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Coronary Computed Tomography Angiography Versus Invasive Coronary Angiography at Gaza Governmental Hospitals: Cost Effectiveness Analysis

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Dedication

To the greatest man I have in my life, the sun of my life... my lovely father

To the biggest heart with the most loving care, who sacrificed a lot for me to become what I am now, my mother

To my wife who supported me through each step of the way and for being for me the greatest source of inspiration... my beloved wife

To the light of my eyes... my kids “Naseem, Waseem &Tala”

To all those who encouraged, supported, and helped me all the way

I dedicate this research for all of them…

With love

Husam

Declaration

I certify that this thesis submitted for the degree of master is the result of my own research, except where otherwise acknowledged, and that this thesis or any of its parts has not been submitted for a higher degree to any other university or institution.

Signed:

Husam Hassan Mansour

Date: --------/---------/---------

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Abstract

The burden of Cardiovascular Diseases (CVDs) is remarkable in Palestine, which is considered the first leading cause of death and placing a huge pressure on healthcare economics. Several imaging approaches exist for diagnosing Coronary Artery Disease (CAD), with varying accuracy and cost. In the Gaza Strip, there is a trend in the Ministry of Health (MoH) toward the need for a sufficient evidence base to justify the cost of any procedure. We aimed to provide cost-effectiveness information to help physicians and decision-makers in selecting the most appropriate testing strategy.

This prospective study was conducted to assess the cost-effectiveness of coronary computed tomography angiography (CCTA) compared with invasive coronary angiography (ICA) in patients with suspected CAD. The overall sensitivity and specificity of CCTA technique was 97.3% and 90.48%, respectively. The positive predictive value was 94.74% and the negative predictive value was 95% of CCTA.

The overall direct costs of ICA (234.23 dollars) were found to be about 4.6 times the cost of CCTA (50.84 dollars). Cost of unnecessary and adverse health outcome of ICA is prominent in this study, about 43.6% of patients have not any benefit from ICA procedure with unjustified cost 26621 dollars for the investigated patients' cohort.

The cost of CCTA per patient increased as a linear function of increasing CAD prevalence. In contrast, the cost per patient for ICA did not increase significantly. Specifically, CCTA showed lower cost than ICA with CAD prevalence <57% but higher costs with CAD prevalence ≥57%.

Regarding cost-effectiveness per CAD correct diagnosis, it is worthy to mention that at CAD prevalence 55% both of CCTA and ICA were equally effective with a cost of 448 dollars. But, the data showed that CCTA is more cost-effective in patients with a prevalence up to 54%, ranging from 1139.1 dollars (10% prevalence) to 449.7 dollars (54% prevalence). In contrast, ICA showed better cost-effectiveness for the prevalence above 55%, ranging from 436.13 dollars (56% prevalence) to 244.23 dollars (100% prevalence).

In term of quality-adjusted life years gained (ΔQALY) with cost-effectiveness, the trend was similar in which at a CAD prevalence of 55% CCTA and ICA were equally effective (150 dollars). But, CCTA was more cost-effective up to a CAD prevalence of 54% ranging from 399.21 dollars (10% prevalence) to 128.06 dollars (54% prevalence). In contrast, ICA shows better cost-effectiveness for the prevalence above 55%, ranging from 146.55 dollars (56% prevalence) and 81.79 dollars (100% prevalence).

The study highly recommends ICA to be considered for patients with CAD whose clinical characteristics indicate a high prevalence of severe stenosis and when the benefits are deemed to exceed the risk. Patients with suspected CAD should receive a comprehensive medical history to assess the probability of CAD prior to additional testing. Furthermore, CCTA can be useful as a first-line test for risk assessment in patients with mild to intermediate probability of suspected CAD.

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List of Abbreviations

CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CBC	Complete Blood Count
CCTA	Coronary Computed Tomography Angiography
CEA	Cost Effectiveness Analysis
CVDs	Cardiovascular Diseases
ED	Emergency Department
ESR	European Society of Radiology
FFR	Fractional Flow Reserve
GS	Gaza Strip
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
ICA	Invasive Coronary Angiography
INR	International Normalized Ratio
MoH	Ministry of Health
MRI	Magnetic Resonance Imaging
MSCT	Multislice Computed Tomography
mSv	Millisievert
NICE	National Institute for Health and Care Excellence
PCBS	Palestinian Central Bureau of Statistics
PCI	Percutaneous Coronary Intervention
PNA	Palestinian National Authority
PT	Prothrombin Time
PTT	Partial Thromboplastin Time
QALYs	Quality-adjusted life-years
SPSS	Statistical Package for Social Science
sq.km	square kilometers
WB	West Bank
WHO	World Health Organization
ΔQALYs	Quality-adjusted life-years gained

Chapter1: Introduction

1.1 Background

The initial diagnosis and treatment of patients with suspected coronary artery disease (CAD) can reduce adverse health events and persist in life (Gibbons et al., 2003). Currently, invasive coronary angiography (ICA) is regarded as the 'gold standard' for the assessment of coronary anatomy and the presence, localization, and severity of CAD. However, ICA has obvious limitations. It has a substantial procedural cost and it is an invasive method associated with serious risks with severe long-term consequences the composite rate of death, stroke or myocardial infarction is 0.1-0.2% in elective procedures (Tavakol et al., 2011). Most importantly, ICA does not directly assess the condition of atherosclerotic disease and change within the vessel wall but merely allows assumptions on its presence and extent based on lumen obstruction. Images are obtained in only two dimensions through the use of multiple projections enables a more comprehensive assessment of an individual lesion. Besides, according to the previous study, more than 50 % of the subjects who undergo elective ICA have no significant coronary artery stenosis (Patel et al., 2010). Therefore, a comparably accurate, non-invasive and reliable screening modality for detecting CAD is of major interest.

Multislice computed tomography (MSCT) as diagnostic equipment has been developing rapidly in recent years. Dramatic improvements in MSCT create high-quality diagnostic images (three dimensions, morphology and functional) (Budoff et al., 2006a). In addition, obvious benefits (i.e., low cost, shorter acquisition time and non-invasive nature) were recorded with the procedure conducted by MSCT, which known as coronary computed tomography angiography (CCTA) (Mowatt et al., 2008a). The role of CCTA was proved in enabling the rapid identification and assessment of atherosclerosis within the moving

coronary arteries and creating considerable interest in the perception that MSCT might potentially reduce the need for ICA (Stein et al., 2006).

The accuracy and reliability of CCTA were validated in 2008 with the publication of three landmark controlled clinical trials (Budoff et al., 2008; Meijboom et al., 2008; Miller et al., 2008). Since the publication of these landmark trials, we have seen frequent technological progression in the field of coronary imaging.

It is generally believed that in the near future, the use of CCTA may replace a substantial proportion of ICA examinations, especially for assessing the degree of stenosis and patency of grafts (Mowatt et al., 2008b). Anyway, it is necessary to address these perspectives by creating a model to project clinical outcomes, and cost-effectiveness of CCTA, as compared with ICA, in the evaluation of patients with suspected CAD.

Cost-effectiveness analysis (CEA) provides a framework of different management strategies for maximizing health benefit within the constraint of inadequate resources (Weinstein and Stason, 1977). Cost-effectiveness analysis is an analytical approach that integrates a test's clinical effectiveness with its economic value (Mark, 2002). The study of CEA provides a rational means to balance health care quality and clinical value in terms of the best outcome at a reasonable price. The economic evaluation suggests that strategies including CCTA are likely to be considered cost-effective for image patients with CAD and cost saving while yielding approximately the same amount of quality-adjusted life-years (QALYs) compared to ICA (Westwood et al., 2013).

Continuous development and upgrading in the radiology departments have remarked over the last seven years in the Gaza Strip (GS) hospitals. This progress open the gate to make comparative studies in the diagnosis of the CAD with health impact and cost containment by different modalities.

1.2 Research problem

Cardiovascular disease (CVD) is a major public health issue over the world. An estimated 17.9 million people died from CVD in 2016, representing 31% of global deaths. Of these deaths, an estimated 7.4 million were due to CAD (WHO, 2017). The burden of CVD is high in Palestine, which is the first leading cause of death in 2016 (30.6% of annual reported deaths) (MoH, 2017).

Coronary Artery Disease is rapidly placing an huge strain on healthcare economics. The diagnosis of CAD is performing through a series of clinical and imaging exams. For patients with evident symptoms of CAD, an initial invasive approach with ICA is usually recommended. Many researchers agree that it is not logical to perform noninvasive imaging prior to ICA on high-risk emergency patients because these procedures could delay treatment. As an alternative to invasive and expensive ICA, non-invasive imaging techniques are used to detect asymptomatic CAD patients at an initial stage and guide optimal patient management thereafter (Meijboom et al., 2006; Scheffel et al., 2007; Bettencourt, 2009; Catalán et al., 2011).

Nowadays, the need for healthcare cost-containment becomes one of the main aims of all health providers. In the Gaza Strip (GS), which is under strict siege and shortage of resources, there is a trend in the Ministry of Health (MoH) toward the need for a sufficient evidence base to justify the cost of any procedure or therapy. Despite the continuing interest in health economic research, little accessible data was recorded on cost-effectiveness analysis. This gap is also noticeable in the diagnosis of different cases with CAD. This vital shortage creates difficulties for decision makers who must allocate scarce resources within the radiology and cardiovascular fields.

1.3 Justification and significance of the study

Patients with CVD risk have a substantial economic burden on the budget of the Gaza strip hospitals. However, observable improvement in the diagnosis and treatment of CAD was achieved in the Gaza strip hospitals. The ICA is considered one of the best choices for diagnosis CAD and remains the cornerstone of diagnosis and treatment of patients with significant or unstable chest pain symptoms. In another hand, ambiguous policy in the patient flow process for the successful diagnostic performance measure. Thus, it can prevent the use of the invasive diagnostic procedure in some patients (non-significant CAD). There is a gap in information about the advantage of MSCT, as a new non-invasive diagnostic technology in the diagnosis of the CAD. Through our literature reviewing there is no previous study touching this subject in Gaza hospitals. In this study, a comparison in cost-effectiveness between CCTA versus ICA was projected at governmental hospitals in the Gaza Strip. Moreover, the diagnostic performance of CCTA was closely measured to test the appropriateness of this comparison with a focus on the diagnostic accuracy and prognostic value in CAD.

1.4 Aim of the study

The overall aim of this study is to assess the cost-effectiveness of coronary computed tomography angiography (CCTA) compared with invasive coronary angiography (ICA) in order to diagnosis patients with suspected coronary artery disease (CAD).

1.5 Specific objectives

1. To assess key principles between CCTA and ICA as cost-effectiveness analysis.
2. To evaluate the accuracy of CCTA as an alternative diagnostic procedure for ICA to improve health outcomes for patients with suspected CAD.

1.6 Research questions

1. What is the relative cost-effectiveness of the CCTA imaging compared to that of ICA for the diagnosis of patients with suspected CAD?
2. Is CCTA accurate and effective non-invasive imaging tool to evaluate patients with CAD?
3. What is the efficacy of patient selection for diagnostic ICA in suspected CAD?
4. Is it time for CCTA to replace ICA in diagnostic CAD?
5. Does the use of CCTA result improve downstream health outcome?

1.7 Context of the study

This study was conducted in MSCT and Catheterization departments at Al-Shifa hospital. Therefore, it is helpful to understand the conditions that contribute to the impact on the Palestinian health care and special departments that we have mentioned and their impact on the Palestinian population in general and the beneficiaries of the service in particular system. So, the researcher represents some basic information on the demographic context, the Palestinian people, and the Palestinian economy, which may interact with each other to influence the health status and health care services in Palestine.

1.7.1 Demographic context of Palestine

Palestine is situated on the eastern coast of the Mediterranean Sea, with an entire area of 27.009 square kilometers (sq.km), it stretches from Ras Al- Nakoura in the north to Rafah in the south. Palestine has an important strategic geographic location as it is situated on the western edge of the continent of Asia, the eastern coastal extremely of the Mediterranean Sea, it is boarded by Lebanon in the north, the Gulf of Aqaba in the south, Syria and Jordan in the east by Egypt and Mediterranean Sea in the west **(Annex1)**. Palestinian National Authority (PNA) controls two geographically separated areas, West Bank (WB) and Gaza Strip (GS). The Palestinian Central Bureau of Statistics (PCBS) estimates that in

2017 the total population of Palestine is 4,781,248 people, about 2,433,196 males compared to 2,348,052 females. The estimated population of West Bank is 2,881,957, 60.3% of which 1,470,293 males compared to 1,411,664 females. On the other hand, the population of Gaza Strip for the same year is about 1,899,291, 39.7% of the total population of Palestine, including 962,903 males compared to 936,388 females (PCBS, 2018). Gaza Strip is a small piece of land located in the southern area of Palestine, It is divided into five governorates: North Gaza, Gaza City, Mid Zone, Khan Younis and Rafah **(Annex 2)**.

1.7.2 Socioeconomic context

The economic situation in the GS is characterized by tragic and limited income, the unemployment rate remarkably increased to 43.9% (PCBS, 2018), the problematical political and economic situation deteriorate the life of people. People suffer from the tight siege that restricts passing of goods and aids across the borders.

The deterioration of both economic and social status in the GS harmfully affects the status of the population and the economic recovery became impossible as long as the siege remains. In the Gaza Strip, the closure and intra-Palestinian political divide create specific challenges, including restrictions on staff movement, access difficulties for patients demanding professional services outside the Gaza Strip. As a result, people have been forced to receive medical services in government hospitals because of their inability to pay for treatment in private centers. Consequently, it has become a great burden rest with the Ministry of Health in the Gaza Strip.

1.7.3 Palestinian health care system

Health care system plays a critically important role in improving health. Well-functioning health system enables the achievement of good health with the efficient use of available resources (McKee et al., 2009). In the Gaza Strip, health care services are provided mainly

through four sectors, governmental health services at Ministry of Health (MoH), Non-Governmental Organizations (NGOs), United Nations Relief and Works Agency (UNRWA), and the Private Sector.

MoH provides primary, secondary, and tertiary health services and purchases the unavailable tertiary health services from domestic and abroad providers. UNRWA provides primary care services for refugees and purchases secondary care services for special cases. NGOs provide primary, secondary and some tertiary services. The private for-profit sector provides the three level of care through a variety of specialized hospitals and investigation centers. The disintegration in the health care system and the lack of coordination between various sectors increase the challenges to provide optimal health care services.

1.7.4 Al-Shifa Medical Complex Center

Al-Shifa complex medical center is the largest hospital in Gaza. It's situated in the west part of Gaza City. It was established in 1946, developed over years until it reaches to higher universal level over 45,000 thousand square meters and located on the western side of the middle of Gaza City. It contains three hospitals Surgery, Internal Medicine and Maternity. The health services delivered to populations through the three hospitals and include the different patients referred by emergency departments or clinics by primary care. Where it is transported to internal departments or hospital outpatients review the complex. Total number of beds are 590 and while the total number of employees is about 1600 divided as follows: Nursing 36.5%, doctors 35.6%, administrators and x-ray technicians in different disciplines17.7%. Bed occupancy rate during the past six months is about 82% (MoH, 2016).

1.7.5 Radiology departments at Al-Shifa hospital

The radiology department at Al Shifa is the largest departments at the level of the Gaza Strip, which receives a large number of patients from Gaza City and other governorate hospitals. Radiology departments of the hospital consist of conventional basic radiography, fluoroscopy, mammography, dental panorama, magnetic resonance imaging (MRI) and multislice computed tomography (MSCT).

1.7.6 Evolution of MSCT in Gaza Strip

The first MSCT department was developed at Public Aid Hospital as a non-governmental organization in January 2012. Coincide with that, another device was developed at the European Gaza Hospital. In January 2015, a new department has been developed at Al-Shifa hospital, bringing the total number of MSCT in the Gaza Strip to three departments. These MSCT machines have advanced options to perform cardiac imaging. Recently, others MSCT machines supplied to Al-Indonesian and Al-Aqsa Hospitals, but still cannot perform cardiac examinations according to absent of cardiac options in these machines.

1.7.7 Evolution of Catheterization in Gaza Strip

The first of cardiac catheterization department was opened in 2006 at Gaza European Hospital, which is directed by the MoH and serves about 1.7 million people. The second catheterization center was also at Gaza European Hospital in 2013 funded from the Islamic Development Bank-Jeddah with implementation from the Qatar Red Crescent and the WHO. In 2014, the opening of a new catheterization department at Al-Shifa medical complex funded by the Qatar Red Crescent. Thus, there are three cardiac catheter devices in MoH hospitals. Moreover, there is four cardiac catheterization centers; two centers in the private sector (Jules Center and life Center), and two centers in non-governmental organizations (Public Aid Hospital and Al Quds Hospital).

1.7.8 Cardiac Catheterization services in the Gaza Strip

In 2017, the number of diagnostic cardiac catheterization cases in the Gaza Strip was 2534 distributed as 1347 at Al-Shifa hospital and 1187 at Gaza European Hospital. Approximately 41% of these cases had neither CAD nor non-obstructive CAD and advised to be followed by medical treatment. In contrast, 59% of cases had significant CAD managed with intervention percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). Semi-annual report for 2018 indicates that the number of diagnostic cardiac catheterization cases was 906 cases (Al-Shifa records, 2018).

1.8 Operational definitions

1.8.1 Significant coronary artery disease

Significant CAD is defined as more than 50% angiographic diameter stenosis in one or more of the epicardial coronary arteries. Based on disease severity, obstructive CAD is classified as single, double, or triple vessel disease (Gauchan et al., 2012; Niccoli et al., 2015). In this study, significant CAD has defined as obstruction ≥ 50% stenosis of any coronary arteries, graft stenosis and stent restenosis.

1.8.2 Coronary artery disease prevalence

Prevalence is the probability of having the disease, also called the pretest likelihood of disease. The likelihood is a given test result would be expected in a patient with the target disorder and used to assess how good a diagnostic test to help in selecting an appropriate diagnostic test. Moreover, means the probability of a patient having the CAD before a diagnostic test result is known (Patterson et al., 1984; Patterson et al., 1995; Dorenkamp et al., 2012). In the current study, we used these definitions in the classification of CAD prevalence in the present study.

1.8.3 Coronary computed tomography angiography

Coronary computed tomography angiography is a diagnostic imaging test that uses MSCT scanner to non-invasively image the coronary arteries of the heart. CCTA has become an integral imaging modality in the evaluation of CAD, facilitated by dramatic technological advances in the last decade, which has resulted in consistent acquisition of high quality images of the coronary arterial lumen as well as the wall with high accuracy and relatively low radiation doses (Yerramasu et al., 2010; Aghayev et al., 2016). In the current study, CCTA was performed through Phillips128 MSCT which have coronary imaging options.

1.8.4 Invasive coronary angiography

Invasive coronary angiography is the most accurate method (the "gold standard") for evaluating and defining CAD. Invasive coronary angiography is used to identify the exact location and severity of CAD. In contrast, it is an invasive test that allows a direct view of the coronary arteries supplying the heart.

1.8.5 Effectiveness of diagnostic tests of CAD

In the current study, the definition of effectiveness is based on the ability of a diagnostic test to accurately identify a patient with CAD. We also used other definition in terms of the clinical outcome for patients enduring the examinations, that is, an increase in the number of quality-adjusted life years for a patient over a 10 year follow-up period (McNeil et al., 1975; Patterson et al., 1984; Patterson et al., 1995; Dorenkamp et al., 2012).

1.8.6 Cost-effectiveness analysis

Cost-effectiveness analysis provides a framework upon which to compare different management approaches through the prism of maximizing health benefit within the restriction resources (Weinstein and Stason, 1977). In the current study, cost-effectiveness is the ratio between the cost of an investigation and the proportion of test effectiveness. A decrease in cost per correct diagnosis indicates improved cost-effectiveness.

Chapter 2: Conceptual framework and literature review

2.1 Conceptual framework

The current chapter describes the mechanism of research steps in terms of choice of the nature of the cases that studied who have undergone CCTA and the cases that have undergone ICA as shown in figure 2.1. At that point, estimation the cost of both procedures with comparing the cost-effectiveness with drawing conclusions and provide a clear vision of the good use of resources to serve the delivery of health care at the lowest cost and best quality for the patient.

- **Coronary artery disease diagnosis**

Although ICA has been the gold standard for evaluating CAD, it should not be routinely performed as an initial test to assess CAD as indicated by the recent guidelines. The role of CCTA for evaluation of CAD becomes of great promise with high diagnostic accuracy. In the current study, the researcher focused on the diagnosis of the CAD with a utilization of the two modalities (ICA and CCTA).

- **Accuracy of CCTA**

The sensitivity, specificity, positive predictive value and negative predictive value of CCTA signify the diagnostic accuracy of CCTA for correct diagnosis of the CAD. The researcher measured the accuracy through the patients who underwent CCTA then they followed by ICA as a reference to more assessment or interventions.

- **Cost effectiveness analysis**

In the current study, we compare the cost-effectiveness of two diagnostic approach (CCTA and ICA) in the diagnosis of the presence or absence of CAD. The cost-effectiveness analysis was measured by performing a mathematical model based on Bayes' theorem and published clinical data was constructed to make these comparisons. This model permits

varying the values of data that are very difficult to obtain, such as the rates and costs of complications due to diagnostic procedures or due to CAD in particular patient groups.

- **Cost analysis**

Detailed activity-based cost analyses of the two modalities were carried out based on direct cost and induced cost. Direct cost includes the total cost of each modality including the cost of equipment, personal salary and procedure requirements and supplies. Induced cost is derived from the complications and mortality resulting from each test, as well as from the complications and mortality resulting from CAD that is inadequately treated because of false negative test results.

- **Effectiveness**

Effectiveness was defined as either the number of patients with CAD correctly diagnosed or as the number of quality-adjusted life years extended by therapy after the diagnosis of CAD.

