



**Arab American University
Faculty of Graduate Studies**

**Evaluating Diagnostic Precision of Non-Enhanced
MRA in Peripheral Arterial Disease**

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**This thesis was submitted in partial fulfillment of the
Requirements for the Degree of Master Degree in CT
and MRI Sciences.**

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Thesis Approval

“Evaluating Diagnostic Precision of Non-Enhanced MRA in Peripheral Arterial Disease”

By

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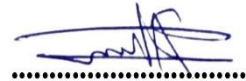
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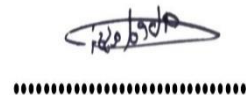
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Declaration

I hereby declare that this thesis represents my work, otherwise referenced, and has not been previously included in a thesis or dissertation submitted elsewhere for a degree, diploma, or other qualifications.

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Dedication

This study is wholeheartedly dedicated to my husband and children, as well as my beloved parents, who have been a constant source of inspiration and strength during times when we contemplated giving up. They consistently provide moral, spiritual, emotional, and financial support. To my brother, sisters, mentor, friends, and classmates, who generously shared their words of advice and encouragement, were propelling me towards the completion of this study.

Lastly, I dedicate this thesis to the Almighty God – I express my gratitude for the guidance, strength, mental acuity, protection, skills, and the gift of a healthy life.

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I would also like to express my heartfelt appreciation and gratitude to my mother and father, my inspiration, for their unwavering support, as well as to my family members.

My greatest thanks go to my husband and children, who have endured years of missed time for themselves due to my absence, as well as the additional workload that has ensued.

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Abstract

In the dynamic landscape of vascular pathology, the early detection of Peripheral Arterial Occlusive Disease (PAOD) plays a crucial role in mitigating substantial morbidity. This study explores the pivotal role of Magnetic Resonance Angiography (MRA) in diagnosing cardiovascular disorders, specifically focusing on the enigmatic realm of peripheral arterial disease (PAD).

Non-contrast MRA techniques, including QISS, 3D-FSE, and VS-MRA, have recently gained prominence in PAD imaging, surpassing traditional methods like TOF and PC-MRA. These advanced techniques offer superior fidelity, outperforming other diagnostic methods such as CTA and digital subtraction angiography. Non-contrast MRA proves particularly valuable for patients with compromised kidney function, pregnant individuals, those with elevated creatinine levels, and individuals with allergic reactions to gadolinium-based contrast agents, ensuring safety in diagnosis.

The study's core objective is to achieve precise and secure diagnoses of PAOD when contrast media (CM) can't be used. Specifically, the research assesses the effectiveness of ECG-triggered 3D-FSE MRA (Inhance-Deltaflow) in evaluating lowerlimb peripheral arterial disease. Utilizing a quantitative, observational, and cross-sectional approach, the study compares the diagnostic precision of non-contrast-enhanced angiography to contrast-enhanced MRA.

The research employed the GE Optima 360, a 1.5 T MRI scanner, and an external ECG signal acquisition system (Magnitude 3200 from the USA) for signal enhancement. Images from 20 patients, 16 males and 4 females, were evaluated by two blinded radiologists, and graded on a scale from 0 to 5. The results demonstrate exceptional sensitivity, with a rate of 98.28% in region 1 (aortoiliac), 100.00% in

region 2 (femoral), and 99.07% in region 3 (leg). The specificity remains unwavering at 100.00% across all regions, underscoring the test's precision in both diagnosis and exclusion.

In summary, this study illuminates the potential of non-enhanced MRA in the realm of PAD diagnosis. By offering a safe and effective alternative for patients at risk due to contrast media, non-enhanced MRA emerges as a beacon of hope. This non-invasive approach, free from the need for contrast agents, not only ensures patient safety but also paves the way for diagnostic enlightenment in the field of vascular pathology.

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List of Abbreviations

AAUP	Arab American University of Palestine
ABI	Ankle Brachial Index
CE-MRA	Contrast-enhanced MR Angiography
CM	Contrast Media
CT	Computed Tomography
CTA	Computed Tomography Angiography
DSA	Digital Subtraction Angiography
ECG	Electrocardiography
eGFR	Estimated Glomerular Filtration Rate
ETS	Echo Train Spacing
FFE	Fast Filled Echo
FBI	Fresh Blood Imaging
FDA	Food and Drug Administration
FOV	Field of View
FSE	Fast Spin Echo
IRB	Institutional Review Board
GBCAs	Gadolinium-based Contrast Agents
GE	General Electric
GFR	Glomerular Filtration Rate
KD	Kawasaki Disease
MIP	Maximum Intensity Projection
MRI	Magnetic Resonance Angiography

MRA	Magnetic Resonance Angiography
NC-MRA	Non-Contrast Enhanced Magnetic Resonance Angiography
NFS	Nephrogenic Systemic Fibrosis
PAD	Peripheral Arterial Disease
PAOD	Peripheral Arterial Occlusive Disease
PC	Phase Contrast
QISS	Quiescent-Inflow Single-Shot
SAAAs	Systemic Artery Aneurysms
SBP	Systolic Blood Pressure
RF	RadioFrequency
SPSS	Statistical Package for the Social Sciences
SSFP	Steady State Free Precession
TE	Time of Echo
TI	Time of Inversion
TOF	Time-of-Flight
TR	Time of Repetition
TRANCE	Triggered Angiography Non-Contrast-Enhanced
TSE	Turbo Spin Echo
US	Ultra-Sound
UV	Ultraviolet
VENC	Velocity Encoding
2D	Two Dimensional
3D	Three Dimensional

Chapter One

Introduction

1.1 Background

Patients with peripheral arterial disease (PAD) are at risk for a variety of quality-of-life concerns, including intermittent claudication, pain at rest, and even gangrene (Liu et al. 2016). PAOD, or peripheral arterial occlusive disease, has been found to have a prevalence of 12 to 20% in people over the age of 65. PAOD was found to be common in patients over the age of 55, with a prevalence of around 20% (Soumya 2016).

PAD patients have poor lower extremity arterial perfusion, also described as "poor circulation." Atherosclerotic plaques typically narrow the arterial flow lumen in PAD, which limits blood flow to the distal extremities (Zemaitis, Boll, and Dreyer, 2019). Walking may result in thigh or calf pain due to transient ischemia of the leg muscles brought on by reduced blood supply. Intermittent claudication, which means "to limp", is the phrase used to describe walking pain caused by PAD. Many PAD patients either show no symptoms at all or present with unusual complaints that do not fully fit the diagnosis of claudication. Others can experience limb-threatening blood flow impairment, demanding urgent surgery (Zemaitis 2022). Cross-sectional diagnostic imaging can determine the severity and location of stenosis, making it essential for interventional and surgical planning.

The gold standard for assessing peripheral arterial disease, conventional intra-arterial angiography or digital subtraction angiography is associated with the risks of an invasive technique, ionizing radiation, nephrotoxic iodinated contrast media, and hospitalization costs (Soumya 2016).

Duplex ultrasound is a well-established noninvasive modality for PAOD with high sensitivity and specificity. The addition of functional (color-flow) imaging can improve the performance of this modality even more. However, duplex ultrasound is operator-dependent and does not provide a "road map" of the vascular system that can be used for treatment planning (Hodnett et al. 2011).

CT Angiography (CTA) provides the spatial resolution of catheter digital subtraction Angiography (DSA) without invasive risks. However, it is directly affected by ionizing radiation and the risk of iodinated contrast nephropathy. Nephropathy caused by contrast medium remains one of the most serious clinical consequences of using iodinated contrast medium (Hodnett et al. 2011). CE-MRA (contrast-enhanced MR angiography) has been demonstrated to be highly accurate for detecting stenosis greater than 50% or occlusion throughout the entire lower extremity arterial tree (Hodnett et al. 2011).

With MRA sequences, the visualization of the arteries over the veins is frequently maximized by using techniques that increase the signal from the vasculature while reducing the signal from the surrounding non-vascular tissues (Kuo et al. 2019). Contrast media (CM) used in MRA and other modalities might even be contraindicated in certain circumstances, such as previous severe allergic reaction to a contrast agent, patients with severe renal disease at risk of nephrogenic systemic fibrosis (NSF), and pregnant patients (Schieda et al. 2018).

As a result, the first cases of severe complication nephrogenic systemic fibrosis were revealed in 1997, and the relation between this disease and gadolinium was discovered in 2006. Nephrogenic systemic fibrosis only occurs in patients with impaired renal function, such as dialysis patients. For these reasons, NC-MRA may be a better

option for avoiding the potentially serious side effects of contrast materials (Morita et al. 2011). However, due to the high prevalence of chronic renal dysfunction in patients with peripheral arterial disease, the risk of nephrogenic NSF following gadolinium exposure has remained a constant concern (Gallo-Bernal et al. 2022).

The concern is focused on developing and using NC-MRA techniques, because of the link between NSF and gadolinium-based contrast agents, which was observed almost exclusively in patients with end-stage renal disease.

Time-of-flight (TOF) and phase-contrast imaging are the most commonly used techniques for NC-MRA. Several novel NC-MRA techniques, however, have since gained popularity. With the proper application of these angiographic techniques, it is possible to diagnose vascular diseases associated with chronic kidney disease without the use of contrast materials (Morita et al. 2011). Fresh blood imaging, native spatial and chemical-shift-encoded excitation (SPACE), and flow-sensitive dephasing are examples of subtractive techniques (Hodnett et al. 2011).

Each of the NC-MRA suggested techniques have benefits and drawbacks, such as long imaging time, signal loss, susceptibility to field artifact, sensitivity to motion, and parameter dependence (Cavallo et al. 2019)(Hodnett et al. 2011).

For NC-MRA, several contrast mechanisms are available, and one of the techniques NC-MRA, is TSE-based. This non-contrast MRA technique is ideal for peripheral Angiography. The core sequence is a 3D-fast (turbo) T2-weighted spin-echo accelerated by partial Fourier acquisition (Navot et al., 2021).

The sequence is either cardiac-gated or peripheral pulse-gated. An arteriogram is created by subtracting co-registered images in diastole and systole. Subtractive 3D fast spin-echo techniques rely on the fact that intra-vascular signal is suppressed in fast spin-

echo images acquired during rapid systolic flow, but relatively preserved during slow or absent diastolic flow (Diering, Maxson & Mitchell, and Freeman 2018).

Therefore, the purpose of this study is to determine the efficacy of ECG-triggered 3D-TSE MRA (Enhance Deltaflow) in the evaluation of lower limb peripheral arterial disease.

1.2 Statement of the Problem

The peripheral arterial occlusive disease is a circulatory problem that causes reduced blood flow through the arteries, with symptoms ranging from none to severe and is primarily caused by atherosclerosis. PAOD affects over 200 million adults worldwide, with the incidence increasing to 20% for people over the age of 70, thus according to epidemiological studies of patients with lower extremity PAD, the annual mortality rate extends between 4% and 6% (ACR, 2023).

It is associated with risk factors for cardiovascular disease such as smoking, diabetes, hypertension, and kidney function impairment (Criqui and Aboyans 2015)

With the aid of gadolinium-based contrast agents (GBCAs), MRI is one of the methods used to diagnose PAOD. In patients with acute renal dysfunction or severe chronic kidney disease, GBCAs may have an unfavorable effect that could lead to NSF. Then the inability of renal failure disease patients, pregnant women, patients with high creatinine levels, and those who had a previous severe allergic reaction to GBCAs to undergo MRA with contrast.

1.3 Objectives

The main objective: The purpose of the study is to determine the efficacy of ECG-triggered 3D-FSE MRA (Enhance Deltaflow) in the evaluation of lower limb peripheral arterial disease.

Secondary objectives:

1. To make a comparison between CE-MRA and NC-MRA using a Q-flow sequence in diagnosing PAOD. diagnose PAOD safely, easily, and accurately in patients with CM risk factors using a Q flow sequence.
2. Introduce an NC-MRA protocol that will patients with risk factors for gadolinium to be diagnosed with PAOD efficiently and safely.

1.4 Study Hypothesis

- * NC-MRA as an alternative to CE-MRA for evaluation of peripheral arterial disease.
- * NC-MRA is safe for patients with kidney failure disease, pregnant patients, and any patient with a risk of MRI contrast media.

1.5 Research Questions

- 1- Is non-contrast-enhanced MRA (NC-MRA) a diagnosable technique for PAOD?
- 2- How can NC-MRA save patients from contrast media and ionizing radiation risks?
- 3- In comparison with CE-MRA;
 - a) How much does the procedure take time?
 - b) Can NC-MRA produce consistent image quality?

1.6 Significance of the Study

CE-MRA is the most accurate diagnostic technique for detecting stenosis (50% or more), with most studies reporting sensitivities and specificities of higher than 90%, but with the highest proportion of adverse events (Alhashlan et al., 2023). Because of the increased risk of NSF, radiologists have withheld GBCAs from patients with acute kidney injury and/or severe chronic kidney disease if the estimated glomerular filtration rate (GFR) is 30 mL/min/1.73 m². NSF is a rare but serious systemic disease that causes fibrosis of the skin and other tissues throughout the body in individuals who are renal impaired. Then the need for NC-MRA is necessary (Weinreb et al., 2021).

