conditions (Zhang et al., 2020) Somatic (physical) stress is associated with physicochemical tissue injury, often called systemic when considered on a larger scale – affecting whole organs or the whole body (Gonzalez et al., 2011) on the other hand, oxidative or excitotoxic stress, which refer to physicochemical changes at the cellular and tissue level (subcategories of somatic stress)(Dimsdale, 2008)

Endothelial dysfunction has also been associated to the physiopathology of restenosis, since it is considered one of the earliest events in the genesis of atherosclerosis and is related to intimal hyperplasia and disease prognosis . (Kitta et al., 2005)

There are, however, reasons to believe that a large proportion of these patients reflect non-ischemic cardiac injury in the form of perioperative stress cardiomyopathy, yet directed studies are needed to confirm this hypothesis.(Iwaszczuk et al., 2021)

1.3. The aim of the study

Therefor current Study was aimed to examine the role of both biomarkers IMA and CHI3L1 in the complication and consequence after PCI in CAD group by the following objectives

- Estimating the level of IMA and CHI3L1in CCS patients who undergoing elective PCI and CA
- Study the Changes in IMA and CHI3L1 after PCI based on the complexity of procedure
- Studying the correlation between serum biomarkers and other causes of PCI complexity
- Investigating the diagnostic preferences of IMA and CHI3L1 using ROC analysis.

Chapter Two

Methodology

2- Materials and Methods

2.1. The study design & setting

A Case-Control Study was conducted at Karbala Center for Heart Diseases and Surgery and Imam Al – Hassan Al Mujtaba teaching hospital in Kerbala city . The study included patients in cardiac care unit (CCU), Catheterization lobby, and cardiac consultancies. The study was conducted from September 2023, through February 2024. The hospital ethics committee approved the study plan, and all patients or their relatives were informed. The study included (120) samples with ages ranging between (29-84 years), 91 males and 29 females, (72) of them underwent elective PCI and (48) as the control group underwent elective diagnostic angiography (CA) with CAD (Figure 2.1).

The stress biomarkers (hs-cTnI , IMA , CHI3L1) were tested for patients and control as pre and post procedure & comorbidities markers (lipid profile) were tested for patients and control.

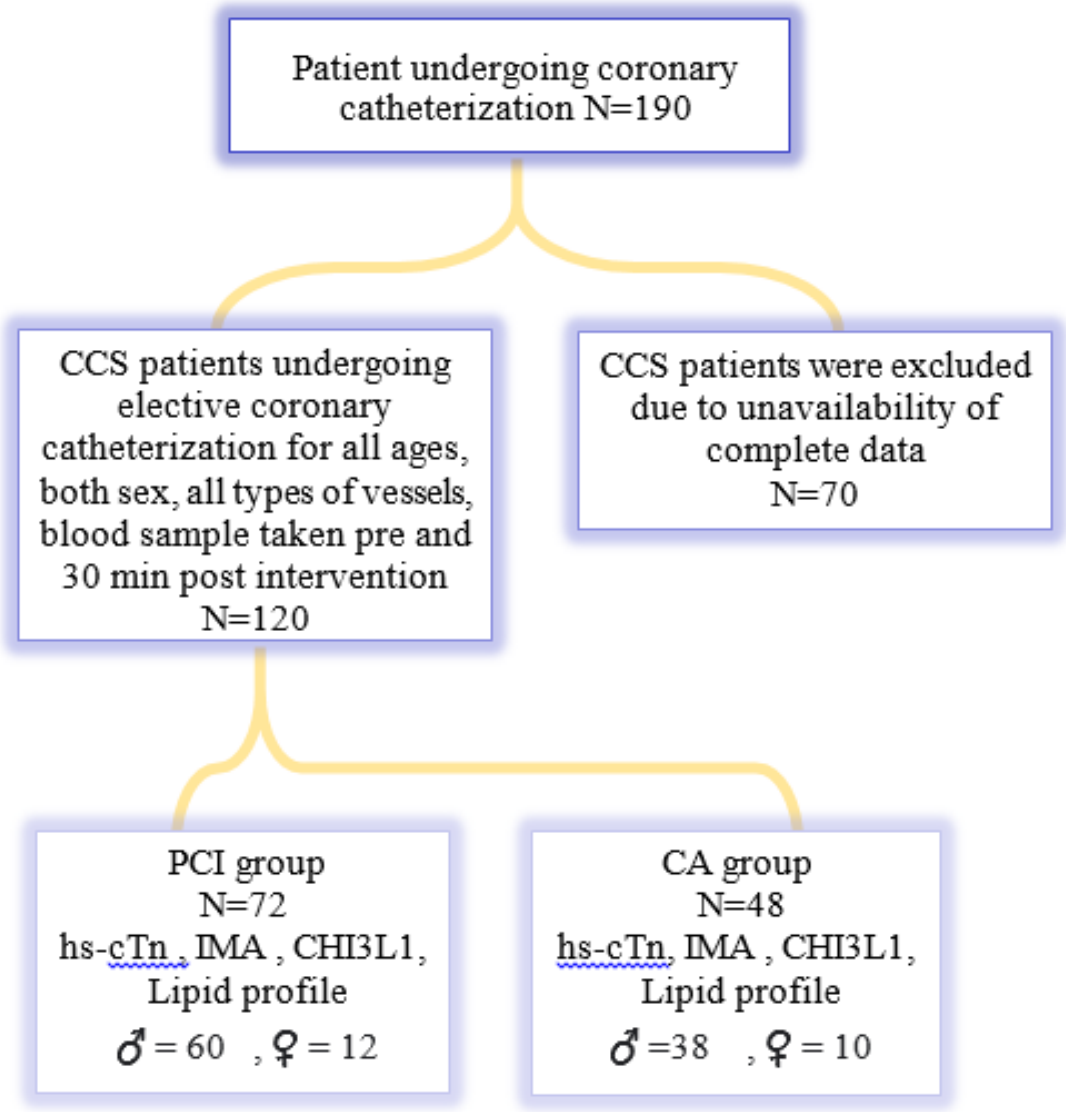

Figure [2.1] Schemed of the study

2.1.1. Inclusion criteria

120 participant with CCS undergoing elective coronary catheterization for all ages , both sex, all types of vessels , one or more vessels with and without bifurcation , one or more lesion , with or without HF were taken ,blood samples taken before and 30 min after intervention, and permission was taken from all patients to participate in current study.

2.1.2. Exclusion criteria

Current study excluded patients with ACS , Peripheral vascular disease (PVD), Chronic kidney disease (CKD) , Stroke , Preeclampsia , cancer, advanced liver insufficiency, prostate diseases, underwent a PCI two weeks ago or less ,and admitted to the emergency department two weeks ago or less .

2.1.3. The ethical approval

The study protocol was approved by the Ethical Committee at Kerbala University- College of Medicine, Karbala Center for Heart Diseases and Surgery and Imam Al – Hassan Al Mujtaba teaching hospital in Kerbala city. Verbal approval was taken from all patients included in the study before sampling.

2.1.4. The specimen collection & storage

The vein samples were collected from all cases and control pre and 30 min post coronary catheterization ; 5 mL of blood was drowned using a syringe, put in a tube containing a gel & clot activator & let for 15-minutes to one hour at room temperature to clot, and then separated into serum by centrifuge at 4000 r/min for 15-min.

The serum was stored in deep freeze at -80 ˚C to check the levels of (IMA), (CHI3L1) and (hs-cTnI) by ELISA.

2.1.5. Patients measurements

Each patient's medicinal & social data was gathered by a questionnaire (Appendix-1), evaluation ECG and echocardiogram (ECO) finding, angiography, and catheterization report, vital signs such as diastolic and systolic, body mass index (BMI). laboratory investigations was

measured for patients and control such as renal function test (RFT), random blood sugar (RBS) ,VIRAL and complete blood count (CBC).

The serum from each patient & control was used for Measurement (IMA, CHI3L1 and hs-cTnI) using ELISA technique (ELISA Reader), Lipid profile (Cholesterol, TG, HDL & LDL) using Spectrophotometric Technique (Architect c 4000).

2.2. The materials

2.2.1. The materials & tools

The materials &Tools with their supplier utilized in this investigation are listed in (Table 2.1).

Table [2.1] The materials & tools use

N	name	Company	Country
1	Pipette(100-1000µl)	Slamed®	Germany
2	Micropipette (10-100 µl)	Slamed®	Germany
3	Multi pipette	Slamed®	Germany
4	Pipette Tips-100µl (yellow)	Kirgen®	China
5	Pipette Tips-1000µl (blue)	Kirgen®	China
6	electronic personal scale	Detecto	USA
8	Gel tubes (6mL)	Nipigon Health LTD	Canada
9	Eppendorf Tubes (1.5 mL)	Kang Gia	China
10	Gloves	MedTech	Malaysia
11	Syringe (5 mL/cc)	JIANGSU KANGYOU MEDICAL INSTRUMENT CO.,LTD	China
12	Tube Rack	Slamed®	Germany
13	Tourniquet	Inzek International Trading	Netherland

14	Cotton	Modawa Medical	Iraq
15	Plaster	Life Plus Medical	China
16	Surgical Spirit	Ameya Fze	UAE
17	Plate Sealer	BT Lab	China
18	Pre-Coated ELISA Plate (96-well)	BT Lab	China
19	Specimen Transport Bag	Hepo International	China
20	Hard Ice Gels Packs	Hepo International	China
21	Laboratory Stopwatches & Timers	Spectrum	USA
22	Graduated Cylinder (1500 mL)	Eterna Duration	Germany
23	Pipette Rack Stand	Slamed®	Germany
24	Blood sugar measuring device	aconlabs	Germany
25	Distilled Water & washing bottle		Iraq

2.2.2. The laboratory kits

Laboratory kits used in the study are listed in (Table 2.2) below with their suppliers: -

Table [2.2] The laboratory kits which were used in current study

N	Name	Company	Country	No. Of Kits
1	Human Ischemia Modified Albumin Elisa Kit	BT Lab	China	3
2	Human Chitinase-3-Like Protein 1 Elisa Kit	BT Lab	China	3
3	Human High sensitivity Troponin I	BT Lab	China	2
4	Lipid profile kit	Abbott laboratories	USA	1

2.2.3. The instruments

All the instruments and tools which were used in current study are shown below in (Table 2.3).

Table [2.3] The instruments used in current study

N	Name	Company	Country
1	Centrifuge	Hettich	Germany
2	Deep freezer (-80 c°)	ALS	UK
3	ELISA Reader	ELX800	USA
4	ELISA Washer	ELX800	USA
5	Refrigerator (-2-8 c°)	Dairei	Denmark
6	Incubator (37°)	Pasteur	France
7	Architect c 4000	Abbott laboratories	USA

2.3. The methods

2.3.1. Measurement of BMI group

The equation determined the BMI : a person's weight in kilograms (Kg) divided by the square of the person's height in meters (m^2) .
The BMI was classified according to the World Health Organization (WHO) in (Table 2.4) (Seo et al., 2019) .

Table [2.4] BMI Status (Seo et al., 2019)

N	BMI (Kg/m^2)	Classification of BMI
1	Below 18.5	Underweight
2	18.5-24.9	Normal Weight
3	25.0 -29.9	Pre-Obesity
4	30.0 -34.9	Obesity Class-1
5	35.0 39.9	Obesity Class-2
6	Above 40	Obesity Class-3

2.3.2 Measurement of the atherogenic indices

- Atherogenic coefficient (AC) is the ratio of non-high-density lipoproteins cholesterol (non-HDL-C) to high-density lipoproteins cholesterol (HDL-C). (Olamoyegun et al., 2016)

$$AC = \text{non-HDL-C} / \text{HDL-C}$$

$$\text{Non- HDL-C} = TC - \text{HDL-C}$$

- Atherogenic index of plasma (AIP): is an unconventional lipid ratio representing the logarithm of the molar ratio of TG to HDL-C. (Gómez-Álvarez et al., 2020)

$$AIP = \log (TG/ \text{HDL-C})$$

- Castelli's risk indexes (I & II): (also called cardiac risk indexes) are two lipid ratios, the Castelli's I is the ratio of TC to HDL-C, while the Castelli's II is the ratio of LDL-C to HDL-C (Igharo et al., 2020),with notable positive correlation with *CAD.* (Tecer et al., 2019)

$$\text{Castelli's I} = TC/ \text{HDL-C ratio}$$

$$\text{Castelli's II} = \text{LDL-C} / \text{HDL-C ratio}$$

- Cholesterol index (C-index): is a simple index that predicts the probability of developing CAD with greater accuracy than the other indices (Ulusoy, 2013)

$$\text{C- index} = (\text{LDL-C}) - (\text{HDL-C})$$

2.3.3. The measurement of serum IMA

- Principle of Assay
  - This sandwich kit is for the accurate quantitative detection of Human Ischemia Modified Albumin (also known as IMA) in serum .
  - This kit is an Enzyme-Linked Immunosorbent Assay (ELISA).

- The Human IMA antibody has been pre-coated on the plate.
- IMA in the sample was added and binded to antibodies coated on the wells.
- A biotinylated human IMA antibody was added and binded to IMA in the sample.
- Streptavidin-HRP was added & linked to the biotinylated IMA antibody.
- The plate was incubated.
- Unbound Streptavidin-HRP was washed away during the washing step.
- A substrate solution was added, and the colour developed proportionately to the amount of Human IMA.
- The reaction was terminated by adding an acidic stop solution, and 450 nm absorbance was recorded.

❖ Preparation of Reagent

- Before use, all reagents (sample and standard) were brought to room temperature.
- It was formed a 320 ng/mL Standard inventory solution by adding 120 µL of the standard (640 ng/mL) to 120µl of standard diluent. The standard was Left to sit for 15 minutes with gentle agitation before diluting. Duplicate standard points were created by serially diluting the stock standard solution (320 ng/mL) 1:2 with standard diluent to produce 160 ng/mL, 80ng/mL, 40ng/mL and 20ng/mL solutions. The standard diluent was acted as the zero standards (0 ng/mL) (Figure 2.2) .
- The dilution of standard solutions suggested are as follows (Table 2.5):

Table [2.5] : Serial dilution of IMA Standard

320ng/mL	Standard No.5	120µl Original Standard + 120µl Standard Diluent
160ng/mL	Standard No.4	120µl Standard No.5 + 120µl Standard Diluent
80ng/mL	Standard No.3	120µl Standard No.4 + 120µl Standard Diluent
40ng/mL	Standard No.2	120µl Standard No.3 + 120µl Standard Diluent
20ng/mL	Standard No.1	120µl Standard No.2 + 120µl Standard Diluent

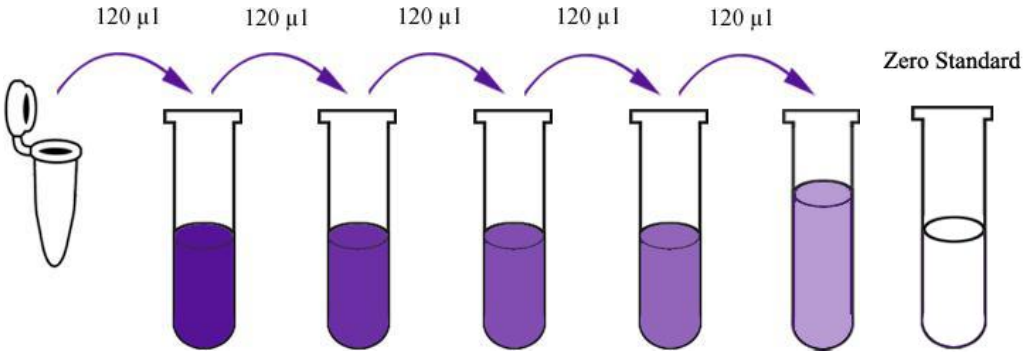

Figure [2.2] Serial dilution of IMA standard

❖ Wash Buffer

- Into Graduated Cylinder 20 mL of wash buffer consternate 25x was added.
- Distilled water (480 mL) was added into Graduated Cylinder and was yielded 500 mL wash buffer dilute.
- Wash buffer dilute in a Graduated Cylinder was added into the washing bottle ELISA.

❖ Procedure of Assay

- Standard (50µl) was added to standard well.
- Sample (40µl) was added to sample wells only.
- Anti- IMA antibody (10µl) was added to sample wells.

- Streptavidin-HRP (50µl) was added to sample & standard wells.
- The wells were mixed.
- The plate was covered with a new sealer.
- The plate was incubated at 37 °C for 60 minutes.
- The sealer was removed from the plate.
- The plate was washed with the wash buffer five times& was blotted the plate onto paper towels.
- Substrate solution A (50µl) & substrate solution B (50µl) were added into each well.
- The plate was covered with a new sealer.
- The plate remained incubated in the dark at 37 °C for 10 minutes.
- The stop solution (50 µl) was added in each well, the blue colour was changed into yellow .
- The plate was directly added to a microplate reader ELISA & was setted to 450nm.
- The optical density (O.D value) was read to determine the absorption level of each well. (Appendix-2)
- The results were printed with the graphic curve stander.

❖ Calculate of Result

The concentration of serum IMA and absorption & concentration of standard was evaluated by a standard curve by the ELISA Dia Reader as shown in the (Table 2.6).

The standard curve was calculated by graphing the average O.D for every standard on the vertical (Y) line versus the concentration on the horizontal (X) line & drawing a best-fit curve through the points on the graph, as shown in (Figure 2.3)

Table [2.6]The standard curve of human IMA

No.of standard (st)	Concentration of standard curve	Optical density (O.D)
st1	0 ng/mL	0.0
st2	20 ng/mL	0.347
st3	40 ng/mL	0.477
st4	80 ng/mL	0.643
st5	160 ng/mL	1.242
st6	320 ng/mL	2.283

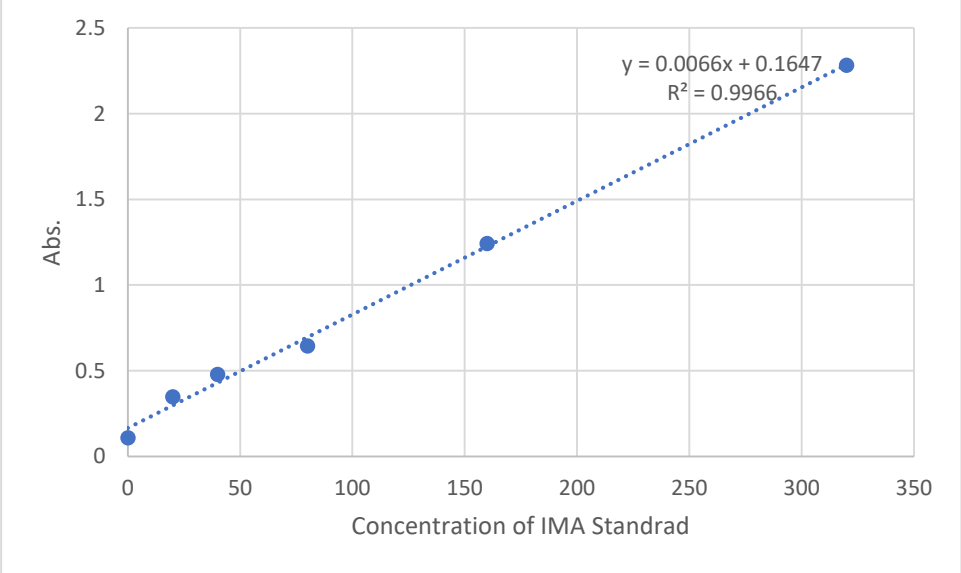

Figure [2.3] The standard curve of human IMA

2.3.4. The measurement of serum CHI3L1

❖ Principle of Assay

- This sandwich kit is intended for the precise quantitative human detection of Chitinase-3-like Protein 1 (also known as CHI3L1) in serum.
- The ELISA kit is an enzyme-linked immunosorbent assay.
- The Human CHI3L1antibody has been pre-coated on the plate.

- CHI3L1in the sample was added and binded to antibodies coated on the wells.
- A biotinylated human CHI3L1Antibody was added and binded to CHI3L1 in the sample.
- Streptavidin-HRP was added & linked to the biotinylated CHI3L1 antibody.
- The plate was incubated.
- Unbound Streptavidin-HRP was washed away during a washing step.
- A substrate solution was added, and the colour developed proportionately to the amount of human CHI3L1.
- The reaction was terminated by adding an acidic stop solution, and 450 nm absorbance was recorded.