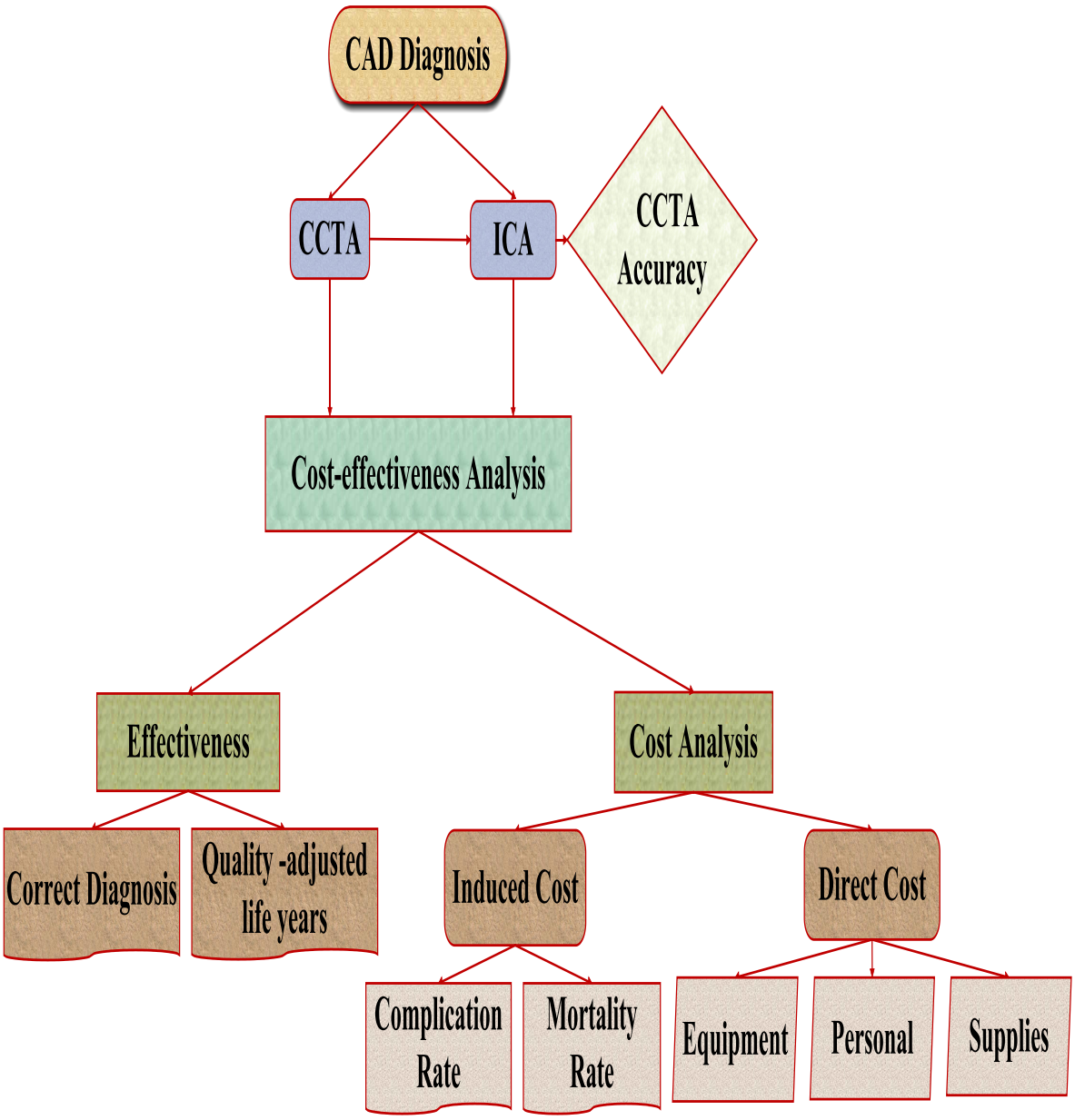

Figure 2.1: Conceptual framework of the study (self-constructed)

2.2 Literature review

This part describes the previous related studies in respect to the efficiency and cost-effectiveness of CCTA which perform through MSCT in the diagnosis of suspected CAD. The review of literature illustrated and has displayed with emphasis since 2004. Starting from this date, several studies were conducted on MSCT to replace ICA due to its non-invasive nature and short time scanning. MSCT has been developing rapidly in recent years starting from 4-slice machines in 1998 up to 320-slice in 2007. The developing of MSCT exhibits many benefits particularly in reducing exam time and dose for patients likewise consequently to health providers. The high sensitivity of MSCT avoids the costs of unnecessary ICA in those referred for investigation CAD, mainly who don't have significant CAD.

2.2.1 Accuracy of CCTA in the detection of CAD compared with ICA

Our review of the literature identified a growing number of studies examining the usefulness of MSCT in a clinical setting. Increasing the number of slices in MSCT clearly confers benefits in terms of improved image quality and diagnostic accuracy for the detection of the significant CAD. In particular, it makes the imaging of smaller vessels more robust, allowing assessment of potentially the whole coronary circulation (Peebles, 2006; Ostrom et al., 2008; Khan et al., 2009).

Another study was done by Hausleiter et al. (2006) on patients with an intermediate risk of the CAD. The study evaluated the presence of coronary calcifications, non-calcified plaques, and lumen narrowing. With the use of 64 MSCT, clearly discernible non-calcified atherosclerotic coronary plaques can be detected in a large group of patients with an intermediate risk for having CAD. The assessment of these plaques by CCTA may allow for improved cardiovascular risk stratification. Hausleiter et al. (2007) conducted a prospective study to assess the clinical usefulness of CCTA for the detection of significant

CAD in patients with risk of having CAD. ICA was used as a reference. Based on the high negative predictive value observed, Hausleiter et al. suggested that CCTA could be a suitable means for the management of patients with an intermediate pre-test likelihood of significant CAD. Gaemperli et al. (2008), obtained a close result which showed a very high negative predictive value for reducing the need for ICA. These results agree with the literature review conducted by Delgado and Williams (2010) to confirm the diagnostic accuracy for CAD of MSCT in comparison to ICA.

A comparison study was done by Meijboom et al. (2007) between CCTA and ICA was achieved on the groups at three levels: patient-by-patient, vessel-by-vessel, and segment-by-segment analysis. Based on their results, Meijboom et al. found that the pretest probability of CAD influences the diagnostic performance of CCTA. Negative CCTA can reliably rule out the presence of significant CAD in symptomatic patients with a low or intermediate estimated probability of having significant CAD. A similar study by Husmann et al. (2008) evaluated patients with suspected CAD to compare the diagnostic accuracy of CCTA in groups of patients with low, intermediate, and high risk of CAD events. Husmann and his colleagues stated, "*Our data suggest that in a clinical setting, CTA would have avoided unnecessary invasive angiography in 56%, 41%, and 24% of patients in the groups with low, intermediate, and high risk for CAD events"*. These results support a distinguished study performed by Budoff et al. (2008). Importantly lies that the 99% negative predictive value at the patient and vessel level establishes CCTA as an effective noninvasive an alternative to ICA to rule out significant CAD.

Janne d'Othée et al. (2008) performed a systematic review of the diagnostic accuracy of CCTA. The study illustrated how CCTA relates to the non-invasive detection of coronary artery stenosis as an alternative to ICA. They included forty-one articles published that evaluated native coronary arteries for significant stenosis and used CCTA as a diagnostic

test and ICA as a reference standard. The study settled that the diagnostic accuracy of CCTA is high. The advances in MSCT technology have resulted in an increase in diagnostic accuracy and proportion of assessable coronary segments. However, per patient, accuracy may be lower and CCTA may have more limited clinical utility in populations at high risk for CAD. Competitive a systematic review and meta-analysis reported by Mowatt et al. (2008a) concluded that given the high sensitivity and negative predictive value, the main role of CCTA may be to rule out significant CAD and reduce the need for ICA.

The appropriate diagnosis of chest pain remains a difficult task in the emergency department (ED). Patient care for chest pain workup requires multiple imaging tests. The serial tests increase the length of the hospital stay and accumulate costs. In response to these problems, CCTA has become helpful in the ED setting. In a prospective observational cohort study, Hoffmann et al. (2006) found that 64-MSCT coronary angiography accurately distinguished a subset of patients with chest pain who could be safely sent home from the emergency department. In order to safeguard appropriate treatment following CCTA, controlled reporting among health providers is critical for the implementation of CCTA. Several studies, confirm that CCTA has been shown in low-risk populations to increase the rate of discharge from the ED, decline the length of hospital stay, increase the rate of detection of CAD, and reduce costs when compared to the current standard of care (Schlett et al., 2011; Litt et al., 2012; Cury et al., 2013; Poon et al., 2013; Hamilton-Craig et al., 2014).

Coincide with evolution MSCT, a study done by Dewey et al. (2009) showed the diagnostic accuracy and less radiation exposure of 320 MSCT compared with cardiac catheterization. The use of emerging technology has the potential to significantly less vulnerable to suboptimal heart rate control and allow image acquisition with lower radiation and contrast doses compared with ICA while maintaining high diagnostic

accuracy. This is confirmed by meta-analysis research by Von Ballmoos et al. (2011) reviewed studies comparing CCTA results with ICA in symptomatic patients with suspected CAD. The analysis found early evidence suggests low-dose CCTA matches the sensitivity of ICA, has low radiation exposure, and is a potentially valid alternative to catheter angiography for triaging symptomatic patients with a clinical suspicion of the CAD. Correspondingly study by Uehara et al. (2013), supported the result of diagnostic accuracy of 320 MSCT for detection of significant coronary artery stenosis in patients with various heart rates and heart rhythms, compared with ICA.

A study was done by Sajjadieh et al. (2013) evaluated the accuracy of CCTA in comparison to ICA in the diagnosis of significant stenosis (≥50%) of the coronary artery tree. The findings of this study revealed that CCTA with 64 MSCT could be considered as a suitable technique for rapid triage of patients presenting to hospitals with chest pain. Inference, the ability of CCTA is obvious to combine anatomical and physiological cardiac evaluation in a single examination is a promising new technique that can provide further optimization for the assessment of patients with suspected or known CAD.

Review article conducted by Alani and his colleagues (2014) to visualization the improvement in CCTA diagnostic accuracy. This review article summarizes CCTA has been a reliable noninvasive imaging test that can substantially contribute to the assessment of CAD with high diagnostic accuracy, guiding clinical decisions in patients with low to intermediate pretest likelihood of CAD.

The accuracy of CCTA was also checked by Joshi et al. (2016) compare ICA in patients undergoing major non-coronary cardiac surgeries regarding true positive and true negative values. The overall sensitivity and specificity of CCTA was 100% and 91.30%. The positive 50% and negative predictive values 100% of CCTA were also high in these

patients. The study suggests that this non-invasive technique may improve pre-operative risk stratification in patients undergoing non-cardiac surgery.

A randomized controlled trial conducted by Dewey et al. (2016) to evaluate whether ICA or CCTA should be performed in patients clinically referred for ICA with an intermediate probability of CAD. The search is ongoing for a gatekeeper that will reliably exclude normal ICA. This randomized trial revealed that patients with atypical symptoms suggestive of CAD, CCTA carefully delayed ICA with no increase in long-term events, reduced minor but not major procedural complications compared with direct ICA and shortened the length of hospital stay. CCTA was associated with reduced ICA rates and increased the diagnostic yield of this procedure but did not reduce exposure to radiation.

Bayar and Feng (2017) assessed the analytic precision of CCTA as a different option for ICA in evaluating CAD. This review study selected 57 patients, who experienced both ICA and additionally CCTA. The study confirmed that CCTA has high accuracy in detection CAD. Moreover, the study settled that indicative precision of MSCT was found to be higher in moderate and extreme stenosis and can be utilized as a substitute to ICA.

Recent interest in fractional flow reserve (FFR) measurements derived from computed tomography (CT-FFR) to evaluate the degree of coronary stenosis. Various studies have been performed comparing the diagnostic performance of CT-FFR to invasive coronary angiography fractional flow reserve (ICA-FFR). Parekh et al. (2017), analyzed studies comparing CT-FFR to ICA-FFR. Regarding this search, CT-FFR has high sensitivity and negative predictive value when compared to ICA-FFR. However, improvements are needed to increase the specificity and positive predictive value. A parallel study conducted by Kueh et al. (2017) which revealed that FFR derived from CCTA has been shown to have excellent correlation with invasive FFR with robust of guiding CAD patients.

2.2.2 Preference of MSCT in illustration of coronary artery anomalies compared to ICA

Early identification of an anomalous coronary anatomy is quite relevant to identify variants without clinical relevance to avoid complications during surgery or angioplasty can occur. For several decades, premorbid diagnosis of coronary artery anomalies has been made with ICA. However, this imaging technique has limitations due to its projections and cannot always adequately provide the required information about the abnormal coronary anatomy. CCTA is robust that has several clinical applications. It not only provides high-resolution anatomical information of the coronary artery tree but also helps define other aspects of the cardiovascular anatomy.

Reviewing CCTA studies by Budoff et al. (2006b) showed the clinical role played by CCTA in the evaluation of different types of coronary arterial anomalies. The results of this review support the use of CCTA as a safe and effective noninvasive imaging modality for defining coronary arterial anomalies in an appropriate clinical setting, providing detailed three-dimensional anatomic information that may be difficult to obtain with ICA.

Obvious advantages were recorded in delineating coronary arterial anomalies and for obtaining an accurate diagnosis for formulating an optimal patient treatment plan. Finally, the results of these studies support the use of CCTA as a harmless and effective noninvasive imaging modality for defining coronary artery anomalies in an appropriate clinical setting, providing comprehensive anatomic information that may be challenging to attain with ICA (Coles, 2004; Schmitt et al., 2005; Kim et al., 2006; Kang et al., 2008; Srinivasan et al., 2008; Van Mieghem and De Feyter, 2009; Fadhil, 2012; Qin et al., 2012; Javoran, 2013; Graidis et al., 2015).

A retrospective study has been done by Yorgun and his colleagues (2010) to evaluate the efficiency of CCTA in the diagnosis of coronary artery fistulas. The study exhibited that

CCTA is an excellent tool with brilliant efficiency for visualization the origin, course, and drainage site of coronary artery fistulas.

ICA has traditionally been indicated to demonstrate the coronary vasculature in detail and has remained the reference standard imaging modality. Owing to the potentially complex three-dimensional anatomy of the coronary anomaly, ICA not infrequently, incompletely delineates the anatomical course of the coronary anomaly. Qin (2015) conducted a study sought to determine the ability of MSCT to detect the origin and course of the anomalous coronary artery. This study confirmed that CCTA is essential detecting method to find coronary anomalies and MSCT clearly depict the origin and course of the anomalous coronary artery.

Recently, a retrospective study on 974 patients who underwent CCTA for detection of coronary anomalies was done by Prasad and Vijayakumar (2017). The study approved that regardless of the complexity of the vascular anatomy, coronary vessel opacification is always possible by CCTA. Additionally, CCTA is an accurate non-invasive imaging modality which suitable to evaluate patients that have an anomalous coronary artery, especially when they have symptoms relating to anomalous vessels.

2.2.3 Assessment of coronary artery stent patency and restenosis using MSCT with compare to ICA

Surveillance ICA is recommended after stent supported PCI due to the unpredictable occurrence of in-stent restenosis. The efficacy of MSCT to assess coronary stent stenosis was approved by several studies, but there was debated in their results. To be specific, increasing the developing of MSCT give more accuracy in evaluation of the stent. The Studies supporting the value of MSCT indicating that CCTA may be most valuable as a noninvasive method of excluding coronary stent stenosis. In additionally, advanced options in MSCT such as luminal density analysis increase it is ability to display the stent lumen

clearly and is extremely helpful for patient follow-up (Cademartiri et al., 2007; Oncel et al., 2007; Sun and Almutairi, 2010; Zhao et al., 2011; Bharati et al., 2012; Dighe et al., 2012; Geyer et al., 2015; Dawoud et al., 2016; Moradi et al., 2017).

In contrast, different studies upset these results and despite the tremendous improvements in MSCT, and still indicate relevant limitations of CCTA imaging of coronary artery stents. These studies settle that the value of CCTA with of coronary stents depends on patient and stent characteristics with a large diameter. Due to these limitations, use of CCTA for evaluation of in-stent restenosis is not considered for routine clinical use. Thus, patient selection is crucial for success (Mahnken et al., 2006; Maintz et al., 2008; Mark et al., 2010; Yang et al., 2012; Windecker et al., 2015).

2.2.4 Diagnostic value of MSCT angiography in the comprehensive assessment of CABG compared to ICA

Plentiful studies undoubtedly pointed that CCTA has high diagnostic accuracy in the proper evaluation of the patency of CABG cases compared with ICA and even with a more brilliant performance than an assessment of native coronaries. This superior diagnostic accuracy may be due to the grafts naturally consider less motion through the cardiac cycle than native coronary vessels, larger vessel diameter of grafts, and lower tendency to develop calcified plaques compared with native coronaries. The modernist technological development of 64 MSCT enables the noninvasive assessment of venous and arterial bypass graft patency and stenosis with high diagnostic accuracy even in patients with arrhythmias during scanning. Furthermore, CCTA is more effective in the evaluation of bypass grafts as compared to heavily calcified native coronary arteries. CCTA is a relatively painless noninvasive procedure when compared to ICA, and it is well tolerated by most of the patients. CCTA can represent a convenient noninvasive method for diagnosis of coronary artery stenosis in CABG patients with a higher diagnostic accuracy,

being greater than of native coronary arteries, and the advantage of visualizing grafts that cannot be detected or accessed by ICA. Evaluation by ICA in patients with prior CABG can be challenging and expose patients to rare complications such as injury to the graft vessel during catheter engagement. Upstream CCTA has the possible to make ICA faster and more efficient due to an improved understanding of CABG anatomy prior to attempting to engage graft evaluation (Schlosser et al., 2004; Chiurlia et al., 2005; Meyer et al., 2007; Hamon et al., 2008; Chaosuwannakit et al., 2014; Pesenti-Rossi et al., 2014; Azizi et al., 2016; Barbero et al., 2016; Barbero et al., 2017; Eisenberg et al., 2017).

2.2.5 Cost-effectiveness analysis of CCTA versus ICA

Given the possible benefits of introducing an extensively accessible non-invasive option for CAD detection. The potential clinical and economic impact that broad adoption of CCTA would have on systems of care, and the uncertainty over the evidence on the net health benefits and appropriate use of CCTA. All healthcare decision makers will benefit from a formal appraisal of the comparative clinical effectiveness and comparative value of CCTA for diagnosis of the CAD.

Cost-effectiveness of CCTA and MRI according to the prevalence of CAD compared with the gold standard ICA was studied by Dewey and Hamm (2007). Their outcomes coincided that CTCA has good cost-effectiveness up to a prevalence of 60%–70%, whereas ICA is more cost-effective in patients with higher prevalence. For patients with a 10% to 50% pretest likelihood of CAD, CCTA was the most cost-effective approach, with costs per correctly identified CAD patient of 4,435 euro (10% likelihood) to 1,469 euro (50% likelihood). ICA to be most cost-effective for a pretest likelihood of at least 70%, with costs per correctly identified CAD patient ranging from 1,153 euro (70% prevalence) to 807 euro (100% prevalence).

In a distinct study, Mowatt et al. (2008b) reported the clinical effectiveness and cost-effectiveness of the CCTA as an alternative to ICA for the investigation of the CAD. They found the main value of CCTA through 64 MSCT to be ruling out significant CAD. A negative CCTA for CAD should avoid the costs of unnecessary ICA, thus resulting in overall cost savings in the diagnostic process of the CAD. However, it is unlikely to replace ICA in the assessment of revascularization cases.

Kreisz et al. (2009) execute a study to evaluates the cost-effectiveness of 64-slice CTCA as an alternative to ICA in an elective outpatient setting for patients otherwise referred to ICA. The results indicate that CTCA is a cost-saving approach contribution a higher health-related quality of life up to approximately 65% pre-test risk of the CAD. Above that threshold, their model predicts a cost-utility trade-off with every gain in health-related quality of life through the use of CTCA as a rule-out test being associated with additional costs when compared to ICA. The health economic analysis of their study predicted that CCTA to be a cost-effective approach in symptomatic patients at low to intermediate risk of significant obstructive CAD otherwise referred to ICA.

A comparable study was done by Stacul et al. (2009) to analyze the costs of 64 MSCT CCTA compared to ICA and to determine the cost-effectiveness of the two modalities. Detailed activity-based cost analyses of the two modalities were carried out at the departments of radiology and cardiology. The differential costs (equipment, variable, personnel), common costs and external costs were estimated. The sum of differential costs, common costs, external costs and hospitalization costs provides the full cost for each examination. The cost of ICA procedure was approximately 9 times of CCTA procedure. In particular, the cost of ICA was 2,027.88 euro versus 230.03euro for CCTA procedure. Cost-effectiveness analysis showed that the cost per correctly identified CAD patient decreased exponentially with increasing pretest likelihoods (prevalence) of CAD. CCTA

was more cost-effective than ICA up to a prevalence of 86%, with a cost per correct diagnosis of CAD ranging from 7,295.10 euro (10% prevalence) to 2,593.9 euro (86% prevalence). By contrast, ICA shows better cost-effectiveness for a prevalence of 87%–100%, with a cost per correct diagnosis of CAD between 2,563.59 euro (87% prevalence) and 2,207.60 euro (100% prevalence). This study approved that CCTA has far lower costs than ICA, and its cost-effectiveness is better in the large majority of patients.