1.7 Outline the Structure of the Thesis

The arrangement of the thesis appears as the following:

Chapter One: Introduction

- 1.1 Provides a general introduction to the study.
- 1.2 States the problem and articulates the research objectives.
- 1.3 Formulates research questions.
- 1.4 Discusses the significance of the study

Chapter Two: Theoretical Framework and Literature Review

- 2.1 Explores peripheral arterial occlusive disease, non-contrast MRA techniques for diagnosing PAOD, and 3D TSE MRA.
- 2.2 Synthesizes relevant literature, highlighting key publications.
- 2.3 Identifies and discusses the knowledge gap in the existing literature.
- 2.4 Evaluate the contributions of the reviewed publications to the addressed issue.

Chapter Three: Research Methodology

- 3.1 Presents the research methodology, encompassing study design, study setting, study population, and sample size.
- 3.2 Describes the study instrument, data collection procedures, data analysis methods, scale correction techniques, and ethical considerations.

Chapter Four: Results

- 4.1 Presents findings obtained from the study.
- 4.2 Includes information about the respondents and supporting research that corroborates the study's outcomes.

Chapter Five: Discussion, Conclusion, Recommendations, Strengths, and Future Work

- 5.1 Engages in a discussion of the results.
- 5.2 Draw conclusions based on the findings.
- 5.3 Offers recommendations derived from the study.
- 5.4 Assesses the strengths of the research.
- 5.5 Proposes avenues for future research.

Chapter Two

Literature Review

2.1 Introduction

The study assessed the “Diagnostic accuracy of non-enhanced MRA in peripheral arterial disease compared to enhanced MRA”. The chapter includes a literature review of non-contrast-enhanced MRA in peripheral arterial disease referring to the variables of study. Published studies in PubMed, Google Scholar, and textbooks were investigated in this study as a search strategy. For this study, the literature review involved a comprehensive search with keywords: non-contrast MRA, peripheral arterial occlusive disease, contrast-enhanced MRA, nephrogenic systemic fibrosis syndrome (NSF), gadolinium, enhanced Deltaflow, General Electric (GE).

2.2 Theory

2.2.1 Peripheral Arterial Occlusive Disease (PAOD):

Peripheral artery occlusive disease (PAOD) is the term that refers to the atherosclerotic narrowing and/or occlusion of all arterial disease that does not involve the coronary arteries or the aorta (carotid and vertebral arteries, coeliac, and mesenteric arteries, renal arteries, and upper and lower limb arteries) (Tran 2021).

Figure (2.1) illustrates lower limb occlusion. In the absence of integrative, multidisciplinary management, PAOD is frequently accompanied by multi-vessel disease, increasing the risk of morbidity and mortality.

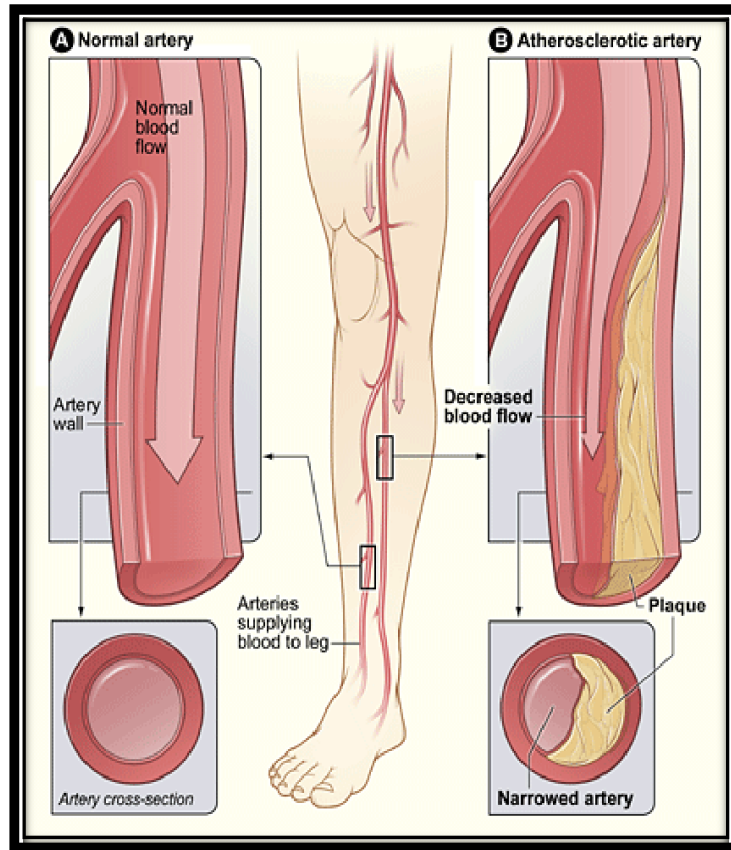


Figure (2.1): Peripheral Arterial Occlusive Disease (Treat-Jacobson et al. 2019)

Endothelial dysfunction and hypercoagulable status cause the development of a thrombogenic and pro-inflammatory status at the inferior vascular axis, which determines the development and progression of both atherosclerotic lesions and their associated complications over time.

Diabetes, hypertension, dyslipidemia, and smoking are the main cardiovascular risk factors that accelerate the progression of the pathophysiological processes, resulting in increased prevalence and mortality in PAOD (Aursulesei Onofrei et al. 2022).

A. Epidemiology and Risk Factors:

PAOD affects 15%-20% of people over the age of 70, with the prevalence probable to be higher if asymptomatic people are included. It is estimated that over 200 million people worldwide have PAD, with symptoms spanning from none to severe. PAD is relatively uncommon in younger people, but its prevalence increases with age and affects a significant proportion of the elderly population (>20% in >80-year-old individuals) (Shu and Santulli 2018).

PAOD is very thrombogenic and is associated with endothelial dysfunction and a hypercoagulable state in a large percentage of diabetics, hyperlipidemias, and smokers. Furthermore, patients with PAOD have an inflammatory state similar to those with unstable angina. PAD is under-recognized: 44% of cases were diagnosed only after enrollment, and despite documentation in medical records, only 49% of primary physicians treating patients with a prior diagnosis of PAD were aware of it. PAD is extremely common (prevalence: 29%) in high-risk individuals (>70 years without other risk factors, or 50-69 years with a history of cigarette smoking or diabetes) (Shu and Santulli 2018).

According to multivariate logistic regression analysis, only high C-reactive protein (CRP) levels were significantly associated with myocardial infarction (Shammas and Shammas 2022).

Smoking, hyperlipidemia, diabetes, and hypertension are the major established risk factors for PAOD, with 95% of people with prevalent PAOD having at least one of these risk factors (Wilcox et al., 2018)

B. Clinical Features of PAOD:

The 2005 (ACC/AHA) guidelines recommended the following clinical presentation of peripheral arterial occlusive disease in patients over the age of 50:

- 20 to 50% asymptomatic
- 40 to 50% atypical leg pain
- 10 to 35% classic claudication
- 1 to 2% threatened limb

The clinical presentation in these patients is usually joint pain associated with exercise, but it can also occur during passive movement of the limb when the symptoms appear. Concerning muscle pains, they rarely present systematically in the same location and are frequently not localized to muscle groups involved in walking (glutei, quadriceps, and calf muscles). Walking distance varies greatly with non-vascular claudication, even throughout the day (Sharma, Norton and Zhu, 2014).

The pain, however, does not disappear simply by stopping walking; instead, the patient must sit, lie down, or adopt a special posture, with the symptoms usually disappearing after a much longer period of rest than with vascular claudication (McDermott et al., 2021).

C. Symptoms:

1. Lower-extremity pain
 - a) Claudication: Exercise causes classic intermittent claudication, relieved by rest.
 - b) It can manifest as buttock, hip, thigh, calf, or foot claudication.
 - c) Extremity pain that is not typical.
 - d) Severe diffuse pain.
2. Non-healing wound/ulcer.
3. Discoloration of the skin /gangrene.

D. Comprehensive Vascular Examination for Identifying PAOD:

Patients who are at significant risk for PAOD should have a thorough vascular examination. The pulses of the femoral, popliteal, dorsal pedis, and posterior tibial arteries should be felt. Bumps in the femoral artery should be heard, and the lower extremities should be examined. Abnormal pulses, audible bruits, non-healing lower extremity wounds, lower extremity gangrene, elevation pallor, dependent rubor, delayed capillary refill, and cool extremities are all symptoms of PAD (Tummala and Scherbel 2018) (Tran, 2021).

2.2.2. Diagnosis of Peripheral Arterial Occlusive Disease:

A careful history and clinical examination remain the gold standard in the diagnosis of PAD and allow for the identification of a risk patient without the need for complex apparatus diagnostic methods.

The traditional gold standard for diagnosing PAOD of the lower extremities is digital subtraction angiography (DSA). Under current therapy guidelines, DSA is not only an excellent diagnostic tool for PAOD, but it is also essential for the interventional treatment of relevant artery stenoses (Posa et al., 2022). Nonetheless, DSA is an invasive procedure with potential complications, so less invasive and more comfortable angiography techniques are preferred when imaging is performed primarily for diagnostic or therapy planning purposes (Klink et al. 2017a).

Clinical examination alone can usually distinguish intermittent claudication from nonvascular causes that mimic claudication (pseudo-claudication). The ankle-brachial index calculation is generally known as the initial screening test (Agency for Healthcare Research and Quality U.S. Department of Health and Human Services

2015).

The ankle-brachial index (ABI) is a simple bedside tool for detecting PAOD in the lower extremities. The ABI of each leg is calculated by dividing the highest ankle systolic blood pressure (SBP) (measured with a blood pressure cuff above the ankle and a doppler of both the dorsal pedis and posterior tibial arteries) by the highest arm SBP, as shown in figure (2.2). A low ABI (0.9) indicates obstructive disease, whereas a very high ABI (>1.4) indicates arterial stiffening due to calcification. Exercise treadmill ABI or pedal plantarflexion (toe raises) ABI increases the sensitivity of the test in patients with claudication symptoms (Tran 2021). ABI has been reported to have a sensitivity of 94% to 97% in detecting angiographically significant stenosis. However, the sensitivity of ABI is decreased in patients with small vessel disease caused by hypertension, diabetes, or chronic kidney disease (Firnhaber and Powell 2019).

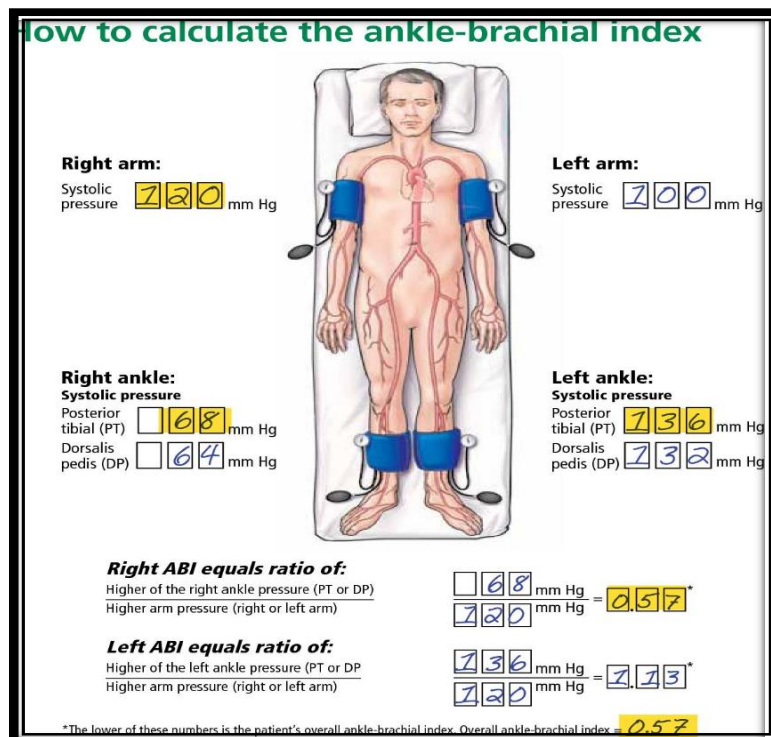


Figure (2.2): Ankle Brachial Index (Kim et al., 2012)

2.2.3 Non-Invasive Diagnostic Tests for PAOD

1. Duplex US

Duplex ultrasound is an excellent screening and diagnostic modality for PAOD. Ultrasound provides information on the location and extent of stenosis, as well as hemodynamics. The evaluation of other arterial vascular stenosis by duplex US is heavily dependent on operator experience and the patient's body habitus (Cheung et al., 2022)

The velocity ratio is used to assess the degree of stenosis. The velocity ratio is calculated by comparing the peak systolic velocity at the site of the stenotic lesion to the uninvolved section of the vessel. A ratio of 1.5 to 2 indicates a stenosis of 30 to 49%, whereas ratios of 2 to 4 and above 4 indicate stenosis of 50 to 75% and more than 75%, respectively. The limb Duplex arterial ultrasound accuracy is determined by the scanned segment and involved levels. Duplex scanning outperforms CT angiography in grading peripheral arterial disease by more than 80%. The other classification considers a peripheral arterial lesion significant when it causes more than 50% stenosis in the presence of an atherosclerotic plaque (Zubair, Lotfollahzadeh 2022).

2. Computed Tomography Angiography (CTA)

CT Angiography (CTA) provides a high-resolution three-dimensional roadmap for diagnosis and can facilitate in determining the most appropriate interventional strategy. The drawbacks of CTA compared to ultrasound are the cost, lack of functional data, radiation exposure, and the requirement for iodinated contrast agents. For vertebral artery disease, subclavian artery disease, mesenteric artery disease, aortoiliac disease, and renal artery disease, CT imaging is more accurate than ultrasound (Tran 2021).