❖ Preparation of Reagent

- Before use, all reagents (sample and standard) were brought to room temperature.
- It was formed a 240 ng/mL Standard inventory solution by adding 120 µL of the standard (480ng/mL) to 120µl of standard diluent. The standard was Left to sit for 15 minutes with gentle agitation before diluting. Duplicate standard points were created by serially diluting the stock standard solution (240ng/mL)1:2 with standard diluent to produce 120ng/mL, 60ng/mL, 30ng/mL and 15ng/mL solutions.The standard diluent was acted as the zero standards (0 ng/mL) (Figure 2.4).
- The dilution of standard solutions suggested are as follows (Table2.7):

Table[2.7] Serial dilution of CHI3L1 standard

240ng/mL	Standard No.5	120µl Original Standard + 120µl Standard Diluent
120ng/mL	Standard No.4	120µl Standard No.5 + 120µl Standard Diluent
60ng/mL	Standard No.3	120µl Standard No.4 + 120µl Standard Diluent
30ng/mL	Standard No.2	120µl Standard No.3 + 120µl Standard Diluent
15ng/mL	Standard No.1	120µl Standard No.2 + 120µl Standard Diluent

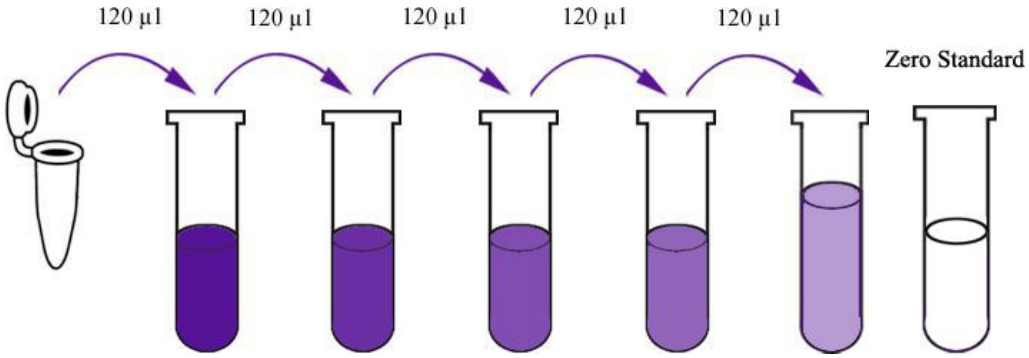

Figure [2.4] Serial dilution of CHI3L1 standard

❖ Wash Buffer

- Into Graduated Cylinder 20 mL of wash buffer consternate 25x was added.
- Distilled water (480 mL) was added into Graduated Cylinder and was yielded 500 mL wash buffer dilute.
- Wash buffer dilute in a Graduated Cylinder was added into the washing bottle ELISA.

❖ Procedure of Assay

- Standard (50µl) was added to standard well.
- Sample (40µl) was added to sample wells only.
- Anti- CHI3L1 antibody (10µl) was added to sample wells.

- Streptavidin-HRP (50µl) was added to sample & standard wells.
- The wells were mixed.
- The plate was covered with a new sealer.
- The plate was incubated at 37 °C for 60 minutes.
- The sealer was removed from the plate.
- The plate was washed with the wash buffer five times& was blotted the plate onto paper towels.
- Substrate solution A (50µl) & substrate solution B (50µl) were added into each well.
- The plate was covered with a new sealer.
- The plate remained incubated in the dark at 37 °C for 10 minutes.
- The stop solution (50 µl) was added in each well, the blue colour was changed into yellow .
- The plate was directly added to a microplate reader ELISA & was setted to 450nm.
- The optical density (O.D value) was read to determine the absorption level of each well. (Appendix-3)
- The results were printed with the graphic curve stander.

❖ Calculate of Result

The concentration of serum CHI3L1 and absorption & concentration of standard was evaluated by a standard curve by the ELISA Dia Reader as shown in the (Table 2.8).

The standard curve was calculated by graphing the average O.D for every standard on the vertical (Y) line versus the concentration on the horizontal (X) line & drawing a best-fit curve through the points on the graph, as shown in (Figure 2.5)

Table [2.8] The standard curve of human CHI3L1

No.of standard (st)	Concentration of standard curve	Optical density (O.D)
St1	0 ng/mL	0.0
St2	15 ng/mL	0.249
St3	30 ng/mL	0.436
St4	60ng/mL	0.715

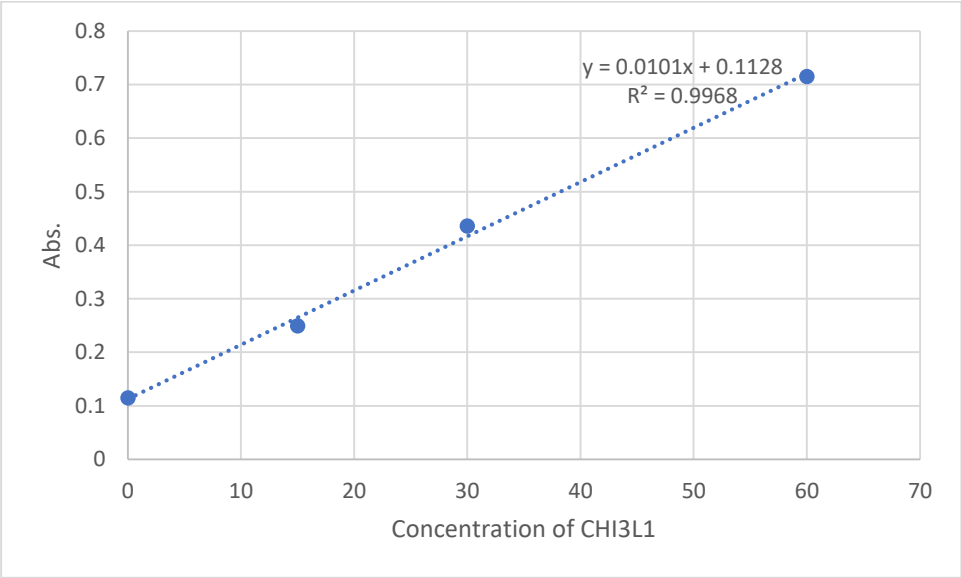

Figure [2.5] The standard curve of human CHI3L1

2.3.5. The measurement of serum HS TNI

❖ Principle of Assay

- This sandwich kit is intended for the precise quantitative human detection of Human High sensitivity Troponin I (also known as HS TNI) in serum.
- The ELISA kit is an enzyme-linked immunosorbent assay.
- The Human HS TNI antibody has been pre-coated on the plate.

- HS TNI in the sample was added and binded to antibodies coated on the wells.
- A biotinylated human HS TNI Antibody was added and binded to HS TNI in the sample.
- Streptavidin-HRP was added & linked to the biotinylated HS TNI antibody.
- The plate was incubated.
- Unbound Streptavidin-HRP was washed away during a washing step.
- A substrate solution was added, and the colour developed proportionately to the amount of Human HS TNI.
- The reaction was terminated by adding an acidic stop solution, and 450 nm absorbance was recorded.

❖ Preparation of Reagent

- Before use, all reagents (sample and standard) were brought to room temperature.
- It was formed a 1200ng/L Standard inventory solution by adding 120 µL of the standard (2400ng/L) to 120µl of standard diluent. The standard was Left to sit for 15 minutes with gentle agitation before diluting. Duplicate standard points were created by serially diluting the stock standard solution (1200ng/L) 1:2 with standard diluent to produce 600ng/L, 300ng/L, 150ng/L and 75ng/L solutions. The standard diluent was acted as the zero standards (0 ng/mL) (Figure 2.6) .

- The dilution of standard solutions suggested are as follows (Table 2.9):

Table [2.9]: Serial dilution of HS TNI standard

1200 ng/L	Standard No.5	120µl Original Standard + 120µl Standard Diluent
600ng/L	Standard No.4	120µl Standard No.5 + 120µl Standard Diluent
300ng/L	Standard No.3	120µl Standard No.4 + 120µl Standard Diluent
150ng/L	Standard No.2	120µl Standard No.3 + 120µl Standard Diluent
75ng/L	Standard No.1	120µl Standard No.2 + 120µl Standard Diluent

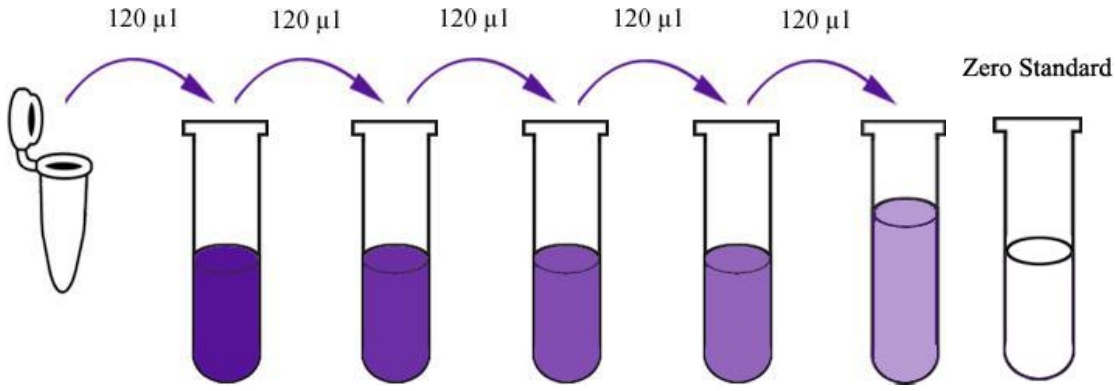

Figure [2.6] Serial dilution of HS TNI standard

❖ Wash Buffer

- Into Graduated Cylinder 20 mL of wash buffer consternate 25x was added.
- Distilled water (480 mL) was added into Graduated Cylinder and was yielded 500 mL wash buffer dilute.
- Wash buffer dilute in a Graduated Cylinder was added into the washing bottle ELISA.

❖ Procedure of Assay

- Standard (50µl) was added to standard well.
- Sample (40µl) was added to sample wells only.
- Anti- HS TNI antibody (10µl) was added to sample wells.

- Streptavidin-HRP (50µl) was added to sample & standard wells.
- The wells were mixed.
- The plate was covered with a new sealer.
- The plate was incubated at 37 °C for 60 minutes.
- The sealer was removed from the plate.
- The plate was washed with the wash buffer five times& was blotted the plate onto paper towels.
- Substrate solution A (50µl) & substrate solution B (50µl) were added into each well.
- The plate was covered with a new sealer.
- The plate remained incubated in the dark at 37 °C for 10 minutes.
- The stop solution (50 µl) was added in each well, the blue colour was changed into yellow .
- The plate was directly added to a microplate reader ELISA & was setted to 450nm.
- The optical density (O.D value) was read to determine the absorption level of each well. (Appendix-4)
- The results were printed with the graphic curve stander.

2.3.6. Serum Cholesterol:

❖ Methodology by Enzymatic

❖ **Principle of Assay**

- The cholesterol assay is used for the quantitation of cholesterol in human serum.
- Cholesterol ester + $H_2O \xrightarrow{\textbf{Cholestrol esterase}}$ Cholesterol + fatty acids
- Cholesterol + $O_2 \xrightarrow{\textbf{Cholesterol oxidase}}$ Cholest-4-ene-3-one + H_2O_2

- H_2O_2 + HBA+ 4-AAP $\xrightarrow{\textbf{Peroxidas}}$ Chromophore (quinoneimine dye)
- The chromophore (a quinonimine dye) was quantitated at 500 nm.

❖ **Normal Value:** in serum according to (Cleeman, 2001)

- < 200 mg/dL---------- > Desirable
- 200-239 mg/dL---------->Borderline
- ≥ 240 mg/dL----------> High

❖ **Procedure of Assay**

The Architect Abbott Laboratories device measures the Cholesterol level. **(Appendix-5)**

2.3.7. Serum Triglyceride:

❖ **Methodology by Enzymatic**

❖ **Principle of Assay**

- The Triglyceride (TG) assay is used to quantify TG in human serum.
- Triglycerides $\xrightarrow{\textbf{Lipase}}$ Free Fatty Acids + Glycerol
- Glycerol + ATP $\xrightarrow{\textbf{glycerol kinase}}$ Glycerol-3-Phosohate + ADP
- Glycerol-3-Phosohate $\xrightarrow{\textbf{glycerol phosohate oxidase}}$ DAP + H_2O_2
- H_2O_2 + 4-AAP + 4-CP $\xrightarrow{\textbf{Peroxidase}}$ Red Colored Dye
- The absorbance of this dye is proportional to the triglyceride concentration present in the sample.

❖ **Normal Value:** in serum according to(Cleeman, 2001)

- < 150 mg/dL---------- > Normal
- 150-199 mg/dL----------> Borderline High
- 200-499 mg/dL----------> High
- ≥ 500 mg/dL----------> Very High

❖ **Procedure of Assay**

The Architect Abbott Laboratories device measures the Triglyceride level. **(Appendix-6)**

2.3.8. Serum High-Density Lipoprotein (HDL):

❖ **The methodology** by Accelerator Selective Detergent.

❖ **Principle of Assay**

- The Ultra High-Density Lipoprotein (UHDL) assay is used to quantify HDL in human serum.
- The UHDL assay is a homogeneous method for directly measuring HDL cholesterol concentrations in serum.
- The method uses a 2-reagent format & properties of a special detergent.
- This method is based on Accelerating The Reaction of Cholesterol Oxidase (CO) With Non-HDL Un-Esterified Cholesterol and Dissolving HDL Cholesterol Selectively Using A Specific Detergent.
- The First Reagent, Non-HDL Un-Esterified Cholesterol, Is Subject to an Enzyme Reaction, and A peroxidase Reaction consumes the Peroxide Generated with DSBMT, Yielding A Colorless Product.
- The Second Reagent Consists of a Detergent (Capable of Solubilizing HDL Cholesterol), Cholesterol Esterase (CE), and a chromogenic coupler to Developer for the quantitative determination of HDL cholesterol.

❖ **Normal Value:** in serum according to(Cleeman, 2001)

- < 40 mg/dL----------> Major Risk Factor For Heart Disease.
- ≥ 60 mg/dL----------> Negative Risk Factor For Heart Disease.

❖ **Procedure of Assay**

The Architect Abbott Laboratories device measures the HDL cholesterol level. **(Appendix-7).**

2.3.9. Serum Very Low-Density Lipoprotein-Cholesterol (VLDL-C):

The Architect Abbott Laboratories device calculated the VLDL-C level according to Friedewald Equation. (Friedewald et al., 1972)

VLDL-C = Triglycerides(mg/dL) /5

❖ **Normal Value:** Less Than 20 mg/dL

2.3.10. Serum Low-Density Lipoprotein-Cholesterol (LDL-C):

The Architect Abbott Laboratories device calculated the LDL-C level according to Friedewald Equation(Friedewald et al., 1972).

LDL-C= Total Cholesterol(mg/dL) – (HDL-VLDL) mg/dL

❖ **Normal Value:** Up to 160 mg/dL

2.4. The statistical analysis

Information from the questionnaire and all test results from study group samples were entered into a data sheet. The data analysis for this work was generated utilising the social sciences statistical package, version 28.0 (IBM, SPSS, Chicago, Illinois, USA), and the Real Statistics Resource Pack software for Mac (Release 8.6) of the resource pack for Excel 2016, (Copyright, 2013 –2020), and graphical pad prism 9.

Descriptive statistics were applied to each group's data. Values were illustrated by n (%) for categorical; scale variables were presented by mean ± 2 standard deviation (SD) for normal data, while for non-normal data, continuous variables were presented by the interquartile range (IQR) and median. The distribution of the data was examined using the Shapiro-Wilk test as a numerical measure of normality.

Analytical and statistical tests confirmed significant differences in categorical variables among the parameters. Results of all hypothesis test with p-values <0.05 (two-sided) were considered statistically significant. The simultaneous confidence level for each confidence interval was calculated using Fisher's LSD technique" This simultaneous confidence level represents the probability that each confidence interval contains the true change." Fisher's LSD method was employed in ANOVA to produce confidence intervals for all pairwise differences between biomarkers and study groups.

The optimal threshold with high specificity and sensitivity for study cases was detected using receiver operating characteristic (ROC) analysis.

Chapter Three

Results

3. Results

3.1. Demographic characteristics and medical history

Table (3.1)summarizes the demographic characteristics of participants in two groups: PCI and CA

Results were shown that the majority of participants in both groups were males: 83.3% in PCI and 79.2% in CA, and Females represented a smaller portion of participants: 16.7% in PCI and 20.8% in CA.

Kerbala was the primary residence for a larger proportion of participants in the group CA (83.3%) compared to PCI (56.9%). Conversely, participants from outside Kerbala were more prevalent in the PCI (43.1%) compared to CA group (16.7%).

The mean age was similar for both groups: 57.7 years old (± 8.5 SD) for PCI and 57.1 years old (± 11.1 SD) for CA, and the mean BMI was higher in the CA group (31.3 kg/m² ± 5.7 SD) compared to the PCI group (29.5 kg/m² ± 5.5 SD).

Table [3.1] Demographics characteristic of the study groups among group:1 PCI, group2: CA

Demographics		PCI (N=72)	CA (N=48)
Sex No.(%)	Male	60(83.3%)	38 (79.2%)
	Female	12(16.7%)	10 (20.8%)
Residence No.(%)	Kerbala	41(56.9%)	40(83.3%)
	Other	31(43.1%)	8 (16.7%)
Age Mean ±2SD (year)		57.7± 8.5	57.1±11.1
BMI Mean ±2SD (kg/m^2)		29.5 ±5.5	31.3 ± 5.7

Table (3.2) compared the medical history of participants in two groups: PCI and CA. Results were indicated a higher percentage of participants in the CA

group reported never smoking (72.9%) compared to the PCI group (61.1%). Current smoking was more prevalent in the PCI group (33.3%) compared to CA (25.0%). Passive smoking was minimal in both groups.

The CA group had a higher proportion of participants with no history of diabetes mellitus (DM) (60.4%) compared to PCI (44.4%). Conversely, the PCI group had a higher percentage of participants with Type 2 DM (55.6%) compared to CA (39.6%).

Antiplatelet use was similar between the two groups, with a vast majority in both groups reporting current use (88.9%)for PCI , (89.6%) for CA. Family history of CAD was uncommon in both groups, with the vast majority (93.1%) for PCI group and (97.9%) for CA group reporting no family history.

Table [3.2] Medical history of the study groups included group:1 PCI , group2: CA

Medical History	PCI (N=72)	CA (N=48)
Smoking No.(%)		
No	44(61.1%)	35 (72.9%)
Active	24(33.3%)	12 (25.0%)
Passive	4(5.6%)	1(2.1%)
DM No.(%)		
No	32(44.4%)	29 (60.4%)
Type 2	40(55.6%)	19 (39.6%)
Anticoagulant No.(%)		
No	8(11.1%)	5 (10.4%)
Yes	64(88.9%)	43 (89.6%)
Family History of CAD No.(%)		
No	67(93.1%)	47 (97.9%)
Yes	5(6.9%)	1(2.1%)

3.2. Mean differences of biomarkers-based on the types of catheterizations

3.2.1. Comparison of pre & post-procedure levels of IMA and CHI3L1 in CA and PCI groups

Table (3.3) and (Figure 3.1) compared the pre- and post-procedure mean levels of two biomarkers, IMA and CHI3L1, between two groups: patients undergoing elective PCI and those undergoing diagnostic CA.

Results were shown that in both CA and PCI groups there was an increase in IMA levels following the procedure. Interestingly, even though that both groups were demonstrated an increasing in the level of post IMA (160.2±57.2 SD, 216.0±131.5 SD) pre &post PCI respectively (P value =0.03) and (157.6±62.9 SD, 219.4±129.4 SD) pre &post CA respectively (P value =0.21), only PCI group was shown a significant difference in the mean level when compared pre & post procedure level. On the other hand, in contrast to IMA, CHI3L1 levels appear to have decreased following the procedure in both groups, (254.2±110.6 SD, 217.2±96.2 SD) pre &post PCI respectively (P value =0.31) and (232.0±118.5 SD, 184.0±82.0 SD) pre &post CA respectively (P value =0.34) .

Table 3.3 Mean differences of Pre & Post procedure IMA and CHI3L1 Levels among group of elective PCI and group of CA.