Decision tree analysis to determine the cost-effectiveness and radiation dose that would result from performing CCTA before ICA employed by Halpern et al. (2010). In their study, they reported that cost reduction with CCTA depends on the prevalence of CAD, but overall costs are reduced as long as the prevalence is less than 85%. At a 50% prevalence of CAD, performing CCTA before ICA results in an average cost saving of 789 dollars per patient with a false-negative rate of 2.5% and average additional radiation exposure of 1–2 mSv. The analysis illustrated that performing CCTA before ICA is a cost-effective strategy in the care of patients without symptoms who have positive stress test results when the probability that the patient has significant CAD is less than 50%. The false-negative rate with this strategy compares favorably with the false-negative rate of stress testing. Thus, the use of CCTA in asymptomatic patients with this role can avoid unnecessary ICA procedures.

Direct costs and comparative cost-effectiveness of new generation MSCT (dual-source CT) and ICA for diagnosing the CAD measured through Dorenkamp et al. (2012). Cost calculations were based on a detailed analysis of direct costs. Based on Bayes' theorem, a mathematical model was used to compare the cost-effectiveness of both diagnostic approaches. Total costs included direct costs, induced costs and costs of complications. Effectiveness was defined as the ability of a diagnostic test to accurately identify a patient with CAD. The study resulted that direct costs amounted to 98.60 euros for CCTA and

317.75 euros for ICA. Analysis of model calculations indicated that cost-effectiveness grew hyperbolically with an increasing prevalence of CAD. Given the prevalence of CAD in the study cohort (24%), CCTA was established to be more cost-effective than ICA (970 euros versus 1354 euros) for one patient correctly diagnosed as having CAD. At a disease prevalence of 49%, CCTA and ICA were equally effective with costs of 633 euros. Above a threshold value of disease prevalence of 55%, proceeding directly to ICA was more cost-effective than CCTA. According to their outcomes, with appropriate patient selection and consideration of disease prevalence are critical for the direction of the patient to the best diagnosis. While ICA remains the gold standard for diagnosing CAD, prudently achieved CCTA may be an economically efficient substitute to ICA, especially in ruling out CAD in patients with an intermediate pretest likelihood.

A study with a wonderful perspective combines tangled aspects of human life conducted by Gorenoi et al. (2012). The researchers evaluated the clinical efficacy, diagnostic accuracy, prognostic value cost-effectiveness as well as the ethical, social and legal inferences of CCTA versus ICA in the diagnosis of the CAD. The result of this study from a medical point of view, CCTA using at least 64 MSCT should be recommended as a test to rule out significant CAD in order to avoid inappropriate ICA in patients with an intermediate pretest probability of CAD. From a health economic point of view, this recommendation should be limited to patients with a pretest probability of CAD of 50% or lower. From a medical and health economic point of view, neither CCTA nor ICA may be recommended as a single diagnostic test for identifying or ruling out functionally relevant coronary stenosis. To diminish any potential negative ethical, social and legal insinuations, the general ethical and moral values of benefit, autonomy, and justice should be considered.

A study by Catalán et al. (2013) explored the cost-effectiveness of two alternative strategies to rule out significant CAD in the pre-operative evaluation of non-coronary cardiovascular surgery. The study concluded the initial CCTA strategy for the pre-operative evaluation of non-coronary cardiovascular surgery in experienced groups represents not only a more comfortable diagnostic strategy for the patient but is also more cost-effective than the ICA strategy. It produces a saving of 411euro per patient as well as a benefit due to the possibility of avoiding potential complications and post-ICA death.

Randomized trials conducted by Hlatky et al. (2013) to reconsideration the projected costs and consequences of CCTA. These randomized trials have shown that FFR guided PCI improves clinical outcome and reduces costs compared with visually guided PCI. FFR has been measured during ICA, but can now be derived noninvasively from CCTA images (FFRCT). Consequences of these trials, the projected initial management costs were highest for the ICA visual strategy (10702 dollars), and lowest for the FFRCT strategy (7674 dollars). A strategy of using FFRCT to guide the selection of patients for ICA and PCI might reduce costs and improve clinical outcomes in patients with suspected CAD.

Respecting to cost-effectiveness matching with test accuracy, a study was achieved by Malagò et al. (2013). The study revealed a proper diagnostic protocol for patients with suspected CAD by the introduction of CCTA. According to the cost-effectiveness analysis based on their data, CCTA costs about 230.03 euro, whereas ICA costs about 1,551 euro. Cost-effectiveness analysis confirmed how the costs for correctly categorizing a patient with CAD decrease significantly as the pretest probability increases. CCTA has a better cost-effectiveness ratio compared with ICA on condition that the pretest probability is <86%, which resembles low to intermediate risk patients. The study confirmed the greater diagnostic performance of CCTA compared with the stress test and its similar accuracy to ICA. The use of CCTA to select patients for ICA has a favorable cost-effectiveness profile.

The costs and cost-effectiveness of CTCA in comparison with ICA for the diagnosis CAD from the point of view of the healthcare provider were studied by Darlington et al. (2014). The average cost of CTCA was estimated to be 180 euros based on the use of a 64MSCT with comparison1,378 euros cost of ICA. The incremental cost-effectiveness ratio is 6,380 euro for each additional correct diagnosis that would be attained with ICA strategy compared to a triage strategy with CCTA that excludes negative CCTA from further testing. A strategy of CTCA triage in the intermediate-risk group, no imaging test in the low-risk group, and ICA in the high-risk group, has good diagnostic accuracy and could significantly cut costs.

The cost-effectiveness of seven coronary diagnostic strategies was assessed through a study implemented by Ferreira et al. (2014). The cost-effectiveness of each strategy was defined as the cost per correct diagnosis (inclusion or exclusion of significant CAD) in an asymptomatic patient. This study of great importance has been proved widely clinical assessment of an individual with suspected stable CAD is usually complemented by noninvasive tests. Furthermore, the diagnostic algorithms that include CCTA are the most cost-effective in symptomatic patients with suspected stable CAD and a pretest likelihood of disease of ≤50%. In these patients, depending on the pretest likelihood of disease and the willingness to pay per correct diagnosis, CCTA may be used as a first-line test or reserved for patients with positive or inconclusive results. In high-risk patients, immediate ICA appears to be the most cost-effective strategy.

Chapter 3: Methodology

This chapter provides comprehensive information about all aspects of research methods and addresses issues related to the methodology that used to achieve the research objectives. It explains the study design, study populations, the setting of the study, period of the study, eligibility criteria, data collection methods, statistical analysis, piloting, and validity of the instruments. In addition, it clarifies the ethical considerations and the limitations of the study as well.

3.1 Study design

The design of this study is triangulated observational, analytical, a prospective study carried out among the patients with suspected CAD and also for evaluation CAD patients (grafts or stent) to investigate accuracy in recurrent ischemic symptoms who underwent CCTA and ICA. Analytic research generates new knowledge about concepts and identifies relationships between variables (Burn and Grove, 2001). The prospective studies refer to the likely prevalence of a phenomenon, situation, problem, attitude or outcome in the future. Such studies attempt to establish the outcome of an event or what is likely to happen (Kumar, 2011). Within the context of this study, the prospective cohort will allow the researcher to follow up cases that with risk CAD and underwent diagnosis with ICA or CCTA over the study period of time.

In the current study, methodological triangulation would provide combination between quantitative and qualitative paradigms to validate findings from one method with another, or to enhance understanding of the facts on the ground (Donovan and Sanders, 2005). Qualitative paradigms are humanistic because it focuses on the personal expert, focused data, and experiential basis of knowledge and practice. It is also holistic because it seeks to situate the meaning of particular behaviors and ways of thinking about or doing things in a given context (Kielmann et al., 2011).

The cost-effectiveness analysis was carried out by using an adaptive mathematical model to assess the relative cost-effectiveness of CCTA imaging and ICA. The accuracy of diagnostic test characteristics of CCTA (sensitivity and specificity) obtained by following the patients with suspected CAD who underwent CCTA and then they were followed by ICA.

3.2 Study setting

The study was carried out in the main governmental hospital in the Gaza Strip. In particular, the study was carried out at the cardiac catheterization and computed tomography departments at Al-Shifa hospital.

3.3 Study population

The study includes two types of the population who were represented the quantitative and qualitative parts.

- **Quantitative part:** the current study comprises three patient populations. The first target is patients presented with a suspected risk of CAD underwent CCTA. The second target is patients presented with a suspected risk of CAD underwent ICA. The third target is patients underwent CCTA then followed up by ICA.
- **Qualitative part:** this part involved a group of key specialists who are involved in diagnosis CAD during the period of the study. This was interesting and enhancing our study to be more valuable and interpreted some results according to their experiences.

3.4 Eligibility criteria

3.4.1 Inclusion criteria:

- Patients providing written informed consent and willing to participate.
- Non-urgent patients with appropriate preparation for both procedure.
- Patients presenting with suspected CAD underwent CCTA and ICA.
- Patients underwent CCTA then followed by ICA.

- Patients with a history of CABG referral for following up.
- Patients with a previous history of PCI to rule out stent restenosis.

3.4.2 Exclusion criteria:

- Emergency patients diagnosed by ICA or CCTA.
- Pediatric patients who presented for assessment cardiac morphology.
- Patients have contraindications to CCTA (Heart rate ≥ 65 beats per minute and contraindication for beta blockers or nitroglycerin drugs).
- Patients with a history of severe allergy to an iodinated contrast agent.
- Patients with impaired kidney function or under dialysis.
- CCTA with poor image quality (poorly visualized coronary segments).

3.5 Study period

The study lasted 20 months executions; it started in March 2017 and completed by October 2018. The research proposal has been submitted to defend in the front of the school of public health assigned a committee in May 2017. Initially, the research proposal described the entire process and provided information about study design, data collection, and analysis methods and tools. After obtaining the committee's approval, the researcher prepared the required tools for this study. The tools were arbitrated by experts and their opinions were taken into considerations. The researcher has consulted a group of 12 experts (two consultant cardiologists, three consultant radiologists, four public health consultants, two medical imaging specialist, and one decision maker at MoH). The arbitration stage lasted for six weeks including the refining of tools in the light of reviewers and the academic supervisor's feedback. In August 2017, the tools were ready to start the data collection and the researcher trained two data collector and carried out the required training prior to piloting and fieldwork. Piloting conducted between 1 and 30 September 2017. Initially, the study constructed to be retrospective, but challenges in data

collection, as incomplete the patient files and limited information about both procedures pushed us to make it as a prospective study. Consequently, the study reconstructed to be prospective and followed up the patients from the appointment period through the final diagnosis. Another piloting was performed and actual data collection of quantitative part and data entry as well started on 2nd January through 30 June 2018. Data entry was performed daily in parallel with data collection. Analysis part of the study was immediately initiated after the completion of data collection. Data management and recoding of variables were done, descriptive analysis and frequency tables were extracted, and then inferential statistics were performed. The accuracy of CCTA was checked and cost-effectiveness analysis model constructed/adopted to appropriate the study objectives. The researcher started to prepare the final report which has been finalized by October 2018.

3.6 Sample size and sampling process

3.6.1 Quantitative part

The sampling process flow chart illustrated in Figure 3.1, which was done in three methods to appropriate the eligibility criteria as follows:

1. Census Survey

The aim of selecting this sample study is to study all patients who underwent CCTA well-matched with study inclusion criteria. The sample size was 131 patient who optimal imaged by CCTA during the study period.

2. Purposive (Typical Case Sampling)

Typical case sampling is a type of purposive sampling useful when a researcher wants to study trend as it relates to what is considered typical members of the affected population. In the current study, about 58 patients imaged by CCTA then referred to ICA were obtained to assess the accuracy of CCTA and added-values of ICA. From this sample, we

calculate the CCTA accuracy (sensitivity, specificity, positive predictive value, and negative predictive value of CCTA) considering the ICA as the golden stander reference of diagnosis patients with suspected CAD.

3. Purposive Sample

This sample was taken into account to explain some of the variables needed to determine the cost analysis. In order to calculate the sample size of the patients underwent ICA, Monkey survey online program was used and resulted in a sample size at least 241 cases for representativeness at 95% confidence interval and 5% margin of error (**Annex 3**). The researcher has taken into consideration the following parameters during the sample size calculation:

- The total number of patients underwent ICA during the year 2017 was 1290 patients at Al-Shifa hospital (Al-Shifa records, 2017). The researcher estimated that the same number of the patient where have been undergone ICA during the year 2018 and half of them (645 patients) were diagnosed in the first half of the year 2018.
- The program revealed that the required sample was 241 at confidence interval 95%., a margin of error 5%, and for more representation, the researcher increased the sample size by additional 9 participants to compensate non-respondents and also to increase the statistical power that the sample size reaches 250 patients.
- From the 250 patients, we ensure that the 58 patients who referral from CCTA were included in this sample.
- In order to establish the appropriateness of the sample size for the total number of patients, the number of patients who underwent ICA was obtained during this period. The number of patients was 609 based on the semi-annual records (Al-Shifa records, 2018).

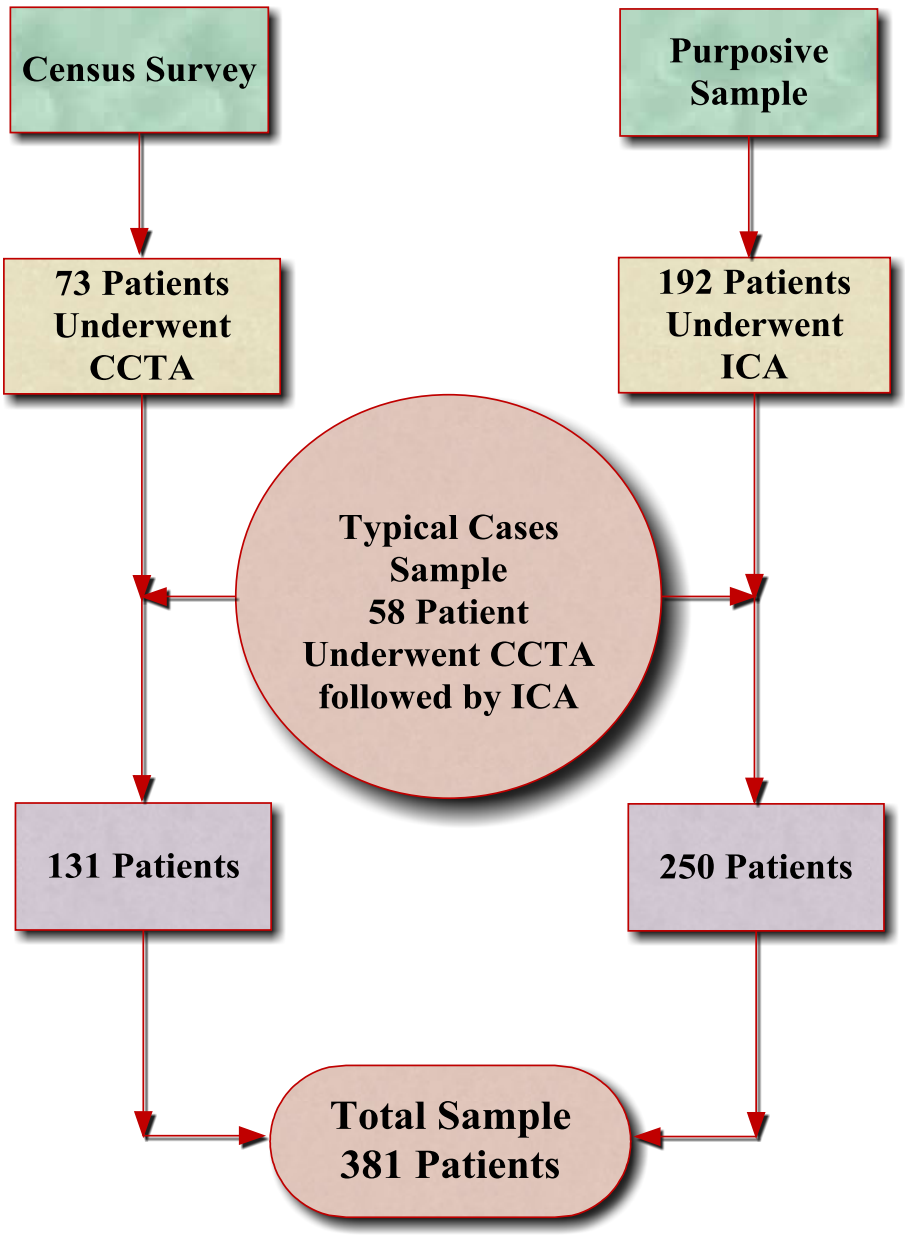

Figure 3.1: Sampling process flow chart

3.6.2 Qualitative part

A purposive sample of seven different medical specialists involved in CAD diagnosis modalities was selected. The integration between quantitative and qualitative data is important to deeply interpretations related results and perspectives. The qualitative component was carried out after finishing the quantitative one in order to deeply explore important issues emerged from the quantitative part.

3.7 Study instruments

- **Quantitative part**

The data were collected by the researcher with the cooperation of trained health providers from Al-Shifa Hospital. To identify the characteristic of the two diagnostic modalities (ICA and CCTA). Two arbitrated questionnaires were constructed to translate research objectives **(Annex 4 for CCTA,** and **Annex 5 for ICA)**; which covered the following areas:

1. **Demographic and personal information**

- Personal information as gender, age, weight, and height.
- Personal habits as lifestyle and smoking.

2. **Medical history and previous cardiac procedures**

- Medical history and patients complain: Family history of heart disease, high cholesterol, high blood pressure, diabetes and chest pain).
- History of cardiac medical intervention: Angioplasty/Stent or Balloon and CABG
- Previous cardiac examinations: Resting Electrocardiography, Exercise Stress Test, Cardiac Echocardiography and Calcium Scoring Test.

3. **Variables for cost-effectiveness analysis**

Additionally, the questionnaire will also cover the differential variables that depend on the patient procedure (ICA or CCTA). These variables are essential for cost analysis and cost-effectiveness analysis such as:

- Pre-procedure preparation blood test such as: Complete Blood Count (CBC), kidney function such as Urea and Creatinine, hepatitis test such as hepatitis C virus (HCV) and hepatitis B virus (HBV), coagulation test such as Prothrombin Time (PT), Partial Thromboplastin Time (PTT), and International Normalized Ratio (INR).

- Drugs administration: preparation's drugs such as beta blockers drugs and sublingual nitroglycerin, and recovery drugs.
- Variables during the procedure: Estimated radiation dose, supplies used during procedures and recovery period, staff procedure and contrast volume.
- Potential complications: bleeding, allergy reactions, shock, and death.
- The diagnostic result of both procedures and categorization of the diseased result to significant CAD ≥ 50% stenosis and non-significant CAD < 50% stenosis.

- **Qualitative Part**

For the qualitative data, the researcher used open-ended (semi-structured) questions **(Annex 6)**. Those questions were asked by the researcher within in-depth interviews with seven medical specialists working in CAD diagnosis field. The interviews focused on the diagnostic process and if there is available standard policy in referral and diagnosis of CAD, the role of imaging modality in the diagnosis, challenges to perform the optimal CCTA procedure and the view of the referring cardiologists in related to CCTA versus ICA.

3.8 Ethical and administrative considerations

An ethical approval was asked for from the School of Public Health at Al-Quds University and Helsinki Committee **(Annex 7)**. Admin approval was obtained from the human resources development directorate general in the MoH **(Annex 8)**. To guarantee patient rights, a covering letter indicating that the participation is voluntary and confidentiality was assured for all of the participants. Moreover, each participant received complete information and explanation about the research purpose, nature, and have a consent form. The researcher assumed that other ethical rights were protected through respect for people and respect for truth.

3.9 Pilot study

Quantitative part: A pilot study included 30 suspected CAD patients who underwent the ICA and 15 suspected CAD patients who underwent the CCTA were done to explore the appropriateness of the study instruments and let the researcher train for data collection. The pilot study improved the study validity and reliability. As a result of this step, few rephrasing and explanation were added to some items in the questionnaire.

Qualitative part: A pilot interview was done with a radiologist, cardiologist and medical imaging specialist which allowed for further improvement of the study validity and reliability. As a result of this stage; asking the questions was improved to be more deeply.

3.10 Data collection technique

After completing the pilot study, the researcher and two data collectors gathered the data from the cardiac catheterization and MSCT departments according to the inclusion and exclusion criteria. The researcher himself filled the questionnaire by reviewing the medical files for all participants. Furthermore, some items were filled through contact with medical staff during the procedure. In case of incomplete records, the researcher contacted the patients in order to bring the required reports. This stage was completed after 6 months. Training was done for the data collectors about the study objectives and vague questions were clarified. In the fieldwork, the researcher began to collect the data in order to help him assistants fully comprehend the questionnaire's items. To monitor the data collection process and make sure of the progress in the data collection, the researcher supervised every day according to his work as CCTA imaging specialist and the presence of the two departments in the vicinity. Confidentiality and privacy were taken into consideration. The CCTA procedure evaluated and reported by CCTA consultant and ICA procedure evaluated and reported by cardiologist consultant. The diagnosed cases sorted to estimate supplies and total cost of the procedure.

3.11 Scientific rigor

3.11.1 Quantitative part (questionnaire)

3.11.1.1 Validity

Face validity: Questionnaires were organized in order to allow smooth data collection. In addition, the data were arranged sequentially in line with the tests under study.

Content validity: Concerning the content validity, adequate reviewing of related topics in the literature about CEA, ICA, CCTA, and CAD were done before designing the study instruments and tools. To assess the relevance of the questionnaires, experts conducted the evaluation process **(Annex 9)**, and comments were taken into consideration. Furthermore, the researcher reviewed some medical files prior to the study and check about the availability of study items. A validation data by identification number and coding number using to excel sheet was used to avoid duplication of cases. The researcher has incorporated experts' suggestions into the data collection tool. This would increase the validity of the questionnaire.

3.11.1.2 Reliability

The following steps were done to assure instruments reliability

1. Standardization of filling the questionnaires.
2. The data entry was filled in the same day of data collection would permit possible interventions to check the data quality or to re-fill the questionnaire when required.
3. Re-entry of 5% of the data after finishing data entry was done to correct the entry procedure and decrease the entry errors.