The status of lower extremity arteries in patients with suspected PAOD can be

accurately assessed utilizing noninvasive CTA. In two systematic reviews by Klink et al. with meta-analyses, single-source, single-energy multi-slice CT scanners (16- and 64-MSCT) had sensitivities of 92% and 95%, respectively, and specificities of 93% and 96% for detecting arterial stenosis of more than 50% (Klink et al. 2017b).

In symptomatic POAD patients, CTA is > 50% accurate in detecting lower extremity artery stenosis. Atherosclerotic calcifications, image quality, and artifacts seemed to not affect CTA sensitivity, but atherosclerotic calcifications significantly reduced and artifacts partially reduced CTA specificity. The overall agreement for stenosis detection and calcified plaque assessment was moderate to substantial (Klink et al. 2017a).

3. Magnetic Resonance Angiography (MRA)

Without the use of ionizing radiation, it provides an accurate, non-invasive, and comprehensive whole-body vascular evaluation. Today's high-performance MR scanners allow for striking angiographic images while avoiding radiation exposure and the complexity of removing overlying bone from 3D reconstructed images. MRA can be performed in two ways: CE-MRA or NC-MRA, both of which take advantage of the differences in signal properties between static tissue and flowing blood via flow-sensitive techniques (Soumya 2016).

MR Angiography techniques can be broadly classified into:

I. Flow-dependent Angiography: It takes advantage of the fact that surrounding tissue remains static while blood flows. This is further subdivided into TOF/inflow angiography and phase contrast MR angiography. These methods are described in detail below.

II. Flow-independent Angiography: Instead of relying on blood flow, this technique is based on T1 and T2 differences and the chemical shift of the different tissues in the voxel. Even areas of slow flow can be easily imaged using this technique.

Another way of classifying MR Angiography is:

- A. Contrast-enhanced MR angiography
- B. Non-contrast enhanced MR angiography.

A. Contrast-enhanced (CE-MRA):

Contrast-enhanced MR angiography (CE-MRA) is a method that combines 3D spoiled gradient-echo sequences with gadolinium-based contrast agents administered (GBCAs). (CE-MRA) can be used to evaluate vascular structures in virtually any part of the body. T1 weighted spoiled gradient-echo sequence (flip angle 25° - 50° allows T1-weighting) is one of its key features (Murphy, Aghayev and Steigner, 2018).

The central acquisition of k-space, which corresponds to the arterial phase of the study, maximizes preferential visualization of arteries by using GBCAs to shorten the T1 interval of the blood, making it appear bright. By providing rapid acquisition of 3D volumes, which have a high signal-to-noise ratio (SNR) of the vessel to the background (Aguet et al., 2021).

Going to follow that, maximum intensity projection images are generated, which are primarily used for MRA interpretation. A dynamic technique is used because it prevents background tissue and venous enhancement. A bolus-chase technique of 0.2 mmol/kg body weight with multi-station MRA can image the aorta and peripheral runoff arteries with the same bolus, in which the aortoiliac, femoropopliteal, and tibial regions are imaged sequentially (Pollak, Norton, and Kramer 2012).

MRA has a reported sensitivity of 95% and a specificity of 90% for stenosis with a

narrowing of 70% to 99%. MRA has a reported sensitivity of 98% and specificity of 86% for all stenosis (Michael and Todd, 2012). The benefits of CE-MRA include minimal invasiveness, the absence of ionizing radiation, high diagnostic accuracy, and cost-effectiveness. Metal implants, pacemakers, claustrophobic patients, and gadolinium-based contrast agents are among the limitations (Nielsen and Thomsen 2012).

GBCAs have been used in healthcare for many decades and are essential to MRI examinations. The half-life of GBCAs in patients with normal renal function is approximately 1.5 hours. Despite GBCAs having a generally excellent safety profile, they are the cause of NSF (Schieda et al. 2018). There is presently no known specific or consistently effective treatment for NSF, a major late adverse event linked to exposure to GBCAs that can develop in patients with severe renal impairment. Even while the correlation between gadolinium exposure and the development of NSF is generally believed, the mechanism is not fully understood.

2.2.4 Nephrogenic Systemic Fibrosis

Nephrogenic systemic fibrosis (NSF) is an iatrogenic fibrosing condition that usually affects patients with renal insufficiency, especially in those with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 ml/min) after exposure to GBCAs during imaging examinations. Skin thickening, tethering, hyperpigmentation; flexion contractures of joints; and extracutaneous fibrosis are all symptoms of NSF. This article examines the epidemiology, histology, pathophysiology, history, and clinical symptoms of this debilitating condition (Alfano et al. 2020).

4. Etiology of NSF:

It is unclear what causes nephrogenic systemic fibrosis exactly. Scarring of tissue occurs throughout the body, most frequently in the skin and subcutaneous tissues, as a result of fibrous connective tissue that develops in the skin and connective tissues. Older gadolinium-based contrast agents (group 1) should be avoided by patients with acute renal dysfunction or chronic kidney disease, according to the Food and Drug Administration (FDA).

5. GFR

According to a recent meta-analysis by Agarwal et al., patients with chronic renal disease who were exposed to gadolinium had a 27-fold higher chance of developing NSF than control participants, who were not exposed to gadolinium (Soumya 2016).

6. Prevention of NSF

Due to the critical, life-saving medical information that GBCAs can provide, physicians should examine the potential risks of gadolinium deposition for every patient before considering whether to do a CE-MRA study. Therefore, avoiding gadolinium is currently suggested as a preventive measure for NSF in patients with severe kidney failure. Gadolinium-containing contrast agents should only be used when strictly necessary, especially in high doses. After gadolinium injection, it could be required to start hemodialysis right away.

A significant risk is inherent for patients with kidney dysfunction whose eGFR is less than 30 ml/min/1.73 m². Studies have demonstrated that doing dialysis instantly after a gadolinium-based MRI can help reduce the risk of NSF in patients on dialysis (Lee 2015).

7. Treatment of NSF:

There are currently no effective treatments for NSF. If possible, recovering renal function is essential to avoiding further progression since it seems to stop or delay the progression. A few studies demonstrated little improvement in skin lesions when intravenous immunoglobulin, photopheresis, and local interferon treatment were used. According to recent studies, cutaneous symptoms may be improved by combining ultraviolet A (UV-A) phototherapy with steroids, methotrexate, and other medications (Shamam & De Jesus, 2022).

B. Non-Contrast-Enhanced MR Angiography (NCE-MRA):

Non-contrast-enhanced MRA has made significant strides in recent years. Compared to CE-MRA and CTA, it provides many advantages, including the ability to repeat scans that have been declared non-diagnostic because of patient movement or technical glitches and the elimination of risks and expenses involved with administering contrast (Diering, et al. 2018). With improvements in MR hardware and software, NCE-MRA methods outweigh the risk of nephrogenic systemic fibrosis caused by gadolinium-based contrast, in patients with vascular or metabolic disorders and moderate to severe renal insufficiency.

Non-contrast MR Angiography sequences include

1. Time of flight (TOF) MR angiography
2. Phase contrast imaging MR angiography
3. SSFP (steady-state free precession) angiography
4. ECG-gated FSE (fast spin echo) MR angiography

1. Time-of-flight (TOF)

Principle: Non-subtractive, inflow-dependent MRA techniques include legacy 2D and 3D TOF methods that are still broadly used for assessing the extracranial carotid arteries and the circle of Willis. Even in slow flow settings, 2D TOF provides efficient head-to-foot coverage and adequate vessel-to-background contrast for the neck vessels. 3D TOF, on the other hand, has less head-to-foot coverage and suffers from saturation effects with slow flow (Diering, Maxson & Mitchell, and Freeman 2018). Background signal is suppressed in TOF by rapid slice-selective radiofrequency excitation pulses due to saturation of the signal from stationary tissue, as shown in figure (2.3) The use of the saturation band on the venous side of the imaging slice aids in the nullification of the signal and masking of the venous flow. In tissue planes with high flow velocity, the incoming blood will be free of the excitation pulse (Cavallo et al. 2019). It is, however, more resistant to signal loss caused by flow-related dephasing caused by a hemodynamically significant stenosis. Due to the rapid, repeated application of the excitation RF pulse along with the tracking venous saturation RF pulse, which is typically placed just downstream of the excitation RF pulse, both techniques are susceptible to artifacts from flow saturation in horizontally directed or tortuous vessel segments (Diering, Maxson & Mitchell, and Freeman 2018). As shown in figure (2.4) 2D-TOF has several limitations, including inadequate signal for vessels deep in the abdomen, flow-related artifacts seen in areas of stenosis, difficulty obtaining perfectly perpendicular imaging planes, and a lengthy scan time (Pollak, Norton, and Kramer 2012).

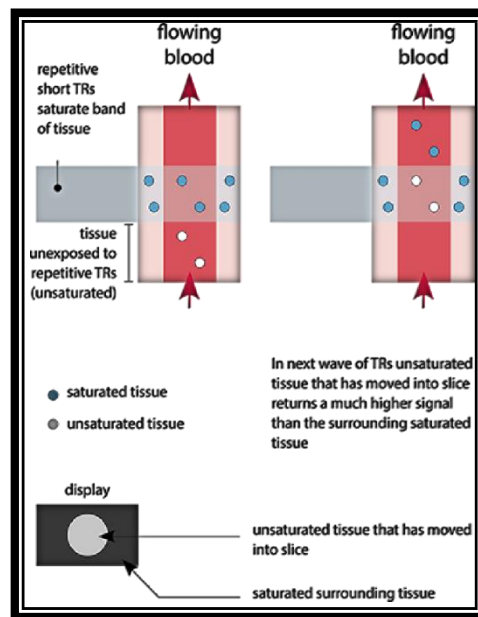


Figure (2.3): Time-Of-Flight (Edelman and Kocktzoglou, 2018).

Advantages of TOF

The great feature of TOF MR Angiography is the simplicity and reliability of imaging and image interpretation because the procedure has been used for a long time and most radiologists and radiologic technologists are familiar with it.

TOF-MRA exhibits certain limitations, including prolonged imaging time, direction-dependent outcomes, susceptibility to signal loss in in-plane, turbulent, or complex flow scenarios, and vulnerability to field heterogeneities. Despite these drawbacks, TOF-MRA finds valuable applications in various medical contexts. Notably, it is employed for 3D imaging of cerebral arteries, as well as 2D imaging of peripheral vessels and head and neck arteries. These applications underscore the versatility and clinical utility of TOF-MRA in visualizing vascular structures within the human body.

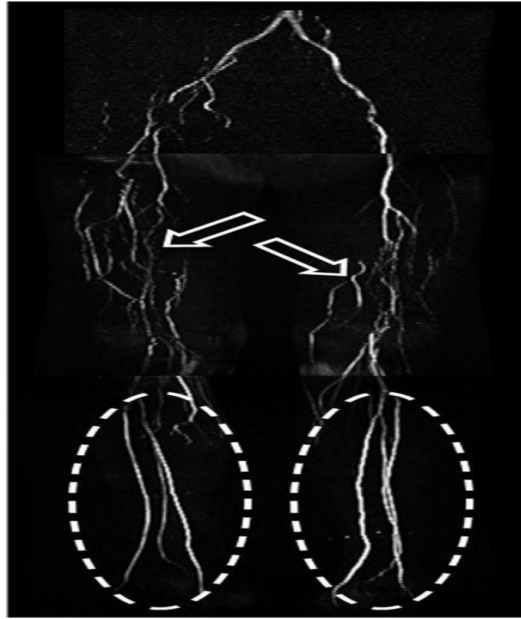


Figure (2.4): Runoff for a 2D time-of-flight MRA.

A patient with bilateral lower extremities claudication brought on by obstruction of the superficial femoral arteries had a 2D time-of-flight MRA of the pelvis, thighs, and calves. Collateral arteries (open arrows) in the thighs that originate from the profunda femoris arteries provide blood flow to the runoff vessels in the calves (ellipses) (Wu and Li, 2012).

2. Phase-contrast

Principle: The magnetic moments of spins moving along a bipolar gradient acquire a phase shift, whereas the magnetic moments of stationary spins do not. The velocity-encoding (VENC) gradients built into the pulse sequence can be used to control the degree and direction of the shift. Stationary spins experience the gradient's positive and negative lobes in equal measure, restoring their magnetic moments to their original phase position. Depending on the flow velocity and direction, the magnetic moments of moving spins become phase-advanced or phase-retarded (Westbrook and talbot 2019).

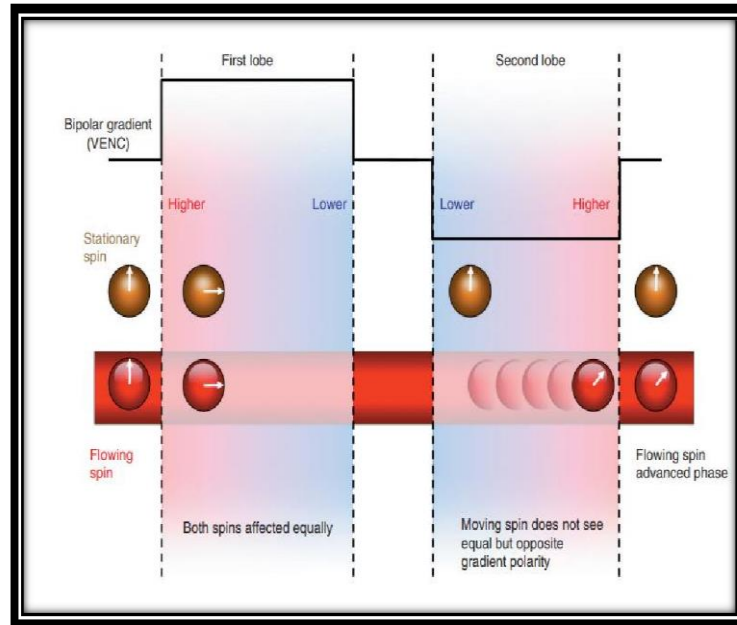


Figure (2.5): Phase contrast (Catherine Westbrook and John Talbot 2019).