Biomarkers	CA (N=48) Mean± 2SD			PCI(N=72) Mean± 2SD		
	Pre-Test	Post -Test	P value	Pre-Test	Post -Test	P value
IMA (ng/mL)	157.6±62.9	219.4±129.4	0.21	160.2±57.2	216.0±131.5	0.03
CHI3L1 (ng/mL)	232.0±118.5	184.0±82.0	0.34	254.2±110.6	217.2±96.2	0.31

(t- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, *: significant at p ≤ 0.001) , CA: Catheter Angiography.**

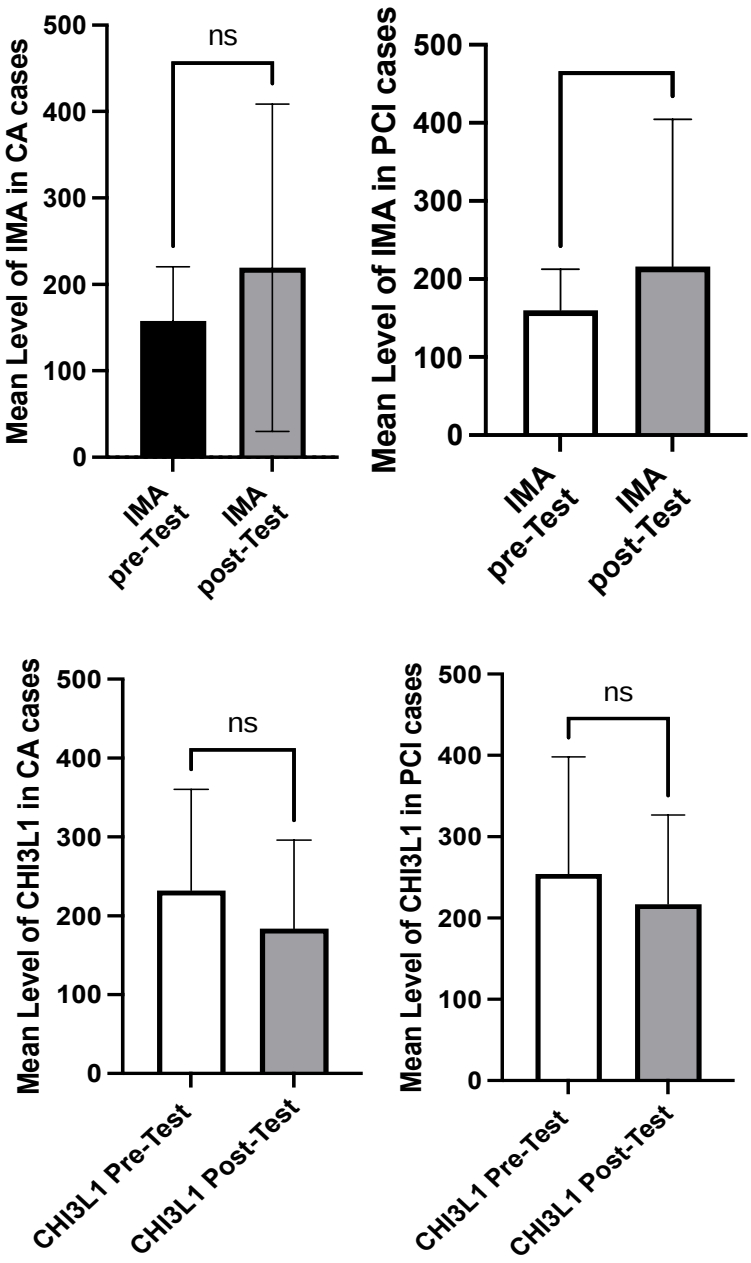

Figure [3.1] Mean differences of Pre & Post procedure IMA and CHI3L1 Levels among group of elective PCI and group of CA**(t- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001)**

3.2.2. Comparison of lipid profile levels in PCI and CA groups

Table (3.4) and (Figure 3.2) demonstrated the mean and SD of lipid profile levels in the two groups. Results were shown that the CA group had a slightly

higher average total cholesterol level (162.1 mg/dL ± 39.9 SD) compared to the PCI group (146.5 mg/dL ± 63.2 SD) (P value = 0.32). Also, the CA group had a considerably higher average LDL level (120.5 mg/dL ± 25.5 SD) compared to the PCI group (74.2 mg/dL ± 32.8 SD) (P value = 0.5). While PCI group had a higher average TG level (194.6 mg/dL ± 117.8 SD) compared to the CA group (134.7 mg/dL ± 34.4 SD) (P value = 0.25). Both groups had relatively low HDL levels, with similar averages: (35.7 mg/dL ± 11.5 SD) in the PCI group and (34.7 mg/dL ± 9.7 SD) in the CA group (P value = 0.71).

Table [3.4] Mean differences of lipid profile levels among group of elective PCI and group of CA

Lipid profile	PCI (N=72) Mean± 2SD	CA (N=48) Mean± 2SD	P value
Total cholesterol (mg/dL)	146.5±63.2	162.1±39.9	0.32
TG (mg/dL)	194.6±117.8	134.7±34.4	0.25
HDL (mg/dL)	35.7±11.5	34.7±9.7	0.71
LDL (mg/dL)	74.2±32.8	120.5±25.5	0.5

(t- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001)

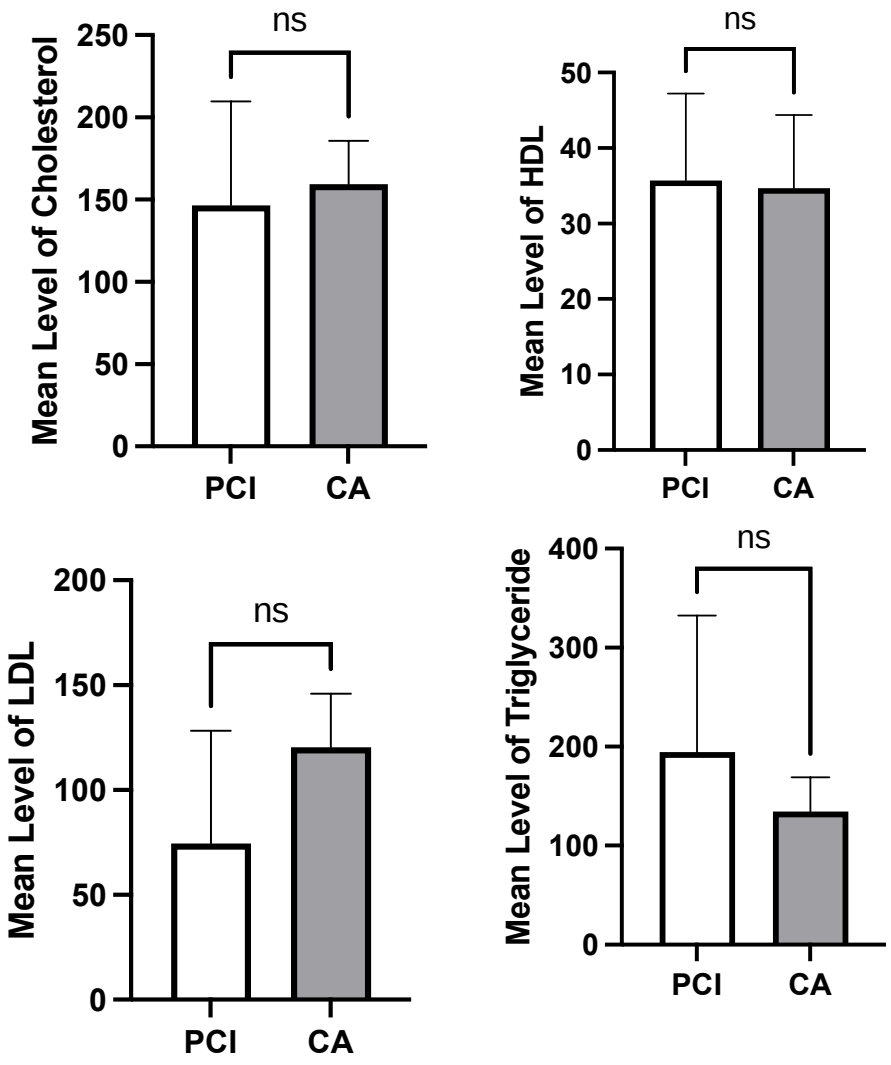

Figure [3.2] Mean differences of lipid profile levels among study groups (t- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001)

3.2.3. Comparison of atherogenic indices in PCI and CA groups

Lipid profile and atherogenic indices differences between PCI and CA groups

Regarding the lipid profile comparisons between patients undergoing PCI and diagnostic CA .The findings reveal interesting differences in cholesterol profiles between the two groups.

The CA group had slightly higher average total cholesterol and significantly higher LDL cholesterol compared to the PCI group. Results were shown a potentially higher burden of atherogenic lipoproteins (LDL) in the CA group.

Conversely, the PCI group had a significantly higher average TG level compared to the CA group. Elevated TG, often associated with metabolic syndrome, can also be a risk factor for cardiovascular disease. Both groups had relatively low HDL levels, with no significant difference between them.

In spite of the differences in the mean levels of lipids, however both study groups were having CAD.

Table (3.5) and (Figure 3.3) presented the mean and SD of atherogenic indices in patients undergoing elective PCI and those undergoing CA.

There was a mean difference in most atherogenic indices between the PCI and CA groups. The CA group has a significantly higher C-index (85.8 ± 18.7 SD) compared to the PCI group (37.1 ± 57.4 SD) (P value = 0.1). A higher C-index generally indicates a greater likelihood of atherosclerotic events. While the PCI group has a slightly higher average AIP (0.7 ± 0.5 SD) compared to the CA group (0.6 ± 0.1 SD) (P value = 0.65). The CA group has higher mean values for both Castelli's Indices (I and II) (5.4 ± 0.7 SD) and (3.6 ± 0.6 SD) compared to the PCI group (4.0 ± 1.9 SD, 2.0 ± 1.8 SD) (P value = 0.17) (P value =0.09). Similar to other indices, the CA group has a higher average AC index (4.4 ± 0.7 SD) compared to the PCI group (3.0 ± 1.9 SD) (P value = 0.17).

Table 3.5 Mean differences of atherogenic indices Levels among group of elective PCI and group of CA

Atherogenic Indices	CA (N=48) Mean± 2SD	PCI (N=72) Mean± 2SD	P value
C-index	85.8±18.7	37.1±57.4	0.1
AIP	0.6±0.1	0.7±0.5	0.65
Castelli's I	5.4±0.7	4±1.9	0.17
Castelli's II	3.6±0.6	2±1.8	0.09
AC index	4.4±0.7	3±1.9	0.17

(T- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, *: significant at p ≤ 0.001), C-index: Cholesterol Index , AIP: Atherogenic Index of Plasma , AC index: Atherogenic Coefficient Index.**

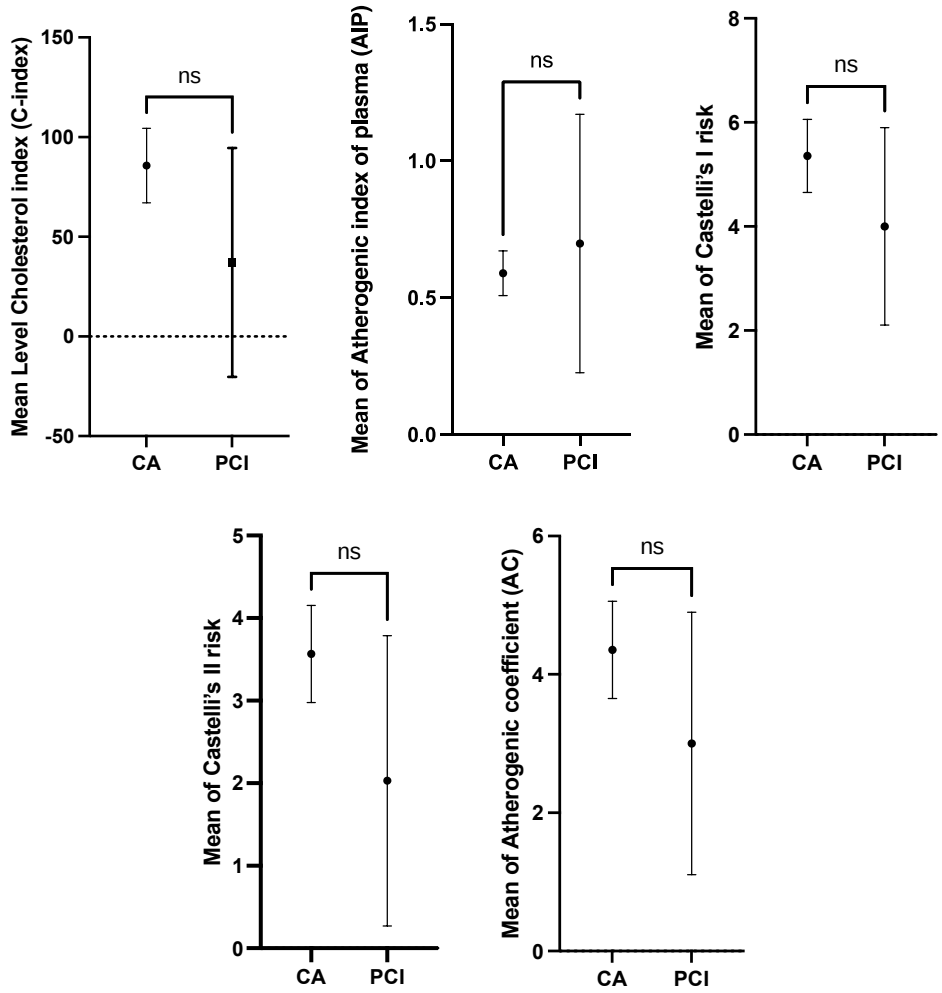

Figure [3.3] Mean differences of atherogenic indices levels among study groups **(T- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001)**

Current study compared atherogenic indices between patients undergoing PCI and diagnostic CA. The findings show that the CA group, despite having a seemingly lipid profile in some aspects, had significantly higher values for most atherogenic indices.

Current findings was highlighted the potential value of atherogenic indices in cardiovascular risk assessment. By incorporating these indices alongside traditional lipid profiles.

The CA group exhibited higher mean values for C-index, Castelli's I & II

indices, and AC index compared to the PCI group.

3.3. Study the angiographic lesion complexity score on IMA and CHI3L1 after PCI

Table (3.6) and (Figure 3.4) and (Figure 3.5) explores the potential association between angiographic lesion complexity score and levels of IMA and CHI3L1 in patients undergoing PCI. This comparison of IMA and CHI3L1 was used to provide a more complete picture of changes following PCI for each complexity score.

Results were shown that there was a trend of increasing average post-procedure IMA levels with higher angiographic lesion complexity scores. In score 0 (absent of complexity) the mean IMA level was (172.1±122.3 SD), score 1 was (138.0±66.0 SD), score 2 was (214.4±119.1 SD) and in score 3 (most complex) IMA level was (530.7±246.6 SD)

On the other hand, Unlike IMA, the trend for CHI3L1 is less clear. In score 0 the mean IMA level was (142.6±88.5SD), score 1 was (129.9±69.7 SD), score 2 was (81.5±23.4 SD) and the highest average post-procedure level

(209.0±112.1 SD) is observed in the most complex lesion score (score 3) group.

These findings indicated a possible link between higher Angiographic Lesion Complexity Scores and post-procedural IMA levels.

Table [3.6] Mean level of post procedure IMA and CHI3L1 among patients group of elective PCI based on Angiographic Lesion Complexity Score the number of scoring included any of the following criteria: Bifurcation, CTO, Type C, UPLMT, and Thrombus Formation

Biomarkers	score 0 N=21 Mean±2SD	score 1 N=23 Mean±2SD	score 2 N=20 Mean±2SD	score 3 N=8 Mean±2SD	p value
IMA (ng/mL)	172.1±122.3a	138.0±66.0a	214.4±119.1a	530.7±246.6b	0.001
CHI3L1 (ng/mL)	142.6±88.5a	129.9±69.7a	81.5±23.4a	209.0±112.1b	0.001

Note: (Post Hoc ANOVA test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, *: significant at p ≤ 0.001), CTO: Chronic Total Occlusion , UPLMT: Unprotected Left Main Trunk. Using the Post Hoc test, the mean's horizontally different in letters differ significantly**

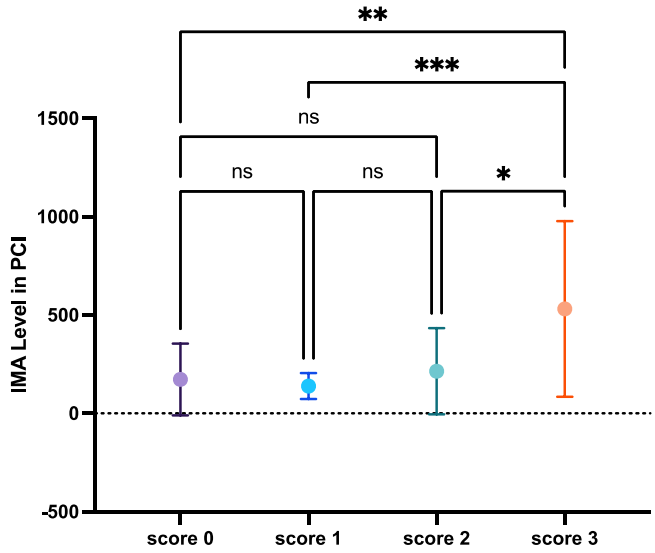

***Figure [3.4] Mean level of post procedure IMA among patients group of elective PCI based on angiographic lesion complexity score* (Post Hoc ANOVA test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001)**

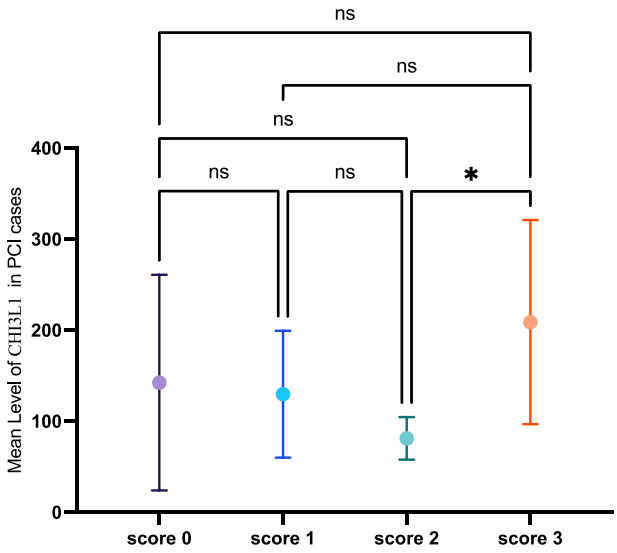

Figure [3.5] Mean differences of post procedure CHI3L1 among patients group of elective PCI based on angiographic lesion complexity score **(Post Hoc ANOVA test was *: significant at $p \leq 0.05$, **: significant at $p \leq 0.01$, ***: significant at $p \leq 0.001$)**

3.4. Study the effect of lesion length on pre & post- PCI levels of IMA and CHI3L1

Table (3.7) and (Figure 3.6) illustrated the potential influence of Lesion Length (less than 30mm vs. 30mm or greater) on pre & post-procedural levels of IMA and CHI3L1 in patients undergoing PCI.

Both lesion length groups showed an increase in IMA levels following PCI. Lesion length < 30mm: Pre-procedure mean was (167.8±63.2 SD), post-procedure level mean was (251.1±117.9 SD) (P value = 0.05), while Lesion length ≥ 30mm: Pre-procedure mean was (175.7±58.9 SD), post-procedure mean was (296.3±129.1 SD) (P value = 0.02), the increase appears to be greater for longer lesions (≥ 30mm).

These findings suggest a possible association between lesion length and changes in IMA levels after PCI, with potentially larger increases for longer lesions.

In contrast to IMA, the trend for CHI3L1 was opposite, since when Lesion length < 30mm: the Pre- procedure level was (273.7±110.9 SD), and in post-procedure level the mean was (174.2±111.7 SD) (P value = 0.09), and in case when the Lesion length ≥ 30mm, the Pre- procedure mean level was (295.6±106.1 SD), while the Post- procedure mean level was (143.5±83.4 SD) (P value = 0.01).