3.11.2 Qualitative part (in-depth interviews)

To safeguard the trustworthiness of the qualitative part in the current study, three steps were considered. First, a peer check was completed by health experts to review in-depth interview questions to assure that they cover all the essential domains. Second, points were taken about

the important issues discussed during the interviews. Third, a debriefing report was written at the end of each interview including the most key points discussed during it.

3.12 Data entry and analysis

Quantitative part: The researcher used the Statistical Package for Social Science (SPSS version 21) program for data entry and analysis. The first stage of data entry was through constructing the entry base and coding of variables, followed by actual data entry. Data entry was performed at the time of data collection. At the analysis stage, data cleaning and data management for the variables of interest were performed.

The management of data depended upon scientific literature, merging and discretizing continuous variables into categories with minimal loss of information. Descriptive analysis cross-tabulation was used to describe the main features of the data. Chi-square test to compare categorical variables. An independent t-test was used to measure the difference in means of normally distributed data between two independent groups.

Logistic regression is a predictive analysis that used to explain the relationship between one dependent binary variable and one or more nominal, ordinal, interval or ratio-level independent variables. Simple logistic regression describes the univariable analysis which was used to select potential independent variables associated with the risk of the CAD. Multiple linear regressions were used to examine the association between risk of the CAD significant independent variables. and These findings were presented as a regression coefficient (*B*), an odds ratio (OR), a 95% confidence interval (CI) and a *P* value < 0.05. The diagnostic performance of CCTA for the detection of the CAD with ICA as the standard of reference was presented as sensitivity, specificity, positive and negative predictive values.

Qualitative part: Open coding thematic analysis technique was used to analyze the transcripts of the in-depth interviews. The researcher would gain the main findings from

the interviews. Then, categorization of related ideas, comparison and integration between the quantitative and the qualitative findings was done to create rich items for discussion and interpretation.

3.13 Cost analysis

The researcher used the Excel program for cost analysis and cost-effectiveness analysis. Concerning the economic evaluation, the costs (in dollars) of both diagnostic approaches (CCTA and ICA) were recognized through a detailed analysis of all involved procedures. Total costs of a diagnostic modality included direct costs and induced costs (expected cost of complications).

3.13.1 Direct cost

Direct costs were classified into three categories: diagnostic-specific equipment costs, materials and supplies costs and personnel costs. Occupancy costs included heating, air-conditioning, light, cleaning, insurance, furniture, security, secretarial and stationery requirements were considered fixed in both departments, so they were excluded from the cost calculation.

3.13.1.1 Equipment costs

Diagnostic-specific equipment cost included purchasing, repair, and maintenance. Installation contracts provided for a defects' liability period. Equipment purchase costs were obtained from the hospital administrative records. The utility of equipment also was taken into account by calculating the equipment lifetime per year divided on all conducted patients. Equipment lifetime, for calculating amortization, was considered to be 10 years, which is the maximum technological lifespan of radiological equipment according to the European Society of Radiology (ESR) (ESR, 2014). Equipment repair identified in six months (the period of data collection). Maintenance and average annual interest payments costs were obtained from the hospital administrative records and purchases contracts

awarded to tender equipment. All items of equipment cost have been taken into consideration through the workload of each diagnostic method. Furthermore, we analyzed this cost by determining the total number of patients who performed any procedure during the study period. Finally, the cost per patient for each modality was calculated.

3.13.1.2 Cost of materials and supplies

Cost of materials and supplies reflected market prices paid to manufacturers and vendors. We calculated all supplies which need to perform the diagnostic procedure for each patient in the two modalities. The supplies consider as single use for one patient was calculated according to the price list. In another hand, the supplies which used for multiple patients were estimated by a factor for each patient. Contrast media which used to visualize the coronary arteries during the diagnostic procedure is varied according to patients, thus we calculated the cost of the amount which used for each patient, then we analyzed the average for all patient for both procedures separately. Blood tests which carried out before and after procedures were taken into account because of differences for both diagnostic strategies. These costs are taken into account regardless of who is responsible for paying the patient himself or the hospital. Hospitalization costs after the procedure, for the observation and recovery period following diagnostic catheterization, were also taken into account. Any comorbidities and other patient-independent factors contributions to the overhead of the procedure were not included.

3.13.1.3 Personnel costs

The salaries of all involved physicians, nurses and medical imaging specialist were also determined. Thus, personnel costs were calculated according to collective agreements for Palestinian civil service law. The number of medical staff required for each patient was determined and multiplied by the average income of this staff. This cost was calculated for all patients and the average was obtained for each patient.

3.13.2 Induced costs

Induced costs included the cost of complications associated with the test false-negative CAD (Patterson et al., 1984; Patterson et al., 1995; Dorenkamp et al., 2012). In the subgroup of patients with false-negative CCTA, a 15% rate of non-fatal myocardial infarction over 10 years was assumed (Patterson et al., 1984). Induced cost also associated with the complication rates for CCTA (0.004%) and elective ICA (0.05%) were derived from the literature (Katayama et al., 1990; Noto et al., 1991; Dewey and Hamm, 2007; Hamm et al., 2008; Stacul et al., 2009).

Costs of complications are difficult to estimate. For this purpose, previously published data were combined. It was assumed that the typical complication of both diagnostic tests or of untreated CAD would be non-fatal myocardial infarction, requiring hospitalization, rehabilitation, chronic medication and repeated follow-up examinations. On average, conservative cost estimates for a serious complication amounted to 20000 dollars (Patterson et al., 1984; Patterson et al., 1995; Dewey and Hamm, 2007; Stacul et al., 2009; Dorenkamp et al., 2012).

3.13.3 Total costs

Total costs were calculated as direct costs and indirect cost (as established by the cost analysis) times the number of patients tested plus the induced costs (the number of patients tested multiplied by the costs of complications produced by test procedures or of CAD missed by false-negative test results). By definition, ICA was the gold-standard test in the cost-effectiveness analysis with a 100% diagnostic accuracy (sensitivity and specificity of ICA=100%) and no non-diagnostic or false results (Montalescot et al., 2014).

3.14 Cost-effectiveness analysis

The researcher used the Origin pro 7.0 program to illustrate the cost-effectiveness analysis. The cost-effectiveness of each strategy was defined as the cost per correct diagnosis.

According to this definition, a lower cost value per correct diagnosis translates into better cost-effectiveness. This straightforward approach assumes that the goal of a test is to make a diagnosis. In the current study, we estimated the costs of the two different strategies relative to their effectiveness intended to correctly diagnose the significant CAD. In particular, the cost-effectiveness of the CCTA and ICA was compared when applied to patient populations with varying CAD pre-test probabilities. Using a mathematical model, we compared the cost-effectiveness for diagnosing the CAD for patient cohorts characterized by different pretest likelihood (prevalence) of CAD.

3.14.1 Model characteristics

The model is based on Bayes' theorem and consequently assesses cost-effectiveness ratios of strategies in hypothetical patient cohorts with different prevalence of disease (Forrester et al., 1979). The mathematical model was initially suggested by Paterson and co-workers to a comparison of cost-effectiveness for diagnosis of CAD (Patterson et al., 1984; Patterson et al., 1995) and was later on applied by others (Stacul et al., 2009; Dorenkamp et al., 2012; Boldt et al., 2013; Moschetti et al., 2014; Berrar, 2018).

3.14.2 Definitions of the effectiveness of tests

When performing a cost-effectiveness analysis, a wide variety of factors and parameters related to the costs and the performances of the tests have to be considered. The model must be able to take into account the costs associated with false-positive results (i.e. costs of unnecessary diagnostic tests) as well as the costs associated with false negative results (i.e. costs of complications because of inappropriate management of the disease).

The most difficult problem in any assessment of cost-effectiveness is to define the effectiveness of healthcare (McNeil et al., 1975; Enthoven, 1978). For our purposes, we defined the effectiveness of diagnostic tests in two ways, the first effectiveness criterion was the ability of a diagnostic test to accurately identify a patient with CAD. This

definition represents a straightforward approach assuming that the single goal of a test is to make a diagnosis (Patterson et al., 1984; Patterson et al., 1995; Stacul et al., 2009; Dorenkamp et al., 2012). The definition of the second effectiveness criterion was more complex and attempted to account for the future health outcome of patients undergoing the tests (Patterson et al., 1984; Patterson et al., 1995). It was assumed that a correct diagnosis of CAD would enable patients to receive optimal therapy resulting in improved survival and well-being. Over the follow-up period, the number of life-years gained (Δ) by CAD therapy was adjusted for quality of life, yielding quality-adjusted life years (QALYs). In line with previous cost-effectiveness analyses, an accurate diagnosis of CAD was projected to increase the number of QALYs by 3 years during a 10-year follow-up (Patterson et al., 1995). Our model describes the patient flow through the two modalities and the diagnostic results and their relationship with the cost and the benefit or adverse health outcome as shown in Figure 3.2:

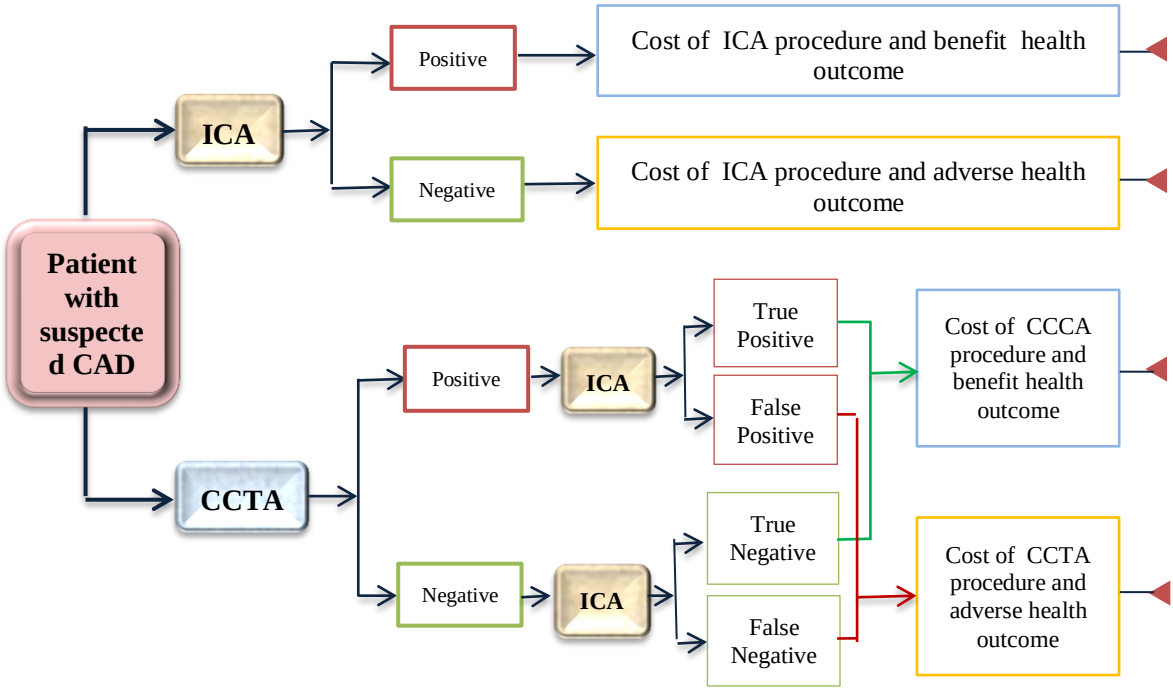

Figure 3.2: Schematic of the decision analytic model patients follow up scenarios for cost analysis and cost-effectiveness

- **The cost analysis and cost-effectiveness analysis statistical model illustrate possible six scenarios**

1. The first scenario, patients underwent ICA with a positive result (significant CAD ≥ 50% stenosis). Cost of ICA procedure was calculated and there was benefit health outcomes due to diagnosis of CAD and appropriate treatment was done.
2. The second scenario, patients underwent ICA with a negative result (non-significant CAD < 50% stenosis or normal with medical treatment). Cost of ICA was calculated, this cost is unjustified and there are adverse health outcomes due to an unnecessary procedure.
3. The third scenario, patients underwent CCTA with a positive result (significant CAD ≥ 50% stenosis), the patients were a referral to ICA and true positive approved by the ICA. Cost of CCTA was calculated and benefit health outcomes were estimated due to the correct diagnosis of CCTA.
4. The fourth scenario, patients underwent CCTA with a positive result (significant CAD ≥ 50% stenosis), the patients were a referral to ICA and false positive approved by the ICA. Cost of CCTA and adverse health outcomes estimated due to an incorrect diagnosis of CCTA.
5. The fifth scenario, patients underwent CCTA with a negative resulted (non-significant CAD < 50% stenosis or normal with medical treatment), the patients were a referral to ICA, and true negative approved by the ICA. Cost of CCTA was calculated and benefit health outcomes were estimated due to the correct diagnosis of CCTA.
6. The six scenario, patients underwent CCTA with a negative resulted (non-significant CAD < 50% stenosis or normal with medical treatment), the patients were a referral to ICA and false negative approved by the ICA. Cost of CCTA and adverse health outcomes incorrect diagnosis of CCTA.

From previous scenarios, the accuracy of CCTA (sensitivity, specificity, positive and negative predictive values) was calculated through the third, fourth, fifth and six scenarios.

3.14.3 Cost-effectiveness Equations

Calculations of cost-effectiveness and utility for CCTA and ICA are involved in the equations below and Table 3.1 shows different parameters and rates required for cost-effectiveness equations.

$$\frac{\textbf{Direct Costs + Induced Costs}}{\textbf{Effectiveness}}$$

- **Cost-effectiveness analysis of CCTA**

1. **Costs** = $N_{CCTA} \times (D_{CCTA} + R_{CCTA} \times C) + N_{ICA} \times (D_{ICA}+R_{ICA} \times C) + FN_{CCTA} \times (R_{FN} \times C)$

whereas

$\mathbf{N_{ICA}} = N_{CCTA} \times (1- FP_{CCTA}) \times [P \times Sn_{CCTA} + (1-P) \times (1-Sp_{CCTA})] + N_{CCTA} \times FP_{CCTA}$

$\mathbf{FN_{CCTA}} = N_{CCTA} \times (1- FP_{CCTA}) \times P \times (1-Sn_{CCTA})$

2. **Effectiveness** = $N_{CCTA} \times (1- FP_{CCTA}) \times P \times Sn_{CCTA} + N_{CCTA} \times P \times FP_{CCTA}$

3. **ΔQALY** = $(CAD_{Dx}) \times (\Delta QALY) - 10 \times (N_{CCTA} \times M_{CCTA} + N_{ICA} \times M_{ICA}) - 5 \times (FN_{CCTA} \times MFN_{CCTA}) - 10 \times (0.1) \times (N_{CCTA} \times R_{CCTA} + N_{ICA} \times R_{ICA} + FN_{CCTA} \times R_{FN})$

- **Cost-effectiveness analysis of ICA**

1. **Costs** = $N_{ICA} \times (D_{ICA}+R_{ICA} \times C)$

whereas $\mathbf{N_{ICA}} = 1$

2. **Effectiveness** = $N_{ICA} \times P$

3. **ΔQALY** = $N_{ICA} \times (\Delta QALY) \times P - 10 \times N_{ICA} \times M_{ICA} - N_{ICA} \times R_{ICA}$

Table 3.1: Parameters and rates required for cost-effectiveness equations

Parameters used in calculations	
N_{CCTA}	Number of patients having CCTA
D_{CCTA}	Direct costs for CCTA
R_{CCTA}	Rate of complications with CCTA
C	Average costs of a complication (assumed to be non-fatal myocardial infarction)
N_{ICA}	Number of patients having ICA
D_{ICA}	Direct and indirect costs for ICA
R_{ICA}	Rate of complications with ICA
FN_{CCTA}	Rate of patients with false-negative CCTA
R_{FN}	Rate of complications per 10-year follow-up period for patients with CAD and false-negative tests
FP_{CCTA}	Rate of false positive CCTA
P	Prevalence of CAD in patient cohort
Sn_{CCTA}	Sensitivity of CCTA
Sp_{CCTA}	Specificity of CCTA
CAD_{Dx}	Effectiveness
ΔQALY	Quality-adjusted life years extended by therapy after making diagnosis of CAD (per 10 years of follow-up)
M_{CCTA}	Mortality rate due to CCTA
M_{ICA}	Mortality rate due to ICA
MFN_{CCTA}	Mortality per 10 years for patients with CAD but false negative CCTA

3.15 Study constraints

The following constraints faced the researcher during carrying out of the study:

- Limited educational resources, particularly professionals in CCTA.
- Limited availability of the up-to-date journals and international publications.
- Lack of local researches on cost-effectiveness resources.
- Cut-off the CCTA and ICA examinations due to break down the equipment at the governmental hospitals.
- Contextual limitation includes the electricity cuts.

Chapter 4: Results and discussion

4.1 Introduction

This chapter presents the results of the statistical analysis of the data and the interpretation of these results in light of other studies. Firstly, it demonstrates the descriptive statistics of the study variables. The descriptive analysis represents the demographic characteristics of the study participants. Secondly, it assesses the inferential analysis to identify the predictors' factors for the significant CAD. Thirdly, it identifies the accuracy of CCTA compared with ICA, which consider as a reference. Finally, for the economic evaluation, the costs of both diagnostic approaches were identified through a detailed analysis of both involved procedures. Additionally, the cost-effectiveness of the two procedures was estimated in which both costs and outcomes are examined concurrently.

4.2 Preliminary descriptive analysis

Descriptive statistics for the key factors in the study, according to the two diagnostic modalities (CCTA and ICA) aims to better understanding of the nature of the data and paving the way to the inferential analysis in the next section.

A total of 381 cases are designated from Al-Shifa hospital. Of these cases, 131 (34.38%) is selected as a census survey who have been diagnosed by CCTA. The rest of the cases are 250 (62.62%) who have been diagnosed by ICA. As well, 58 cases out of 250 have been referred from CCTA to ICA to confirm the diagnosis during the study period.

4.2.1 Demographic characteristics

Gender distribution in the sample shows that there are 243 (63.8%) male and 138 (36.2%) female. Patients are distributed almost consistently according to the diagnostic modalities as given in Table 4.1. Furthermore, the Chi-square test of independence reveals that the patients' gender has an insignificant incidence of the diagnostic modality, where (Chi-square test = 0.121 and *P*-value = 0.728).

Table 4.1: Cross tabulation of diagnostic modalities versus gender, (*n* =381)

Diagnostic Modalities	Gender	
	Male ***n*** **(%)**	**Female** ***n*** **(%)**
CCTA	82 (62.6%)	49 (37.4%)
ICA	161 (64.4%)	89 (35.6%)
Total	**243 (63.8%)**	**138 (36.2%)**

It is noticeable from these results that the proportion of males far exceeds the proportion of females, even if the diagnostic modality varies. Within in-depth interviews, experts cardiologist interpret our results as one said*:*

> *"Symptoms in females are often vague and common with other symptoms. From our experience, we note that a high proportion of male patients presented with CAD compared to female patients. Hence, we prefer to use the initial diagnosis (Stress ECG, ECG and ECHO) without exposing the females to the risk of radiation which they receive from the CCTA or ICA. Also, male patients have excess risk factors than females such as smoking and stress".*

This interpretation is parallel with a local study conducted by Jamee et al. (2013) for identifying the gender difference and characteristics attributed to CAD in Gaza-Palestine and revealed that myocardial infarction was the male has two times higher than female in admitted patients (53.3% males versus 25.7% females); this difference is statistically significant (*P*-value = 0.004).

Concerning to age, the mean age of all patients in the sample is 54.31 years with standard deviation of 8.26 years. Independent samples t-test shows that there is a significant difference between the means of age with respect to the diagnostic modalities at 0.05 level of significance (*P*-value = 0.012) as given in Table 4.2, where the mean age of patients diagnosed by CCTA is 55.77 years while the mean age of patients diagnosed by ICA is 53.55 years.

Table 4.2: Independent samples t-test for difference between the means of age with respect to the diagnostic modalities.

Diagnostic modalities	Mean (year)	Standard deviation	Mean difference	T- value	*P*-value
CCTA	55.77	9.452	2.223	2.337	0.012*
ICA	53.55	7.461			

* Significant at 0.05 level of significance.

Ageing predisposes to a high incidence and prevalence of CAD in both men and women. Knowing the prevalence of CAD in the population helps the physician to estimate pretest probability. Our results indicate that the mean age of the study populations is 54.31 years, which is close to previous studies. The age is a risk factor that increases the likelihood of CAD when associated with other risk factors. In men, the risk for CAD increases starting at age 45 and in women, the risk for CAD increases starting at age 55 (Ridker et al., 2007; Min et al., 2011; Nakazato et al., 2014). Risk factors associated with CAD in Gaza studied by Khwaiter (2009) indicate that distribution of risk factor value of mean age was 57.3 years. Another local study accompanied by Eljedi and Mushtaha (2015) showed that 78% of the CAD group were male and 36% of them aged between 50-59 years old. Consequently, it necessary to CAD risk stratification according to age group with respect to clinical data to a direction of optimal diagnosis approach.

4.2.2 History of cardiac medical intervention

The history of cardiac medical intervention was categorized into three categories, where 32 (8.4%) of patients are with prior angioplasty (stent or balloon), 63 (16.5%) patients are with prior CABG and 286 (75.1%) patients have never had any cardiac medical intervention. Furthermore, the Chi-square test of independence reveals that the history of cardiac medical intervention has a significant incidence on the diagnostic modality, where (Chi-square test = 79.995 and *P*-value <0.001).