Flow direction independent, because images can be obtained in planes parallel to the vessels without severe saturation effects, image acquisition time for 2D imaging can be shorter than for TOF angiography. Moreover, the technique provides excellent background signal suppression (Morita et al. 2011).

The utilization of phase contrast magnetic resonance angiography (PC MRA) comes with certain limitations. Firstly, there is a prolonged imaging time, especially in the case of three-dimensional (3D) imaging. Secondly, the technique is susceptible to signal loss in turbulent flow conditions. Additionally, PC MRA is sensitive to motion, which can pose challenges in acquiring clear and accurate images. Furthermore, the method is parameter-dependent, requiring careful consideration of various factors for optimal results. Despite these limitations, PC MRA finds valuable applications in medical imaging.

3. Steady State Free Precession MRA

Principle: SSFP Angiography, also known as Balanced FFE (fast field echo), TrueFISP (fast imaging with steady-state precession), FIESTA (fast imaging employing steady-state acquisition), and True SSFP, is a gradient-echo-based sequence that employs a series of equidistant RF pulses to maintain steady-state longitudinal and transverse magnetization. T2-/T1-weighted image contrast gives blood a high signal intensity with little reliance on inflow. Angiographic images with a high signal-to-noise ratio are produced using 3D acquisition (Morita et al. 2011) Figure (2.6) shows the principle of SSFP.

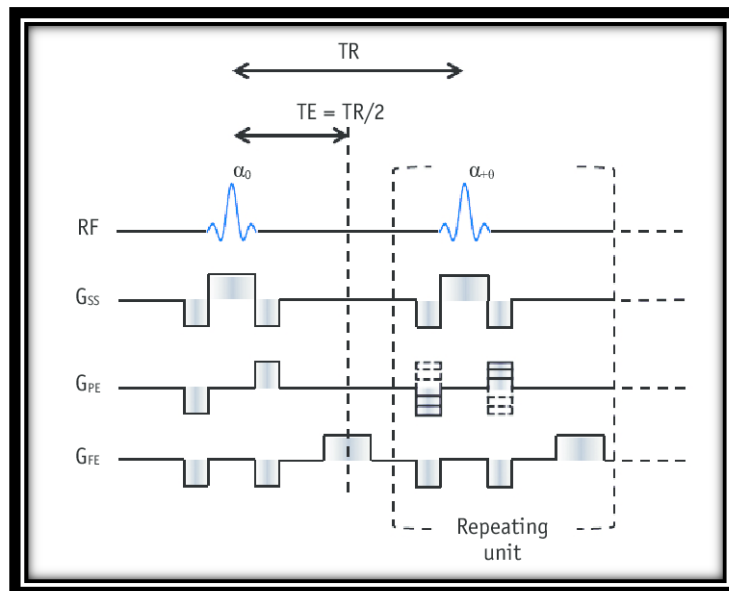


Figure (2.6): SSFP MRA pulse sequence (Park et al., 2015)

SSFP offers several advantages making it a valuable imaging technique. Firstly, it boasts a short imaging time, enhancing efficiency in medical diagnostics. Secondly, SSFP MRA provides a high signal- to-noise ratio, ensuring clear and detailed imaging results. Additionally, it exhibits relative flow independence, contributing to its versatility in capturing vascular structures. However, like any imaging method, SSFP

MRA has its limitations. It is prone to high background signals and susceptibility to field heterogeneities, potentially affecting the precision of the acquired images.

Despite these constraints, SSFP MRA finds notable applications in specific vascular assessments. It is particularly well-suited for imaging the renal arteries and proves effective in visualizing the aorta and coronary arteries, showcasing its utility in cardiovascular and renal evaluations.

4. ECG-gated FSE MR Angiography

Principle: The flow void effect of fast arterial flow during systole is used in ECG-gated FSE MR Angiography under the names FBI (fresh blood imaging), Delta Flow, NATIVESPACE (sampling perfection with application of optimized contrasts using different flip angle evolutions), TRANCE (triggered angiography non-contrast-enhanced), and FlowPrep. It generates bright-blood angiography by subtracting systolic images, in which signals from fast-flowing arteries are voided, from diastolic images, in which signals from slow-flowing arteries remain at high intensity on T2-weighted images (Morita et al. 2011). To allow for appropriate T1 recovery ECG or pulse wave-gated data is typically collected every two or three heartbeats (R-R intervals). In the readout direction, flow-spoiling gradient pulses are used to increase the flow systolic dephasing effect (Soumya 2016). Reduced data sampling duration is useful for maximizing the differences in signals between systole and diastole, reducing T2-weighted blurring, and reducing motion-related artifacts to produce images of sufficient quality (Morita et al. 2011).

The principle of the 3D ECG-gated FSE sequence is shown in figure (2.7). Every slice partition uses ECG gating to start each slice encoding at the same cardiac phase. FSE-related sequences generally result in "black blood" or "flow void" images,

however, the FBI method allows for "bright blood" depiction without the need for contrast agents. This is accomplished through the use of ECG-synchronized half-Fourier FSE, which minimizes echo train spacing (ETS) to eliminate motion-related artifacts and minimize susceptibility effects, which leads to a short single-shot acquisition time. The short T2 values in the blood produce blurring in the phase-encode direction in half-Fourier FSE, yet this blurring enhances the "bright blood" signal when aligned with the orientation of blood vessels.

The application of central k-space ordering in half-Fourier FSE decreases flow voids in the phase-encode direction even further. Signal enhancement and reduced flow dephasing can be used for fast-flow depiction by aligning the phase-encode direction parallel to the vessel of interest (Zhang et al. 2018).

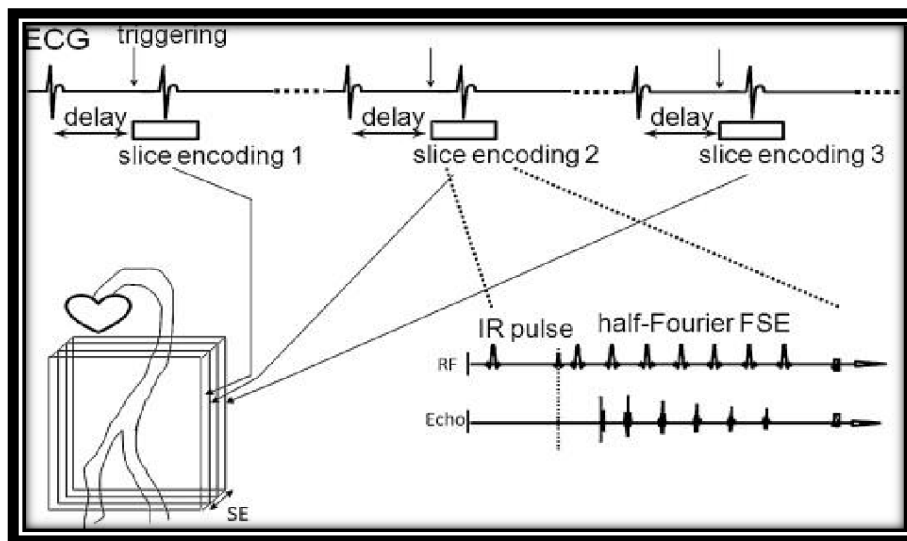


Figure (2.7): 3D ECG-gated FSE principle (Miyazaki and Isoda 2011).

ECG-gated fast spin-echo (FSE) imaging offers several advantages in medical diagnostics. Firstly, it boasts a relatively short imaging time, making it a time-efficient technique. Secondly, its sensitivity to slow flow enhances its capability to detect and visualize such vascular dynamics. Additionally, ECG-gated FSE exhibits a reduced

susceptibility to field heterogeneities, contributing to enhanced image quality. However, this imaging method comes with its set of limitations. Its complexity poses a challenge, and the direction- dependent nature of the process can be a drawback. Moreover, ECG-gated FSE is sensitive to motion artifacts, potentially impacting the precision of results. Despite these limitations, the technique finds valuable applications in imaging peripheral arteries and the aorta, showcasing its significance in cardiovascular diagnostics and assessment.

2.3 Literature Review

Minju, Minjung, et al. 2021 said, that this study investigated the ability of NE-MRA to image the feline aorta and the external iliac arteries. In contrast to human medicine, it was shown that ECG-FSE in cats caused picture quality to deteriorate (venous contamination, artifacts, and diminished arterial delineation), and repeatable and reproducible images could not be acquired due to their quick and shallow cardiac cycle. Because TOF produces good image quality that is sufficient for identifying the aorta and external iliac arteries in clinically healthy cats, it is more dependable and reproducible than 3D ECG-FSE. Consequently, it is anticipated that it will be utilized in the future to identify thromboembolism, evaluate the severity of the condition, select the best course of treatment, and analyze the prognosis for patients with feline arterial thromboembolism (FATE) (Nonaka et al. 2021).

Haruki, Takanori, et al. 2020 said Systemic artery aneurysms (SAAs) are a rare side effect of Kawasaki disease (KD), which also causes coronary aneurysms (SAAs). Hence, both coronary and systemic arterial aneurysms should be assessed in KD patients. The diastolic phase image of the three-dimensional fast spin echo during non-

contrast magnetic resonance Angiography was used to analyze two cases of SAA in this research. The first case involved a male 1-year-old who was given a KD diagnosis at 2 months of age. Scanning for 94 seconds revealed several aneurysms in the right axillary artery measuring 6.0 mm and 2.5 mm and the left axillary artery measures 12.0 mm, 4.0 mm, and 3.0 mm.

The second example involved a 13-year-old boy with KD who was diagnosed at 4 months of age after having a 7.0-mm right axillary artery aneurysm for 101 seconds, of scanning. Diastolic phase electrocardiogram-gated three-dimensional fast spin echo can assess SAA in patients with KD and does not need a lengthy scanning period or contrast material (Nonaka et al. 2021).

Gesine, Marie-Teres, et al. 2021 said Due to data loss, unexpected discoveries, and test termination due to claustrophobia, four out of 49 patients were unable to participate in this study. Out of the remaining 45 patients, three more had incomplete exams (no FSE-MRA, no CE-MRA, and no QISS-MRA without MIP reconstruction). All 45 patients were included in the time analysis; however, only complete exams (n = 42 participants) were examined for the image quality study. Fontaine stage IIa, stage IIb, and stage III PAD were present in 38 out of 45 patients (mean age, 66.11 years, 17 female) (Knobloch et al. 2021).

Schubert et al evaluated pedal vasculature in 20 PAD patients using cardiac-gated 3D FSE and CE-MRA, with DSA as the standard reference. The NC-MRA technique resulted in a significantly higher rate of non-diagnostic vessel segments. The NC-MRA had 96% sensitivity and 97% negative predictive value, while specificity and positive predictive value were 80% and 69% for >50% stenosis, respectively (Cavallo et al. 2019).

Gutzeit et al used DSA as a reference standard to study cardiac gated 3D FSE in the lower limb arteries. The analysis revealed that both the thigh and calf segments had a very high negative predictive value (>95%) and a high diagnostic accuracy (>90%) (Cavallo et al., 2019).

Hanrahan, Lindley, et al. in 2018 said 16.9% (97/573, 19/20 patients) of the 573 vascular segments that were examined showed hemodynamically significant anomalies. In 98% of segments with Gd MR Angiography, 93% with QIR/ECG-FSE, and 95% with QISS, reader confidence was sufficient for diagnosis. For all 3 stations combined, reader trust was generally better with QISS than QIR/ECG-FSE (P .05 Sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and k agreement for all three stations were 81.4/87.2/57.0/95.8/86.2%/0.578 for QIR/ECG-FSE and 75.0/90.6/61.6/94.7/88.0%/0.597 for QISS when low confidence segments were classified as misdiagnosis. QISS and QIR/ECG-FSE had no statistically significant differences in agreement with Gd MR Angiography when using TASC II criteria to determine severity (Hanrahan et al. 2018).

Amy, Norton, et al. in 2012 said when contemplating a potential intervention for lower extremity PAD, noninvasive imaging is recommended to locate and assess the degree of artery stenosis. Depending on patient-specific considerations, local knowledge, and safety profiles, the major guidelines (TASC II, ESC, and ACC/AHA) advocate the use of either duplex US, CTA, or MRA. New knowledge is being gained from promising research investigations about the use of noninvasive imaging for assessing the physiology of the lower extremities and characterizing atherosclerotic plaques (Pollak, Norton, and Kramer 2012).

Kengo, Yasuhiro, et al. in 2010 said due to its increased capacity to identify

arterial stenosis, CE-MRA is often used in body and extremity examinations. It is advised that CE-MRA be replaced by the three-dimensional electrocardiogram-synchronized fast spin echo approach. Using non-contrast MRA on 3.0 T. MRI, a few papers in the literature assess the detectability of vascular stenosis. Using an original vascular phantom, non-contrast MRA at 3.0 T was used in this investigation to assess the detectability of vascular stenosis. The silicon tubes that made up the vascular phantom. The luminal diameter was stenosed by 30% and 70%, respectively. Each silicon tube has a pump attached to it that creates a pulsating flow. In this investigation, a flowing substance was employed to demonstrate the similarities of the intensity to blood on MRI.