Both lesion length groups exhibited a decrease in CHI3L1 levels following PCI, as presented in Table 3.7

Table [3.7] Mean differences of pre & post procedure IMA and CHI3L1 among patients group of elective PCI based on the lesion length by comparing the mean level of pre & post procedure markers in (A) the lesion length <30mm, (B) lesion length ≥30mm

A	Lesion length <30mm N=44		P value
	Pre procedure Mean±2SD	Post procedure Mean±2SD	
IMA (ng/mL)	167.8±63.2	251.1±117.9	0.05
CHI3L1 (ng/mL)	273.7±110.9	174.2±111.7	0.09

B	Lesion length ≥30mm N=28		P value
	Pre procedure Mean±2SD	Post procedure Mean±2SD	
IMA (ng/mL)	175.7±58.9	296.3±129.1	0.02
CHI3L1 (ng/mL)	295.6±106.1	143.5±83.4	0.01

(T- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, *: significant at p ≤ 0.001)**

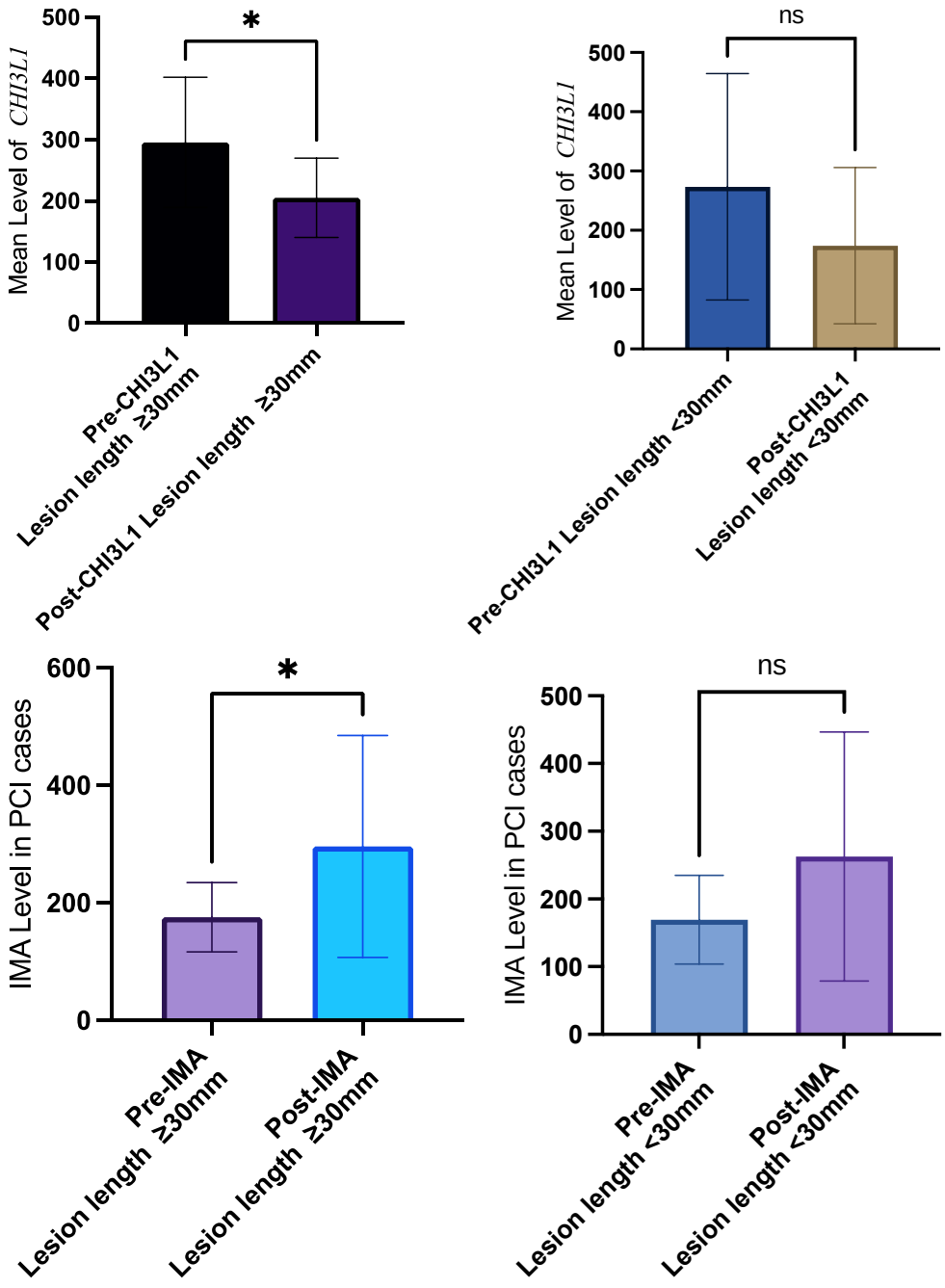

Figure [3.6] Mean differences of pre & post procedure IMA and CHI3L1 among patients group of elective PCI based on the lesion length **(T- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001)**

3.5. Study the effect of number of vessel disease on pre & post procedure levels of IMA and CHI3L1 after PCI

3.5.1. Single-vessel compared to single-vessel with bifurcation

Table (3.8) and (Figure 3.7) demonstrated the potential effect of the number of vessel disease (single vessel vs. single vessel with bifurcation) on pre & post- procedure levels of IMA and CHI3L1 in patients undergoing PCI.

Both groups displayed an increase in IMA levels following PCI. In case of Single vessel, Pre- procedure IMA mean was (169.5±63.6 SD), and the post-procedure level was (273.4±124.3 SD) (P value = 0.005) While in Single vessel with bifurcation, the Pre- procedure IMA level was (154.5±60.2 SD), and post- procedure IMA was (335.5±166.2 SD) (P value = 0.03). The increase appears to be larger in the group with bifurcation, while might be reflect the degree of the complexity.

For CHI3L1 the trend shown that in both groups it was decrease after PCI. In Single vessel group the Pre- procedure CHI3L1 was (191.7±61.6 SD), and in post-PCI was (132.2±41.9 SD) (P value = 0.42). On the other hand, in Single vessel with bifurcation, the pre- procedure CHI3L1 level was (191.2±63.8 SD), and the Post- procedure CHI3L1 was (135.5±43.0 SD) (P value = 0.48). The magnitude of decrease seems slightly less pronounced in the bifurcation group.

These findings suggest a possible link between the presence of a bifurcation and the magnitude of change in IMA levels after PCI, with potentially larger increases for bifurcations.

Table [3.8] Mean differences of pre & post- procedure IMA and CHI3L1among patients group of elective PCI based on the number of vessel diseases by comparing the mean level of Pre & Post procedure markers in (A) single-vessel compared to (B) single-vessel with bifurcation

A	Single vessel N=35		P value
	Pre procedure Mean±2SD	Post procedure Mean±2SD	
IMA (ng/mL)	169.5±63.6	273.4±124.3	0.005
CHI3L1 (ng/mL)	191.7±61.6	132.2±41.9	0.42

B	Single vessel with bifurcation N=16		P value
	Pre procedure Mean±2SD	Post procedure Mean±2SD	
IMA (ng/mL)	154.5±60.2	335.5±166.2	0.03
CHI3L1 (ng/mL)	191.2±63.8	135.5±43.0	0.48

(T- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, *: significant at p ≤ 0.001)**

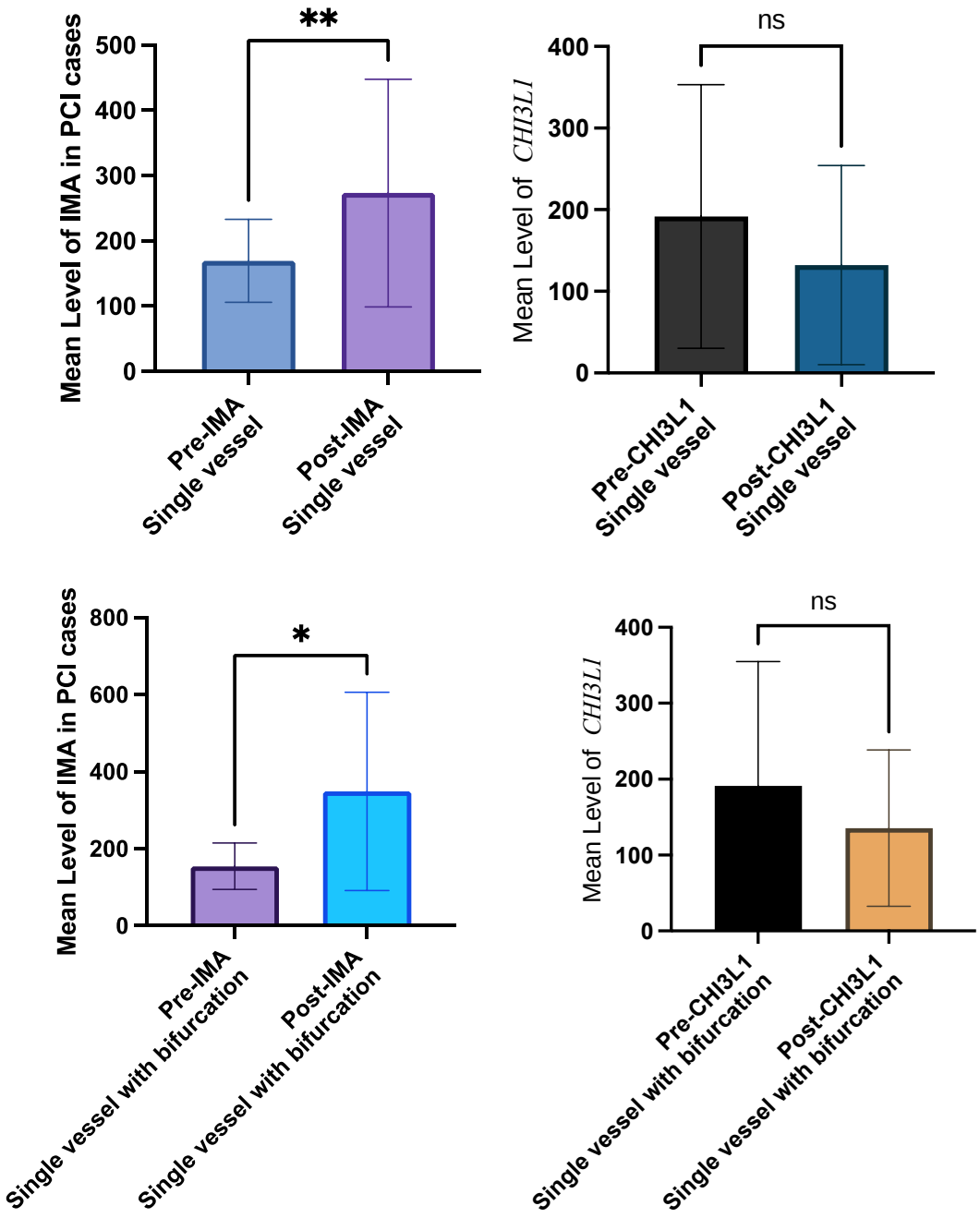

Figure [3.7] Mean differences of pre & post procedure IMA and CHI3L1 among patients group of elective PCI based on whether the PCI was for single vessel or single vessel with bifurcation **(T- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001)**

3.5.2. Multi-vessel compared to multi-vessel with bifurcation

Table (3.9) and (Figure 3.8) compared the mean levels of Pre & Post procedure IMA and CHI3L1 in case of multi-vessel compared to multi-vessel with bifurcation.

Both groups showed an increase in IMA levels following PCI. In Multi-vessel, Pre- procedure IMA was (165.9±61.7 SD), and post- procedure IMA was (355.9±51.7 SD) (P value = 0.01).

In case of multi-vessel with bifurcation, the pre- procedure IMA was (190.8±11.8 SD), and Post- procedure IMA was (332.7±83.4 SD) (P value = 0.01). The increase appears to be similar in both groups, despite the presence of a bifurcation.

IMA levels were shown a significant Differences when compared to the pre & post procedure level in multi-vessel PCI, and a significant difference when compared the pre & post procedure level in multi-vessel with bifurcation. Interestingly, even when compared the pre- procedure multi-vessel PCI and post procedure level in multi-vessel with bifurcation. These findings were highly indicated the power of IMA to reflect the stress on the blood vessel when PCI deal with multi-vessel or multi-vessel with bifurcation

The trend for CHI3L1 is markedly different between the two groups. In Multi-vessel: Pre- procedure CHI3L1 was (191.2±83.8 SD), and Post-procedure CHI3L1 was (135.5±63.0 SD) (P value = 0.4), while in Multi-vessel with bifurcation: Pre- procedure CHI3L1 was (280.5±87.9 SD), and the Post- procedure level was (79.5±33.6 SD) (P value = 0.008).

Table [3.9] Mean differences of pre & post procedure IMA and CHI3L1 among patients group of elective PCI based on the number of vessel disease by comparing the mean level of pre & post procedure markers in (A) multi-vessel compared to (B) multi-vessel with bifurcation

A	multi-vessel N=11		P value
	Pre procedure Mean±2SD	Post procedure Mean±2SD	
IMA (ng/mL)	165.9±61.7	355.9±51.7	0.01
CHI3L1 (ng/mL)	191.2±83.8	135.5±63.0	0.4

B	multi-vessel with bifurcation N=10		P value
	Pre procedure Mean±2SD	Post procedure Mean±2SD	
IMA (ng/mL)	190.8±11.8	332.7±83.4	0.01
CHI3L1 (ng/mL)	280.5±87.9	79.5±33.6	0.008

(T- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, *: significant at p ≤ 0.001)**

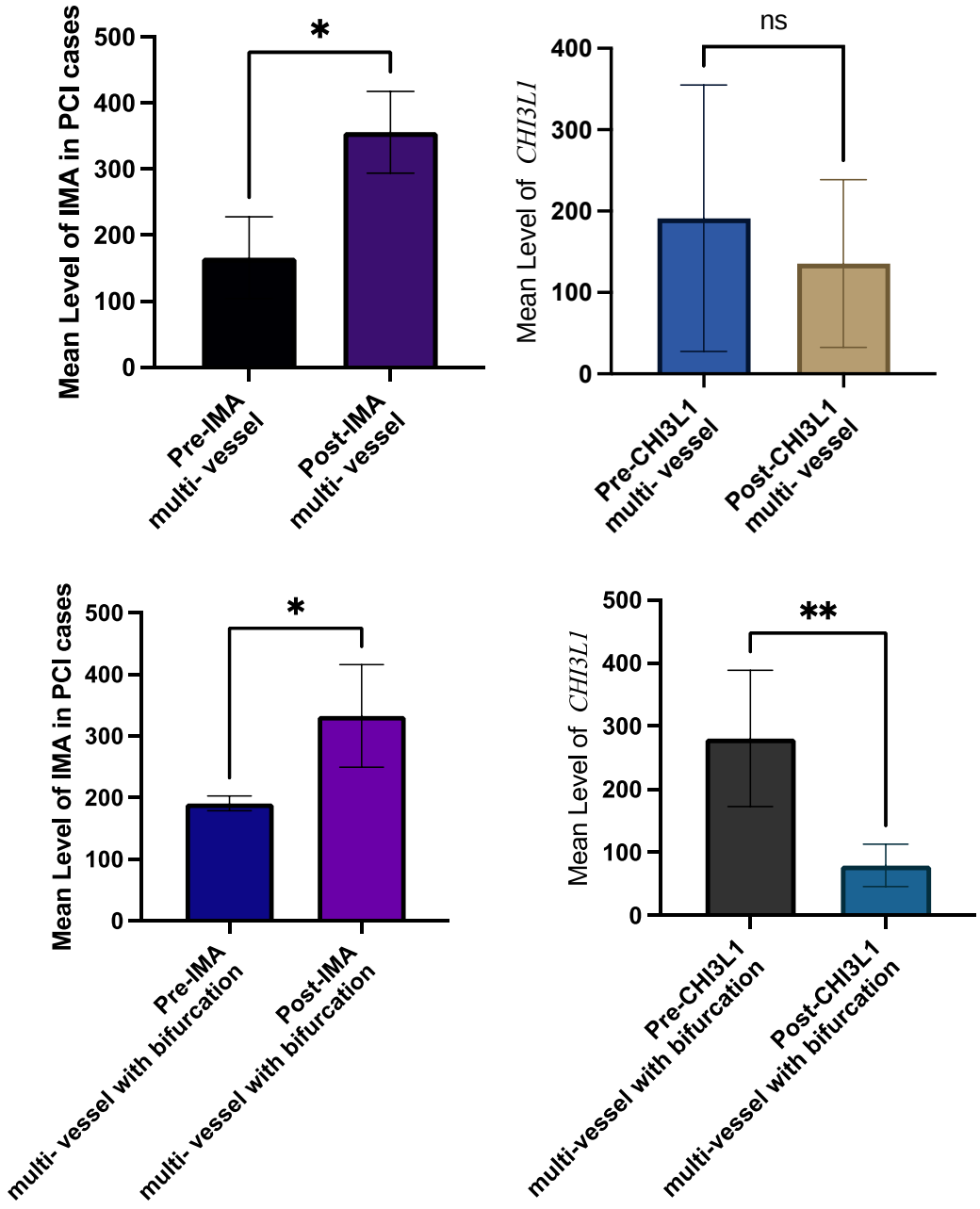

Figure [3.8] Mean differences of pre & post- procedure IMA and CHI3L1 among patients group of elective PCI based on whether the PCI was for multi- vessel or multi- vessel with bifurcation**(T- test was *: significant at p ≤ 0.05, **: significant at p ≤ 0.01, ***: significant at p ≤ 0.001)**

3.6. Correlation coefficients between biomarkers in PCI patients

Considering the important role of the measured parameters in PCI cases, the Pearson analysis of such group was used to show the response relationship between parameters. The correlation study demonstrated significant relationships among the measured parameters, P values were (< 0.05).

The (Figure 3.9) and (Figure 3.10) shows a range of correlation coefficients, indicating both positive and negative relationships between different biomarkers. Results were indicated that there is a moderate negative correlation between post- procedure IMA level and CHI3L1 (r =-0.5233).

post-procedure IMA has a moderate positive correlation with post-procedure hs-Tn levels (r = 0.4372) (P value = 0.05). This suggests that higher levels of IMA might be associated with some degree of myocardial injury after PCI.

On the other hand, weak to moderate negative correlations exist between various lipid profile markers (Total Cholesterol, TG, LDL, non-HDL-c) and post- procedure levels of IMA and CHI3L1. This suggests a potential inverse relationship in such cases after PCI.

Also, post- procedure IMA and CHI3L1 levels show weak negative correlations with some atherogenic indices (AC, AIP, Castelli's I & II risk, C-index). This might indicate that higher levels of these markers are associated with a less atherogenic profile. However, the correlations are weak and non-significant, details about the correlation coefficient (r) and p values were presented in Appendix (9) and Appendix (10)

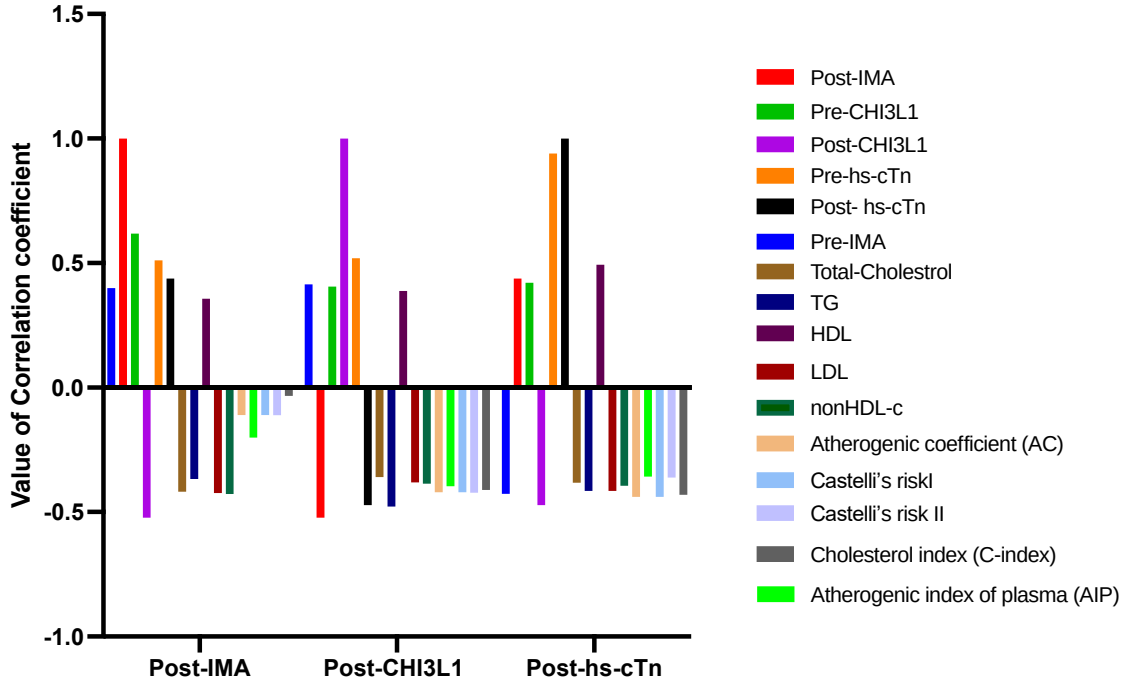

Figure [3.9] The correlation coefficient (r) between biomarkers among group of elective PCI

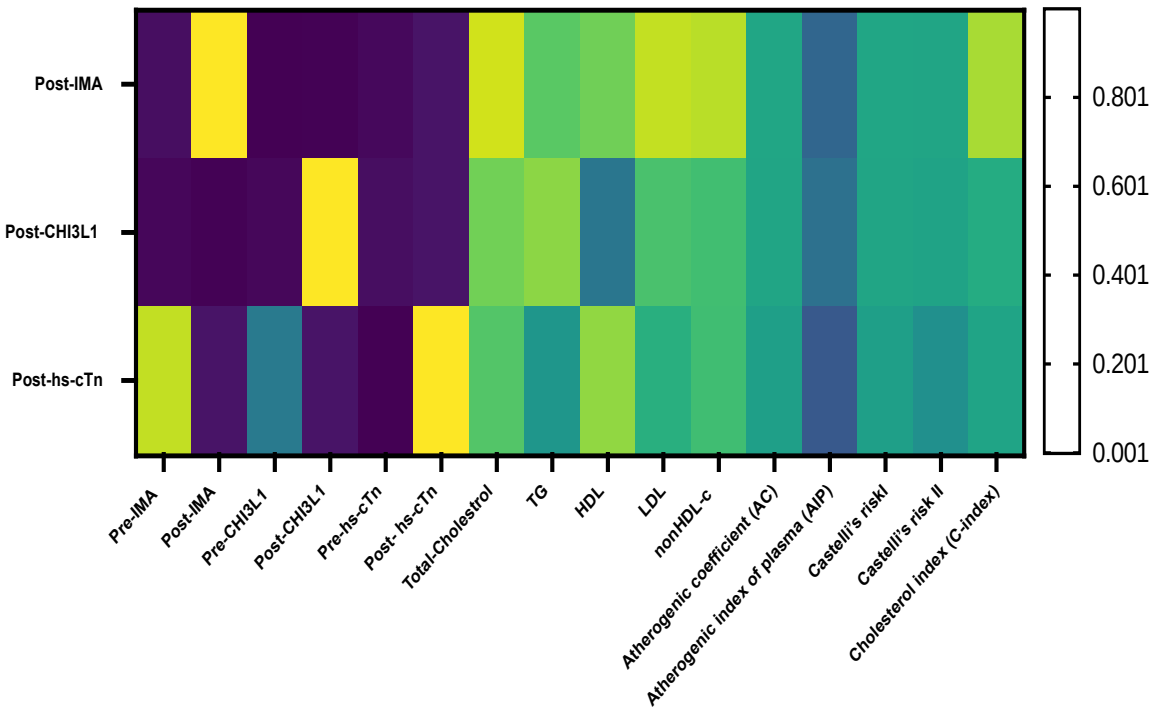

Figure [3.10] The significance of P value for the correlation between biomarkers among group of elective PCI

3.7. Receiver operating characteristics (ROC) curve

Receiver operating curve (ROC) curve and AUC analysis were performed for the IMA, and CHI3L1 as possible diagnostic parameters for PCI complexity. PCI complexity has been stated as PCI with at least 1 of the following characteristics: 1) 3 vessels treated; 2) ≥3 lesions treated;3) ≥3 stents implanted; 4) total stent length >60 mm;5) bifurcation with 2 stents implanted; 6) left main PCI; and 7) chronic total occlusion PCI.(Jin et al., 2024)

Table (3.10) and (Figure 3.11) summarizes the diagnostic performance of IMA levels in identifying patients who underwent a more complex PCI procedure.