Results from cross tabulation in Table 4.3 show that there are 88.4% of those diagnosed with ICA versus 49.6% of those diagnosed with CCTA has no previous cardiac medical intervention. Alternatively, there are 4.8% of those diagnosed with ICA versus 38.9% of those diagnosed with CCTA had previously CABG. Furthermore, there are 6.8% of those diagnosed with ICA versus 11.5% of those diagnosed with CCTA had previously angioplasty (stent or balloon).

Table 4.3: Cross tabulation of diagnostic modalities versus the history of cardiac medical intervention, (*n* =381)

Diagnostic modalities	**History of cardiac medical intervention**		
	Angioplasty/Stent or Balloon ***n* (%)**	***Coronary Artery Bypass Graft*** ***n* (%)**	***Non-cardiac medical intervention*** ***n* (%)**
CCTA	15 (11.5%)	51 (38.9%)	65 (49.6%)
ICA	17 (6.8%)	12 (4.8%)	221 (88.4%)
Total	**32 (8.4%)**	**63 (16.5%)**	**286 (75.1%)**

The previous cardiac medical intervention of the patient is necessary to be obtained because it will be the guide to direct the patient to the optimal procedure. From our results, about 11.5% of cases that conducted CCTA had previous angioplasty. This in line with previous literature that showed some limitations of CCTA in assessment coronary artery stent patency and restenosis (Mark et al., 2010; André et al., 2014). Due to these limitations, CCTA is not yet recommended for stents <3.0 mm in diameter. However, the recent introduction of new options with CCTA may improve the accuracy of the evaluation of in-stent restenosis (Fuchs et al., 2013; Yoo et al., 2018). Surveillance ICA is recommended after stent supported PCI due to the unpredictable occurrence of in-stent restenosis (Zhao et al. 2011; Moradi et al., 2017).

Regarding the history of CABG, the current results indicate the high proportion of patients undergo CCTA (38.9%) compared to only 4.8% undergo ICA. Given the inherent

challenges in performing ICA in patients who have CABG, non-invasive techniques CCTA has been great to assess graft patency. Clinically, such an evaluation is often required when patients present with symptoms suggestive of ischemia for follow up. Barbero and colleagues (2016) conducted a systematic review and meta-analysis of ten studies representing 959 patients with prior CABG surgery. The pooled sensitivity and specificity of detecting complete graft occlusions was 99% as compared to the standard of ICA. These impressive estimates of accuracy persisted across all studies regardless of the age of patients or grafts. Certain clinical scenarios may have a compelling role for CCTA over ICA. CCTA may be much more recommended in the evaluation of proximal or bypass graft aneurysms (Hulten and Blankstein, 2012; Mushtaq et al., 2014; Pesenti-Rossi et al., 2014). CCTA evaluates patients with unknown previous CABG surgical details to know the number, location, and pathways of grafts before planning management by ICA. Additionally, CCTA before ICA has the potential to the procedure faster and more efficient due to an improved understanding of graft anatomy. Given the economic costs and the risk of ICA compared with non-invasive CCTA, it would appear attractive to reserve ICA only for patients with an elevated risk of disease in the grafts or native vessels distal to the surgical anastomoses (Barbero et al., 2017; Eisenberg et al., 2017).

Concerning to patients without previous cardiac intervention and underwent the diagnostic procedures for the first time, the majority of patients that diagnosed with ICA (88.4%) has no previous cardiac intervention (angioplasty or CABG). This result disagrees with the clinical guideline in a recent publication. The high sensitivity of CCTA makes it the non-invasive test of choice in the evaluation of CAD. This has now been ratified in national guidelines with NICE that recommending CCTA as the first-line investigation for all patients presenting with chest pain due to suspected CAD in elective cases with a low

probability of CAD risk (Moss et al., 2017). Within in-depth interviews, experts cardiologist interpret our results as one said:

> *"We prefer to perform ICA for the patient for several reasons, including the inability to regulate and reduce the patient's heart rate to the limit which required to conduct CCTA. In addition, there is unreliable in the accuracy and effectiveness of local CCTA. Moreover, the availability of ICA is more than CCTA and we have cultural difficulties for convincing patients to perform the new CCTA procedure".* This view is followed by experts radiologist and medical imaging specialist as they said*: "The CCTA need high experience from medical imaging specialist and radiologist, and, most importantly need complete cooperation from the cardiologist to good preparation of patients to perform optimal CCTA procedure".*

4.2.3 Estimated Radiation Dose

The mean radiation dose given for all patients in the sample is 7.987 millisievert (mSv) with a standard deviation of 3.23 mSv. Independent samples t-test shows that there is a significant difference between the means estimated radiation dose with respect to the diagnostic modalities at 0.05 level of significance (*P*-value <0.001) as given in Table 4.4, where the mean radiation dose of patients diagnosed with CCTA is 11.589 mSv while the mean radiation dose patients diagnosed with ICA is 6.100 mSv.

Table 4.4: Independent samples t-test for the difference between the means of estimated radiation dose with respect to the diagnostic modalities

Diagnostic modalities	Mean (mSv)	Standard deviation	Mean difference	T- value	*P*-value
CCTA	11.589	2.3162	5.489	24.0373	<0.001*
ICA	6.100	1.662			

* Significant at 0.05 level of significance

Ionizing radiation during ICA or CCTA has serious negative biological effects on humans. Any cancer risk due to radiation exposure from a single cardiac imaging test depends on age (higher with younger age at exposure) and sex (greater for women) (Einstein et al., 2007; Hausleiter, 2009; Smith-Bindman, 2009). Consequently, an optimal strategy is judgmentally to diagnose significant CAD without unnecessary exposing to radiation (Neglia et al., 2015). According to our results, the average estimated radiation dose enclosed within the strategy of saving radiation dose. In the report conducted by Coles et al. (2006), they revealed that radiation dose and attendant risk associated with CCTA versus selective diagnostic ICA in the same patients were 14 mSv and 6 mSv, respectively. If no dose-saving strategy is applied, it is estimated that effective doses of CCTA may reach up to 30 mSv, thus, there is a potential risk of associated radiation-induced malignancy (Xu and Zhang, 2010). Within in-depth interviews, experts medical imaging specialist interpret our results as one said*:*

> *"Radiation doses differ from one patient to another depending on the size of the patient and the imaged area, but in any case, the modern equipment's have the property of reducing radiation doses to diminish the risk of radiation".* Experts cardiologist interpret our results as one said*: "Radiation doses in ICA highly dependent on the experience of the cardiologist who performs the ICA procedure regarding the time which needs to access to the origin of coronary arteries and the ability of visualization the arteries in different views".*

4.2.4 Diagnosis Results

The diagnostic results of the ICA and CCTA have been categorized into three categories for all patients who underwent the two procedures as given in Table 4.5. The relative frequency of diagnosis results reveals that about one fourth (24.7%) of patients have been diagnosed as normal, followed by (28.3%)of patients were diagnosed as non-significant

CAD (stenosis < 50%). In contrast, there are 47% of patients were diagnosed as significant CAD (stenosis ≥ 50%).

Furthermore, results from cross tabulation in Table 4.5 show that there are 31.3% of those diagnosed through CCTA versus 21.2% of those diagnosed through ICA diagnosed as normal without CAD. Additionally, there are 39.7% of those diagnosed through CCTA versus 22.4% of those diagnosed through ICA have non-significant CAD (stenosis < 50%). On the other hand, there are 29% of those diagnosed through CCTA versus 56.4% of those diagnosed through ICA have significant CAD (stenosis ≥ 50%).

Table 4.5: Cross tabulation of diagnostic modalities versus diagnosis result,(*n* =381)

Diagnosis Result	**Diagnostic modalities**		**Total**
	CCTA ***n* (%)**	*ICA* ***n* (%)**	
Normal	41 (31.3%)	53 (21.2%)	94 (24.7%)
Non-significant CAD	52 (39.7%)	56 (22.4%)	108 (28.3%)
Significant CAD	38 (29%)	141 (56.4%)	179 (47%)
Total	131(100%)	250 (100%)	381 (100%)

Our results indicate that two third of patients (71%), who underwent CCTA are diagnosed without significant disease (31.3% normal and 39.7% non-significant CAD). This result exhibits that no need for interventions for those patients with ICA, and only medical treatment was advised. Several related studies coincided with our results, and they recommended the use of CCTA for the evaluation of low to intermediate risk patients presenting with acute chest pain (Chow and Sheth, 2011; Zeb et al., 2014; Gongora et al., 2017). CCTA can provide more information than ICA on the type and the burden of atherosclerotic plaque in the coronary tree. In addition to these high diagnostic and prognostic values, CCTA may play an important role as a gatekeeper to avoid inadequate performance of ICA. From a similar study, Shaw et al. (2012) examined the impact of

CCTA to avoid unnecessary ICA. They observed that the anatomical assessment of CAD by CCTA provides not only accurate diagnostic and prognostic implications, but also the additional notable benefit of avoiding the unnecessary ICA. Based on this concept, CCTA can safely reduce unnecessary ICA as a gatekeeper.

Regarding patients underwent ICA, results indicate that 43.6% of patients are diagnosed without significant disease (21.2% normal and 22.4% non-significant CAD). Additionally, 56.4% of patients have significant CAD, and they need intervention (PCI or CABG). Close to this result a local observational study conducted by Abed and Jamee (2015) studied the characteristics and risk factors attributed to CAD in women attended health services in Gaza-Palestine, ICA data showed that 55.2% had significant CAD, and 44.8% had no CAD. Obviously, the low diagnostic yield of the ICA was reported by these results, which is close to an important study conducted by Patel et al. (2010), that revealed a low diagnostic yield for obstructive CAD in 38% of patients undergoing the first-time ICA. So, highlight the need for improvement in risk stratification strategies to enhance the yield of ICA. Furthermore, it raises the question about clinical signs and pre-test investigations that should be considered before ICA. In parallel, Therming et al. (2017) confirm the very low diagnostic yield of non-invasive and invasive assessment of CAD in current clinical practice, particularly in women and in patients with atypical symptoms. Within in-depth interviews, experts cardiologist interpret our results as one said*:*

> *"Although the high proportion of those who do not have either any CAD or non-significant CAD, this percentage is declining from previous years, and this attributed to enhance the concept of initial clinical diagnosis. Furthermore, the training of junior cardiologists to identify groups with a high probability of CAD and direct toward to complete investigations for the patient then referred to an expert cardiologist to judgment if need ICA or not".*

4.3 Inferential analysis

4.3.1 Predictors for significant CAD and efficacy patients selection for ICA

The final result of ICA for diagnosis eligible patients who had suspected CAD is categorized into two categories: first category with significant obstructive CAD which is defined as more than 50% angiographic diameter stenosis in one or more of the epicardial coronary arteries, and the second category is non-significant obstructive CAD who has angiographic diameter stenosis less than 50% (Gauchan et al., 2012; Niccoli et al., 2015). Regarding patients in stable clinical conditions, guidelines are recommended for straightforward ICA to patients have a high probability of significant CAD, and clinical follow-up in those with a low probability of non-significant CAD (Montalescot et al., 2013). In the current study, out of 250 patients diagnosed by ICA, there are 141 (56.4%) patients were considered to have a significant CAD, and 109 (43.6%) of them were considered to have non-significant CAD.

Logistic regression is a predictive model for a categorical dependent variable based on a set of independent predictors. This section aims to identify the associated factors and independent predictors for significant CAD via logistic regression. A set of 9 independent variables are considered to build up the logistic regression, specifically (gender, age, obesity, lifestyle, smoking status, family history of heart disease, high cholesterol, high blood pressure and diabetes).

4.3.1.1 Baseline characteristics of the ICA patients

The descriptive statistics of the independent categorical variables are summarized in Table 4.6. The chi-square test reveals that there is a significant association between the diagnosis result of ICA and the all independent variables at 0.05 level of significance.

Table 4.6: Chi-square test of independent categorical variables associated with CAD

Variable	Categories	Diagnosis Result of ICA			Chi-square test	*P*-value
		Significant (CAD)	Non-Significant (CAD)	Total		
Gender	Male	106 (42.4%)	55 (22.0%)	161 (64.4%)	16.384	< 0.001*
	Female	35 (14.0%)	54 (21.6%)	89 (35.6%)		
Obesity	Obese	65 (26.0%)	31 (12.4%)	96 (38.4%)	8.104	0.004*
	Non-Obese	76 (30.4%)	78 (31.2%)	154 (61.6%)		
Lifestyle	Sedentary lifestyle	114 (45.6%)	57 (22.8%)	171 (68.4%)	23.195	< 0.001*
	Regular exercise	27 (10.8%)	52 (20.8%)	79 (31.6%)		
Smoking Status	Smokers	79 (31.6%)	27 (10.8%)	106 (42.4%)	24.594	< 0.001*
	Non-Smokers	62 (24.8%)	82 (32.8%)	144 (57.6%)		
Family history of heart disease	Yes	32 (12.8%)	6 (2.4%)	38 (15.2%)	14.094	< 0.001*
	No	109 (43.6%)	103 (41.2%)	212 (84.8%)		
High cholesterol	Yes	47 (18.8%)	15 (6.0%)	62 (24.8%)	12.627	< 0.001*
	No	94 (37.6%)	94 (37.6%)	188 (75.2%)		
High blood pressure	Yes	36 (14.4%)	14 (5.6%)	50 (20.0%)	6.158	0.013*
	No	105 (42.0%)	95 (38.0%)	200 (80.0%)		
Diabetes	Yes	18 (7.2%)	3 (1.2%)	21 (8.4%)	8.012	0.005*
	No	123 (49.2%)	106 (42.4%)	229 (91.6%)		

* Significant at 0.05 level of significance.

4.3.1.2 Simple Logistic Regression

We calculated the unadjusted odds ratios for 9 independent variables using the univariate logistic regression model to determine the risk factors associated with CAD.

The results of the simple logistic regression analysis. enabled us to determine which characteristics were independently associated with the presence of CAD, while the other factors remain constant as illustrated in Table 4.7.

Table 4.7:Risk factors associated with CAD from Simple Logistic Regression analysis

Variable		β Coefficient	Standard error	Unadjusted Odds Ratio (95.0% CI)	Wald statistics	*P*-value
Gender	**Male**	1.09	0.27	2.97 (1.74-5.08)	15.90	<0.001*
	Female	-	-	1 [Reference]	-	-
Age		0.13	0.02	1.14 (1.09-1.2)	32.61	<0.001*
Obesity	**Obese**	0.77	0.27	2.15 (1.26-3.66)	7.98	0.005*
	Non-Obese	-	-	1 [Reference]	-	-
Lifestyle	**Sedentary lifestyle**	1.35	0.29	3.85 (2.19-6.77)	22.02	<0.001*
	Regular exercise	-	-	1 [Reference]	-	-
Smoking	**Currently smoking**	1.35	0.28	3.87 (2.24-6.69)	23.47	<0.001*
	Non-smoking	-	-	1 [Reference]	-	-
Family history of heart disease	**Yes**	1.62	0.47	5.04 (2.02-12.55)	12.07	0.001*
	No	-	-	1 [Reference]	-	-
High cholesterol	**Yes**	1.14	0.33	3.13 (1.64-5.99)	11.94	0.001*
	No	-	-	1 [Reference]	-	-
High blood pressure	**Yes**	0.84	0.35	2.33 (1.18-4.58)	5.98	0.014*
	No	-	-	1 [Reference]	-	-
Diabetes	**Yes**	1.64	0.64	5.17 (1.48-18.04)	6.64	0.010*
	No	-	-	1 [Reference]	-	-

* Significant at 0.05 level of significance.

Among these characteristics, the male has an odds ratio of 2.97, which means that a male patient has an approximately 3 times higher risk of CAD than they are for female. Age has an odds ratio of 1.14, which indicates that with an increase of 1 year in age, the associated risk of CAD will also be increased by 14%. The predicted odds for having a significant CAD are 2.15 times higher for patients who are obese than they are for non-obese. Regarding lifestyle, the sedentary lifestyle is independent of physical activity associated with an increased risk of CAD 3.85 times than they are for a regular exerciser. Current smokers were 3.87 times at higher risk of developing CAD than non-smokers.

The family history of heart disease has a high odds ratio, the odds of having a significant CAD are 5 times more likely to have a significant CAD as patients who without a family history of heart disease. The odds of having a significant CAD are more than 3 times higher for patients who have high cholesterol than they are for patients who do not have high cholesterol. The odds of having a significant CAD are 2.33 times higher for patients who have high blood pressure than they are for patients who do not have high blood pressure. Interestingly diabetes has the highest odds ratio, the odds of having a significant CAD are 5.17 times higher for diabetic patients than non-diabetic patients.

4.3.1.3 Multiple Logistic Regression

The final effect model was obtained using forward RL variable selection. Based on the results of simple logistic regression analysis, the all independent variables with a *P*-value <0.05 were included in the multiple logistic regression analysis. Table 4.8 presents all the independent variables appearing in the final model that remained significantly associated with CAD.

The Omnibus Tests of Model Coefficients for the proposed model gives the value of -2 log likelihood is 248.78 with an associated value of Chi-square test equals 93.69 at 7 degrees of freedom and *P*-value <0.001, which reveals the existence of an association between the independent variable and significant CAD status. Furthermore, the Cox and Snell R^2 and Nagelkerke R^2 statistics show that the independent variables explained 31.3% and 41.9% of significant CAD variability, respectively. Hosmer and Lemeshow Test for the goodness of model fit reveal that significance equals 0.418 (no significant differences between actual and predicted values) which indicate well-fitting of our predicting logistic regression model. A marked improvement showed correct classification rate in our logistic model for 76.4% of the cases compared to 56.4% in the null model.

Table 4.8: Risk factors associated with CAD from Multiple Logistic Regression

Variable		Adjusted β Coefficient	Standard error	Adjusted Odds Ratio (95.0% CI)	Wald statistics	*P*-value
Age		0.12	0.03	1.12 (1.06-1.18)	18.65	<0.001*
Obesity	**Obese**	0.87	0.33	2.39 (1.26-4.55)	7.09	0.008*
	Non-Obese	-	-	1 [Reference]	-	-
Lifestyle	**Sedentary lifestyle**	0.76	0.35	2.14 (1.09-4.22)	4.90	0.027*
	Regular exercise	-	-	1 [Reference]	-	-
Smoking	**Currently smoking**	1.06	0.33	2.89 (1.51-5.52)	10.53	0.001*
	Non-smoking	-	-	1 [Reference]	-	-
Family history of heart disease	**Yes**	1.13	0.52	3.12 (1.11-8.68)	4.68	0.030*
	No	-	-	1 [Reference]	-	-
High blood pressure	**Yes**	1.01	0.42	2.74 (1.22-6.18)	5.90	0.015*
	No	-	-	1 [Reference]	-	-
Diabetes	**Yes**	1.47	0.69	4.35 (1.13-16.76)	4.55	0.033*
	No	-	-	1 [Reference]	-	-

* Significant at 0.05 level of significance.

Not surprisingly, in multiple logistic regression analysis, we observed that the stronger independent predictors for the presence of significant CAD at the ICA were the traditional risk factors age, obesity, lifestyle, smoking, the presence of family history of heart disease, high blood pressure and diabetes. The strongest association was found for diabetes, the odds of having a significant CAD are 4.35 times higher for diabetic patients than non-diabetic patients. Family history of heart disease although decreased in odds it still has significantly high odds ratio 3.12 times, which expressively odds of contributing towards the development of CAD. Regarding smoking, it was assessed only qualitatively through patient reports, whereas quantitative characteristics such as exposure time and intensity of consumption were not considered. Remarkably, current smokers were 2.89 times at higher risk of developing CAD than non-smokers. High blood pressure and obesity are more

likely developing CAD with slightly increased in odds 2.74 and 2.39, respectively. Concerning lifestyle, regular exercise is associated with significant reductions in the incidence of CAD and at lower risk 2.15 times than the sedentary lifestyle.

Nearby to our results, Khwaiter (2009) identified the risk factors associated with CAD in Gaza, he found that CAD patients who are at higher risk of overweight are female patients, CAD with high relation with diabetic female patients, CAD patients who are at higher risk of CAD are sedentary to light activity patients, and the relation between smoking and CAD occurrence risks.

In accord with our results, a case-control study conducted by Eljedi and Mushtaha (2015) to identify the risk factors of CAD in Palestinian patients undergoing ICA, their study revealed that the most common risk factors were physical inactivity (OR 3.96, P=0.002), hypertension (OR 2.73, P<0.001), diabetes (OR 2.21, P=0.006), smoking (OR 1.96, P=0.031), and positive family history (OR 2.12, P=0.012). Furthermore, persons with hypertension and diabetes are more vulnerable to CAD and had 2.73 and 2.18 times the odds of developing CAD respectively. Positive family history of CAD was strongly correlated with developing CAD among the case group.

Close to these results, Costa et al. (2015) assessed the efficacy of patient selection for ICA in suspected CAD. Their results indicate that the odds of having a significant CAD male gender 3.95 times higher female, odds of having a significant CAD 1.15 times higher for a patient with one more year old, the odds of having a significant CAD are 2.02 times higher for patients who have high cholesterol than they are for patients who do not have high cholesterol.

4.4 Diagnostic accuracy of CCTA compared to ICA

In the current study, we tested CCTA as a gatekeeper to ICA and the possibility to reduce the number of ICAs by reliably identifying CAD and improve patient safety while maintaining diagnostic accuracy. The accuracy was conducted on 58 patients who diagnosed through CCTA and were referred for ICA within the study period either as part of clinical work-up (full investigation) or as part of the accurate diagnosis. Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of CCTA were calculated. ICA is considered the golden standard diagnostic approach.

Based on per-patient analysis of 58 patients, results from cross tabulation in Table 4.9 shows that there are 38 patients with positive CAD (significant CAD ≥50% stenosis) and 20 patients with negative CAD (non-significant CAD) revealed from CCTA. By performing ICA to confirm the diagnosis, only 36 patients were correctly diagnosed by CCTA (true positive) and two patients incorrectly diagnosed by CCTA (false positive). Regarding non-significant CAD diagnosed with CCTA (20 patients), 19 of them were correctly diagnosed (true negative), and only one patient was incorrectly diagnosed (false negative).