By adjusting the image matrix, static magnetic field strength, and flow velocity, MRA was carried out in the vascular phantom without the need for a contrast agent (NATIVE sequence). Except from that Flow compensation was applied with or without NATIVE sequence. By measuring the signal intensities in non-contrast MRA pictures, the amount of vascular stenosis was quantitatively calculated. 30% of the vessels are thought to be stenotic at slow flow rates. Yet, in situations with high flow velocity, 30% stenosis was overestimated. The MRA using the NATIVE sequence overstated the stenosis by 70%. Using a flow compensation procedure increased the estimation of 70% stenosis. The flow compensation technique enhances the accurate assessment of vascular stenosis in MRA with a NATIVE sequence. MRA with NATIVE sequence is considered to be a promising method for the evaluation of patients with severe renal dysfunction as a substitute for CT angiography or CE-MRA (Nakato, Hiai, and Tomiguchi 2010).

Mitsue, Satoshi, et al in 2000 said the development of a non-contrast-enhanced

three-dimensional (3D) magnetic resonance angiography (MRA) method that acquires pictures quickly and doesn't use a contrast agent. The thoracic and iliac areas of 16 healthy participants were examined at 0.5 and 1.5 T using an electrocardiographically (ECG) synchronized 3D half-Fourier fast spin echo (FSE) technique with a proper ECG delay time for each slice encoding in 3D terms. Each 3D fresh blood imaging (FBI) experiment began with an ECG preparation scan (ECG-prep), and the right ECG triggering time was chosen to provide the best possible image of the target vessel during 3D FBI capture. Good-quality 3D MRA pictures of the thoracic and abdominal regions were obtained. Also, the weighted subtraction of two photos captured at various times enhances the contrast between arteries and veins (Miyazaki et al. 2000).

Chapter Three

Methodology

The research presents subsequent sections in this chapter, study design, study settings, Study population and sample size, study instrument, data collection, data analysis method, scale correction, and ethical considerations.

3.1 Study Design and Setting

The research employed a quantitative, observational diagnostic, cross-sectional design. After securing approval from the Palestinian Ministry of Health (see appendix C), and Institutional Review Board (IRB) approval (see appendix A), the investigation involved conducting tests on patients presenting with peripheral arterial occlusive disease at the vascular clinic of Palestine Medical Complex. Before implementation, the procedural details were communicated to the vascular physicians, directing the replacement of lower limb computed tomography angiography (CTA) with lower limb magnetic resonance angiography (MRA) for patients with identified risk factors for contrast media. Participants underwent a comprehensive explanation of the testing procedure, and their informed consent was obtained through the signing of a written consent form.

3.2 Study Instrument

Using MRI scanner of MRI department in Palestine Medical Complex (GE optima 360, 1.5T). For signal detection, the combination of a 16-channel anterior array coil with the posterior coil will be used. The ECG signal will be received via an external system (Magnitude 3200, USA).

3.3 Study Population and Sample Size

The study population is the entire diagnosed patient with peripheral arterial occlusive disease in Palestine Medical Complex. The sample consisted of 20 patients who arrived at the vascular clinic of Palestine Medical Complex from March 2023 till August 2023.

3.4 Inclusion Criteria

Individuals presenting symptoms indicative of lower limb peripheral arterial disease, undergoing contrast-enhanced MRA at Palestine Medical Complex.

3.5 Exclusion Criteria

The study's exclusion criteria encompass several specific conditions to ensure the reliability and safety of the research. Firstly, individuals with metallic implants are excluded, as the presence of such implants may interfere with the accuracy of magnetic resonance imaging (MRI). Secondly, patients who decline to provide consent for MRI are excluded from participation. Thirdly, individuals who are unable to cooperate during the MRI procedure are excluded, as cooperation is crucial for obtaining precise imaging results. Additionally, patients with arrhythmias, which can affect the stability of imaging data, are excluded from the study. Finally, the research focuses on adults, and thus, individuals below the age of 18 are not included in the participant pool. These exclusion criteria are carefully defined to enhance the study's validity and ensure the well-being of the participants.

3.6 Ethical Considerations

The Palestinian Ministry of Health granted the researcher permission to conduct the necessary examinations on the participating patients (Appendix C). The researcher also supplied a consent form (Appendix D) that indicates that participation is voluntary and that the participant's information would be kept confidential and used exclusively for scientific research reasons. Patient privacy and confidentiality were preserved, and participants were guaranteed that they did not need to provide any information that could be used to identify them, such as their name, address, or any other information. Then, all patients' consent was confirmed, and their signatures were obtained. The Arab American University's Scientific Research Ethics Committee (IRB) approved the study (Appendix A). The facility's approval for graduate studies (Appendix B).

3.7 Non-Contrast-Enhanced MR Angiography

Electrocardiography-gated, three-step, 3D ECG-gated FSE MRA (Enhance Deltaflow) sequence was performed in the axial plane with the following parameters as shown in the table below (table 3.1).

Table 3.1: 3D delta inflow parameters

TR	TE	TI	Slice thickness	Spacing	Matrix	Flip angle	FOV	NEX
2145	62.3	174	2.4	1.2	288*192	80	40*40	0.38

To determine the individual Diastolic Trigger Delay (DTD) an ECG-gated segmental SSFP coronal image was obtained with the following parameters (Table 3.2) with DTD of (280/ 170/ 90 cm/s) at the first step, second step, and third step respectively.

Table 3.2: Coronal SSFP parameters

TR	TE	TI	Slice Thickness	Spacing	Matrix	Flip angle	FOV	NEX
4615	79.9	0	150	0	320*224	90	40*40	0.54

3.8 Contrast-Enhanced MR Angiography (CE-MRA)

Three-dimensional spoiled gradient echo, fast-field-echo MRA as mask sequence was used with the following parameters as shown in Table 3.3. The start of the imaging sequence (step 1 of C_e MRA) was adapted to the enhancement of the abdominal aorta using a coronal smart prep; fluoro triggered technique. Dual-phase injections of 25 ml gadolinium Cyclolux were used with an overall injection duration of 0.24s. In the first phase, 15 ml of Cyclolux at a flow rate of 2 ml/second was injected. For the second phase, 10 ml of Cyclolux at a flow rate of 0.7 ml per second- and 30-ml saline solution were administered into the right antecubital vein, and the parameters for the arterial phase are shown on table 3.4.

Table 3.3: Mask parameters

TR	TE	TI	Slice Thickness	Spacing	Matrix	Flip angle	FOV	NEX
3.3	1.1	0	3.6	1.8	320*224	30	46*41.4	1

Table 3.4: Arterial sequences parameters:

TR	TE	TI	Slice Thickness	Spacing	Matrix	Flip angle	FOV	NEX
3.3	1.1	0	3.6	1.8	320*224	30	46*41.4	1

3.9 Data Analysis Techniques

For the statistical manipulation of our data; both descriptive and inferential statistical methods are used with a focus on the descriptive approach. The statistical analysis was carried out using the IBM SPSS version 25.0 statistical software. On one hand, descriptive statistical methods such as percentages, means, and charts were suggested by the nature and goals of our study where we evaluate the accuracy of non-contrast-enhanced MRA as an alternative to contrast-enhanced MRA for evaluation of peripheral arterial occlusive disease. On the other hand, when we consider the three different MRA acquisition steps collectively, along with five categories, it became reasonable (to a good degree) to conduct inferential parametric statistics where we utilized the Chi-Square, KAPPA Test, and Reliability test comparing two independent population means with unknown and possibly unequal population. This tool of analysis will be used on a larger scale in our future studies. A value of $p < 0.05$ was used as a significance standard.

3.10 Image Analysis

The data sets (source images, maximum intensity projections (MIP), and individual multi-planar images) were evaluated by consensus of two radiologists experienced 5 years in radiology. To prevent bias, the observers were blind to NC-MRA parameters as well as to any clinical information available. In the three different MRA acquisition steps, the MR image quality was graded using five categories: not assessable (score 1; vessels not visible or diagnostic information cannot be obtained), poor (score 2; image quality is degraded because of low signal intensity or blurring artifacts), moderate (score 3; low signal intensity and blurring artifacts), good (score 4;

high signal intensity and no blurring artifacts but post-processed MIP are of inferior quality for example due to background signal), and excellent (score 5; high signal intensity without blurring artifacts, also MIP reconstructions show relevant vessel lesions) evaluating the image quality.

Table 3.5 shows the abdominal aorta, pelvic arteries, femoral arteries, popliteal arteries, and the lower leg arteries segment included in this study.

Table 3.5: Lower limb artery segments.

Aorta	
Abdominal aorta	
Pelvic Arteries	
Right common – external iliac artery	Left common – external iliac artery
Right internal iliac artery	Left internal iliac artery
Femoral Arteries	
Right common femoral artery	Left common femoral artery
Right superficial femoral artery	Left superficial femoral artery
Popliteal Artery	
Right popliteal artery	Left popliteal artery
Lower Leg Arteries	
Right anterior tibial artery (ATA)	Left anterior tibial artery (ATA)
Right common peroneal artery (CPA)	Left common peroneal artery (CPA)
Right posterior tibial artery (PTA)	Left posterior tibial artery (PTA)

In total, 340 arterial segments have been evaluated across all of the 20 patients. Each artery was then separately assessed and graded qualitatively and quantitatively by two radiologists.

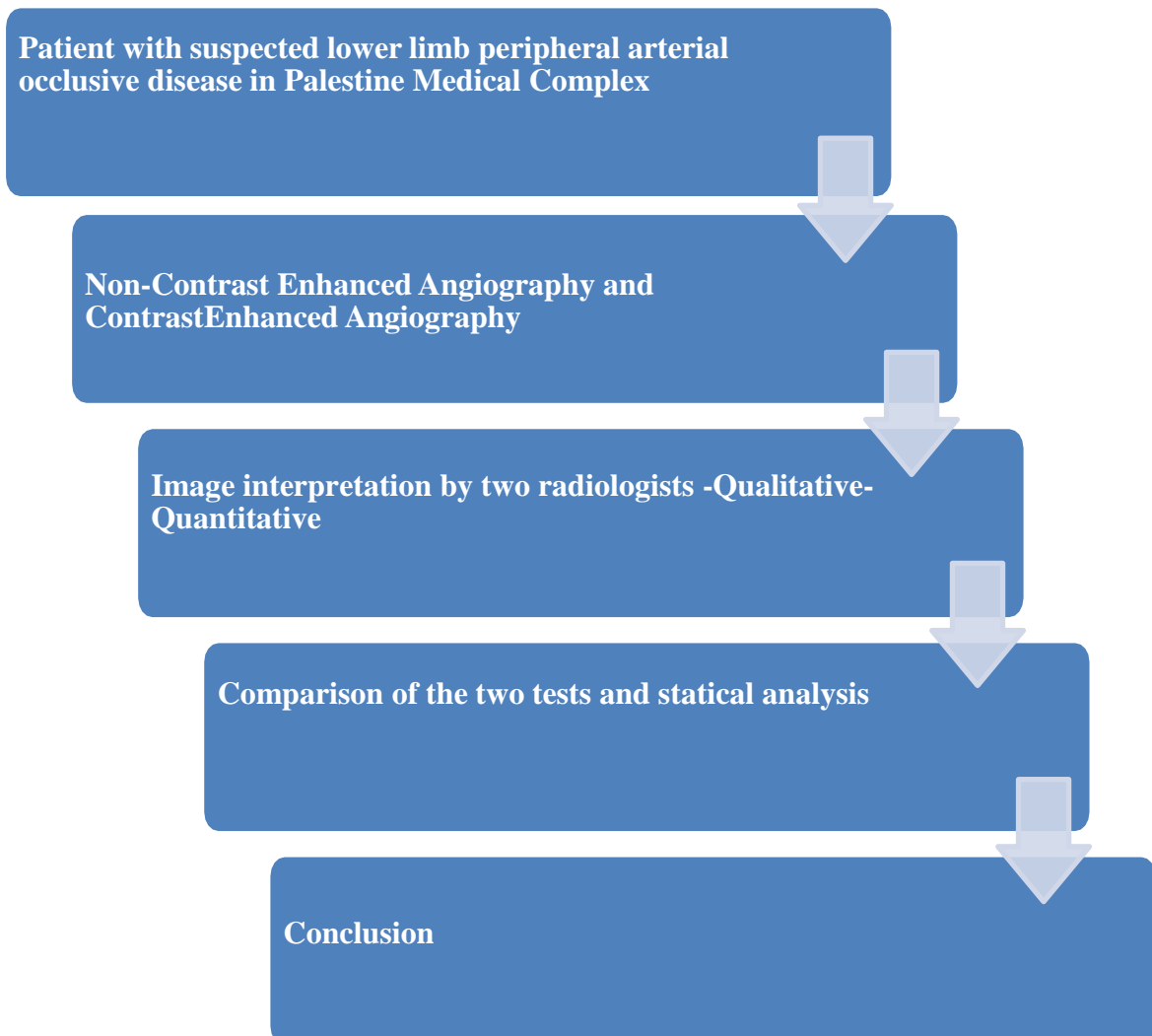
The image quality for each artery segment was qualitatively assessed as follows:

- Not assessable (vessels not visible or diagnostic information cannot be obtained)
- Poor (image quality is degraded because of low signal intensity or blurring artifacts)

- Moderate (low signal intensity and blurring artifacts)
- Good (high signal intensity and no blurring artifacts but post-processed MIPs are of inferior quality for example due to background signal)
- Excellent (high signal intensity without blurring artifacts, also MIP reconstructions show relevant vessel lesions)

3.11 Algorithm of the Methodology

This algorithm sets forth the systematic data collection, processing, and interpretation, resulting in an exhaustive and efficient approach for determining the accuracy of non- enhanced MRA in diagnosing PAOD.