Both Pre-procedure IMA and Post- procedure IMA have AUC values around 60%, indicating a moderate ability to distinguish between simple and complex PCI cases. Post- procedure IMA has a higher sensitivity (84.6%) compared to Pre- procedure IMA (58.6%). This means post-procedure IMA is better at correctly identifying patients who had complex PCI. Pre- procedure IMA has a higher specificity (69.7%) compared to post- procedure IMA (37%). This means Pre- procedure IMA is better at correctly identifying patients who did not have risk of complex PCI. Results of the Sensitivity & Specificity were confirmed using Youden's J statistics to the parameters. The table provides cut-off values for IMA levels along with their 95% confidence intervals. These values can be used to classify patients into high or low risk for complex PCI based on their pre- or post- procedure IMA levels.

Overall, the results suggest that IMA levels have some potential in identifying complex PCI cases. Post-procedure IMA might be better for detecting complex PCI, while pre procedure IMA might be better for ruling out patients who have risk of complex PCI.

Table (3.10) AUC, optimal threshold, sensitivity and specificity of IMA levels pre and post procedure based on the criteria of more complex PCI

Variable	AUC	Sensitivity %	Specificity %	Cut-off points	CI (95%)	P value
Pre-IMA (ng/mL)	60.4%	58.6%	69.7%	104.4425	0.414-0.714 (ng/mL)	> 0.05
Post-IMA (ng/mL)	60.7%	84.6%	37%	122.6045	0.400-0.714 (ng/mL)	> 0.05

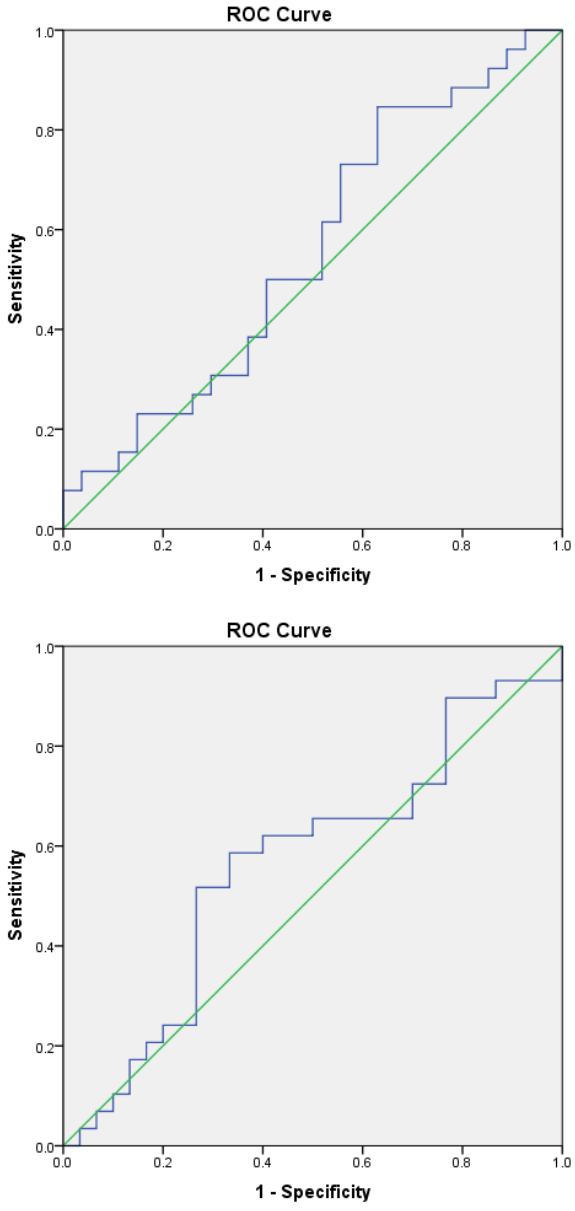

Figure (3.11) ROC curves for pre-& post procedure IMA in CCS patients undergoing PCI to analyse the optimal diagnostic points for predicting complex PCI compared to Non-complex group

Table (3.11) and (Figure 3.12) demonstrated the diagnostic performance of CHI3L1 levels in identifying patients who underwent a more complex PCI procedure.

Both Pre- procedure CHI3L1 and Post- procedure CHI3L1 have AUC values around 61-63%, indicating a moderate ability to distinguish between simple and complex PCI cases.

Pre- procedure CHI3L1 has a higher sensitivity (88.2%) compared to Post-procedure CHI3L1 (58.8%). This means Pre-procedure CHI3L1 is better at correctly identifying patients who had risk of complex PCI. Post-procedure CHI3L1 has a higher specificity (78.9%) compared to Pre-procedure CHI3L1 (36.8%). This means Post-procedure CHI3L1 is better at correctly identifying patients who did NOT have complex PCI.

Table also was presented cut-off values for CHI3L1 levels along with their 95% confidence intervals. These values can be used to classify patients into high or low risk for complex PCI based on their pre- or post-procedural CHI3L1 levels.

Table (3.11) AUC, optimal threshold, sensitivity, and specificity of CHI3L1 levels pre and post procedure based on the criteria of more complex PCI

Variable	AUC	Sensitivity %	Specificity %	Cut-off points	CI (95%)	P value
Pre-CHI3L1 (ng/mL)	62.9%	88.2%	36.8%	362.075 (ng/mL)	0.335-0.724	> 0.05
Post-CHI3L1 (ng/mL)	61.6%	58.8%	78.9%	93.738 (ng/mL)	0.368-0.783	> 0.05

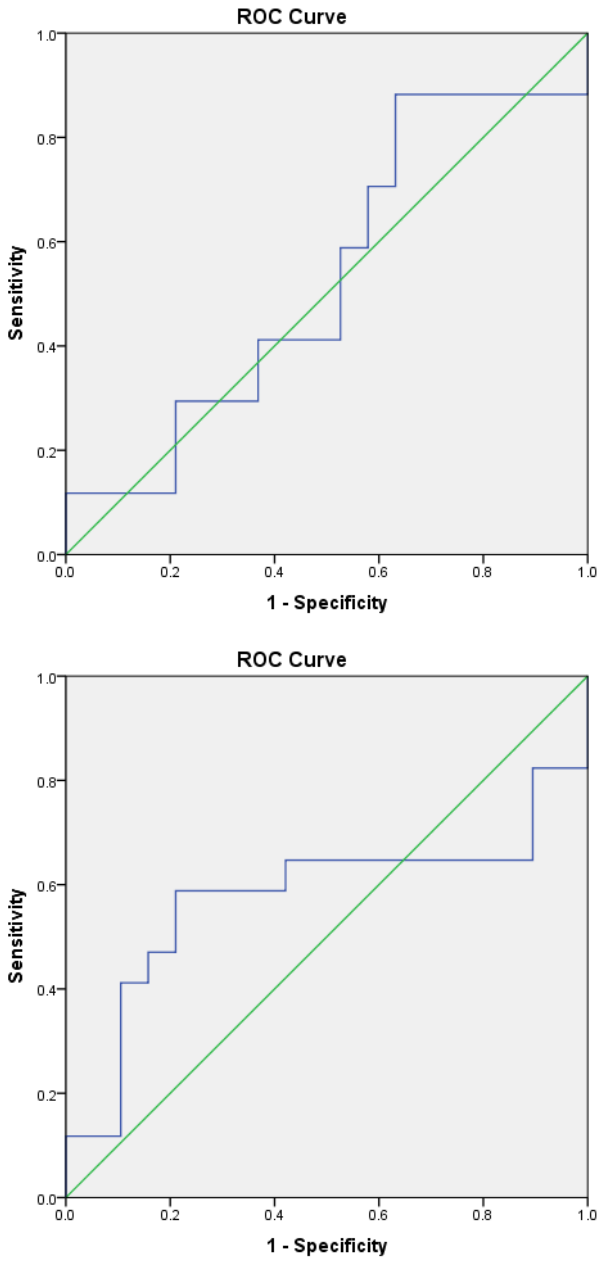

Figure (3.12) ROC curves for pre & post procedure CHI3L1 in CCS patients undergoing PCI to analyse the optimal diagnostic points for predicting complex PCI compared to Non-complex group

Chapter Four

Discussion

4- Discussion

In the current study, results were shown that the majority of participants in both groups were males. It has been found that women were less likely to be revascularized than men, either in the management of stable angina (Daly et al., 2006) or in acute coronary syndromes. (Heer et al., 2006)

Procedural and post interventional hospital complications were significantly higher in women compared to men, even after adjustment for age. This has been described before (Kleopatra et al., 2011) but the reasons for this finding are speculative (smaller vessel size in women, higher comorbidity, differences in endothelial function, variability in correct dosage of adjunctive medical therapy).(Heer et al., 2017)

Interestingly, sex differences in vascular complications after PCI were comparable to that after lone diagnostic coronary angiography, and they were lower compared to former reports, which may reflect the decreasing use of aggressive anticoagulation regimes, the use of weight-adjusted heparin dosing, and the introduction of smaller sheath sizes and early sheath removal.(Lansky et al., 2005)

High percentage of males was found to be suffering from the CHD than females. This does not seem to be by chance, rather shows increased prevalence of the disease among males in the selected study group as well as the general population(Shabana et al., 2020). Secondary causes, such as high values for mean TC, LDL-C, smoking rate, DM and low values for HDL-C in males than females may be due to higher prevalence in males than females.(Shabana et al., 2020)

In the current study, the mean age was similar for both PCI and CA group. The elderly have more cardiovascular risk factors and a greater burden of ischemic disease than younger patients needing PCI and, therefore, derive greater benefit from revascularization. (Wang et al., 2011)

Saada et al in 2022 found that all-cause death, cardiac mortality, and bleeding rates at 1-year were higher for elderly patients compared to patients younger than 80 years old. (Saada et al., 2022)

In the current study, the mean BMI was higher in the CA group compared to the PCI group. Wilson et al showed that obesity determined by BMI in men and women followed for up to 44 years was associated with an increased incidence of CVD.(Wilson et al., 2002)

The risk of CVD mortality rose progressively with increasing BMI in men < 65 years old. In a previous study these investigators showed that in men ≥ 65 years old no association between BMI and CVD mortality was noted.(Baik et al., 2000)

Brown et al demonstrated that a BMI of 19-24 kg/m^2 was the optimal BMI for minimizing CVD risk.(Katta et al., 2021)

Smoking increases mortality from all causes and has a crucial role in atherosclerotic cardiovascular disease(Gallucci et al., 2020).In the current study, current smoking was more prevalent in the PCI group compared to CA group. Bernhard and colleagues. showed that metals contained in cigarette smoke play a crucial role in damaging the vascular endothelium (Bernhard et al., 2005).The increased cardiovascular risk seems to be related to the adrenergic effects of nicotine that result in an increased heart rate, increased inotropic status, increased coronary microvascular resistance and reduced insulin sensitivity.(General, 2010)

Diabetes mellitus is a risk factor for CHD, independent of traditional risk factors such as hypertension, hyperlipidemia, and tobacco smoking(Goodarzi and Rotter, 2020).In the current study, the PCI group had a higher percentage of participants with Type 2 DM compared to CA. A small coronary angiographic study showed that the cardiovascular complications that occur in Type 2 DM patients depend on angiographic status rather than diabetes status, meaning that in the absence of obstructive

CAD on angiography, there is little difference in the incidence of cardiovascular events among patients with or without diabetes(Saely et al., 2004). Diabetic patients constitute one quarter of all cases undergoing coronary revascularisation procedures such as PCI(Rajbhandari et al., 2021). Among patients undergoing angiography (excluding those with known diabetes mellitus), rates of newly discovered impaired glucose tolerance and diabetes mellitus correlated with the extent of coronary artery disease (CAD).(Doerr et al., 2011)

Since IMA is generated immediately following myocardial ischemia, the causes of the increases in IMA have been shown to be endothelial or extracellular hypoxia, acidosis, and free oxygen radicals. It is the only marker of myocardial ischemia approved by the U.S. Food and Drug Administration (Demir et al., 2018). One recent study found that IMA rose rapidly 5–10 min after myocardial ischemia and could be detected in the reversible stage of ACS. It is, therefore, a stable, early, sensitive, and inexpensive biomarker for ACS (Turan et al., 2017). IMA content also depends on the duration of ischemic events: its levels after prolonged ischemia (25-60 min) are much higher than levels observed after short-term (15-21 min) ischemia (Gaze, 2013).Wahab et al. showed a distinct advantage of measuring IMA in patients presenting to the emergency department with acute chest pain to rule out a final diagnosis of ACS (Wahab, 2017). Several studies also indicated that IMA is a highly sensitive marker and has a high predictive value, which might prove the usefulness of this biomarker for early detection of myocardial ischemia (Gurumurthy et al., 2014) . Their research data showed a possible role of the IMA test in the early triage of patients with chest pain. Additionally, Mehta et al. also reported that serum IMA levels are significantly higher in patients with ACS compared to healthy controls, and have important clinical value in the early

diagnosis and risk stratification of ACS (Mehta et al., 2015). Consistent with above studies, current study indicated that serum IMA was closely related to the occurrence and severity of ACS after PCI and might become a novel marker for diagnosis complexity of PCI.

IMA reflects the magnitude and duration of ischemia during PCI, and is not just a simple marker of free radical injury, the evaluation of its content may provide valuable information regarding the duration of diseases and possible complications, and it can be used in the differential diagnosis of certain pathological conditions.

IMA is a sensitive marker of PCI-induced ischemia in the PCI setting, and may have a role in clinical practice. (Shevtsova et al., 2021b, Kandeel Fathi Kandeel et al., 2022)

4.1. Comparison of pre & post-procedure levels of IMA and CHI3L1 in CA and PCI groups

This study investigated the changes in IMA and CHI3L1 levels following two cardiac procedures: PCI and CA.

Both the PCI and CA groups showed an increase in IMA levels following the procedure. However, only the PCI group had a statistically significant difference between pre- and post-procedure levels. This suggests that PCI might induce a more significant degree of myocardial ischemia compared to CA which might reflect indirectly the complexity of PCI

In contrast to IMA, CHI3L1 levels were decreased following the procedure in both groups. This finding is not entirely clear and requires further investigation. CHI3L1 is a protein with anti-inflammatory properties (Zhao et al., 2020). Its decrease after both procedures could be due to a temporary suppression of the inflammatory response triggered by the cardiac intervention.

The Possible Explanation for Increased IMA after PCI might due to being PCI involves manipulating coronary arteries, which can temporarily reduce blood flow to the heart muscle (ischemia) (Mungee, 2023) . IMA is a marker of ischemia, and its increase in the PCI group likely reflects this temporary ischemic event. On the other hand, the lack of a significant rise in IMA following CA suggests minimal ischemia during this diagnostic procedure, which typically involves less manipulation of the coronary arteries.

4.2. Comparison of lipid profile levels and atherogenic indices in PCI and CA groups

Regarding the lipid profile comparisons between patients undergoing PCI and diagnostic CA .The findings reveal interesting differences in cholesterol profiles between the two groups.

The CA group had slightly higher average total cholesterol and significantly higher LDL cholesterol compared to the PCI group. Results were shown a potentially higher burden of atherogenic lipoproteins (LDL) in the CA group, current was agreed with the previous research who shown the role of LDL in the contribution of coronary artery plaque formation.) Mortensen et al., 2022(

Conversely, the PCI group had a significantly higher average TG level compared to the CA group. Elevated TG, often associated with metabolic syndrome, can also be a risk factor for cardiovascular disease. Both groups had relatively low HDL levels, with no significant difference between them.

In spite of the differences in the mean levels of lipids, however both study groups were having coronary artery disease. Dyslipidemia is an independent major risk factor for CAD. This variation might be due to lifestyle interventions and a wide range of risk factors resulting in CAD progression (Shahid et al., 2020)

Studies have reported a higher prevalence of dyslipidemia among such cases(Ganesan Karthikeyan, 2009). A combination of low HDL-C and high TG referred to as atherogenic dyslipidemia, have been implicated as important predictors of CAD.(K.E.L Harchaoui, 2009)

Current study compared atherogenic indices between patients undergoing PCI and diagnostic CA. The findings show that the CA group, despite having a seemingly lipid profile in some aspects, had significantly higher values for most atherogenic indices.

Current findings was highlighted the potential value of atherogenic indices in cardiovascular risk assessment. By incorporating these indices alongside traditional lipid profiles. The specific components contributing to a high atherogenic index can inform targeted managements.

The CA group exhibited higher mean values for C-index, Castelli's I & II indices, and the AC index compared to the PCI group. These indices generally reflect a higher risk of atherosclerotic events. These findings were consistence with others who suggests that atherogenic indices might provide a more comprehensive picture of cardiovascular risk compared to traditional lipid profiles alone.(Deng et al., 2023)

Recently, it has been confirmed that Atherogenic index of plasma (AIP) represents a novel marker in the current era of cardiovascular diseases (Wang et al., 2023, Zheng et al., 2022, Qin et al., 2020).considered AIP as a continuous variable, and found a significant positive correlation between AIP level and risk of all-causes mortality (Kasapkara and Erdoğan, 2023) .The disbalance of these plasma lipids leads to dyslipidemia, which is characterized by high levels of LDL-C, TG, and total cholesterol and low levels of HDL-C (Hoogeveen and Ballantyne, 2021) . Although reducing LDL-C levels is a treatment goal in CAD, even after attaining this target, a notable residual cardiovascular risk remains present, encouraging the exploration of more accurate risk factors in these patients (Ikezaki et al.,

2021) . Regarding a practical predictor, the AIP strongly predicts cardiovascular events by reflecting the atherogenic lipid profile and providing valuable insights into the residual cardiovascular risk. Other current investigation (Wang et al., 2023) yielded evidence that patients exhibiting elevated AIP levels were at a greater risk of MACE compared to those with lower AIP levels, primarily due to the heightened likelihood of unplanned repeat revascularization. Previous research has demonstrated a positive association between AIP levels and the severity of coronary artery lesions as well as plaque stability(Hu et al., 2023).

This meant that patients exhibiting elevated AIP levels are more susceptible to accelerated progression and rupture of coronary plaques, thereby elevating the likelihood of unplanned repeat revascularization. Secondly, several studies have demonstrated significant associations between elevated AIP level and insulin resistance, which is associated with an augmented susceptibility to cardiovascular events (Salazar et al., 2013) . Thirdly, patients with a high AIP level were more likely to be obese (Zhu et al., 2018), and manifest a greater incidence of hypertension, diabetes mellitus, and metabolic syndrome (Shi and Wen, 2023), all of which are essential players in poorer clinical outcomes following PCI.