Table 4.9: Cross tabulation of diagnostic Results of CCTA versus diagnostic Results of ICA, (*n* =58)

		Diagnostic Results of ICA		**Total**
		Positive	**Negative**	
Diagnostic Results of CCTA	**Positive**	36	2	38
	Negative	1	19	20
Total		37	21	58

Calculations of CCTA accuracy are summarized in Table 4.10. The overall sensitivity and specificity of CCTA technique was 97.3% (95% CI: 85.84% to 99.93%) and 90.48% (95% CI: 69.62% to 98.83%), respectively. The positive predictive value was 94.74% (95% CI: 82.79% to 98.54%) and negative predictive value was 95% (95% CI: 73.23% to 99.25%) of CCTA.

Table 4.10: Calculations of CCTA accuracy

Sensitivity	True positive/(True positive +False negative)	36/(36 +1)	97.3%
Specificity	True negative/(True negative +False positive)	19/(19 +1)	90.48%
PPV	True positive/(True positive +False positive)	36/(36 +2)	94.74%
NPV	True negative/(True negative +False negative)	19/(19+1)	95%
Accuracy	(Total positive +Total negative)/Total	36+19/58	94.83%

The current results are close to previous studies, very high sensitivity ranging between 85% and 99% and negative predictive value (NPV) ranging between 83% and 99% were reported in three multicenter (Budoff et al., 2008; Meijboom et al., 2008; Miller et al., 2008). Opolski et al. (2015) studied the accuracy of CCTA compare to ICA by per-patient analysis. Their study confirms that CCTA has high sensitivity (98%) and negative predictive values (94%). Other study conducted by Joshi et al. (2016) revealed that the overall sensitivity and specificity of CCTA were 100% (95% CI: 39.76%–100%) and 91.30% (95% CI: 79.21%–97.58%), respectively. In the same study, the positive predictive value was 50% (95% CI: 15.70%–84.30%) and the negative predictive value was 100% (95% CI: 91.59%–100%) of CCTA was also fairly high in these patients. In inference, recent studies, systematic review and meta-analysis confirm that CCTA is considered as a gatekeeper for ICA due to the diagnostic accuracy of CCTA for CAD when compared to other diagnostic modalities (Budoff et al., 2017; Chaikriangkrai et al., 2018; Meinel et al., 2018).

4.5 Cost analysis

A cost analysis is an important first step before engaging in cost-effectiveness analysis of economic evaluation and to determine the suitability or feasibility of a potential procedure. The costs of both diagnostic methods were identified through a detailed analysis of all involved procedures. In our cost analysis, the following general considerations were taken into account:

1. Operational hours

Operational hours for MSCT and cardiac catheterization systems were 7 hours/day, 250 days/year according to the Ministry of Health regulations based on the Palestinian civil service law, which regulating working hours and official holidays.

2. Equipment lifetime

Equipment lifetime of MSCT equipment and cardiac catheterization was set at 10 years, which determined according to categories annually number utilization cases based on the European Society of Radiology (ESR) (ESR, 2014).

3. Procedure time period

Independent samples t-test shows that there is a significant difference between the means of the procedure time period with respect to the diagnostic modalities (CCTA and ICA) at 0.05 level of significance (*P*-value <0.001) as given in Table 4.11. The mean procedure time of CCTA is 10.24 minutes while the mean procedure time of ICA is 37.00 minutes.

Table 4.11: Independent samples t-test for difference between the means of the procedure time period with respect to the diagnostic modalities

Diagnostic modalities	Mean (minute)	Standard deviation	Mean difference	T-value	*P*-value
CCTA	10.24	1.894	-26.756	-64.373	<0.001*
ICA	37.00	6.029			

* Significant at 0.05 level of significance.

4. Reporting Time Period

Independent samples t-test shows that there is a significant difference between the means of the reporting time with respect to the diagnostic modalities at 0.05 level of significance (*P*-value <0.001) as given in Table 4.12. The mean reporting time of CCTA result is 42.02 minutes while the mean reporting time of ICA result is 12.32 minutes.

Table 4.12: Independent samples t-test for difference between the means of the reporting time period with respect to the diagnostic modalities

Diagnostic modalities	Mean (minute)	Standard deviation	Mean difference	T-value	*P*-value
CCTA	42.02	11.073	29.703	30.543	<0.001*
ICA	12.32	1.568			

* Significant at 0.05 level of significance

5. Cost of contrast medium

Independent samples t-test shows that there is a significant difference between the means of the cost of contrast medium per patient with respect to the diagnostic modalities at 0.05 level of significance (*P*-value <0.001) as given in Table 4.13. The mean cost of contrast medium of CCTA procedure per patient is 17.47 dollars while the mean cost of contrast medium of ICA procedure per patient is 11.68 dollars.

Table 4.13: Independent samples t-test for difference between the means of the cost of contrast medium per patient with respect to the diagnostic modalities

Diagnostic modalities	Mean (dollar)	Standard deviation	Mean difference	T-value	*P*-value
CCTA	17.47	1.753	5.786	23.950	<0.001*
ICA	11.68	2.954			

* Significant at 0.05 level of significance

4.5.1 Cost analysis of CCTA procedure

Direct costs for CCTA are defined as the sum of the equipment costs, personnel costs and medical supplies cost of CCTA procedures.

4.5.1.1 Equipment costs

- Equipment or unit costs of equipment were the sum of purchasing cost and guaranty cost which include service contract and maintenance.
- Costs of equipment per CCTA procedure were calculated as shown in Table 4.14.

Table 4.14: Calculation steps of equipment cost per CCTA procedure

Steps	Calculations	Result
Cost per year	= total cost of MSCT equipment/10 year equipment lifetime = 1172500 dollars /10 year	117250 dollars
Cost per day	= cost per year/250 working days = 117250 dollars /250 days	469 dollars
Cost per hour	= cost per day/7 working hours = 469 dollars/7 hours	67 dollars
Cost per minute	= cost per hour/60 minute = 67 dollars/60	1.12 dollars
Cost per CCTA procedure	= cost per minute x average CCTA procedure time = 1.12 x 10.24 minute	11.43 dollars
Total equipment cost per CCTA procedure 11.43 dollars		

4.5.1.2 Personal salaries cost

- Personal salaries were determined based on the procedure need highly experienced employees with a period of time in the work. Thus there is a salary in accordance with the years of experience and their certificates. Thus, the salary of the most experienced employee was calculated according to civil service law.

- Personnel cost is the total salaries of medical imaging specialists, consultant radiologist and nursing. Personal cost was estimated on the basis of the procedure time, which spends for each patient also the time of reporting.
- On specific time requirements for CCTA, medical imaging specialists and nursing spend only the time of the procedure (10.24 min), but the radiologist spends time procedure and time of reporting (10.24 min+42.02 min).
- Steps for calculations of salary cost per CCTA procedure as the following:
    1. Salary cost per year = Salary per month (dollar) x12 month
    2. Salary cost per day = Salary cost per year /250 working days
    3. Salary cost per hour = Salary cost per day/7 working hours
    4. Salary cost per minute = Salary cost per hour/60 minute
    5. Salary cost per CCTA procedure = Salary cost per minute x average CCTA procedure time
- Costs of personal cost per CCTA procedure were calculated as shown in Table 4.15.

Table 4.15: Personal cost per CCTA procedure

Personal	Salary per month	Cost per min	No. of employee	Time	Cost per procedure
Medical Imaging Specialists	850 dollars	0.10	1	10.24	0.99
Consultant Radiologist	2000 dollars	0.23	1	52.26	12.02
Expert Nurse	800 dollars	0.09	1	10.24	0.94
Total personal salaries cost per CCTA procedure 13.95 dollars					

4.5.1.3 Medical supplies and blood tests cost

- Medical supplies cost is the total cost of materials used during the CCTA procedure, cost of contrast medium used to visualize the coronary arteries and cost of preparation.
- Supplies cost and preparation cost were calculated for each patient. Contrast medium was calculated as an average of contrast cost for all patients.
- Costs of supplies per CCTA procedure were calculated as shown in Table 4.16.

Table 4.16: Medical supplies cost per CCTA procedure

Medical supplies	Costs of supplies per procedure (dollar)
Cannula	0.22
Cotton	0.1
Alcohol	0.1
Extension tube	1
Plaster	0.1
Normal saline	1.5
Drugs	1.18
Blood test	3.8
Contrast medium	17.46
Total medical supplies cost per CCTA procedure 25.46 dollars	

4.5.1.4 Direct cost of CCTA

Direct cost of CCTA per procedure is equal the sum of total equipment cost per procedure 11.43 dollars, total personal cost per procedure 13.95 dollars and total medical supplies cost per procedure 25.46 dollars. Table 4.17 shows summary for the total direct cost per CCTA procedure.

Table 4.17: Summary for the total direct cost per CCTA procedure

Total equipment cost per CCTA procedure	11.43 dollars
Total personal cost per CCTA procedure	13.95 dollars
Total medical supplies cost per CCTA procedure	25.46 dollars
Total direct cost per CCTA procedure 50.84 dollars	

4.5.2 Cost analysis of ICA procedure

Direct costs for ICA are defined as the sum of the equipment costs, medical supplies cost, recovery period and personnel costs of ICA procedures.

4.5.2.1 Equipment costs of ICA procedure

- Unit costs of equipment were the sum of purchasing cost and guaranty cost which include service contract and maintenance.
- Costs of equipment per ICA procedure were calculated as shown in Table 4.18.

Table 4.18: Calculation steps of equipment cost per ICA procedure

Steps	Calculations	Result
Cost per year	= total cost of Catheterization equipment/10 years equipment lifetime = 1147500 dollars /10 years	114750 dollars
Cost per day	= cost per year /250 working days = 114750 dollars /250 days	459 dollars
Cost per hour	= cost per day /7 working hours = 459 dollars/7 hours	65.57 dollars
Cost per minute	= cost per hour/60 minutes = 67/60	1.09 dollars
Cost per ICA procedure	= cost per minute x average ICA procedure time = 1.09 x 37 minute	40.44 dollars
Total equipment cost per ICA procedure 40.44 dollars		

4.5.2.2 Personal salaries cost of ICA procedure

- Personnel salaries cost of medical imaging specialists, consultant cardiologist and nursing were also determined. Personal cost was estimated on the basis of the procedure time which spends for each patient also the time of reporting and recovery.
- On specific time requirements for ICA, medical imaging specialists and nursing spend only the time of the procedure (37 min), and others nursing spends only the time of the recovery (11.40 min), but the cardiologist spends time procedure and time of reporting (37 min+12.32 min). The time requirements for ICA is considered direct cost, but the recovery time spends not only for one patient, so we calculated by indirect cost as attributed to the cost of the procedure.
- Steps for calculations of salary cost per ICA procedure as the same mentioned in CCTA.
- Costs of direct personal cost per ICA procedure were calculated as shown in Table 4.19.

Table 4.19: Total personal direct cost per ICA procedure

Personal	Salary per month	Cost per min	No. of employee	Time	Cost per procedure
Medical Imaging Specialists	850 dollars	0.10	1	37	3.59
Consultant Cardiologist	2000 dollars	0.23	2	49.32	22.55
Expert Nurse	800 dollars	0.09	2	37	6.77
Total personal salaries direct cost per ICA procedure 32.91 dollars					

- The indirect cost of the salary of recovery nurse per ICA procedure was calculated as the annual salary is divided by the average number of cases conducted per year. Then

multiplied by a number of the nurse who service all patients during the recovery period. Table 4.20 shows the indirect cost of nurse salary during the recovery period.

Table 4.20 Indirect cost estimated from recovery per ICA procedure

Personal	Salary per month	Salary per year	No. of annual cases	Nurse salary cost per procedure	No. of nurses	Cost per procedure
Recovery Nurse	800	9600	1684	5.7	2	11.40
Indirect cost of the salary of the recovery nurse per ICA procedure 11.40 dollars						

Finally, total personal cost per ICA procedure was estimated from the summation of direct and indirect cost as shown in Table 4.21.

Table 4.21: Total of personal cost per ICA procedure

Personal cost	Cost per procedure
Direct cost	32.91 dollars
Indirect cost	11.40 dollars
Total of personal cost per ICA procedure	44.31 dollars

4.5.2.3 Medical supplies and blood test cost of ICA procedure

- Medical procedure supplies cost were included the materials used during the ICA procedure, cost of contrast medium which used to visualization the coronary arteries and cost of preparation.
- Supplies cost and preparation cost were calculated for each patient. Contrast medium was calculated as an average of contrast cost of all patients. Other supplies which used during the recovery period were also calculated.
- Costs of supplies per CCTA procedure were calculated as shown in Table 4.22.

Table 4.22: Total medical supplies cost per ICA procedure

Medical supplies	Costs of supplies per procedure (dollar)
Cannula	0.22
Cotton	0.2
Alcohol	0.1
Extension tube	1
Plaster	0.1
Normal saline	1.5
Femoral sheath F6 11 cm (Kit)	15
Coronary Guide wire J TIP 0.035 - 150 cm	18
Jodkins left JL 4 catheter Fr 6	22
Jodkins right JR 4 catheter Fr 6	22
Lower lock syringe 12c	2
Manifold 3 way- right off	5
Pressure line male – female 100 cm	5
Puncture needle G 18, 7cm	3
Gauze	2
Poledin 10 %	0.3
Syringe 3ml -10 ml -20 ml	0.21
Needle G21	0.02
Intravenous set	0.15
Blood test	35
Contrast medium	11.68
Recovery supplies	5
Total medical supplies cost per ICA procedure 149.48 dollar	

Finally, the total cost of ICA per procedure is equal to the sum of equipment cost per ICA procedure (40.44 dollars), total personal cost per examination (44.31 dollars) and total medical supplies cost per ICA procedure (149.48 dollars). Table 4.23 shows the total cost (direct and indirect) per ICA procedure.

Table 4.23: Total cost per ICA procedure

Total equipment cost per ICA procedure	40.44 dollars
Total personal cost per ICA procedure	44.31 dollars
Total medical supplies cost per ICA procedure	149.48 dollars
Total direct and indirect cost per ICA procedure 234.23 dollars	

4.6 Cost comparison CCTA versus ICA

Summarized cost categories for both diagnostic approaches are displayed in table 4.24. The overall direct costs of ICA were found to be about 4.6 times the cost of CCTA, mainly due to higher materials and supplies costs (5.9 times), equipment costs (3.5 times), and personnel costs (3 times). This ratio is markedly lower than those reported in previous studies, which have found that the cost of ICA exceeds that of CCTA up to a factor of nine (Dewey and Hamm, 2007; Stacul et al., 2009; Halpern et al., 2010). However, the latter studies have, at least partly, applied inconsistent cost-accounting practices, and thus, the results might not be directly comparable. However, the main factor that contributes to the low-cost ratio between CCTA and ICA is the relatively low direct costs of machines, reflecting an increasingly different equipment manufactures specifications costs. In contrast, the current results are nearly close to the study conducted by Dorenkamp et al. (2012), which revealed that the overall direct costs of ICA were found to be about three times the cost of CCTA, mainly due to a partial similarity of MSCT equipment specifications.

Table 4.24: Cost comparison CCTA versus ICA

Cost category	CCTA (in dollar)	ICA (in dollar)
Equipment	11.43	40.44
Materials and supplies	13.95	44.31
Personnel	25.46	149.48
Total	50.84	234.23

4.6.1 Cost of unnecessary and adverse health outcome of ICA

The cost to patients and healthcare systems is considerable in parallel to patient safety which is a critical policy issue. Many adverse events can be systematically prevented through better policy and practice, with the cost of prevention typically much lower than the cost of harm. ICA is valuable in patients with high risk of CAD, but, many individuals currently undergoing ICA will not benefit from ICA. Therefore, if there are noninvasive alternatives to guide decisions about the use of ICA to spare individuals from undergoing unnecessary ICA, there is potential to improve health outcomes.

Based on Figure 3.2 which show the scenario in case of unnecessary to ICA, Table 4.5 which show the number of patients with non-significant CAD and cost of ICA procedure from Table 4.24, we estimate the cost of unnecessary and adverse health outcome of ICA according to ICA cost equation as the following:

- Total cost of unnecessary and adverse health outcome the selected sample (250 patients)

$$= N_{ICA} \times (D_{ICA} + R_{ICA} \times C)$$

$$= 109 \text{ x } (109 + 0.05\% \text{ x } 20000)$$

$$= 26621 \text{dollars}$$

4.7 Cost per patient tested

Figure 4.1 shows the cost per patient tested in relation to different prevalence of CAD. These results indicate that the cost of both CCTA and ICA are equally at prevalence 57%. The cost of CCTA increased as a linear function of CAD prevalence (direct relation between false diagnosis and prevalence). In contrast, the cost for ICA did not increase significantly (no false diagnosis, both sensitivity and specificity are 100%). Cost increases with CAD prevalence for CCTA but not significantly for ICA. CCTA showed lower cost than ICA with CAD prevalence <57% but higher costs with CAD prevalence >57%.

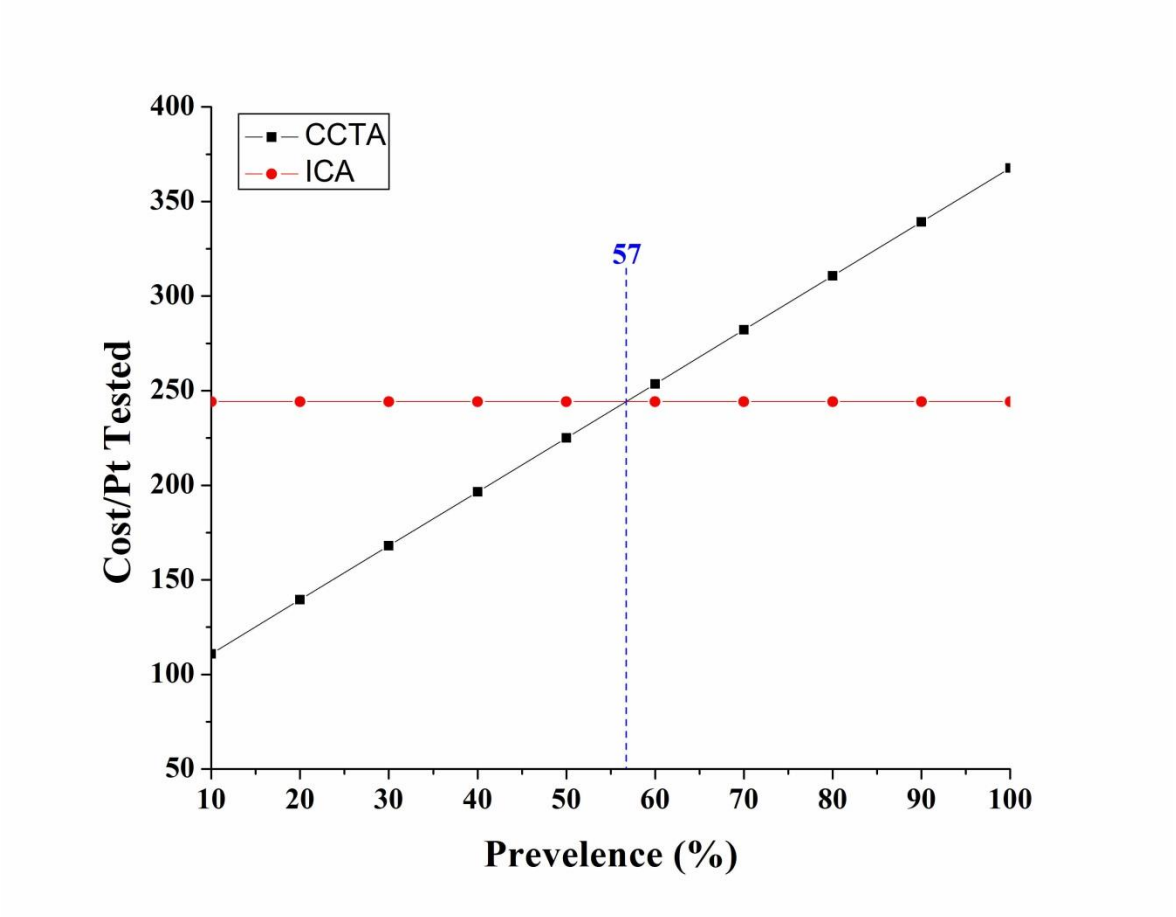

Figure 4.1 Effects of disease prevalence on cost

4.8 Impact of CAD prevalence on cost-effectiveness in term cost per effect

As cost per effect is the inverse of cost-effectiveness, the hyperbolic decrease in cost per effect indicates increased cost-effectiveness. Despite the increase in total cost with increasing prevalence of CAD especially in CCTA, cost-effectiveness improved with different CAD prevalence for both diagnostic tests. Figure 4.2 plots cost per effect (cost per patient with CAD diagnosed accurately) versus increasing prevalence of CAD.