Chapter Four

Results

This chapter outlines the results of the study, the study sample, with a discussion of the results.

4.1 Study Sample

Table 4.1 shows the distribution of participants according to their demographic and medical condition characteristics. The study sample of 20 patients was distributed by gender with 15 males and 5 females. The age of patients ranged from 20 to 81 years with a mean of 54.7 from both genders.

Table 4.1: Sample Characteristics

Sex	Female	5
	Male	15
Diabetes	No	12
	Yes	8
Hypertension	No	12
	Yes	8
Obesity	No	12
	Yes	8
Smoker	No	11
	Yes	9

4.2 Non-Enhanced MRA

Table 4.2 presents a detailed examination of image quality assessments by arterial segments as conducted by two radiologists (referred to as "Dr1" and "Dr2").

Table 4.2: Assessments of image quality for different arterial segments, performed by two radiologists.

Variable	Non-contrast	
	Dr 1	Dr2
	Mean	Mean
Aorta	3.35	3.20
Right common iliac artery	3.80	3.90
Left common iliac artery	3.73	3.90
Right external iliac artery	3.80	3.95
Left external iliac artery	3.80	3.90
Right common femoral artery	3.90	4.05
Left common femoral artery	3.90	4.00
Right superficial femoral artery	4.00	4.05
Left superficial femoral artery	4.00	4.05
Right popliteal artery	4.05	4.15
Left popliteal artery	4.05	4.15
Right anterior tibial artery (ATA)	4.05	4.10
Right common peroneal artery (CPA)	4.05	4.10
Right posterior tibial artery (PTA)	3.95	3.90
Left anterior tibial artery (ATA)	3.95	3.90
Left common peroneal artery (CPA)	3.95	3.90
Left posterior tibial artery (PTA)	3.95	3.90

4.2.1 Aorta

The mean quality rating for the Aorta was 3.35 for Dr1 and 3.20 for Dr2, indicating a moderate level of agreement between the two radiologists. While for contrast studies both rated with a mean of 5.

4.2.2 Right Common – External Iliac Artery

For right common iliac artery, both radiologists assigned relatively high mean quality ratings for the Right Common Iliac Artery, with Dr1 and Dr2 providing ratings of 3.80 and 3.90, respectively. While for contrast studies both rated with a mean of 5.

4.2.3 Left Common – External Iliac Artery

The left common iliac artery exhibits mean quality ratings of 3.73 for Dr1 and 3.90 for Dr2, suggesting overall agreement between the radiologists. While for with contrast studies both rated with a mean of 5.

4.2.4 Right Internal Iliac Artery

The right internal iliac artery receives reasonably high mean quality ratings from both radiologists, with Dr1 and Dr2 assigning ratings of 3.80 and 3.95, respectively. While for with contrast studies both rated with a mean of 5.

4.2.5 Left Internal Iliac Artery

The left external iliac artery also demonstrates agreement among the radiologists, with mean quality ratings of 3.80 (Dr1) and 3.90 (Dr2). While for with contrast studies both rated with a mean of 5.

4.2.6 Right Common Femoral Artery

The right common femoral artery receives moderately high mean quality ratings from both radiologists, with Dr1 and Dr2 assigning ratings of 3.90 and 4.05, respectively. While for with contrast studies both rated with a mean of 5.

4.2.7 Left Common Femoral Artery

The left common femoral artery demonstrates agreement between the radiologists. Dr1 assigns a mean quality rating of 3.90, while Dr2 provides a slightly higher mean rating of 4.00. While for with contrast studies both rated with a mean of 5.

4.2.8 Right Superficial Femoral Artery

The right superficial femoral artery receives high mean quality ratings from both radiologists, with Dr1 and Dr2 assigning ratings of 4.00 and 4.05, respectively. While for with contrast studies both rated with a mean of 5.

4.2.9 Left Superficial Femoral Artery

The left superficial femoral artery exhibits high mean quality ratings from both radiologists.

Dr1 assigns a mean quality rating of 4.00, while Dr2 provides a slightly higher mean rating of 4.05. While for with contrast studies both rated with a mean of 5.

4.2.10 Right Popliteal Artery

The right popliteal artery exhibits high mean quality ratings from both radiologists, with

Dr1 and Dr2 assigning ratings of 4.05 and 4.15, respectively. While for with contrast studies both rated with a mean of 5.

4.2.11 Left Popliteal Artery

The left popliteal artery receives high mean quality ratings from both radiologists, mirroring the ratings for the right popliteal artery, with Dr1 and Dr2 assigning ratings of 4.05 and 4.15, respectively. While for with contrast studies both rated with a mean of 5.

4.2.12 Right Anterior Tibial Artery

The right anterior tibial artery receives high mean quality ratings from both radiologists, with Dr1 and Dr2 assigning ratings of 4.05 and 4.10, respectively. While for with contrast studies both rated with a mean of 5.

4.2.13 Left Anterior Tibial Artery

The left anterior tibial artery exhibits moderate agreement between the radiologists, mirroring the ratings for the right anterior tibial artery. Dr1 and Dr2 assign mean quality ratings of 3.95 and 3.90, respectively. While for with contrast studies Dr1 and Dr2 rated 4.50 and 4.0, respectively.

4.2.14 Right Common Peroneal Artery

The right common peroneal Artery also garners high mean quality ratings from both radiologists, with Dr1 and Dr2 providing ratings of 4.05 and 4.10, respectively. While for with contrast studies both rated with a mean of 5.

4.2.15 Left Common Peroneal Artery

The left common peroneal artery demonstrates agreement between the radiologists,

similar to the right common peroneal artery. Dr1 and Dr2 provide mean ratings of 3.95 and 3.90, respectively. While for with contrast studies Dr1 and Dr2 rated 4.50 and 4.0, respectively.

4.2.16 Right Posterior Tibial Artery

The right posterior tibial Artery demonstrates moderate agreement between the radiologists. Dr1 assigned a mean quality rating of 3.95, while Dr2 provided a slightly lower mean rating of 3.90. While for with contrast studies Dr1 and Dr2 rated 4.50 and 4.0, respectively.

4.2.17 Left Posterior Tibial Artery

The left posterior tibial artery reflects a moderate agreement between the radiologists, akin to the right posterior tibial artery. Dr1 and Dr2 assign mean quality ratings of 3.95 and 3.90, respectively, with consistent median ratings of 4.00. While for with contrast studies Dr1 and Dr2 rated 4.50 and 4.0, respectively.

The main results of the image quality assessments for various arterial segments, as conducted by two radiologists (Dr1 and Dr2), indicate varying degrees of agreement and consensus in their evaluations. There is generally good to high agreement in image quality assessments for the majority of arterial segments as indicated by mean ratings ranging from 3.35 to 4.15. Several segments consistently receive moderate to high mean quality ratings, reflecting reliability and consistency in image quality assessments. However, some segments, such as the Aorta and the right common iliac artery, exhibit notable discrepancies in image quality assessments between the two radiologists, with differences in median ratings suggesting potential variability.

The non-contrast-enhanced MRA yielded a mean value of 3.82, while the contrast-enhanced MRA produced a mean value of 4.82, as shown in table (4.3). This signifies a disparity

of one degree between the two methods, suggesting an admissible level of differentiation.

Table 4.3: Mean and Median Overall segments quality

		Non- contrast	With contrast
Quality of the image	Mean	3.82	4.82
	Median	4.0	5
	Std. Dev.	0.65	0.08

The temporal disparity between the acquisition times of contrast-enhanced MRA and non-contrast-enhanced MRA was marginal, indicating a comparable duration for both techniques. Consequently, non-contrast-enhanced MRA presents as a viable method of preference for certain patients. This assertion is supported by the mean acquisition time of 31.1 minutes for non-contrast-enhanced MRA, only slightly exceeding the 25-minute acquisition time for contrast-enhanced MRA, spanning from the initiation to the conclusion of the examination.

Each arterial region was then analyzed using Cohen's Weighted Kappa to assess the goodness of agreement between the contrast enhanced and non-contrast enhanced MRA in the field of image quality diagnosis. Kappa weight was also used to evaluate the agreement between the D1 and D2 assessments. Table 4.4 shows the interpretation of the Kappa statistic, a measure of agreement between two methods that classify items into mutually exclusive categories.

The Kappa value ranges from 0 to 1, where 0 indicates no agreement beyond chance, and 1 indicates perfect agreement. The most important relevant indicators were calculated by testing variance, predictive values, and odds. Grades 1 and 2 were considered negative and grades 4 and 5 were considered positive for stenosis. Class 3 was neglected.

Table 4.4: Interpretation of Cohen's kappa

Value of Kappa	Level of Agreement	% of Reliable Data
0–.20	None	0–4%
.21–.39	Minimal	4–15%
.40–.59	Weak	15–35%
.60–.79	Moderate	35–63%
.80–.90	Strong	64–81%
Above.90	Almost Perfect	82–100%

4.3 Region-Wise Analysis

The arteries of the lower limbs were divided into three areas as follows:

- a. Region 1 (Aorto-Iliac) abdominal aorta, bilateral common iliac arteries, and bilateral external iliac arteries.
- b. Region 2 (Femoro-Popliteal) bilateral common femoral arteries, superficial femoral arteries, and bilateral popliteal arteries.
- c. Region 3 (Arteries in the Leg) bilateral common peroneal, posterior tibial, and anterior tibial arteries.

The efficacy of the index test was then evaluated for each of the arterial regions using Cohen's Weighted Kappa. Weighted Kappa was used to quantify the agreement in image quality between the two techniques. Sensitivity, specificity, positive predictive value, and negative predictive value of non-contrast MRA for image quality.

Region 1: Table (4.5) shows the cross-tabulation between the techniques and the degree of Agreement in Region 1, and table (4.6) shows sensitivity specificity and accuracy.

Table 4.5: Symmetric Measures Results- CE-MRA and NC-MRA Degree of Agreement in Region 1

		Value	Asymptotic Standard Error	Approximate T ^b	Approximate Significance
Measure of Agreement	Kapp a	.933	.067	7.593	.0001
N of Valid Cases		66			
a. Not assuming the null hypothesis.					
b. Using the asymptotic standard error assuming the null hypothesis.					

Testing Kappa against Null Hypothesis (H_0): Kappa = 0, Test Results: P Value <0.001

Table 4.6: Diagnostic performance of NCE-MRA in region 1

Statistic	Value	95% Confidence Interval
Sensitivity	98.28%	90.76% to 99.96%
Specificity	100.00%	63.06% to 100.00%
Disease prevalence (*)	0.74%	
Positive Predictive Value (*)	100.00%	93.73% to 100.00%
Negative Predictive Value (*)	99.99%	99.91% to 100.00%
Accuracy (*)	99.99%	
KAPPA:	0.9325	
Observed Agreement:	98.48%	

The table provides important statistics related to the diagnostic test. The test has a sensitivity of 98.28%, which means that it correctly identifies 98.28% of the diagnostic potential of the images in this case. The specificity is 100.00%, indicating that the test accurately identifies all individuals who do not have this condition. The kappa statistic, which is a measure of

agreement between the test and the reference standard, is 0.9325, indicating a high level of agreement between techniques. And 98.48% agreement between the two radiologists.

Region 2: Table (4.7) shows the cross-tabulation between the techniques and the degree of Agreement in Region 2, table (4.8) shows sensitivity specificity and accuracy.

Table 4.7: Symmetric Measures results- CE-MRA and NC-MRA Agreement in region 2

Symmetric Measures						
			Value	Asymptotic Standard Error	Approximate T ^b	Approximate Significance
Measure of Agreement	of	Kapp	.741	.175	7.973	0.0001
		a				
N of Valid Cases			108			
a. Not assuming the null hypothesis.						
b. Using the asymptotic standard error assuming the null hypothesis.						

Testing Kappa against Null Hypothesis (H_0): Kappa = 0, Test Results: P - Value <0.001

Table 4.8: Diagnostic performance of NCE-MRA in region 2

Statistic	Value	95% Confidence Interval
Sensitivity	100.00%	96.48% to 100.00%
Specificity	75.00%	19.41% to 99.37%
Disease prevalence (*)	0.93%	
Positive Predictive Value (*)	3.60%	0.68% to 16.95%
Negative Predictive Value (*)	100.00%	29.24% to 100.00%
Accuracy (*)	75.23%	65.95% to 83.07%
Observed Agreement:	98.15%	

The table displays important statistics related to another diagnostic test. The test has a sensitivity of 100.00%, indicating that it correctly identifies all image diagnoses in this area. The

kappa statistic, which is a measure of agreement between the test and the reference standard, is 0.741, indicating a moderate level of agreement. And 98.15% agreement between the two radiologists.

Region 3: Table (4.9) shows the Cross tabulation between the techniques group and the agreement of degree in region 3, table (4.19) shows sensitivity specificity and accuracy.

Table 4.9: Symmetric Measures results- CE-MRA and NC-MRA Agreement of degree in region3

Symmetric Measures					
		Value	Asymptotic Standard Error	Approximate T ^b	Approximate Significance
Measure of Agreement	Kappa	.491	.310	5.147	0.0001
N of Valid Cases		110			
a. Not assuming the null hypothesis.					
b. Using the asymptotic standard error assuming the null hypothesis.					