On the other hand, results were shown that patients undergoing coronary angiography tend to have higher Castelli's I (CRI) and (CRII) values compared to those undergoing elective PCI, this finding was consistence with other research in different context who investigate the relationship between Castelli's I and II and ischemia severity (Doğanay, 2023) . It was found that Higher CRI levels were detected in patients with ischemia, while CRI-II levels was correlated with ischemia severity, but not CRI-I. CRI-II was a co-independent predictor of presence and severity of ischemia and CRI-II threshold levels showed a gradual increase in predicting ischemia severity. (Doğanay, 2023)

AD is primarily caused by atherosclerosis, while atherosclerosis-related diseases often have a poor prognosis (Shao et al., 2020) . It is known that mechanisms such as lipid accumulation in the arterial intima, activation of inflammatory cells such as monocytes and T lymphocytes, and production of matrix proteins play a role in the pathogenesis of atherosclerosis (Koelwyn et al., 2018).This is consistent with the detection of impaired lipid metabolism, elevated monocytes and CRP levels in patients with presence or severity of ischemia. Previous studies have demonstrated the role of CRI created from lipid profiles in predicting cardiovascular disease. Zhang et al. (Zhang et al., 2012) reported that CRI-I, which reflects coronary plaque formation, is associated with the risk of ischemic stroke in both men and women. Dai et al. (Dai et al., 2022) reported that aortic calcification exhibits a positive correlation with both CRI-I and CRI-II. Afsin et al. (Afsin et al., 2021)showed that CRI-II is an independent predictor of slow coronary flow. Although these findings support that CRI can be an important screening tool in predicting CAD,

Inflammatory activation can accelerate atherosclerosis (Wu et al., 2017). Following tissue damage, an inflammatory response causes macrophages to accumulate in the damaged tissue. It has also been suggested that HDL may inhibit leukocyte activation and migration (Spirig et al., 2013). Activated monocytes transform into macrophages by engulfing oxidized LDL cholesterol molecules. HDL cholesterol plays a role in reducing monocyte activation and reversing the effects of oxidized LDL (Nazir et al., 2020). This results in the secretion of pro- and anti- inflammatory cytokines and increased CRP production. Thus, an inflammatory response accelerates atherosclerosis (Badimon et al., 2018).

This mechanism was consistent with the positive correlation between CRIs and markers of inflammation. Previous studies reported a positive correlation between CRP levels and ischemia severity in CAD patients (Liu

et al., 2020). These mechanisms may explain the diagnostic performance power of CRI-II derived from LDL and HDL cholesterol levels. Moreover, CRI-II offered a gradual threshold values for distinguishing ischemia severity. CRI-II can be an inexpensive and easy screening tool to predict the severity of ischemia beyond presence of ischemia.

This study compared atherogenic indices between patients undergoing percutaneous coronary intervention (PCI) and diagnostic catheter angiography (CA). The findings show that the CA group, despite having a seemingly lipid profile in some aspects, had significantly higher values for most atherogenic indices.

This finding was highlighted the potential value of atherogenic indices in cardiovascular risk assessment. By incorporating these indices alongside traditional lipid profiles. The specific components contributing to a high atherogenic index can inform targeted managements.

The CA group exhibited higher mean values for C-index, Castelli's I & II indices, and the AC index compared to the PCI group. These indices generally reflect a higher risk of atherosclerotic events. These findings were consistence with other who suggests that atherogenic indices might provide a more comprehensive picture of cardiovascular risk compared to traditional. parameters such as AIP, AC, CR I&II which can be calculated more easily and that can better reflect the complex lipid metabolism, should be taken into account in daily practice in addition to follow-up of traditional lipid parameters.

4.3. Study the angiographic lesion complexity on the levels of IMA and CHI3L1 after PCI

A trend of increasing average post-procedure IMA levels was observed with higher Angiographic Lesion Complexity Scores. This suggests that more

complex lesions (Score 3) might be associated with greater myocardial ischemia during the procedure, as reflected by higher IMA levels.

The possible explanation might be due to Complex lesions which are likely to involve more significant blockage of coronary arteries, potentially leading to a greater degree of myocardial ischemia during the procedure. IMA is a marker of ischemia, and its elevation in patients with complex lesions supports this notion.

Also, it might reflect the Severity of Intervention, since More complex lesions could necessitate more extensive procedures to open the blockage, potentially causing more temporary ischemia compared to simpler lesions.(Hu., 2024)

For CHI3L1 , no previous studies were reported such findings. It is known to have anti-inflammatory effects. The lack of a clear trend might be due to the complex interplay between inflammation and ischemia during the procedure. More research is needed to understand how CHI3L1 levels are affected by angiographic lesion complexity and their potential role as a biomarker in this context.

In current study the Pre-procedural assessment of lesion complexity could help identify patients at higher risk for ischemia during procedures. This information could be valuable for guiding management strategies and potentially improving patient outcomes.

4.4. Study the effect of lesion length on pre & post- procedure levels of IMA and CHI3L1

Current study investigated the impact of lesion length on changes in IMA and CHI3L1 levels following PCI. The findings suggest a possible association between lesion length and these biomarkers. These findings were reported for the first time in current study, no previous results have

performed such comparison in IMA and CHI3L1 after PCI based on the Lesion Length

Both lesion length groups (less than 30mm and greater than or equal to 30mm) showed an increase in IMA levels following PCI. However, the increase appeared to be greater for lesions longer than 30mm. This indicated a potential link between lesion length and the degree of myocardial ischemia during the procedure. Longer lesions might restrict blood flow to a larger area of the heart, leading to more significant ischemia(Tomey et al., 2014), and in our case its more pronounced rise in IMA. The increase in IMA with longer lesions supports its role as a marker of ischemia. More extensive blockage by longer lesions likely leads to more ischemia, reflected by a higher rise in IMA.

In contrast to IMA, CHI3L1 levels decreased after PCI in both lesion length groups. This decrease might be due to the complex interplay between ischemia and inflammation during the procedure.

4.5. Study the effect of number of vessel disease on pre & post procedure levels of IMA and CHI3L1

Furthermore, the current study examined the potential impact of having a coronary bifurcation (single or multi vessel with bifurcation) on the pre- and post-procedural levels of IMA and CHI3L1in patients undergoing PCI. The findings suggest a possible association between bifurcation and the changes in these biomarkers.

Both groups (single and multi vessel, single and multi vessel with bifurcation) showed an increase in IMA levels after PCI. However, the increase appeared to be larger in the bifurcation group. This suggests a potential link between the presence of a bifurcation and the degree of myocardial ischemia during PCI(Hak Seung Lee 2022). Bifurcations might

be technically more challenging to treat, potentially leading to more ischemia stress and a more pronounced rise in IMA.

CHI3L1 levels decreased after PCI in both single vessel and single vessel with bifurcation groups. The decrease, however, appeared slightly less pronounced in the bifurcation group.

The larger increase in IMA with bifurcation might reflect the greater complexity of these lesions and potentially a higher degree of ischemia during PCI. PCI procedures involving bifurcations are often technically more complex, requiring additional maneuvers that could prolong ischemia time and contribute to a more significant rise in IMA.

4.6. Correlation coefficients between biomarkers in PCI patients

Regarding the interrelationships between biomarkers after PCI. The negative correlation between IMA and CHI3L1 could be due to the complex interplay between ischemia and inflammation. While ischemia might trigger an initial inflammatory response (leading to a decrease in CHI3L1), the overall burden of ischemia might overwhelm this response.

The positive correlation between IMA and hs-Tn suggests that higher levels of ischemia (IMA) might be associated with some degree of myocardial injury (hs-Tn) after PCI. This could be due to damage caused by prolonged or severe ischemia during the procedure. (Gjin Ndrepepa 2016)

The correlation between pre-procedural hs-Tn and post-procedural biomarkers suggests that pre-existing myocardial injury might worsen the ischemic response and potentially lead to further injury during PCI.

These findings highlight the potential of IMA as a marker for not only ischemia but also potential myocardial injury after PCI, especially when correlated with hs-Tn.

By considering pre-procedural hs-Tn levels and monitoring IMA during PCI, healthcare professionals might be able to tailor strategies to minimize ischemia and potential injury.

For overall results, the previous research shown a wide range of evaluation of IMA in different types of heart disease. Reddy et al. (2014) demonstrated that IMA can be an early predictor of Tn-I results after 6-24 hours in patients with ACS, suggesting an association between IMA and Tn-I.(Reddy et al., 2014) Increased levels of IMA evidently forecasted adverse results in patients and increased the hospitalization days (Nepal et al., 2017). (Nepal et al., 2017)

Evaluation of serum IMA is recommended not only for early detection of myocardial ischemia but also as a prognostic indicator of the disease severity. (Shevtsova et al., 2021b)

Mowafy et al. (2013)(Mowafy, 2013) reported that there was a statistically significant positive correlation between IMA levels and TIMI risk score of the study patients. Also, there was significant positive correlation between IMA levels and the extent of the coronary artery disease, defined by number of vessels affected in ischemic patients but not the severity of the disease. As a predictor of mortality, IMA at a level of 9.65 ng/mL had a sensitivity of 66.6% and specificity of 88.6%. Although the mean level of IMA was higher in morbid patients (during the follow-up period) when compared with non-morbid patients, this difference was statistically insignificant.

Patients were divided into three groups based on the number of coronary lesions: one vessel, two vessels, or three vessels. Serum IMA levels were significantly different between subgroups of patients with ACS ($P < 0.05$), and increased with the number of coronary lesions. (Fumeng Yang, 2019)

In current study, we investigated the association between serum IMA and CHI3L1 in CCS patients who having elective PCI to provide evidence that the serum levels of both markers were in line with the complexity of PCI.

This is the first study to evaluate whether IMA levels correlate with increasing vessels stress, as assessed by relation to PCI complexity.

Previously, It was found that the only variables independently related to post-PCI IMA levels were balloon inflation pressure, inflation duration, and number of inflations. There is some scatter in the correlations reported in current study, probably a reflection that the duration and number of inflations are some of the variables that may be involved in IMA production during PCI. Factors such as the severity and extent of the lesion and the presence or absence of collateral blood supply may also play a role in IMA levels. The results of study suggest that IMA is not only a marker of the occurrence of an ischemic event but also an indicator of the severity of ischemia. (Quiles et al., 2003)

The results of study highlighted that serum IMA level was significantly higher in CCS group after PCI, thus supporting the fact that patients with evidence of myocardial ischemia and ACS have reduced cobalt binding to HSA. (Kandeel Fathi Kandeel et al., 2022) Various mechanisms have been proposed for the generation of IMA. Cardiac ischemia may induce hypoxia, acidosis, increased free radical damage, membrane energy-dependent sodium and calcium pump disruptions, free iron and copper ion exposure, all of which involves damage of the amino terminal of HSA (Patil et al., 2013). The release of fatty acids in myocardial ischemia results in the binding of fatty acid to albumin, inducing a conformational change in albumin, thus reducing its binding with Co (II) (Mishra et al., 2018).(Mishra et al., 2018) Study has reported that IMA values during balloon angioplasty, showed correlation with the number, pressure and inflation duration, suggesting that IMA reflects to the magnitude and duration of ischemia during PCI, and is not just a simple marker of free radical injury. While in the same study, CK-MB and Mb showed no alterations immediately after PCI.

Lin et al. (2011) compared between the means of IMA before and after PCI that showed that IMA was higher after PCI than before.(Lin et al., 2011)

Studies by other investigators that used PCI as a model of transient myocardial ischemia have also shown that IMA levels increased very early after balloon inflation.(Bar-Or et al., 2001)

IMA levels in all patients increased significantly after PCI from baseline to post-PCI (59.9 to 80. 9 U/mL, p 0.0001). IMA levels were higher in patients with more balloon inflations, higher pressure inflations, and longer inflation duration.(Quiles et al., 2003)

Regarding the CHI3L1 This is the first study to evaluate whether CHI3L1 levels correlate with increasing vessels stress, as assessed by relation to PCI complexity.

Only a few studies were reported some correlation with other case of heart disease which might be used as indirect evidence to reflect their role in the severity of the disease.

The acute phase protein CHI3L1 is a new potential biomarker of inflammation in patients with coronary heart disease, and macrophages in atherosclerotic plaques express CHI3L1, with the highest expression seen in macrophages from early atherosclerotic lesions.(Fang et al., 2022a)

Inflammation is of great importance in the long-term development of atherosclerotic lesions and ischaemic heart disease. Since 2007, multiple pro-inflammatory cytokines have been confirmed to play an important role in promoting cardiovascular diseases, especially elevated levels of serum CHI3L1 in patients with stable ischaemic heart disease (Kucur et al., 2007). This finding has further been replicated in many studies from different countries, revealing a positive correlation between CHI3L1 levels and number of main coronary vessel diseases with >50% stenosis (Kastrup et al., 2009). Importantly, whether baseline elevated serum CHI3L1 levels are

associated with risks of later promotion of ischaemic heart disease is being elucidated.(Deng et al., 2020)

It was found that plasma CHI3L1 was elevated 7 fold in STEMI patients and 4 fold in patients with chronic IHD compared to controls. These findings indicate that CHI3L1 could play a role in both the acute inflammatory process eliciting the plaque instability and in the recovery and remodelling process after an acute STEMI by promoting the growth of new cardiomyocytes and inducing vasculogenesis.(Wang et al., 2008)

It could be speculated that CHI3L1 may protect cardiomyocytes from undergoing apoptosis under ischemia since in cancer cells CHI3L1 expression is up-regulated following hypoxia (Junker et al., 2005). It has recently been shown that serum CHI3L1 is associated with the extent of CAD defined by the number of vessels with stenosis (Kucur et al., 2007).

It is not known which type of cells that is the main source of the increased plasma level of CHI3L1 in patients with acute and chronic IHD. The lack of relation between maximal serum CK-MB and plasma CHI3L1 in STEMI patients suggests that cardiomyocytes are not the major and only source of this marker during acute ischemia.(Wang et al., 2008) Others have found that the maximum serum CHI3L1 was correlated with CK-MB in non-thrombolysed AMI patients but not in thrombolysed AMI patients (Nøjgaard et al., 2008). The thrombolytic therapy activates the inflammatory system and this could release CHI3L1from other cell types such as activated monocytes, macrophages and neutrophils.(Wang et al., 2008)

The results of previous studies showed that (Pala et al., 2018) serum CHI3L1 had prognostic significance in AMI patients, and plasma CHI3L1was significantly increased in AMI patients and remained higher than that in healthy subjects after one month, and was associated with elevated serum BNP, diastolic dysfunction, and long-term increased total mortality. Yang et

al (Yang et al., 2019b) further studied patients with acute STEMI who underwent primary coronary intervention (PCI) and were followed up for 24 months. Found that the incidence of MACE was significantly higher in the high CHI3L1 group than in the low CHI3L1 group during the follow-up period. Therefore, high serum CHI3L1 levels are an independent predictor of MACE, and serum CHI3L1 can be used as a biomarker to predict the long-term prognosis of STEMI patients after PCI.

Further studies showed that serum CHI3L1 had a high diagnostic value in predicting the occurrence of MACE within 30 days after PCI in STEMI patients, with a sensitivity of 74.1%, a specificity of 76.3%, and an AUC of 0.768 when serum CHI3L1 was > 1383.91 ng/dL. These results indicate that serum CHI3L1 levels may be an important indicator for predicting the occurrence of MACE within 30 days after PCI in STEMI patients. Possibly, CHI3L1 is a highly conserved protein secreted by macrophages and released when stimulated, so it is an indicator of inflammation and severity in MI. MI causes myocardial ischemia, which causes an inflammatory response, resulting in further damage to myocardial tissue releasing more inflammatory mediators (Nøjgaard et al., 2008), regulation of MI scar formation, and impact on prognosis.(Fang et al., 2022a)

It was also shown that there was no statistical difference in intervention related parameters between patients in the MACE group and those in the non-MACE group . The possible reason for the results may be that the subjects of the study were STEMI patients, who themselves had severe conditions, so there was no significant difference in interventional therapy(Fang et al., 2022a)

Harutyunyan et al (Harutyunyan et al., 2013) showed a linear relationship between CHI3L1 levels and both short- and long-term all-cause mortality in patients with stable coronary artery disease.

Yang et al (Yang et al., 2019b) hypothesized that CHI3L1 may be a useful biomarker for predicting long-term out- comes in patients with STEMI undergoing PCI. After dividing patients into 2 groups, the incidence of MACE was higher in patients with high CHI3L1 levels than in those with low CHI3L1 levels at 24-month follow-up.

Alterations in serum CHI3L1 levels in patients with AMI after PCI have also been deeply investigated. In a clinical trial containing 72 patients with AMI treated with primary PCI, the authors showed that the increased serum CHI3L1 levels at baseline were reduced to normal serum concentrations at one month after PCI, and the maximum serum CHI3L1 levels were confirmed to be negatively associated with the left ventricular ejection fraction (LVEF) (Hedegaard et al., 2010).

The authors showed that patients with acute STEMI undergoing primary PCI who presented higher serum CHI3L1 levels were more likely to suffer from dyslipidaemia, type 2 diabetes mellitus, advanced Killip classification, and intra-aortic balloon pump (Yang et al., 2019b). During the follow-up period, the prevalence of MACEs was notably increased in patients with higher CHI3L1 levels. These results indicate that serum CHI3L1 could be used as a biomarker to predict the long-term outcome in patients with STEMI after PCI.(Deng et al., 2020)

Interestingly, CHI3L1 is markedly increased in the early period after the acute onset of MI symptoms with medical or invasive treatment and in patients with non-STEMI. Thus, if increased CHI3L1 is induced by macrophages in unstable atherosclerotic plaques and is not released from the myocardium during early necrosis of the infarcted myocardium, serum CHI3L1 could potentially be used for early detection of unstable plaques. Given that serum CHI3L1 is an acute-phase reactant, it is indeed plausible that the acute inflammatory reaction could be the origin of elevated serum CHI3L1 .(Deng et al., 2020)

4.7. Diagnostic performance of biomarkers using receiver operating characteristics (ROC) curve

There have been very few studies assessing the prognostic value of IMA no previous study was reported the IMA and CHI3L1 threshold based on the complexity of PCI in CCS group. Nepal et al. (2017) reported that people with higher IMA above 93.3U/mL showed higher short-term end points and higher 1-year mortality rates that high IMA was independent predictor of both of these outcomes.(Nepal et al., 2017) Levels of IMA were also found to be in chest pain high in another study (Güldoğan et al., 2017).(Güldoğan et al., 2017)

Chawla et al. found IMA's sensitivity and specificity for detecting ACS to be 78.0% and 82.7%, respectively, compared to 58.0% and 60.0% for the CK-MB assay (Chawla R., 2006). Lee et al. obtained other results, finding the sensitivity and specificity of IMA for identifying ACS to be 93% and 35.6%, respectively, and the negative and positive predictive values to be 91.8% and 39.6%, respectively. The combination of myoglobin, CK-MB, and TnT demonstrated 80.2% of sensitivity and 57% of specificity for ACS diagnosis. Sensitivity increased to 94.5%, and specificity fell to 45.1% when IMA was included in the cardiac marker panel (Yong-Wha Lee 2007).

Chapter Five

Conclusion

&

Recommendation

5.1. Conclusions

- Results were shown that in both CA and PCI groups there was an increase in IMA levels following the procedure. CHI3L1 levels appear to have decreased following the procedure in both groups Interestingly, even though that both groups were demonstrated an increasing in the level of IMA, only PCI group was shown a significant difference in the mean level when compared pre & post procedure level.
- Results were shown that there was a trend of increasing average post-procedure IMA levels and decrease CHI3L1with higher Angiographic Lesion Complexity Scores. Also, in both lesion length groups, they were shown an increase in IMA levels following PCI. Results were demonstrated a possible link between the presence of a bifurcation and the magnitude of change in IMA levels after PCI, with potentially larger increases for bifurcations.
- IMA levels were shown a significant Differences when compared to the Pre & Post procedure level in multi-vessel PCI, and a significant difference when compared the Pre & Post procedure level in multi-vessel with bifurcation. Interestingly, even when compared the pre-multi-vessel PCI and Post procedure level in multi-vessel with bifurcation. These findings were highly indicated the power of IMA to reflect the stress on the blood vessel when PCI deal with multi-vessel or multi-vessel with bifurcation
- IMA levels have some potential in identifying complex PCI cases. Post- procedure IMA might be better for detecting complex PCI, while pre- procedure IMA might be better for ruling out patient who had risk of complex PCI.

5.2. Recommendations & future work

- Could be used as a novel marker for early detection of coronary artery disease before the rise of troponin
- As a novel factor for the diagnosis of ACS .
- Used as a biomarker for the complexity of coronary interventions.
- CHI3L1 could be used as an emerging prognostic factor for atherosclerosis.
- Further studies are recommended to asses the prognosis of patients with myocardial infarction after coronary intervention used these markers.
- It would be a good idea to study and compared IMA levels with TIMI flow grade & MPG. TIMI evaluates blood flow along the main epicardial artery, MPG evaluates the microvascular patency of the distal capillaries perfusing the myocardium.
- Since Medina classification were significantly associated with periprocedural myocardial infarction in contemporary elective PCI, it would be worth comparing with IMA levels and demonstrate the most prevalent coronary bifurcation lesion subtypes.
- Study the diagnostic performance of IMA level in patients with coronary dissection due to PCI.