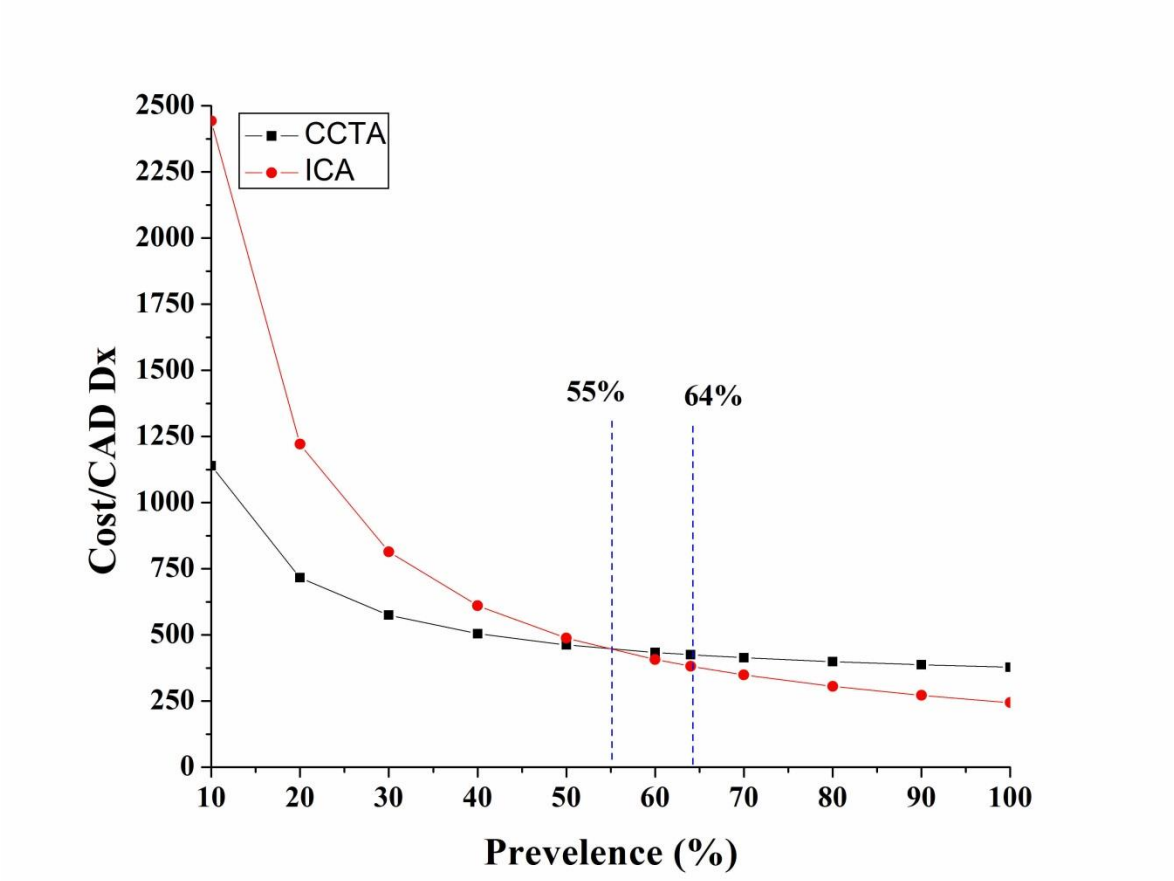

Figure 4.2: Effects of disease prevalence on cost-effectiveness in term cost per effect

In comparison, CCTA was more cost-effective up to a CAD prevalence of 54%, the cost for one patient correctly diagnosed as having CAD was 449.7 dollars with CCTA and 452.3 dollars with ICA. Given the 64% CAD prevalence of the investigated patient cohort in the current study, the cost for one patient correctly diagnosed as having CAD was 425.2 dollars with CCTA and 381.6 dollars with ICA. At a CAD prevalence of 55%, CCTA and

ICA were equally effective with costs of 448 dollars. With higher disease prevalence (>55%), ICA became more cost-effective. In particular, the data demonstrate that CCTA is more cost-effective in patients with a prevalence up to 54%, with a cost per correct diagnosis of CAD ranging from 1139.1dollars (10% prevalence) to 449.7 dollars (54% prevalence). By contrast, ICA shows better cost-effectiveness for a prevalence of 56%–100%, with a cost per correct diagnosis of CAD between 436.13 dollars (56% prevalence) and 244.23 dollars (100% prevalence). Cost and prevalence are inversely proportional in both CCTA and ICA as shown in Table 4.25.

Table 4.25: Cost-effectiveness of CCTA and ICA at different levels of CAD prevalence in term cost per effect

Cost-effectiveness (dollar) Cost/CAD Dx		
Prevalence	**CCTA**	**ICA**
10%	1139.1	2442.3
20%	716	1221.2
30%	575	814.1
40%	504.5	610.6
50%	462	488.5
54%	449.7	452.3
55%	448	448
56%	443.9	436.13
60%	434	407.1
70%	413.9	384.9
80%	398.8	305.3
90%	387	271.4
100%	377.6	244.23

4.9 Impact of CAD prevalence on cost-effectiveness in terms of ΔQALY

Figure 4.3 plots cost per cost-effectiveness in terms of ΔQALY versus increasing prevalence of CAD. The decrease in cost per ΔQALY indicates increased cost-effectiveness. Regardless of the increase in cost with increasing prevalence of CAD especially in CCTA, ΔQALY improved with different CAD prevalence for both diagnostic tests. At a CAD prevalence of 55%, CCTA and ICA were equally effective in term ΔQALY with costs of 150 dollars. CCTA was more cost-effective in term ΔQALY up to a CAD prevalence of 54% ranging from 399.21 dollars (10% prevalence) to 128.06 dollars (54% prevalence). By contrast, ICA shows better cost-effectiveness for a prevalence of 56%–100%, with a cost per in term ΔQALY of CAD between 146.55 dollars (56% prevalence) and 81.79 dollars (100% prevalence) as shown in Table 4.26.

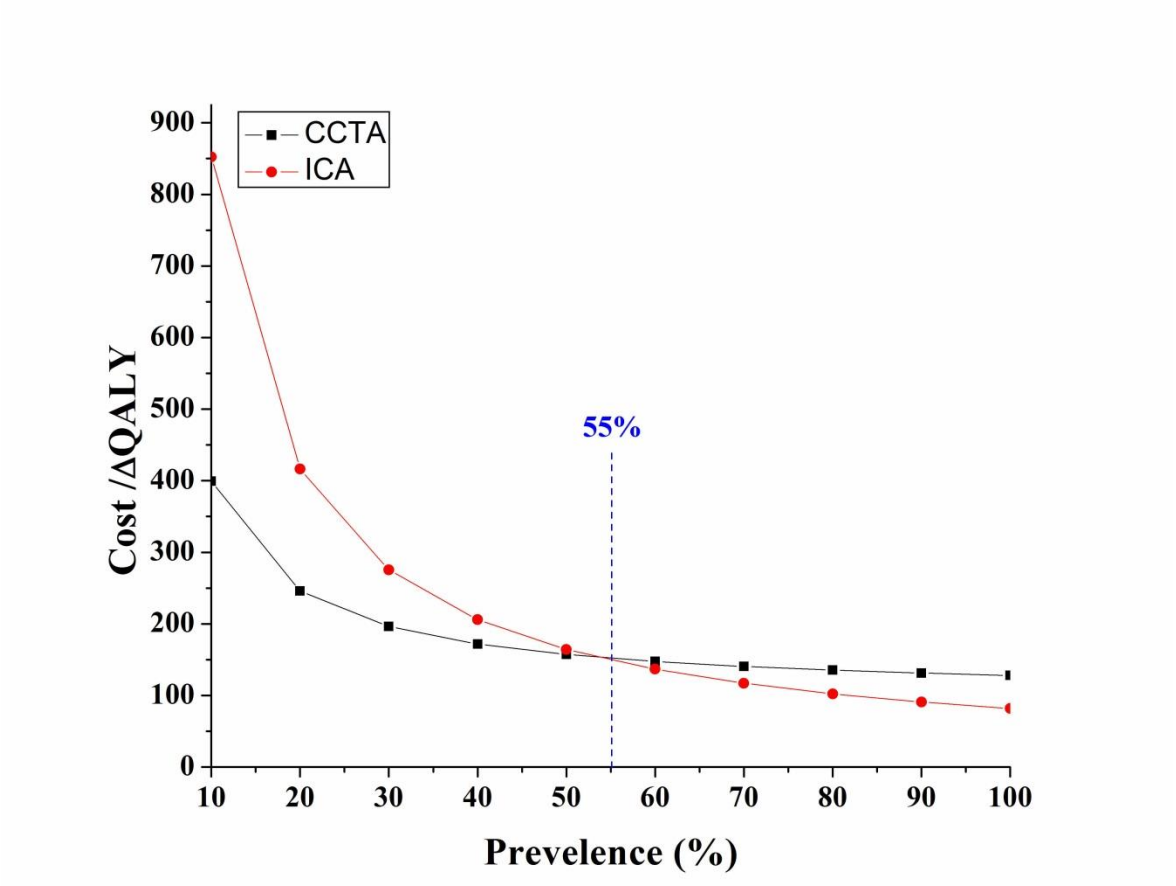

Figure 4.3 Effects of disease prevalence on cost-effectiveness in terms of ΔQALY

Table 4.26: Cost-effectiveness of CCTA and ICA at different levels of CAD prevalence in terms of ΔQALY

Cost-effectiveness (dollar) QALYs		
Prevalence	**CCTA**	**ICA**
10%	399.21	852.46
20%	245.84	416.42
30%	196.42	275.5
40%	171.89	205.84
50%	157.24	164.3
54%	128.06	152.03
55%	150	150
56%	150.92	146.55
60%	147.49	136.71
70%	140.55	117.05
80%	135.34	102.34
90%	131.30	90.91
100%	128.06	81.79

From a cost-effective point of view, our results indicate that the range of patients eligible for CCTA is smaller than previously believed and that ICA becomes the more cost-effective diagnostic approach at a disease prevalence > 55%. These findings are supported by guidelines on the assessment and diagnosis of recent onset chest pain issued by the NICE. According to NICE guidelines, CCTA is recommended if a patient has a 10-29% prevalence for CAD. The guideline further recommends ICA as the most cost-effective first test if the prevalence of CAD is >61% (Skinner et al., 2010). Close to our results, a study conducted by Dorenkamp et al. (2012) that revealed above a threshold value of disease prevalence of 55%, proceeding directly to ICA was more cost-effective than CCTA. In contrast to our results, two previous studies applied different cost-accounting practices and largely overestimated the costs of ICA or the rate of severe complications

associated with ICA. One of these previous studies demonstrated that CCTA is cost-effective in patients up to 60-70% prevalence for CAD, whereas ICA is the most cost-effective preferred approach in patients with a higher prevalence (Dewey and Hamm, 2007). The second study found CCTA to be more cost-effective than ICA even up to a prevalence for CAD of 86% (Stacul et al., 2009).

4.10 Sensitivity analysis of variables influencing cost-effectiveness

A sensitivity analysis was performed to evaluate whether some key parameters used in the mathematical model are robust within a certain range of uncertainty. Thus, cost-effectiveness calculations were repeated after:

1. Increasing and decreasing the rates of complications associated with invasive coronary angiography (R_{ICA}= 0.1% and 0.01%) (Patterson et al., 1984; Patterson et al., 1995; Dorenkamp et al., 2012; Boldt et al., 2013).
2. Taking into account higher and lower costs of complications (C=25000 dollars and 10000 dollars) (Patterson et al., 1984; Patterson et al., 1995; Dorenkamp et al., 2012; Boldt et al., 2013).
3. Increasing and decreasing CCTA sensitivity (Sn_{CCTA}= 85.84 and 99.93) and specificity (Sp_{CCTA}= 69.62 and 98.83) concerning to our accuracy calculations.

We systematically changed the numerical values of previous key parameters in the equations. Increasing (0.1%) or decreasing (0.01%) the rates of complications associated with ICA changed the cost-effectiveness threshold of CCTA marginally (56% and 53% CAD prevalence, respectively). With higher (25000 dollars) costs of complications, the cost-effectiveness of CCTA decreased marginally up to a CAD prevalence of 51%, but with lower (10000 dollars) costs of complications, the cost-effectiveness of CCTA was significantly increased up to a CAD prevalence of 62%. The most substantial changes occurred at maximally decreased and increased diagnostic accuracies. However, CCTA

remained prominent significantly more cost-effective than ICA up to a disease prevalence of 77%, in contrast with maximum decreased diagnostic accuracies, the cost-effectiveness decreased dramatically to 14%.

Finally, one of the key requirements of cost-effectiveness analysis is the identification cost per effect, which means is decrease cost with high benefit indicates increase cost-effectiveness. Likewise, as the prevalence of CAD increased, there were decreased costs per utility unit in terms of QALYs gained indicating increased cost-utility at higher disease prevalence. Thus, despite the fact that total costs increased with increasing prevalence of CAD, cost per effect and cost per utility improved. The hyperbolic relationship between CAD prevalence and cost per effect or cost per utility implicates very high costs per effect or utility unit at low disease prevalence. At a low prevalence of CAD, the rank order of cost per utility unit was principally the same as that of cost per effect in CCTA. Again, the rank order of tests changed at high disease prevalence and performing ICA as the first and only test was the most cost-effective diagnostic approach at high disease prevalence.

Our analysis shows cost-effectiveness CCTA for diagnosing CAD in patients suspected as having mild to intermediate CAD. Thus, the most important step for physicians in selecting the appropriate diagnostic approach (CCTA versus ICA) is based on a clinical estimation of disease prevalence. The score by Morise et al. (1997) provides an easy, memorable and accurate method for categorizing and subcategorizing patients with suspected CAD into probability groups upon which decisions concerning diagnostic testing could be based. Although ICA remains the gold standard for diagnosing CAD, carefully performed CCTA may be an economically efficient alternative to ICA, especially in ruling out CAD in patients with an intermediate pretest likelihood.

Chapter 5: Conclusion and Recommendations

5.1 Conclusion

The health economics of care pathways in the Gaza Strip have become under greater scrutiny due to increasing financial pressures on healthcare providers due to a scarcity of medical supplies. Cost-effective care pathways are fundamental to provide sustainable healthcare programs. Due to the overestimation of CAD using traditional risk tables, non-invasive testing has been utilized to improve risk stratification and initiate appropriate management to reduce the dependence on invasive investigations. In line with recent technological developments, CCTA is a modality that offers a detailed anatomical assessment of CAD comparable to ICA. The present study was carried out for project clinical outcomes, health care costs, and cost-effectiveness of CCTA, as compared with ICA, in the evaluation of patients with suspected CAD. Two group sample considered of 381 cases are elected from Al-Shifa hospital. Of these cases, 131 (34.38%) is selected as a census survey who have been diagnosed by CCTA. The rest of the cases are 250 (62.62%) selected who have been diagnosed by ICA. As well, 58 cases out of 250 have been referred from CCTA to ICA to confirm the diagnosis. Gender distribution shows that there are 243 (63.8%) male and 138 (36.2%) female with mean age of all patients in the sample is 54.31 years. The majority of patients that diagnosed with ICA (88.4%) has no previous cardiac intervention (angioplasty or CABG). This result disagrees with the clinical guideline ratified CCTA as the first-line investigation for all patients with suspected CAD. Regarding the estimated radiation dose, patients diagnosed with CCTA is receive approximately twice radiation with ICA, however, these doses enclosed within the strategy of saving radiation doses.

The low diagnostic yield of elective ICA was prominent in our study, about 56.4% of patients underwent ICA were considered to have a significant CAD, about 43.6% were

considered to have non-significant CAD. Consequently, baseline characteristics, such as gender, age, obesity, lifestyle, smoking status, family history of heart disease, high cholesterol, high blood pressure and diabetes were collected to predict the efficacy of patient selection for ICA in suspected CAD. The simple logistic regression analysis showed all variables significantly associated ($P < 0.05$) with the presence of significant CAD (stenosis ≥ 50). Multiple logistic regression showed that the stronger independent predictors for the presence of significant CAD at the ICA were the traditional risk factors age, obesity, lifestyle, smoking, the presence of family history of heart disease, high blood pressure and diabetes. The diagnostic yield and accuracy of CCTA in patients referred for ICA based on clinical concern for CAD and clinical criteria determined by cardiologist according to patients complain. We enrolled 58 patients underwent CCTA prior to ICA, then we analyzed the prevalence of potentially significant CAD (≥ 50% stenosis) on CCTA and calculated the diagnostic accuracy of ≥ 50% stenosis on CCTA for the detection of clinically significant CAD on ICA. ICA is the gold standard with a 100% sensitivity and 100% specificity. Compared to ICA, CCTA's sensitivity, specificity, NPV, PPV for diagnosis CAD were, 97.3%, 90.48%, 95% and 94.83%, respectively. These results confirm that CCTA appears to be an effective noninvasive alternative to exclude CAD.

Cost of CCTA and ICA per patient tested in relation to different prevalence of CAD shows that CCTA increased as a linear function of CAD prevalence. In dissimilarity, the cost for ICA did not increase significantly. Cost increases with CAD prevalence for CCTA but not significantly for ICA. In parallel, CCTA showed lower cost than ICA with CAD prevalence < 57%, but higher costs with CAD prevalence > 57%. Although the increase in total cost with increasing prevalence of CAD, cost-effectiveness improved with different CAD prevalence for both diagnostic tests. In comparison, CCTA was more cost-effective

up to a CAD prevalence of 54%, cost for one patient correctly diagnosed as having CAD was 449.7 dollars with CCTA and 452.3 dollars with ICA. Given the 63.8% CAD prevalence of the investigated patient cohort, cost for one patient correctly diagnosed as having CAD was 425.5 dollars with CCTA and 382.9 dollars with ICA. At a CAD prevalence of 55%, CCTA and ICA were equally effective with costs of 448 dollars. With higher disease prevalence (>55%), ICA became more cost-effective.

The decrease in cost per ΔQALY indicates increased cost-effectiveness. Regardless of the increase in cost with increasing prevalence of CAD, ΔQALY improved with different CAD prevalence for both diagnostic tests. At a CAD prevalence of 55%, CCTA and ICA were equally effective in term ΔQALY with costs of 150 dollars.

CCTA was more cost-effective in term ΔQALY up to a CAD prevalence of 54% ranging from 399.21 dollars (10% prevalence) to 128.06 dollars (54% prevalence). By contrast, ICA shows better cost-effectiveness for prevalence of 56%–100%, with a cost per in term ΔQALY of CAD between 146.55 dollars (56% prevalence) and 81.79 dollars (100% prevalence)

Finally, data call for a more rational approach to avoid unnecessary testing and appropriate utilization of noninvasive diagnostic testing is important to ensure that patients with CAD are referred to ICA for diagnosis and that patients who do not have CAD can avoid unnecessary invasive testing. Although ICA has been the gold standard for evaluating CAD, it should not be routinely performed as an initial test to assess CAD in patients with suspected CAD by the recent guidelines, due to cost, invasiveness, and measurable risk (Montalescot et al., 2014). CCTA is a rapidly growing, non-invasive imaging modality that developed quickly over the last decade, and its role for evaluation of CAD becomes of great promise with high diagnostic accuracy (Meijboom et al., 2008; Miller et al., 2008).

5.2 Recommendations

Based on the study analysis, findings and conclusions, the researcher propose the following recommendations:

1. Invasive coronary angiography should be considered for patients with CAD whose clinical characteristics and results of noninvasive testing indicate a high likelihood of severe stenosis and when the benefits are deemed to exceed the risk.
2. Patients with suspected CAD should receive a thorough history and physical examination to assess the probability of CAD prior to additional testing.
3. Coronary computed tomography angiography might be reasonable for patients with a low to intermediate pretest probability of CAD who have at least moderate physical functioning or no disabling comorbidity.
4. Patients with CAD diagnosed by CCTA should be carefully followed to monitor the progression of disease, complications and adherence.
5. Choices regarding diagnostic options should be made through a clear policy of shared decision-making with explaining information about risks, benefits, and costs to the patient.
6. Coronary computed tomography angiography can be useful as a first-line test for risk assessment in patients with suspected CAD to an adequate workload.
7. Invasive coronary angiography is not recommended to assess risk in asymptomatic patients with no evidence of ischemia on CCTA.
8. The low cost and high sensitivity of CCTA make it the non-invasive test of choice in the evaluation of non-significant CAD.
9. The supervising cardiologist should have advanced knowledge and expertise in CCTA. Certification of advanced expertise in CCTA is desirable.

10. Avoidance of unnecessary ICA may result in cost savings, even if positive results require confirmation by ICA.
11. In higher risk population a strategy of sending all patients directly to ICA is likely to be cost-effective.
12. The performance and interpretation of CCTA require special training is recommended to maintain competence in the procedure.
13. The rapid technological advances of CCTA have raised promise that this imaging modality may fulfill the role of a gold-standard non-invasive investigation of the CAD.

5.2.1 Recommendation for further researches

1. Enhancement researches to focus on investigating the merit of integrating CCTA into patient management and to determine its effect on treatment and clinical outcomes.
2. Future study protocols should delineate, a priori, possible adverse events and consequences (including those related to psychological aspects of testing and radiation exposure) and report their occurrence per the protocol.
3. Forthcoming studies should incorporate standardized, validated measures for patient-reported outcomes and document the impact of testing, including downstream testing, on patient psychological status (particularly with false positive results), health status and resource use.
4. Additional sufficiently powered studies examining the impact of testing on hard clinical outcomes (death, myocardial infarction) at longer-term follow up (>12 months) are needed.
5. Studies (randomize control trials, pragmatic trials or methodologically rigorous comparative cohort studies) that compare functional tests using more state of the art technology and methods with each other and with anatomic tests are needed.