Testing Kappa Against Null Hypothesis (H_0): Kappa = 0, Test Results: P - Value <0.001

Table 4.10: Diagnostic performance of NCE-MRA in region 3

Statistic	Value	95% Confidence Interval
Sensitivity	99.07%	94.95% to 99.98%
Specificity	50.00%	1.26% to 98.74%
Disease prevalence (*)	0.96%	
Positive Predictive Value (*)	1.89%	0.48% to 7.16%
Negative Predictive Value (*)	99.98%	99.80% to 100.00%
Accuracy (*)	50.47%	40.78% to 60.14%
KAPPA	0.9407	
Observed Agreement	96.43%	

The table displays important statistics related to another diagnostic test. The test has a sensitivity of 99.07%, indicating that it correctly identifies most image diagnoses in this area. The kappa statistic, which is a measure of agreement between the test and thereference standard, is 0.491, indicating a weak level of agreement. And 96.43% agreement between the two radiologists.



Figure 4.1: CE-MRA



Figure 4.2: NC_MRA
3D ECG gated FSE

This scholarly image presents a meticulously balanced pair of lower limb Magnetic Resonance Angiography (MRA) scans. The composition places the contrast-enhanced MRA on the right side and the non-contrast-enhanced counterpart on the left. A striking observation emerges from this visual dichotomy: both images exhibit an exceptionally uniform quality in their depiction of the lower limb vascular structures.

Despite the absence of contrast enhancement in the left image, the delineation of anatomical details, blood vessels, and surrounding tissues remains remarkably consistent with its contrast-enhanced counterpart on the right.

This remarkable congruence underscores the inherent diagnostic value of non-contrast MRA techniques, reaffirming their role as a viable, cost-effective, and radiation-free alternative in clinical settings. It also serves as a testament to the advanced capabilities of modern imaging technology in providing high-quality, information-rich medical images for diagnostic purposes.

Chapter Five

Discussion & Conclusion

This section discusses the study investigating the diagnostic accuracy of non-enhanced magnetic resonance angiography (MRA) in peripheral arterial disease (PAD) compared to enhanced MRA for patients with contrast media risk factors provides valuable insights into the potential of non-enhanced MRA as a safe and effective alternative imaging modality.

5.1 Discussion

The present investigation was conceived to assess the applicability of NC-MRA, utilizing 3D ECG-gated FSE in comparison with CE-MRA, in the evaluation of peripheral arterial disease affecting the lower limbs. Patients diagnosed with peripheral arterial disease, who were undergoing MRA at the PMC MRI department, constituted the study cohort. These patients underwent non-contrast MRA 3D ECG-gated FSE, as well as contrast MRA. Each non-contrast MRA procedure required approximately 20-35 minutes, as well as contrast MRA studies were completed within approximately 25 minutes.

Subsequently, two independent radiologists evaluated the obtained images. The assessment encompassed qualitative appraisal of images acquired from various arterial segments. The data thus acquired were subjected to comprehensive analysis, to assess the diagnostic efficacy of the non-contrast technique and evaluate inter-observer variability.

In this study, involving 340 arterial segments across 20 patients, the data derived from the two radiologists were meticulously recorded and subjected to rigorous statistical analysis using SPSS. Parameters including sensitivity, specificity, positive predictive value, negative predictive value, and Cohen's weighted Kappa were estimated to elucidate the diagnostic performance and

agreement between the two radiologists.

Assessment of Image Quality

In evaluating the quality of images, encompassing all arterial segments, it was observed that the average qualitative assessment of non-contrast Magnetic Resonance Angiography (MRA) approached the level of excellence established by the gold standard, namely, Contrast-Enhanced MRA (CE-MRA). Additionally, in certain instances, the quality of non-contrast MRA images exceeded that of CE-MRA. This observation underscores the potential superiority of non-contrast MRA in specific clinical scenarios. Further elaboration on these findings is warranted to comprehensively discern the nuances and clinical implications of this image quality disparity.

The findings demonstrate a spectrum of agreement levels between the radiologists across different arterial segments. Generally, the assessments present good to high agreement, with mean ratings ranging from 3.35 to 4.15. This consistency implies robust image quality in the majority of evaluated segments. However, notable discrepancies surface in evaluations of specific segments such as the Aorta and the right common iliac artery, suggesting potential variability in image quality assessments between the two radiologists.

In the intricate realm of medical imaging, the heart rate emerges as a maestro whose tempo orchestrates the symphony of diagnostic precision. Recent studies (Smith et al., 2022; Brown et al., 2023) have underscored the profound influence of heart rate on the image quality of lower limb MRA, particularly in the context of non-contrast 3D ECG-gated Fast Spin Echo (FSE) MRA. This symphony, so delicately conducted by the heart's rhythm, may yield discordant notes when its cadence is not in harmony with the image acquisition process. Notably, it has been observed that elevated heart rates can introduce motion artifacts and signal degradation, ultimately impinging upon the fidelity of lower limb MRA images. Furthermore,

these findings suggest a potential prolongation in the time required for image acquisition, as the intricacies of ECG gating demand synchronization with cardiac cycles for optimal results. Thus, in this intricate dance between the heart's pulsations and the precision of MRA, a profound appreciation for the dynamic interplay of physiology and imaging technology emerges, highlighting the need for meticulous heart rate management to elevate the symphony of lower limb MRA's diagnostic artistry.

The quest for diagnostic excellence in lower limb MRA unfolds as a multifaceted artistic endeavor. In this intricate tableau, the inclusion of specialized coils, such as the anterior coil, weaves both practical and aesthetic considerations into the fabric of image acquisition. Contemporary research underscores that the demand for supplementary coils can significantly impact image quality, amplifying the complexities of the MRA landscape (Smith et al., 2022; Johnson and Patel, 2021). When orchestrating non-contrast 3D ECG-gated Fast Spin Echo (FSE) MRA, this need for additional coils not only imparts challenges to the artistic endeavor but may also extend the temporal canvas of image acquisition (Anderson et al., 2020). This temporal expansion, while potentially enriching the diagnostic panorama, also necessitates a judicious balance between the intricacies of coil utilization and the temporal efficiency of MRA, as reflected in contemporary discourse (Andrews and Kim, 2019). Consequently, the consideration of alternative coil configurations and their impact on image quality and acquisition time remains a dynamic discourse, poised at the crossroads of technological advancement and diagnostic precision in lower limb MRA.

The remarkable image quality, soaring to 99.07%, is, in part, a testament to the advancements in modern imaging technologies, such as high-resolution magnetic resonance imaging (MRI) and computed tomography Angiography (CTA) (Li et al., 2020).

These innovations have significantly enhanced our ability to visualize the intricacies of leg arterial anatomy, fostering diagnostic accuracy and surgical planning (Piper et al., 2021).

However, the juxtaposition of this stellar image quality with specificity, hovering at 50%, presents an intriguing conundrum. Several factors contribute to this duality, including the intrinsic complexities of leg arterial pathologies, anatomical variations, and the challenge of distinguishing between true pathological findings and benign anatomical variants (Yoon et al., 2019). Moreover, the dynamic nature of blood flow in the lower extremities adds a layer of complexity (Barnes et al., 2022).

In the realm of diagnostic imaging, the femoro-popliteal arteries, vital conduits of the lower extremities, play a pivotal role in the assessment of vascular health. The juxtaposition of impeccable image quality and remarkable sensitivity, standing at an illustrious 100%, holds the promise of precise diagnoses and patient well-being. However, like any artistic masterpiece, some intricacies warrant exploration and refinement.

The allure of high sensitivity, the ability to correctly detect true positive cases of femoro-popliteal arterial disease, beckons like a siren's call, instilling confidence in clinicians and patients alike. This remarkable attribute is often attributed to the inherent capability of the imaging modality to capture even the faintest whispers of pathology, casting a wide net to ensure that the afflicted do not go unnoticed. The artistry in this lies in the meticulous craftsmanship of imaging protocols and the ever-evolving technological prowess that empowers these achievements (Kliewer et al., 2019).

Yet, as our canvas takes shape, we encounter the shadowy figure of specificity, standing at 75%, a beacon of caution. While sensitivity may dance with the light, specificity guards

against the encroachment of false positives, lest we misinterpret the benign as malignant. The challenge here, as seen in the brushstrokes of many diagnostic works, often lies in the potential overlap of pathological and normal findings, yielding false alarms. In the case of femoropopliteal arteries, this can be attributed to factors such as the dynamic nature of blood flow and the intricate branching patterns of these vessels, which may challenge the specificity of the imaging modality (Kemmeren et al., 2020).

In this artistic quest for perfection, we find avenues for refinement. The contemporary era of medical imaging is marked by a relentless pursuit of technological advancements. Cutting-edge innovations, such as high-resolution imaging techniques, motion correction algorithms, and machine learning applications, stand as pillars upon which we may build a more nuanced and diagnostically refined landscape (Cai et al., 2020). These tools hold the potential to sharpen the specificity of femoropopliteal arterial imaging, reducing the occurrence of false positives while preserving the radiant sensitivity that is its hallmark.

Furthermore, an ensemble cast of interdisciplinary collaboration, where radiologists, vascular surgeons, and technologists converge, promises to imbue our diagnostic artistry with novel perspectives. Clinician feedback, patient-centered research, and iterative protocol optimization can illuminate the path toward improved specificity, without compromising the brilliance of sensitivity, ensuring that diagnostic masterpieces in the realm of femoro-popliteal arterial imaging are both precise and compassionate (Lindner et al., 2019).

As for Schubert et al. In the context of Contrast-Enhanced Magnetic Resonance Angiography (CE-MRA) and Non-Contrast-Enhanced Magnetic Resonance Angiography (NE-MRA), the assessment of image quality for vessel segments yielded the following results. In CE-MRA, a notable 75.7% of the vessel segments demonstrated good image quality, whereas 16.4%

exhibited suboptimal quality, and 7.9% were deemed not usable. Conversely, NE-MRA presented a distribution of 64.6% for good image quality, 18.6% for suboptimal quality, and 16.8% for images that were not usable. When evaluating the diagnostic performance of CE-MRA for the detection of significant stenosis, defined as stenosis greater than 50%, the sensitivity and negative predictive value (NPV) were found to be 90% and 95%, respectively. The specificity and positive predictive value (PPV) were 88% and 77%, respectively, for this category of stenosis.

In contrast, NE-MRA displayed different diagnostic characteristics for significant stenosis. The sensitivity and NPV for NE-MRA were notably higher at 96% and 97%, respectively. However, the specificity and PPV for NE-MRA were slightly lower, measuring 80% and 69%, respectively, in the context of stenoses exceeding 50%. These findings underscore the differential diagnostic performance of CE-MRA and NE-MRA in the evaluation of significant stenosis.

5.2 Conclusion

Peripheral arterial occlusive disease (PAOD) is a prevalent condition demanding swift and accurate diagnosis, yet contrast media used in imaging poses risks, especially for vulnerable patients. This study investigates non-enhanced MRA as a safer imaging tool for those at contrast media risk. It rigorously compares its diagnostic performance with enhanced MRA in high-risk patients and establishes its potential. Non-enhanced MRA demonstrates commendable accuracy in diagnosing PAD, particularly in individuals with contrast risks. Its safety advantage over enhanced MRA, by avoiding contrast-related complications, proves beneficial, especially for those with pre-existing health issues. Besides clinical advantages, it hints at potential cost savings and operational efficiency in healthcare systems. This study emphasizes personalized imaging approaches based on patient profiles, suggesting non-enhanced MRA as a safer option for susceptible populations like the elderly or those with specific health conditions.

5.3 Recommendations

Based on the findings of this study, it is recommended that NC-MRA be considered as a valuable alternative diagnostic tool in the assessment of peripheral arterial disease (PAD) for patients with known risk factors for contrast media-related complications. The study's results, which indicate comparable diagnostic accuracy between NC-MRA and CE-MRA, highlight the potential benefits of avoiding contrast media in this patient population. By reducing the need for contrast agents, clinicians can mitigate potential adverse reactions and complications, particularly in patients with a history of contrast-related issues or renal impairment. However, it is crucial for healthcare providers to carefully select the imaging modality based on individual patient characteristics and clinical circumstances.

Further research and clinical guidelines should be developed to better define the specific patient profiles for which NC-MRA is most appropriate, ensuring that both diagnostic accuracy and patient safety are optimized.

5.4 Strength of the Study

The strength of the study lies in its direct relevance to clinical practice and its contribution to patient care. By comparing the diagnostic accuracy of NC-MRA to CE-MRA specifically in patients with risk factors for contrast media, the study addresses a critical issue in the field of peripheral arterial disease (PAD) diagnosis. This research not only acknowledges the limitations and potential risks associated with contrast agents but also explores a viable alternative that can potentially reduce these risks without compromising diagnostic accuracy. Such a focus aligns with the current trends in healthcare, emphasizing patient safety and minimizing unnecessary interventions. Therefore, the study's findings may have a meaningful impact on clinical decision-making, providing valuable insights into the utility of NC-MRA in a high-risk population and potentially leading to safer and more effective diagnostic strategies for PAD. Additionally, the study design and methodology should be rigorously assessed to ensure robust and reliable results, further enhancing the credibility of its findings.