Chapter Six

References

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Appendix

6.1. References

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6.2. Appendix

Appendix-1

Questionnaire

Questionnaire

Name : _____

Age : _____

Phone number :

Sex : male ☐ female ☐

Smoking: active ☐ passive ☐ No ☐

Diabetes mellitus: Type 1 ☐ Type 2 ☐ No ☐

Use of anticoagulant (e.g. Aspirin) : Yes ☐ No ☐

Family history of CAD ? Yes ☐ No ☐ (male<40 , female<50)

No.of PCI : _____

Chronic kidney disease: Yes ☐ No ☐

Stroke: Yes ☐ No ☐

Preeclampsia: Yes ☐ No ☐

Other (cancer): Yes ☐ No ☐

He underwent a PCI two weeks ago or less : Yes ☐ No ☐

He was admitted to the ER two weeks ago or less : Yes ☐ No ☐

Weight: _____ Height: _____

BMI (kg/m2) : _____ Obesity stage : _____

DIA : _____ SYS : _____

HbA1c : _____ RBS : Pre PCI _____ Post PCI _____

Urea : _____ Creatinine: _____

eGFR : _____ Atherogenic index : _____

Date of admission: / / Time admission: :

Flouro time of operation: Total fluoro min	Total K mGy	Total DAP Gy.cm2	Exposure DAP Gy.cm2	Fluoro DAP Gy.cm2

Contrast amount : _____

Number of vessel disease : _____

Type of vessel : LMS ☐ LCX ☐ LAD ☐ RCA ☐

ECG finding: LBBB _____

T inv _____

Pathological Q wave _____

ECO finding: EF% (_____)

Viability of myocardial: : Yes ☐ No ☐

TIMI Flow : .....

Complexity of PCI

Factor	Yes	No
Bifurcation with 2 stents implanted		
Total stent length >60mm		
Treatment of a CTO		
Multivessel PCI		
≥3 lesions treated		
≥3 stents implanted		
Vein bypass graft PCI		
Left main lesion proximal LAD		
Bifurcation lesion with side branch ≥2.5mm		
Lesion length ≥30mm		

No. of prestent inflation ..... Tortuous : Yes ☐ No ☐

No. of stent..... Collateral : Yes ☐ No ☐

No.of poststent inflation..... Prior Stent : Yes ☐ No ☐

No of ballon ..... NC ballon : Yes ☐ No ☐

Medina ..... PTCA : Yes ☐ No ☐

EKG Changes : Normal ☐ Non Specific ☐ ST Depression ☐

Complex PCI patient

Factor	Yes	No
Heart failure		
Prior surgery		
Calcification		

Angiographic Lesion Complexity Score

Factor	Yes	No
Bifurcation		
Chronic Total Occlusion (CTO)		
Type C		
Unprotected Left Main Trunk (UPLMT)		
Thrombus Formation		

Investigation: Cardiac Tests

Hs-Troponin: pre PCI _____ post PCI _____

Ischemia Modified Albumin : pre PCI _____ post PCI _____

Chitinase-3-like protein 1: pre PCI _____ post PCI _____

lipid profile : HDL(ch) : _____ LDL(ch) : _____

TG : _____ Total Cholesterol : _____ HDL (non ch) : _____

CHARACTERISTICS OF ACC/AHA TYPE A, B, AND C LESIONS

Type A Lesions: (High Success, >85%; Low Risk)

- Discrete (<10 mm length) ☐
- Concentric ☐
- Readily accessible ☐
- Nonangulated segment <45° ☐
- Smooth contour ☐
- Little or no calcification ☐
- Less than totally occlusive ☐
- Not ostial in location ☐
- No major branch involvement ☐
- Absence of thrombus ☐

Type B Lesions (Moderate Success, 60% to 85%; Moderate Risk)

- Tubular (10–20 mm length) ☐
- Eccentric ☐
- Moderate tortuosity of proximal segment ☐
- Moderately angulated, 45°–90° ☐
- Irregular contour ☐
- Moderate to heavy calcification ☐
- Ostial in location ☐
- Bifurcation lesions requiring double guidewires ☐
- Some thrombus present ☐
- Total occlusion <3 months old ☐

Type C Lesions (Low Success, <60%; High Risk)

- Diffuse (>2 cm length) ☐
- Excessive tortuosity of proximal segment ☐
- Extremely angulated, >90° ☐
- Inability to protect major side branch ☐
- Degenerated vein grafts with friable lesions ☐
- Total occlusion >3 months old ☐

Appendix-2

Human Ischemia Modified Albumin ELISA Kit

USER INSTRUCTION

Cat.No E1172Hu

Standard Curve Range: 2-600ng/mL

Sensitivity: 1.08ng/mL

Size: 96 wells / 48 wells

Storage: Store the reagents at 2-8°C. For over 6-month storage refer to the expiration date keep it at -20°C. Avoid repeated thaw cycles. If individual reagents are opened it is recommended that the kit be used within 1 month.

***This product is for research use only, not for use in diagnosis procedures. It's highly recommended to read this instruction entirely before use.**

Precision

Intra-Assay Precision (Precision within an assay) Three samples of known concentration were tested on one plate to assess intra-assay precision.
Inter-Assay Precision (Precision between assays) Three samples of known concentration were tested in separate assays to assess inter-assay precision.
CV(%) =
SD/mean x
100 Intra-
Assay:
CV<8%
Inter-Assay:
CV<10%

Intended Use

This sandwich kit is for the accurate quantitative detection of Human Ischemia Modified Albumin (also known as IMA) in serum, plasma, cell culture supernates, Ascites, tissue homogenates or other biological fluids.

Assay Principle

This kit is an Enzyme-Linked Immunosorbent Assay (ELISA). The plate has been pre-coated with Human IMA antibody. IMA present in the sample is added and binds to antibodies coated on the wells. And then biotinylated Human IMA Antibody is added and binds to IMA in the sample. Then Streptavidin-HRP is added and binds to the Biotinylated IMA antibody. After incubation unbound

Streptavidin-HRP is washed away during a washing step. Substrate solution is then added and color develops in proportion to the amount of Human IMA. The reaction is terminated by addition of acidic stop solution and absorbance is measured at 450 nm.

Reagent Provided

Components	Quantity (96T)	Quantity (48T)
Standard Solution (640ng/mL)	0.5mL x1	0.5mL x1
Pre-coated ELISA Plate	12 * 8 well strips x1	12 * 4 well strips x1
Standard Diluent	3mL x1	3mL x1
Streptavidin-HRP	6mL x1	3mL x1
Stop Solution	6mL x1	3mL x1
Substrate Solution A	6mL x1	3mL x1
Substrate Solution B	6mL x1	3mL x1
Wash Buffer Concentrate (25x)	20mL x1	20mL x1
Biotinylated Human IMA Antibody	1mL x1	1mL x1
User Instruction	1	1
Plate Sealer	2 pics	2 pics
Zipper bag	1 pic	1 pic

Material Required But Not Supplied

- 37°C±0.5°C incubator
- Absorbent paper
- Precision pipettes and disposable pipette tips
- Clean tubes
- Deionized or distilled water
- Microplate reader with 450 ± 10nm wavelength filter

Precautions

- Prior to use, the kit and sample should be warmed naturally to room temperature 30 minutes.
- This instruction must be strictly followed in the experiment.
- Once the desired number of strips has been removed, immediately reseal the bag to protect the remain from deterioration. Cover all reagents when not in use.
- Make sure pipetting order and rate of addition from well-to-well when pipetting reagents.
- Pipette tips and plate sealer in hand should be clean and disposable to avoid cross-contamination.
- Avoid using the reagents from different batches together.
- Substrate solution B is sensitive to light, don't expose substrate solution B to light for a long time.
- Stop solution contains acid. Please wear eye, hand and skin protection when using this material. Avoid contact of skin or mucous membranes with kit reagent.
- The kit should not be used beyond the expiration date.

Specimen Collection

Serum Allow serum to clot for 10-20 minutes at room temperature. Centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatant without sediment.

Plasma Collect plasma using EDTA or heparin as an anticoagulant.After mix 10-20 minutes, centrifuge samples for 20 minutes at 2000-3000 RPM. Collect the supernatant without sediment. **Urine/Ascites/ Cerebrospinal fluid** Collect by sterile tube. Centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatant without sediment.

Cell culture supernatant Collect by sterile tubes. When detecting secrete components, centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatants. When detecting the components in the cell, use PBS (pH 7.2-7.4) to dilute cell suspension , the cell concentration of approximately 1 million/mL. Damage cells through repeated freeze-thaw cycles to let out the inside components. Centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatant without sediment.

Tissue Rinse tissues in ice-cold PBS (pH 7.4) to remove excess blood thoroughly and weigh before homogenization. Mince tissues and homogenize them in PBS (tissue weight (g): PBS (mL) volume=1:9) with a glass homogenizer on ice. To further break down the cells, you can sonicate the suspension with an ultrasonic cell disrupter or

subject it to freeze-thaw cycles. The homogenates are then centrifuged for 5 minutes at 5000×g to get the supernatant.

Note

- Sample concentrations should be predicted before being used in the assay. If the sample concentration is not within the range of the standard curve, users must **contact us** to determine the optimal sample for their particular experiments.
- Samples to be used within 5 days should be stored at 2-8°C. Samples should be aliquoted or must be stored at -20°C within 1 month or -80°C within 6 months. Avoid repeated freeze thaw cycles.
- Samples should be brought to room temperature before starting the assay.
- Centrifuge to collect sample before use.
- Samples containing NaN3 can't be tested as it inhibits the activity of Horse Radish Peroxidase (HRP).
- Collect the supernatants carefully. When sediments occurred during storage, centrifugation should be performed again.
- Hemolysis can greatly impact the validity of test results. Take care to minimize hemolysis.

Sample can't be diluted with this kit. Owing to the the material we use to prepare the kit, the sample matrix interference may falsely depress the specificity and accuracy of the assay.

Summary

1. Prepare all reagents, samples and standards.
2. Add sample and ELISA reagent into each well. Incubate for 1 hour at 37℃.
3. Wash the plate 5 times.
4. Add substrate solution A and B. Incubate for 10 minutes at 37℃.
5. Add stop solution and color develops.
6. Read the OD value within 10 minutes.

Appendix-3

Human Chitinase-3-like Protein 1 ELISA Kit

USER INSTRUCTION

Cat.No E2063Hu

Standard Curve Range: 1-400ng/mL

Sensitivity: 0.61ng/mL

Size: 96 wells / 48 wells

Storage: Store the reagents at 2-8°C. For over 6-month storage refer to the expiration date keep it at -20°C. Avoid repeated thaw cycles. If individual reagents are opened it is recommended that thekit be used within 1 month.

***This product is for research use only, not for use in diagnosis procedures. It's highlyrecommended to read this instruction entirely before use.**

Precision

Intra-Assay Precision (Precision within an assay) Three samples of known concentration weretested on one plate to assess intra-assay precision.
Inter-Assay Precision (Precision between assays) Three samples of known concentration weretested in separate assays to assess inter-assay precision.
CV(%) =
SD/mean x
100Intra-
Assay:
CV<8%
Inter-Assay:
CV<10%

Intended Use

This sandwich kit is for the accurate quantitative detection of Human Chitinase-3-like Protein 1 (also known as CHI3L1) in serum, plasma, cell culture supernates, Ascites,

tissue homogenates orother biological fluids.

Assay Principle

This kit is an Enzyme-Linked Immunosorbent Assay (ELISA). The plate has been pre-coated with Human CHI3L1 antibody. CHI3L1 present in the sample is added and binds to antibodies coated on the wells. And then biotinylated Human CHI3L1 Antibody is added and binds to CHI3L1 in thesample. Then Streptavidin-HRP is added and binds to the Biotinylated CHI3L1 antibody. After

incubation unbound Streptavidin-HRP is washed away during a washing step. Substrate solution isthen added and color develops in proportion to the amount of Human CHI3L1. The reaction is terminated by addition of acidic stop solution and absorbance is measured at 450 nm.

Reagent Provided

Components	Quantity (96T)	Quantity (48T)
Standard Solution (480ng/mL)	0.5mL x1	0.5mL x1
Pre-coated ELISA Plate	12 * 8 well strips x1	12 * 4 well strips x1
Standard Diluent	3mL x1	3mL x1
Streptavidin-HRP	6mL x1	3mL x1
Stop Solution	6mL x1	3mL x1
Substrate Solution A	6mL x1	3mL x1
Substrate Solution B	6mL x1	3mL x1
Wash Buffer Concentrate (25x)	20mL x1	20mL x1
Biotinylated Human CHI3L1 Antibody	1mL x1	1mL x1
User Instruction	1	1
Plate Sealer	2 pics	2 pics
Zipper bag	1 pic	1 pic

Material Required But Not Supplied

- 37°C±0.5°C incubator
- Absorbent paper
- Precision pipettes and disposable pipette tips
- Clean tubes
- Deionized or distilled water
- Microplate reader with 450 ± 10nm wavelength filter

Precautions

- Prior to use, the kit and sample should be warmed naturally to room temperature 30 minutes.
- This instruction must be strictly followed in the experiment.
- Once the desired number of strips has been removed, immediately reseal the bag to protect theremain from deterioration. Cover all reagents when not in use.
- Make sure pipetting order and rate of addition from well-to-well when pipetting reagents.
- Pipette tips and plate sealer in hand should be clean and disposable to avoidcross-contamination.
- Avoid using the reagents from different batches together.
- Substrate solution B is sensitive to light, don't expose substrate solution B to light for a longtime.
- Stop solution contains acid. Please wear eye, hand and skin protection when using thismaterial. Avoid contact of skin or mucous membranes with kit reagent.
- The kit should not be used beyond the expiration date.

Specimen Collection

Serum Allow serum to clot for 10-20 minutes at room temperature. Centrifuge at 2000-3000 RPMfor 20 minutes. Collect the supernatant without sediment.

Plasma Collect plasma using EDTA or heparin as an anticoagulant.After mix 10-20 minutes, centrifuge samples for 20 minutes at 2000-3000 RPM. Collect the supernatant without sediment. **Urine/Ascites/ Cerebrospinal fluid** Collect by sterile tube. Centrifuge at 2000-3000 RPM for 20minutes. Collect the supernatant without sediment.

Cell culture supernatant Collect by sterile tubes. When detecting secrete components, centrifugeat 2000-3000 RPM for 20 minutes. Collect the supernatants. When detecting the components in the cell, use PBS (pH 7.2-7.4) to dilute cell suspension , the cell concentration of approximately 1million/mL. Damage cells through repeated freeze-thaw cycles to let out the inside components. Centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatant without sediment.

Tissue Rinse tissues in ice-cold PBS (pH 7.4) to remove excess blood thoroughly and weigh before homogenization. Mince tissues and homogenize them in PBS (tissue weight (g): PBS (mL)volume=1:9) with a glass homogenizer on ice. To further break down the cells, you can sonicate the suspension with an ultrasonic cell disrupter or

subject it to freeze-thaw cycles. The homogenates are then centrifuged for 5 minutes at 5000×g to get the supernatant.

Note

- Sample concentrations should be predicted before being used in the assay. If the sampleconcentration is not within the range of the standard curve, users must **contact us** to determine the optimal sample for their particular experiments.
- Samples to be used within 5 days should be stored at 2-8°C. Samples should be aliquoted ormust be stored at -20°C within 1 month or -80°C within 6 months. Avoid repeated freeze thaw cycles.
- Samples should be brought to room temperature before starting the assay.
- Centrifuge to collect sample before use.
- Samples containing NaN3 can't be tested as it inhibits the activity of Horse Radish Peroxidase(HRP).
- Collect the supernatants carefully. When sediments occurred during storage, centrifugationshould be performed again.
- Hemolysis can greatly impact the validity of test results. Take care to minimize hemolysis.

Sample can't be diluted with this kit. Owing to the the material we use to prepare the kit, thesample matrix interference may falsely depress the specificity and accuracy of the assay.

Summary

1. Prepare all reagents, samples and standards.
2. Add sample and ELISA reagent into each well. Incubate for 1 hour at 37°C.
3. Wash the plate 5 times.
4. Add substrate solution A and B. Incubate for 10 minutes at 37°C.
5. Add stop solution and color develops.
6. Read the OD value within 10 minutes.

Appendix-4

Human High sensitivity Troponin I ELISA Kit

USER INSTRUCTION

Cat.No E6717Hu

Standard Curve Range: 10-2000ng/L

Sensitivity: 5.18ng/L

Size: 96 wells / 48 wells

Storage: Store the reagents at 2-8°C. For over 6-month storage refer to the expiration date keep it at -20°C. Avoid repeated thaw cycles. If individual reagents are opened it is recommended that the kit be used within 1 month.

***This product is for research use only, not for use in diagnosis procedures. It's highly recommended to read this instruction entirely before use.**

Precision

Intra-Assay Precision (Precision within an assay) Three samples of known concentration were tested on one plate to assess intra-assay precision.
Inter-Assay Precision (Precision between assays) Three samples of known concentration were tested in separate assays to assess inter-assay precision.
CV(%) =
SD/mean x
100 Intra-
Assay:
CV<8%
Inter-Assay:
CV<10%

Intended Use

This sandwich kit is for the accurate quantitative detection of Human High sensitivity Troponin I (also known as HS TNI) in serum, plasma, cell culture supernates, Ascites, tissue homogenates or other biological fluids.

Assay Principle

This kit is an Enzyme-Linked Immunosorbent Assay (ELISA). The plate has been pre-coated with Human HS TNI antibody. HS TNI present in the sample is added and binds to antibodies coated on the wells. And then biotinylated Human HS TNI Antibody is added and binds to HS TNI in the sample. Then Streptavidin-HRP is added and binds to the Biotinylated HS TNI antibody. After

incubation unbound Streptavidin-HRP is washed away during a washing step. Substrate solution is then added and color develops in proportion to the amount of Human HS TNI. The reaction is terminated by addition of acidic stop solution and absorbance is measured at 450 nm.

Reagent Provided

Components	**Quantity (96T)**	**Quantity (48T)**
Standard Solution (2400ng/L)	0.5mL x1	0.5mL x1
Pre-coated ELISA Plate	12 * 8 well strips x1	12 * 4 well strips x1
Standard Diluent	3mL x1	3mL x1
Streptavidin-HRP	6mL x1	3mL x1
Stop Solution	6mL x1	3mL x1
Substrate Solution A	6mL x1	3mL x1
Substrate Solution B	6mL x1	3mL x1
Wash Buffer Concentrate (25x)	20mL x1	20mL x1
Biotinylated Human HS TNI Antibody	1mL x1	1mL x1
User Instruction	1	1
Plate Sealer	2 pics	2 pics
Zipper bag	1 pic	1 pic

Material Required But Not Supplied

- 37°C±0.5°C incubator
- Absorbent paper
- Precision pipettes and disposable pipette tips
- Clean tubes
- Deionized or distilled water
- Microplate reader with 450 ± 10nm wavelength filter

Precautions

- Prior to use, the kit and sample should be warmed naturally to room temperature 30 minutes.
- This instruction must be strictly followed in the experiment.
- Once the desired number of strips has been removed, immediately reseal the bag to protect the remain from deterioration. Cover all reagents when not in use.
- Make sure pipetting order and rate of addition from well-to-well when pipetting reagents.
- Pipette tips and plate sealer in hand should be clean and disposable to avoid cross-contamination.
- Avoid using the reagents from different batches together.
- Substrate solution B is sensitive to light, don't expose substrate solution B to light for a long time.
- Stop solution contains acid. Please wear eye, hand and skin protection when using this material. Avoid contact of skin or mucous membranes with kit reagent.
- The kit should not be used beyond the expiration date.

Specimen Collection

Serum Allow serum to clot for 10-20 minutes at room temperature. Centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatant without sediment.

Plasma Collect plasma using EDTA or heparin as an anticoagulant.After mix 10-20 minutes, centrifuge samples for 20 minutes at 2000-3000 RPM. Collect the supernatant without sediment. **Urine/Ascites/ Cerebrospinal fluid** Collect by sterile tube. Centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatant without sediment.

Cell culture supernatant Collect by sterile tubes. When detecting secrete components, centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatants. When detecting the components in the cell, use PBS (pH 7.2-7.4) to dilute cell suspension , the cell concentration of approximately 1 million/mL. Damage cells through repeated freeze-thaw cycles to let out the inside components.

Centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatant without sediment.

Tissue Rinse tissues in ice-cold PBS (pH 7.4) to remove excess blood thoroughly and weigh before homogenization. Mince tissues and homogenize them in PBS (tissue weight (g): PBS (mL) volume=1:9) with a glass homogenizer on ice. To further break down the cells, you can sonicate the suspension with an ultrasonic cell disrupter or subject it to freeze-thaw cycles. The homogenates are then centrifuged for 5 minutes at

5000×g to get the supernatant.

Note

- Sample concentrations should be predicted before being used in the assay. If the sample concentration is not within the range of the standard curve, users must **contact us** to determine the optimal sample for their particular experiments.
- Samples to be used within 5 days should be stored at 2-8°C. Samples should be aliquoted or must be stored at -20°C within 1 month or -80°C within 6 months. Avoid repeated freeze thaw cycles.
- Samples should be brought to room temperature before starting the assay.
- Centrifuge to collect sample before use.
- Samples containing NaN3 can't be tested as it inhibits the activity of Horse Radish Peroxidase (HRP).
- Collect the supernatants carefully. When sediments occurred during storage, centrifugation should be performed again.
- Hemolysis can greatly impact the validity of test results. Take care to minimize hemolysis.

Sample can't be diluted with this kit. Owing to the the material we use to prepare the kit, the sample matrix interference may falsely depress the specificity and accuracy of the assay.

Summary

1. Prepare all reagents, samples and standards.
2. Add sample and ELISA reagent into each well. Incubate for 1 hour at 37℃.
3. Wash the plate 5 times.
4. Add substrate solution A and B. Incubate for 10 minutes at 37°C.
5. Add stop solution and color develops.
6. Read the OD value within 10 minutes.

Appendix-5

Cholesterol

This package insert contains information to run the Cholesterol assay on the ARCHITECT c SystemsTM and the AEROSET System.

INTENDED USE

The Cholesterol assay is used for the quantitation of cholesterol in human serum or plasma.

PRINCIPLES OF PROCEDURE

Cholesterol esters are enzymatically hydrolyzed by cholesterol esterase to cholesterol and free fatty acids. Free cholesterol, including that originally present, is then oxidized by cholesterol oxidase to cholest-4-ene-3-one and hydrogen peroxide. The hydrogen peroxide combines with hydroxybenzoic acid (HBA) and 4-aminoantipyrine to form a chromophore (quinoneimine dye) which is quantitated at 500 nm.

Methodology: Enzymatic

REAGENTS

Reagent Kit

REF 7D62 Cholesterol is supplied as a liquid, ready-to-use, single reagent kit which contains:

R1 10 x 84 mL

Estimated tests per kit: 3,032

Calculation is based on the minimum reagent fill volume per kit.

Reactive Ingredients ---------- > Concentration

Cholesterol Oxidase (Microbial) ---------- > more than 200 *U/L*

Cholesterol Esterase (Microbial)---------- > more than 500 *U/L*

Peroxidase (Horseradish)---------- > more than 300 *U/L*

4-Aminoantipyrine---------- > 0.25 *mmol/L*

HBA---------- > 10 *mmol/L*

The Abbott Clinical Chemistry Cholesterol reagent is certified to be traceable to the National Reference System for Cholesterol, against the Abell-Kendall reference method in a CDC-Certified Cholesterol Reference Method Laboratory Network (CRMLN).

REAGENT HANDLING AND STORAGE

Reagent Handling

Remove air bubbles, if present in the reagent cartridge, with a new applicator stick. Alternatively, allow the reagent to sit at the appropriate storage temperature to allow the bubbles to dissipate. To minimize volume depletion, do not use a transfer pipette to remove the bubbles.

CAUTION: Reagent bubbles may interfere with proper detection of reagent level in the cartridge, causing insufficient reagent aspiration which could impact results.

Reagent Storage

Unopened reagents are stable until the expiration date when stored at 2 to 8°C.

Reagent stability is 30 days if the reagent is uncapped and onboard.

SPECIMEN COLLECTION AND HANDLING

Suitable Specimens

Serum and plasma are acceptable specimens. The National Cholesterol Education Program (NCEP) recommends using fasting specimens.

• **Serum**: Use serum collected by standard venipuncture techniques into glass or plastic tubes with or without gel barriers. Ensure complete clot formation has taken place prior to centrifugation. Separate serum from red blood cells or gel as soon after collection as possible.

Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may take longer to complete their clotting processes. Fibrin clots may subsequently form in these sera and the clots could cause erroneous test results.

• **Plasma:** Use plasma collected by standard venipuncture techniques into glass or plastic tubes. Acceptable anticoagulants are lithium heparin (with or without gel barrier) and sodium heparin. Ensure centrifugation is adequate to remove platelets. Separate plasma from red blood cells or gel as soon after collection as possible.

Specimen Storage Serum and plasma

Temperature	**Maximum Storage**
20 to 25°C	> 7 days
2 to 8°C	> 7 days
-20°C	> 3 months

Guder et al. suggest storage of frozen specimens at -20°C for no longer than the time interval cited above. However, limitations of laboratory equipment make it necessary in practice for clinical laboratories to establish a range around -20°C for specimen storage. This temperature range may be established from either the freezer manufacturer's specifications or your laboratory standard operating procedure(s) for specimen storage.

NOTE: Stored specimens must be inspected for particulates. If present, mix and centrifuge the specimen to remove particulates prior to testing.

Appendix-6

TRIGLYCERIDE

This package insert contains information to run the Triglyceride assay on the ARCHITECT c SystemsTM and the AEROSET System.

INTENDED USE

The Triglyceride assay is used for the quantitation of triglyceride in human serum or plasma.

PRINCIPLES OF PROCEDURE

Triglycerides are enzymatically hydrolyzed by lipase to free fatty acids and glycerol. The glycerol is phosphorylated by adenosine triphosphate (ATP) with glycerol kinase (GK) to produce glycerol-3-phosphate and adenosine diphosphate (ADP). Glycerol-3-phosphate is oxidized to dihydroxyacetone phosphate (DAP) by glycerol phosphate oxidase (GPO) producing hydrogen peroxide (H2O2). In a color reaction catalyzed by peroxidase, the H2O2 reacts with 4-aminoantipyrine (4-AAP) and 4-chlorophenol (4-CP) to produce a red colored dye. The absorbance of this dye is proportional to the concentration of triglyceride present in the sample. This analytical methodology is based on the reaction sequence described by Fossati et al. and by McGowan et al.5 In this reagent, 4-chlorophenol is used rather than 2-hydroxy-3,5-dichlor- obenzenesulfonate, used in the Fossati and McGowan studies.

Methodology: Glycerol Phosphate Oxidase

REAGENTS

Reagent Kit

REF 7D74 Triglyceride is supplied as a liquid, ready-to-use, single reagent kit which contains:

R1 10 x 84 mL

Estimated tests per kit: 3,032

Calculation is based on the minimum reagent fill volume per kit.

Reactive Ingredients	**Concentration**
ATP	> 2.5 *mmol/L*
Mg2+	> 2.5 *mmol/L*
4-Aminoantipyrine	> 0.4 *mmol/L*
4-Chlorophenol	> 2 *mmol/L*
Peroxidase (Horseradish)	> more than 2,000 *U/L*
GK (Microbial)	> more than 600 *U/L*
GPO (Microbial)	> more than 6,000 *U/L*
Lipoprotein Lipase (Microbial)	> more than 3.000 *U/L*

REAGENT HANDLING AND STORAGE

Reagent Handling

Remove air bubbles, if present in the reagent cartridge, with a new applicator stick. Alternatively, allow the reagent to sit at the appropriate storage temperature to allow the bubbles to dissipate. To minimize volume depletion, do not use a transfer pipette to remove the bubbles.

CAUTION: Reagent bubbles may interfere with proper detection of reagent level in the cartridge, causing insufficient reagent aspiration which could impact results.

Reagent Storage

Unopened reagents are stable until the expiration date when stored at 2 to 8°C.

Reagent stability is 42 days if the reagent is uncapped and onboard.

SPECIMEN COLLECTION AND HANDLING

Suitable Specimens

Serum and plasma are acceptable specimens. The National Cholesterol Education Program (NCEP) recommends using fasting specimens.

• **Serum**: Use serum collected by standard venipuncture techniques into glass or plastic tubes with or without gel barriers. Ensure complete clot formation has taken place prior to centrifugation. Separate serum from red blood cells or gel as soon after collection as possible.

Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may take longer to complete their clotting processes. Fibrin clots may subsequently form in these sera and the clots could cause erroneous test results.

• **Plasma**: Use plasma collected by standard venipuncture techniques into glass or plastic tubes. Acceptable anticoagulants are lithium heparin (with or without gel barrier) and sodium heparin. Ensure centrifugation is adequate to remove platelets. Separate plasma from red blood cells or gel as soon after collection as possible.

Specimen Storage

Serum and plasma

Temperature **Maximum Storage**

20 to 25°C----------> 2 days

2 to 8°C---------- > 7 days

-20°C---------- >1 year

Guder et al. suggest storage of frozen specimens at -20°C for no longer than the time interval cited above. However, limitations of laboratory equipment make it necessary in practice for clinical laboratories to establish a range around -20°C for specimen storage. This temperature range may be established from either the freezer manufacturer's specifications or your laboratory standard operating procedure(s) for specimen storage.

NOTE: Stored specimens must be inspected for particulates. If present, mix and centrifuge the specimen to remove particulates prior to testing.

Appendix-7

Ultra HDL

This package insert contains information to run the Ultra HDL assay on the ARCHITECT c SystemsTM and the AEROSET System.

INTENDED USE

The Ultra HDL (UHDL) assay is used for the quantitation of high-density lipoprotein (HDL) cholesterol in human serum or plasma.

PRINCIPLES OF PROCEDURE

The Ultra HDL assay is a homogeneous method for directly measuring HDL cholesterol concentrations in serum or plasma without the need for off-line pretreatment or centrifugation steps.

The method uses a two-reagent format and depends on the properties of a unique detergent. This method is based on accelerating the reaction of cholesterol oxidase (CO) with non-HDL unesterified cholesterol and dissolving HDL cholesterol selectively using a specific detergent. In the first reagent, non-HDL unesterified cholesterol is subject to an enzyme reaction and the peroxide generated is consumed by a peroxidase reaction with DSBmT yielding a colorless product. The second reagent consists of a detergent (capable of solubilizing HDL cholesterol), cholesterol esterase (CE), and chromagenic coupler to develop color for the quantitative determination of HDL cholesterol.

Methodology: Accelerator Selective Detergent.

REAGENTS

Reagent Kit

REF 3K33 Ultra HDL is supplied as a liquid, ready-to-use, two-reagent kit which contains:

R1 4 x 84 *mL*

R2 4 x 32 *mL*

Estimated tests per kit: 1,440

Calculation is based on the minimum reagent fill volume per kit.

Reactive Ingredients **Concentration**

R1 Cholesterol oxidase (E. coli) ---------- > < 1,000 *U/L*

Peroxidase (Horseradish)---------- > < 1,300 *ppg U/L*

N, N-bis (4-sulphobutyl)-m-toluidine-disodium--------- > < 1.0 *mmol/L*

(DSBmT)

Accelerator---------- > < 1.0 *mmol/L*

Ascorbic oxidase (Curcubita sp.) ----------> < 3,000 *U/L*

R2 Cholesterol esterase (Pseudomonas sp.) ---------- > < 1,500 *U/L*

4-Aminoantipyrine ---------- > < 0.1%

Detergent---------- > < 2.0%

The Ultra HDL reagent is certified as traceable to the HDL cholesterol designated comparison method, covering the NCEP medical decision points, by the CDC-Certified Cholesterol Reference Method Laboratory Network (CRMLN).

REAGENT HANDLING AND STORAGE

Reagent Handling

Remove air bubbles, if present in the reagent cartridge, with a new applicator stick. Alternatively, allow the reagent to sit at the appropriate storage temperature to allow the bubbles to dissipate. To minimize volume depletion, do not use a transfer pipette to remove the bubbles.

CAUTION: Reagent bubbles may interfere with proper detection of reagent level in the cartridge, causing insufficient reagent aspiration which could impact results.

Reagent Storage

• Unopened reagents are stable until the expiration date when stored at 2 to 8°C.

• DO NOT FREEZE.

• Protect reagents from direct sunlight.

• Reagent stability is 28 days if the reagent is uncapped and onboard.

Indications of Deterioration

• Quality control results outside of the acceptance criteria defined by your laboratory.

• Presence of turbidity.

SPECIMEN COLLECTION AND HANDLING

Suitable Specimens

Serum and plasma are acceptable specimens. The National Cholesterol Education Program (NCEP) recommends using fasting specimens for

a lipoprotein profiles. If the specimen is nonfasting, only the values for total cholesterol and HDL cholesterol are usable.

• **Serum**: Use serum collected by standard venipuncture techniques into glass or plastic tubes with or without gel barriers. Ensure complete clot formation has taken place prior to centrifugation. When processing samples, separate serum from blood cells or gel according to the specimen collection tube manufacturer's instructions.

Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may take longer to complete their clotting processes. Fibrin clots may subsequently form in these sera and the clots could cause erroneous test results.

• **Plasma**: Use plasma collected by standard venipuncture techniques into glass or plastic tubes. Acceptable anticoagulants are sodium heparin, lithium heparin (with or without gel barrier), and spray-dried EDTA. * Ensure centrifugation is adequate to remove platelets. When processing samples, separate plasma from blood cells or

gel according to the specimen collection tube manufacturer's instructions.

***NOTE**: Lower HDL cholesterol results obtained from EDTA plasma have been attributed to an osmotic dilution effect. The NCEP has suggested

multiplying EDTA plasma results by a factor of 1.03 to correct the EDTA result to a serum equivalent value.

Specimen Storage

Serum and Plasma

Temperature	**Maximum Storage**
20 to 25°C	> 2 days
2 to 8°C	> 7 days
-20°C	>1 year

Guder et al. suggest storage of frozen specimens at -20°C for no longer than the time interval cited above. However, limitations of laboratory equipment make it necessary in practice for clinical laboratories to establish a range around -20°C for specimen storage. This temperature range may be established from either the freezer manufacturer's specifications or your laboratory standard operating procedure(s) for specimen storage.

NOTE: Stored specimens must be inspected for particulates. If present, mix and centrifuge the specimen to remove particulates prior to testing.

Appendix-8

certificate

Appendix-9

Table (6.1) ***The correlation coefficient (r) between biomarkers among group of elective PCI***

Markers	Pre-IMA	Post-IMA	Pre-CHI3L1	Post-CHI3L1	Pre-hs-cTn	Post- hs-cTn	Total-Cholestrol	TG	HDL	LDL	nonHDL-c	(AC)	(AIP)	Castelli's riskI	Castelli's risk II	(C-index)
Post-IMA	0.40	1.00	0.62	-0.52	0.51	0.44	-0.42	-0.37	0.36	-0.42	-0.43	-0.11	-0.20	-0.11	-0.11	-0.03
Post-CHI3L1	0.41	-0.52	0.41	1.00	0.52	-0.47	-0.36	-0.48	0.39	-0.38	-0.39	-0.42	-0.40	-0.42	-0.42	-0.41
Post-hs-cTn	-0.43	0.44	0.42	-0.47	0.94	1.00	-0.38	-0.42	0.49	-0.42	-0.39	-0.44	-0.36	-0.44	-0.36	-0.43

Appendix-10

Table (6.2) ***The significance of P value for the correlation between biomarkers among group of elective PCI***

Markers	Pre-IMA	Post-IMA	Pre-CHI3L1	Post-CHI3L1	Pre-hs-cTn	Post- hs-cTn	Total-Cholestrol	TG	HDL	LDL	nonHDL-c	nt (AC)	(AIP)	Castelli's riskI	**Castelli's risk II**	(C-index)
Post-IMA	0.03	1.00	0.00	0.00	0.02	0.05	0.93	0.74	0.78	0.91	0.89	0.59	0.32	0.59	**0.59**	0.87
Post-CHI3L1	0.01	0.00	0.01	1.00	0.03	0.05	0.79	0.83	0.39	0.71	0.70	0.58	0.37	0.58	0.58	0.62
Post-hs-cTn	0.91	0.05	0.41	0.05	0.00	1.00	0.73	0.52	0.84	0.63	0.69	0.56	0.27	0.56	0.50	0.58

الملخص

الخلفية: إن مسببات إصابة عضلة القلب أثناء العملية الجراحية واحتشاء عضلة القلب من النوع 4 أ (type 4a MI) متعددة العوامل وقد تنتج عن أحداث أو مضاعفات مرتبطة بالتدخل التاجي عن طريق الجلد (PCI). قد يؤدي إعادة التروية بعد نقص تروية عضلة القلب إلى تسريع إصابة عضلة القلب وتفاقم النتائج السريرية. أحد أهم الآليات المرضية في إصابة إعادة التروية هو الإجهاد التأكسدي، وهو اختلال التوازن بين نظام مضادات الأكسدة والإنتاج المفرط لأنواع الأكسجين التفاعلية (ROS)، مما يؤدي إلى تراكم سام لـ(ROS). وقد ثبت أيضًا أن الألبومين المعدل بالإقفار (IMA) مرتفع لدى المرضى بعد PCI نتيجة لإصابة نقص التروية وإعادة التروية. والهدف هو دراسة دور المؤشرات الحيوية IMA و Chitenase 3 like protein 1 (CHI3L1) في المضاعفات والعواقب بعد التدخل التاجي عن طريق الجلد في مرض الشريان التاجي.

الطرق: أجريت دراسة حالة وشاهد في مركز كربلاء لأمراض وجراحة القلب ومستشفى الإمام الحسن المجتبى التعليمي في مدينة كربلاء . شملت الدراسة الحالية 120 مشاركًا تتراوح أعمارهم بين (29- 84) عامًا. خضع (72) منهم لتدخل قسطري اختياري في الشريان التاجي وخضع (48) منهم لتصوير القسطرة التشخيصي (CA) كمجموعة ضابطة. تم قياس مستوى المؤشرات الحيوية في المصل , تم قياس مستويات IMA و CHI3L1 باستخدام تقنية ELISA. تم إجراء قياس مستويات ملف الدهون في مصل الإنسان باستخدام تقنية القياس الطيفي.

النتائج: أظهرت النتائج وجود اتجاه لزيادة متوسط مستويات IMA بعد العملية مع ارتفاع درجات تعقيد آفة تصوير الأوعية الدموية. في الدرجة 0 (بدون تعقيد)، كان متوسط مستوى IMA (122.3±172.1)، وكانت الدرجة 1 (66.0±138.0)، وكانت الدرجة 2 (119.1±214.4) وفي الدرجة 3 (الأكثر تعقيدًا) كان مستوى IMA (246.6±530.7). يتمتع IMA بعد العملية بحساسية أعلى (84.6٪) مقارنة بـ IMA قبل العملية (58.6٪). وهذا يعني أن IMA بعد العملية أفضل في التعرف بشكل صحيح على المرضى الذين يعانون من PCI معقد. أظهرت كلتا مجموعتي طول الآفة زيادة في مستويات IMA بعد PCI. طول الآفة > 30 مم: كان متوسط ما قبل الإجراء (63.2±167.8)، كان متوسط مستوى ما بعد الإجراء (117.9±251.1)، بينما كان طول الآفة ≤ 30 مم: كان متوسط ما قبل الإجراء (58.9±175.7)، كان متوسط ما بعد العملية (129.1±296.3)، ويبدو أن الزيادة تكون أكبر بالنسبة للآفات الأطول (≤ 30 مم). وعلى النقيض من IMA، وكان

الاتجاه بالنسبة لـ CHI3L1 معاكسًا. كانت مستويات IMA قبل الإجراء في حالة الوعاء الواحد (63.6±169.5)، وكان مستوى ما بعد الإجراء (124.3±273.4) بينما في حالة الوعاء الواحد مع التفرع، كان مستوى IMA قبل الإجراء (60.2±154.5)، وكان مستوى IMA بعد الإجراء (166.2±335.5). ويبدو أن الزيادة أكبر في المجموعة مع التفرع، في حين قد تعكس درجة التعقيد. بالنسبة للـCHI3L1 أظهر الاتجاه أنه في كلتا المجموعتين انخفض بعد الPCI.

في حالة الأوعية المتعددة مع التفرع، كان IMA قبل الإجراء (190.8 ± 11.8)، وكان IMA بعد الإجراء (332.7 ± 83.4). ويبدو أن الزيادة متشابهة في كلتا المجموعتين، على الرغم من وجود تفرع. أظهرت مستويات IMA اختلافات كبيرة عند مقارنتها بمستوى ما قبل وبعد الإجراء في PCI متعدد الأوعية، واختلافًا كبيرًا عند مقارنة مستوى ما قبل وبعد الإجراء في الأوعية المتعددة مع التفرع. كان اتجاه CHI3L1 مختلفًا بشكل ملحوظ بين المجموعتين وأظهر انخفاضًا عامًا. كل من IMA قبل الإجراء وIMA بعد الإجراء لهما قيم AUC حوالي 60٪، مما يشير إلى قدرة معتدلة على التمييز بين حالات PCI البسيطة والمعقدة.

الاستنتاج: IMA، إلى جانب العوامل السريرية الأخرى، يمكن استخدامها لتحسين تصنيف المخاطر للمرضى الذين يخضعون للإجراءات، وخاصة تلك التي من المتوقع أن تكون معقدة. العلاقة بين تعقيد الآفة التصويرية للأوعية الدموية، وطول الآفة، وعدد الأوعية الدموية التي بها تفرع، وهذه المؤشرات الحيوية، يمكن للباحثين تطوير استراتيجيات أفضل لإدارة نقص التروية أثناء العمليات وتحسين رعاية المرضى. يمكن استخدام مستويات IMA كعلامة لتقييم درجة نقص التروية التي يعاني منها المريض أثناء الـ PCI، وخاصة في المرضى الذين لديهم تفرعات.

جمهورية العراق

وزارة التعليم العالي والبحث العلمي

جامعة كربلاء- كلية الطب

فرع الكيمياء والكيمياء الحياتية

تقييم المؤشرات الحيوية المحتملة قبل وبعد التدخل القسطري للشرايين التاجية

رسالة مقدمة الى

جامعة كربلاء - فرع الكيمياء والكيمياء الحياتية - مجلس كلية الطب

كجزء من متطلبات نيل درجة الماجستير في الكيمياء السريرية

من قبل

رشا محمد شرموخ

بكالوريوس علوم كيمياء / جامعة كربلاء / ٢٠١٢

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