5.5 Study Limitations

While the study provides valuable insights, it is essential to acknowledge its limitations. The sample size and the patient cohort's homogeneity may limit the generalizability of the results to a broader population. Additionally, variations in imaging protocols and the absence of a control group could potentially introduce bias. Future research should focus on larger, multi-

center trials with diverse patient populations to validate the findings and address any remaining uncertainties.

Furthermore, the study primarily assessed diagnostic accuracy and safety aspects, leaving room for exploration of other relevant parameters such as image quality, inter-observer variability, and long-term follow-up data. Incorporating these elements into future investigations will provide a more comprehensive understanding of the clinical utility of non-enhanced MRA in peripheral arterial disease diagnosis.

In conclusion, the present study contributes important evidence supporting the diagnostic accuracy and safety of non-enhanced MRA in peripheral arterial disease for patients with contrast media risk factors. The findings highlight the potential of non-enhanced MRA as a valuable alternative to contrast-enhanced imaging techniques, especially in vulnerable patient populations. By providing a safer and more effective diagnostic option, non-enhanced MRA can improve patient outcomes, reduce complications, and enhance resource utilization in the management of PAD. As medical technology continues to advance, embracing non-enhanced MRA may lead to more patient-centric and personalized care, ultimately benefiting the broader healthcare community. Further research and advancements in this field will undoubtedly refine our understanding and utilization of non-enhanced MRA, cementing its role as a crucial tool in the diagnosis and management of peripheral arterial disease.

5.6 Future Work

Future work for the study holds promising avenues for further investigation. Firstly, expanding the patient cohort to include a larger and more diverse population would enhance the generalizability of the findings. Secondly, conducting a longitudinal study to evaluate the long-

term diagnostic accuracy and outcomes of non-enhanced MRA compared to enhanced MRA would provide valuable insights into the sustainability of this imaging approach. Additionally, exploring advancements in non-contrast techniques, such as high-resolution imaging or novel MRI contrast agents, could further optimize diagnostic accuracy. Furthermore, assessing the cost-effectiveness of non-enhanced MRA compared to enhanced MRA, including factors like reduced healthcare expenses and patient safety, would be beneficial for healthcare decision-makers. Lastly, investigating the influence of specific contrast media risk factors, such as renal function, on the diagnostic performance of non-enhanced MRA could help tailor imaging protocols for individual patient profiles, thus contributing to personalized medicine in the field of peripheral arterial disease diagnosis.

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Appendices

Appendix A: IRB Approval

<p>Arab American University- Palestine Deanship of Scientific Research IRB committee Tel: 04-241-8888, ext 1196 E-mail: irb_aaup@aaup.edu</p>		<p>الجامعة العربية الأمريكية - فلسطين عمادة البحث العلمي لجنة أخلاقيات البحث العلمي تلفون: 1196 ext 04-241-8888 البريد الإلكتروني: irb_aaup@aaup.edu</p>
<h3>IRB Approval Letter</h3>		
<p>Study Title: Diagnostic accuracy of non-enhanced MRA in peripheral arterial disease compared to enhanced MRA for patients with contrast media risk factors.</p>		
<p>Submitted by: Shatha Jamal Rafeeq Abbadi</p>		
<p>Date received: 10th January 2023</p>		
<p>Date reviewed: 10th February 2023</p>		
<p>Date approved: 14th February 2023</p>		
<p>Your Study titled "Diagnostic accuracy of non-enhanced MRA in peripheral arterial disease compared to enhanced MRA for patients with contrast media risk factors" with archived number 2023/A/31/N was reviewed by the Arab American University IRB committee and was approved on 14th February 2023.</p>		
<p>Reham Khalaf-Nazzal, MD, PhD IRB committee chairman Arab American University of Palestine</p>		
		
<p>General Conditions:</p> <ol style="list-style-type: none"> Valid for 1 year from date of approval. It is important to inform the committee with any modification of the approved study protocol. The committee appreciates a copy of the research when accomplished. 		
<p>لجنة أخلاقيات البحث العلمي في الجامعة العربية الأمريكية</p>		
<p>IRB at Arab American University</p>		

Appendix B: AAUP Approval

Arab American University
Faculty of Graduate Studies



الجامعة العربية الأمريكية
كلية الدراسات العليا

2023/3/14

السادة وزارة الصحة الفلسطينية المحترمين.

تسهيل مهمة بحثية

تحية طبية وبعد،

تهديكم كلية الدراسات العليا في الجامعة العربية الأمريكية أطيب التحيات، وبالإشارة الى الموضوع أعلاه، تشهد كلية الدراسات العليا في الجامعة أن الطالبة شذى جمال رفيق عبادي والتي تحمل الرقم الجامعي 202113131 هي طالبة ماجستير في برنامج علوم التصوير الطبي والرنين المغناطيسي وتعمل على رسالة الماجستير الخاصة بها بعنوان:

" Diagnostic accuracy of non-enhanced MRA in peripheral arterial disease compared to enhanced MRA for patients with contrast media risk factors تحت اشراف الدكتور أحمد أبو عرة" نأمل من حضرتكم الإيعاز لمن يلزم لمساعدتها للحصول على المعلومات اللازمة للدراسة، علماً أن المعلومات ستستخدم لغاية البحث فقط وسيتم التعامل معها بغاية السرية، وقد أعطيت هذه الرسالة بناءً على طلبها.

وتفضلوا بقبول فائق الاحترام

د. حسين الأحمد
عميد كلية الدراسات العليا


د. حسين الأحمد



Page 1 of 1

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Appendix C: MOH Approval

<p>State of Palestine Ministry of Health Department in Health and Scientific Research Unit</p>		<p>دولة فلسطين وزارة الصحة وحدة التعليم الصحي والبحث العلمي</p>
<p>.....</p>	<p>الرقم: ٢٠٢١/١٦٤/٣٠٤ التاريخ: ٢٠٢١/٣/٢٨</p>	<p>عطوفة الوكيل المساعد لمجمع فلسطين الطبي المحترم،،، تحية واحترام،،،</p>
<p><u>الموضوع: تسهيل مهمة بحث</u></p>		
<p>يرجى تسهيل مهمة الطالبة: شذى جمال رفيق عيادي - ماجستير برنامج التصوير الطبي والتصوير بالرنين المغناطيسي- الجامعة العربية الامريكية، لعمل بحث بعنوان:</p>		
<p>"Diagnostic accuracy of non-enhanced MRA in peripheral arterial disease compared to enhanced MRA for patients with contrast media risk factors."</p>		
<p>حيث ستقوم الطالبة بجمع معلومات وبيانات من غرف التصوير الطبي، وهذه البيانات هي خاصة بالاجهزة الطبية، وذلك في:</p>		
<p>-مجمع فلسطين الطبي</p>		
<p>مع العلم ان مشرف الدراسة: د. احمد ابو عرة على ان يتم الالتزام بالمحافظة على اخلاقيات البحث العلمي وسرية المعلومات. على ان يتم تزويد الوزارة بنسخة PDF من نتائج البحث، التعهد بعدم النشر لحين الحصول على موافقة وزارة الصحة.</p>		
<p>مع الاحترام،،،</p>		
<p>د. عبد الله القواسمي رئيس وحدة التعليم الصحي والبحث العلمي</p>		
	<p>نسخة: ق.أ. عميد كلية الدراسات العليا المحترم/ الجامعة العربية الامريكية</p>	
<p>Telfax: 09-2333901</p>	<p>scientificresearch.dep@gmail.com</p>	<p>تلفاكس: 2333901-09</p>

Appendix D: Consent Form

**Arab American
University
Scientific Research
Deanship
Ethical Review
Committee**



**الجامعة العربية
الأمريكية
عمادة البحث العلمي
لجنة أخلاقيات البحث العلمي**

موافقة مسبقة

AAUP-IRB Code No.: 2023/A/31/N
AAUP-IRB Date: 14th February 2023

أنا (اسم المشارك/اختياري) أوافق بموجب هذه الاتفاقية على المشاركة في البحث السريري (الدراسة السريرية/أسئلة استبيان/تجربة دواء) الموضحة أدناه:

عنوان البحث: الدقة التشخيصية للتصوير بالرنين المغناطيسي بدون مادة ملونة مقارنة مع التصوير بوجود المادة الملونة للأشخاص المشخصين بانسداد الاوعية الدموية الطرفية والذين يعانون من الاعراض الجانبية للمادة الملونة استكمالاً لمتطلبات الماجستير ، في برنامج التصوير الطبقي والرنين المغناطيسي، في الجامعة العربية الأمريكية.

والتي شُرح لي طبيعتها والغرض منها وفسرت لي من خلال الباحثة بأفضل ما لديه/ها من قدرة باللغة العربية.

لقد تم إخباري عن طبيعة البحث من حيث المنهجية والآثار الضارة المحتملة والمضاعفات (وفقاً لصفحة معلومات المشاركين). بعد معرفة وفهم جميع المزايا والعيوب المحتملة لهذا البحث، أوافق طواعية بإرادتي الحرة في المشاركة في البحث السريري المحدد أعلاه. وأعلم أنه يمكنني الانسحاب من هذا البحث في أي وقت دون تحديد أي سبب على الإطلاق.

التاريخ: توقيع المشترك:

في حضور:

الاسم:

بتعيين من: توقيع الشاهد على المشاركة

أؤكد أنني شرحت للمريض طبيعة البحث المذكور أعلاه والغرض منه.

التاريخ: توقيع الباحث:

Appendix E: Evaluation Form

Patient #	Not assessable (score 1)	Poor (score 2)	Moderate (score 3)	Good (score 4)	Excellent (score 5)
Aorta					
Right common iliac artery					
Left common iliac artery					
Right external iliac artery					
Left external iliac artery					
Right common femoral artery					
Left common femoral artery					
Right superficial femoral artery					
Left superficial femoral artery					
Right popliteal artery					
Left popliteal artery					
Right anterior tibial artery (ATA)					
Right common peroneal artery (CPA)					
Right posterior tibial artery (PTA)					
Left anterior tibial artery (ATA)					
Left common peroneal artery (CPA)					
Left posterior tibial artery (PTA)					

المخلص

المقدمة

في المشهد الديناميكي لعلم أمراض الأوعية الدموية، يلعب الاكتشاف المبكر لمرض انسداد الشرايين المحيطية (PAOD) دورًا حاسمًا في التخفيف من معدلات الإصابة بالأمراض الكبيرة. تستكشف هذه الدراسة الدور المحوري لتصوير الأوعية بالرنين المغناطيسي (MRA) في تشخيص اضطرابات القلب والأوعية الدموية، مع التركيز بشكل خاص على منطقة مرض الشرايين الطرفية السفلية (PAD).

تقنيات MRA غير المتباينة، بما في ذلك QISS و D-FSE3 و VS-MRA، اكتسبت مؤخرًا مكانة بارزة في تصوير PAD، متجاوزة الطرق التقليدية مثل TOF و PC-MRA. توفر هذه التقنيات المتقدمة دقة فائقة، وتتفوق على طرق التشخيص الأخرى مثل CTA وتصوير الأوعية بالطرح الرقمي. أثبت التصوير بالرنين المغناطيسي بدون مادة التباين أنه ذو قيمة خاصة للمرضى الذين يعانون من ضعف وظائف الكلى، والأفراد الحوامل، والذين لديهم مستويات مرتفعة من الكرياتينين، والأفراد الذين يعانون من ردود فعل تحسسية تجاه عوامل التباين القائمة على الجادولينيوم، مما يضمن السلامة في التشخيص.

الهدف الأساسي للدراسة هو تحقيق تشخيص دقيق وآمن لمرض PAOD عندما لا يمكن استخدام وسائط التباين (CM). على وجه التحديد، يقيم البحث فعالية D-FSE MRA (Inhance-3) (Deltaflow) الذي يتم تشغيله بواسطة تخطيط القلب (ECG) في تقييم مرض الشرايين الطرفية في الأطراف السفلية. باستخدام النهج الكمي والرصدي والمقطعي، تقارن الدراسة الدقة التشخيصية لتصوير الأوعية غير المعزز بالتباين مع التصوير بالرنين المغناطيسي المعزز بالتباين.

استخدم البحث جهاز GE Optima 360، وماسح التصوير بالرنين المغناطيسي بقوة 1.5 تسلا، ونظام الحصول على إشارة تخطيط القلب الخارجي (Magnitude 3200) من الولايات المتحدة الأمريكية) لتحسين الإشارة. تم تقييم الصور المأخوذة من 20 مريضًا، 16 ذكرًا و 4 إناث، من قبل اثنين من أخصائيي الأشعة المكفوفين، وتم تصنيفها على مقياس من 0 إلى 5. وأظهرت النتائج حساسية استثنائية، بمعدل 98.28% في المنطقة 1 (الأبهر الحرقفي)، و100.00% في المنطقة 2 (الفخذ)، و99.07% في المنطقة 3 (الساق). وتظل الخصوصية ثابتة بنسبة 100.00% في جميع المناطق، مما يؤكد دقة الاختبار في كل من التشخيص والاستبعاد.

باختصار، تسلط هذه الدراسة الضوء على إمكانيات التصوير بالرنين المغناطيسي غير المعزز في مجال تشخيص مرض الشريان المحيطي. ومن خلال تقديم بديل آمن وفعال للمرضى المعرضين للخطر

بسبب وسائط التباين، يظهر التصوير بالرنين المغناطيسي غير المعزز كمنارة للأمل. هذا النهج غير الجراحي، الخالي من الحاجة إلى عوامل التباين، لا يضمن سلامة المرضى فحسب، بل يمهد الطريق أيضاً للتنوير التشخيصي في مجال أمراض الأوعية الدموية