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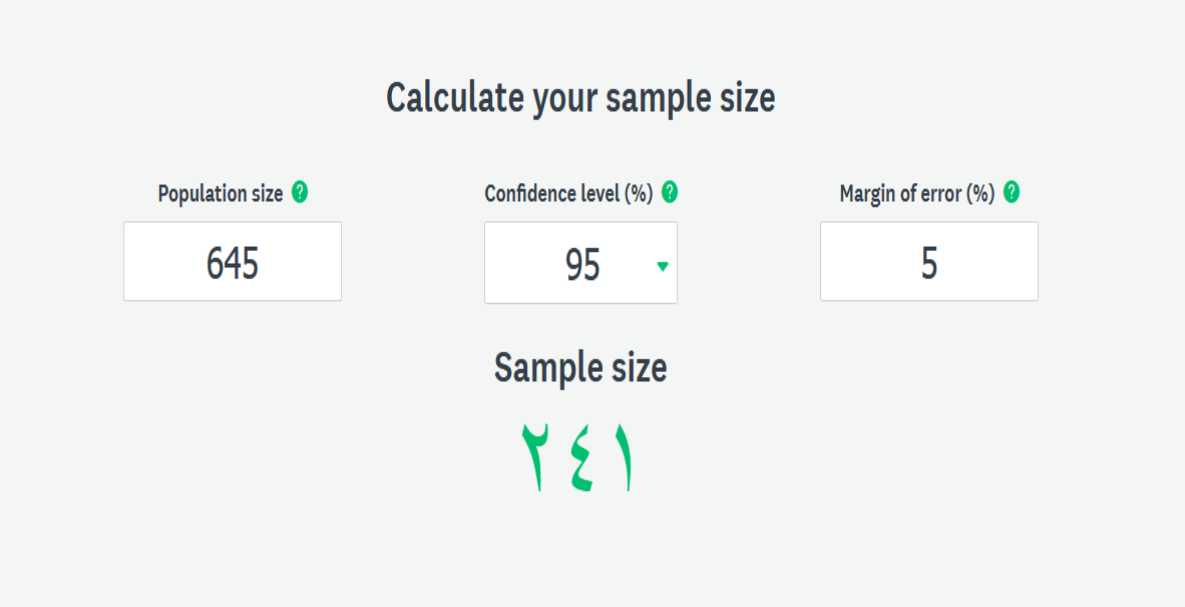
Annexes

Annex 1: Map of Palestine

Annex 2: Map of Gaza Strip

Annex 3: Sample size calculation



Annex 4 Questionnaire for Patient undergo CCTA Procedure

Serial number		**ID number**		**Date: / / 2018**	
Hospital:		**Al-Shifa Hospital**			
A. Personal Information					
A1	**Gender**		**Male**		**Female**
A2	**Age ---------- Years**	**A3**	**Weight ---------- kg**	**A4**	**Height ---------- cm**
B. Personal Habits					
B1	**Lifestyle**	**B1.1**	**Sedentary lifestyle**		
		B1.2	**Regular exerciser (30mins more than 5 days/week)**		
		B1.3	**Hard and stress work**		
B2	**Smokinghabit**	**B2.1**	**Currently smoking**		
		B2.2	**Non smoker**		
		B2.3	**Ex-smoker < 12 months**		
		B2.4	**Ex-smoker >12 months**		
C. Medical History					
C1	**Family history of heart disease**		**C2**	**Heart attack**	
C3	**Rapid or irregular heartbeats**		**C4**	**Chest pain or discomfort**	
C5	**High cholesterol**		**C6**	**High blood pressure**	
C7	**Asthmaor lung disease**		**C8**	**Shortness of breath**	
C9	**History of allergies**		**C10**	**Diabetes**	
C11	**Impaired kidney function**		**C12**	**Others**……	

D. History of Cardiac Medical Intervention					
D1	**Angioplasty/Stent or Balloon**		**D2**	**Heart Valve Replacement**	
D3	**Coronary artery bypass Graft**		**D4**	**Thoracic Vessels Surgery**	
D5	**Pacemaker**		**D6**	**Non cardiac intervention**	

E. Previous Cardiac Examination					
E1	**Resting Electrocardiography**		**E2**	**Exercise Stress Test**	
E3	**Cardiac Echocardiography**		**E4**	**Cardiac Catheterization**	
E5	**Prior Calcium Score CT**		**E6**	**Coronary artery CT**	
E7	**Others**……				

F. Pre-Procedure Preparation						
F1	**Pulse**	**_ _ _ _beats per minute**				
F2	**Blood Pressure**	**_ _ _ _mm Hg**				
F3	**Kidney Function**	**Urea_ _ _ _mg/dL**		**Creatinine_ _ _ _mg/dL**		
F4	**Hepatitis Test**		**Hepatitis C (HCV)**		**Hepatitis B (HBV)**	
F5	**Coagulation Test**	**PT_ _ _ _**	**PTT_ _ _ _**	**INR_ _ _ _**		
F6	**Beta Blockers Drugs**		**Yes**		**No**	
F7	**Sublingual Nitroglycerin**		**Yes**		**No**	

G. Appointment Period					
G1	**Emergency Appointment**		**G2**	**Elective Appointment**	

G3	**Appointment time period**	**G3.1**	**Within 24 hours**	
		G3.2	**More than 24 hours to 72 hours**	
		G3.3	**More than 72 hours to One weak**	
		G3.4	**More than One weak to two weak**	
		G3.5	**More than two weak**	
H. Items during CCTA procedure				
H1	**Estimated Radiation Dose _ _ _ _ mSv**			
H2	**Contrast Volume _ _ _ _mL**			
H3	**Procedure time period _ _ _ _ minute**			
H4	**Supplies Used**	**H4.1**	**Cannula**	
		H4.2	**Cotton**	
		H4.3	**Alcohol**	
		H4.4	**Extension tube**	
		H4.5	**Plaster**	
		H4.6	**Normal saline**	
H5	**Staff of Procedure**	**H5.1**	**Medical Imaging Specialists**	
		H5.2	**Radiologist**	
		H5.3	**Nurse**	

I. Potential Complications of CCTA					
I1	**Allergic reaction**		**I2**	**Shock**	
I3	**Death**		**I4**	**Others**……	
J. Diagnosis of CCTA					
J1	**Normal**		**J2**	**Inconclusive result**	
J3	**Congenital anomaly**		**J4**	**Extra-Cardiac Pathology**	
J5	**Coronary**		**J5.1**	**Plaque without stenosis**	
			J5.2	**Mild Stenosis <50%**	
			J5.3	**Moderate Stenosis 50%-70%**	
			J5.4	**High stenosis >70%**	
J6	**Grafts**		**J6.1**	**Occlusion**	
			J6.2	**Significant stenosis**	
J7	**Stent**		**J7.1**	**Stent Restenosis**	
			J7.2	**Blooming and motion artifacts**	
K. Reporting Period					
K1	**Reporting time period**		**_ _ _ _ minute**		

Annex 5: Questionnaire for Patient undergo ICA Procedure

Serial number		**ID number**		**Date: / / 2018**	
Hospital:		**AL Shifa Hospital**			
A. Personal Information					
A1	**Gender**		**Male**		**Female**
A2	**Age ---------- Years**	**A3**	**Weight ---------- kg**	**A4**	**Height ---------- cm**
B. Personal Habits					
B1	**Lifestyle**	**B1.1**	**Sedentary lifestyle**		
		B1.2	**Regular exerciser (30mins more than 5 days/week)**		
		B1.3	**Hard and stress work**		
B2	**Smokinghabit**	**B2.1**	**Currently smoking**		
		B2.2	**Non smoker**		
		B2.3	**Ex-smoker < 12 months**		
		B2.4	**Ex-smoker >12 months**		
C. Medical History					
C1	**Family history of heart disease**		**C2**	**Heart attack**	
C3	**Rapid or irregular heartbeats**		**C4**	**Chest pain or discomfort**	
C5	**High cholesterol**		**C6**	**High blood pressure**	
C7	**Asthmaor lung disease**		**C8**	**Shortness of breath**	
C9	**History of allergies**		**C10**	**Diabetes**	
C11	**Impaired kidney function**		**C12**	**Others**……	

D. History of Cardiac Medical Intervention					
D1	**Angioplasty/Stent or Balloon**		**D2**	**Heart Valve Replacement**	
D3	**Coronary artery bypass Graft**		**D4**	**Thoracic Vessels Surgery**	
D5	**Pacemaker**		**D6**	**Non cardiac intervention**	

E. Previous Cardiac Examination					
E1	**Resting Electrocardiography**		**E2**	**Exercise Stress Test**	
E3	**Cardiac Echocardiography**		**E4**	**Cardiac Catheterization**	
E5	**Prior Calcium Score CT**		**E6**	**Coronary artery CT**	
E7	**Others**……				

F. Pre-Procedure Preparation							
F1	**Pulse**	**_ _ _ _beats per minute**					
F2	**Blood Pressure**	**_ _ _ _mm Hg**					
F3	**Kidney Function**	**Urea_ _ _ _mg/dL**		**Creatinine_ _ _ _mg/dL**			
F4	**Hepatitis Test**		**Hepatitis C (HCV)**		**Hepatitis B (HBV)**		
F5	**Coagulation Test**	**PT_ _ _ _**		**PTT_ _ _ _**		**INR_ _ _ _**	
F6	**Complete Blood Count (CBC)**		**Yes**		**No**		
F7	**Chest X-Ray (CXR)**		**Yes**		**No**		

G. AppointmentPeriod					
G1	**Emergency Appointment**		**G2**	**Elective Appointment**	

G3	**Appointment time period**	**G3.1**	**Within 24 hours**	
		G3.2	**More than 24 hours to 72 hours**	
		G3.3	**More than 72 hours to One weak**	
		G3.4	**More than One weak to two weak**	
		G3.5	**More than two weak**	

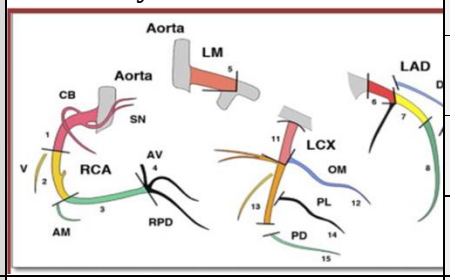
H. Items during ICA procedure

H1	**Site of Incision**		**Femoral**		**Radial**
H2	**Estimated Radiation Dose**		**_ _ _ _ mSv**		
H3	**Contrast Volume**		**_ _ _ _mL**		
H4	**Procedure time period**		**_ _ _ _ minute**		

H5	**Supplies Used**	**H5.1**	**Cannula**	
		H5.2	**Cotton**	
		H5.3	**Alcohol**	
		H5.4	**Extension tube**	
		H5.5	**Plaster**	
		H5.6	**Normal saline**	
		H5.7	**Femoral sheath F6 11 cm (Kit)**	
		H5.8	**Coronary Guide wire J TIP 0.035 - 150 cm**	
		H5.9	**Jodkins left JL 4 catheter Fr 6**	

		H5.10	**Jodkins right JR 4 catheter Fr 6**		
		H5.11	**lower lock syringe 12c**		
		H5.12	**Manifold 3 way- right off**		
		H5.13	**Pressure line male – female 100 cm**		
		H5.14	**Puncture needle G 18, 7cm**		
		H5.15	**Gauze**		
		H5.16	**Poledin 10 %**		
		H5.17	**Syringe 3ml -10 ml -20 ml**		
		H5.18	**Needle G21**		
		H5.19	**Heparin 2 ml**		
		H5.20	**IV sit**		
H6	**Staff of Procedure**	**H6.1**	**Medical Imaging Specialists**	**No.1**	
				No.2	
		H6.2	**Cardiologist**	**No.1**	
				No.2	
				No.3	
		H6.3	**Nurse**	**No.1**	
				No.2	
				No.3	
				No.4	
				No.5	

I. Potential Complications of ICA					
I1	**Trauma of the arteries, veins and nerves**		**I2**	**Bleeding**	
I3	**Infection**		**I4**	**Allergic reaction**	

I5	**Thrombosis**		**I6**	**Embolism**	
I7	**Myocardial infarction**		**I8**	**Shock**	
I9	**Cerebral insult**		**I10**	**Emergency operation**	
I11	**Cardiopulmonary resuscitation**		**I1**	**Coronary dissection**	
I13	**Death**		**I4**	**Others**……	
J. Diagnosis Results of ICA					
J1	**Normal**		**J2**	**Inconclusive result**	
J3	**Congenital anomaly**		**J4**	**Ectasia**	
J5	**Coronary** 		**J5.1**	**Plaque without stenosis**	
			J5.2	**Mild Stenosis <50%**	
			J5.3	**Moderate Stenosis 50%-70%**	
			J5.4	**High stenosis >70%**	
J6	**Grafts**		**J6.1**	**Occlusion**	
			J6.2	**Significant stenosis**	
J7	**Stent**		**J7.1**	**Stent Restenosis**	
K. Reporting Period					
K1	**Reporting time period**		**_ _ _ _ minute**		
L. Post ICA Procedure					
L1	**Recovery time period**		**_ _ _ _ hours**		
L2	**Recovery Supplies and Examination**		**Normal saline**		
			IV sit		
			Gauze		
			Plaster		
			Drugs		
			Resting Electrocardiography		

Annex 6: Semi-structured in-depth interviews questions

- **For Cardiologists**

1. Is there a standard protocol or clear policy to refer suspected CAD patients to diagnosis approach correlated with up to date the international guidelines?
2. Is the patient gender has an effect on selecting diagnostic modality (CCTA or ICA)?
3. What do you explain that the majority of patients are male and that the proportion of females in both diagnostic modality is limited?
4. Is the previous cardiac medical intervention of the patient is affected in direct the patient to the diagnostic modality?
5. How satisfied are you with the coronary CT diagnoses performed at our hospital?
6. What the causes which influence on the radiation dose which received during the ICA?
7. Which explains that a high proportion of patients who underwent ICA with unnecessary for ICA?

- **For Radiologist and medical imaging specialist**

1. What the challenges to perform the optimal CCTA procedure?
2. There is an application to radiation safety protocol?
3. What the reasons which influence the radiation dose which received during the CCTA?

Annex 7: Approval from Helsinki committee –Gaza governorate

المجلس الفلسطيني للبحث الصحي

Palestinian Health Research Council

تعزيز النظام الصحي الفلسطيني من خلال مأسسة استخدام المعلومات البحثية في صنع القرار

Developing the Palestinian health system through institutionalizing the use of information in decision making

Helsinki Committee

For Ethical Approval

Date: 2017/08/07 **Number:** PHRC/HC/236/17

Name: HUSAM H. MANSOUR الاسم:

We would like to inform you that the committee had discussed the proposal of your study about:

نفيدكم علماً بأن اللجنة قد ناقشت مقترح دراستكم حول:

Coronary Computed Tomography Angiography Versus Invasive Coronary Angiography at Gaza Governmental Hospitals: Cost Effectiveness Analysis

The committee has decided to approve the above mentioned research. Approval number PHRC/HC/236/17 in its meeting on 2017/08/07

و قد قررت الموافقة على البحث المذكور عاليه بالرقم والتاريخ المذكوران عاليه

Signature

Member **Member**

Chairman

Genral Conditions:-

1. Valid for 2 years from the date of approval.
2. It is necessary to notify the committee of any change in the approved study protocol.
3. The committee appreciates receiving a copy of your final research when completed.

Specific Conditions:-

E-Mail:pal.phrc@gmail.com

Gaza - Palestine غزة - فلسطين

شارع النصر - مفترق العيون

Annex 8: An agreement letter from MoH Hospitals General Administration

State of Palestine
Ministry of health

دولة فلسطين
وزارة الصحة

السيد : رامي عيد سليمان العبادله المحترم

التاريخ:27/11/2017
رقم المراسلة 178870

مدير عام بالوزارة /الإدارة العامة لتنمية القوى البشرية - /وزارة الصحة

السلام عليكم ,,,

الموضوع/ تسهيل مهمة باحث/ حسام منصور

التفاصيل //
بخصوص الموضوع أعلاه، يرجي تسهيل مهمة الباحث/ حسام حسن منصور
الملتحق ببرنامج ماجستير الصحة العامة – مسار الإدارة الصحية- جامعة القدس أبوديس بغزة في إجراء بحث بعنوان -:
"Coronary Computed Tomography Angiography Versus Invasive Coronary Angiography At Gaza Governmental Hospitals: cost Effectiveness Analysis "
حيث الباحث بحاجة للاطلاع على الملف الطبي وتعبئة استبانة من عدد من مرضى القلب الذين خضعوا للقسطرة القلبية والاشعة المقطعية في مجمع الشفاء الطبي ومستشفى غزة الأوربي.
نأمل توجيهاتكم لذوي الاختصاص بضرورة الحصول على الموافقة المستنيرة من المرضى الذين هم على استعداد للمشاركة في البحث ومن ثم تمكين الباحث من التواصل معهم، بما لا يتعارض مع مصلحة العمل وضمن أخلاقيات البحث العلمي، ودون تحمل الوزارة أي أعباء أو مسئولية.
وتفضلوا بقبول التحية والتقدير،
ملاحظة / تسهيل المهمة الخاص بالدراسة أعلاه صالح لمدة 6 أشهر من تاريخه.

محمد ابراهيم محمد السرساوي
مدير دائرة/الإدارة العامة لتنمية القوى البشرية -

التحويلات

■ محمد ابراهيم محمد السرساوي(مدير دائرة)	← رامي عيد سليمان العبادله(مدير عام بالوزارة)	إجراءاتكم بالخصوص(27/11/2017)
■ رامي عيد سليمان العبادله(مدير عام بالوزارة)	← عبد اللطيف محمد محمد الحاج(مدير عام بالوزارة)	إجراءاتكم بالخصوص(28/11/2017)
■ عبد اللطيف محمد محمد الحاج(مدير عام بالوزارة)	← مدحت عباس خضر حسن (مدير عام بالوزارة)	إجراءاتكم بالخصوص(28/11/2017)
■ عبد اللطيف محمد محمد الحاج(مدير عام بالوزارة)	← يوسف فوزي اسماعيل العقاد(مدير مستشفى)	إجراءاتكم بالخصوص(28/11/2017)
■ مدحت عباس خضر حسن (مدير عام بالوزارة)	← ()	إجراءاتكم بالخصوص(28/11/2017)
■ مدحت عباس خضر حسن (مدير عام بالوزارة)	← رافت حامد يوسف حمدونه(مدير دائرة)	إجراءاتكم بالخصوص(28/11/2017)
■ مدحت عباس خضر حسن (مدير عام بالوزارة)	← زهير محمود احمد نوفل(مدير دائرة التمريض)	إجراءاتكم بالخصوص(28/11/2017)
■ مدحت عباس خضر حسن (مدير عام بالوزارة)	← ()	إجراءاتكم بالخصوص(28/11/2017)
■ يوسف فوزي اسماعيل العقاد(مدير مستشفى)	← اتحاد شكري شاكر شبير(رئيس قسم اداري)	لعمل اللازم(28/11/2017)
■ يوسف فوزي إسماعيل العقاد(مدير مستشفى)	← كمال صبحي عبدالحميد موسى(مدير إداري)	لعمل اللازم(28/11/2017)

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تلفون. 8-2846949 (+970)
فاكس. 8-2826295 (+970)

Annex 9: List of experts (interviewees)

Name	Affiliation
Radiologists	
Dr. Mohammad Mattar	Al-Shifa hospital- MoH
Dr. Saadi Jaber	Gaza European hospital- MoH
Dr. Marwan Mattar	Gaza European hospital- MoH
Cardiologists	
Dr. Mohammed Habeeb	Al Shifa hospital- MoH
Dr. Mohammed Abu Hasiera	Al Shifa hospital- MoH
Medical Imaging Specialist	
Mr. Moussa Abo zour	Al Shifa hospital- MoH
Mr. Moussa Al Nahal	Gaza European hospital- MoH

Annex 10: List of experts (arbitrators)

No.	Name	Affiliation
1.	Dr. Yahia Abed	Al- Quds University
2.	Dr. Ahmed Najim	Al Azhar University
3.	Dr. Samy Alagha	Al Azhar University
4.	Dr. Mazen Abo Qamar	Al Azhar University
5.	Dr. Ihab Naser	Al Azhar University
6.	Dr. Mohammed Matter	MoH
7.	Dr. Mohammed Habeeb	MoH
8.	Dr. Saadi Jaber	MoH
9.	Dr. Mohammed Abu Hasiera	MoH
10.	Mr. Ibrahiem Abass	MoH
11.	Mr. Moussa Abo zour	MoH
12.	Mr. Maher Soliman	MoH

Abstract in Arabic

"تصوير الشرايين التاجية بواسطة الأشعة المقطعية مقابل القسطرة القلبية التشخيصية في مستشفيات غزة الحكومية: تحليل فعالية التكلفة"

إعداد: حسام حسن حسين منصور

إشراف: الدكتور/ ياسر صالح العجرمي

ملخص الدراسة

مقدمة

الأمراض القلبية تمثل عبء ملحوظ في فلسطين ، والذي يعتبر أول سبب رئيسي للوفاة والذي يرهق كاهل موازنات الرعاية الصحية. توجد عدة طرق للتشخيص الإشعاعي لمرض الشريان التاجي (CAD)بدرجات متفاوتة من الدقة والتكلفة. في قطاع غزة ، هناك اتجاه في وزارة الصحة نحو الحاجة إلى قاعدة أدلة كافية لتبرير تكلفة أي إجراء وذلك سعيا لتوفير معلومات كافية لفعالية التكلفة من أجل مساعدة الأطباء وصناع القرار في اختيار استراتيجية التشخيص الأكثر فاعلية.

الهدف من الدراسة

هدفت هذه الدراسة لتحديد فعالية التكلفة من تصوير الشرايين التاجية بواسطة الأشعة المقطعيةCCTA مقارنة مع القسطرة القلبية التشخيصية ICA في المرضى الذين يشتبه بتعرضهم لمرض الشريان التاجي.

منهجية الدراسة

الدراسة عبارة عن دراسة تحليلية لبيانات تم جمعها (كمية و نوعية)، الكمية باستخدام استبانة لجمع البيانات لتتبع الحالات التي خضعت لتصوير الشرايين التاجية بواسطة الأشعة المقطعيةCCTA وكان عددها 131 حالة. اضافة لذلك تم دراسة 250 حالة خضعوا للقسطرة القلبية بحيث شملت على 58 حالة قد خضعوا من قبل لتصوير الشرايين التاجية بواسطة الأشعة المقطعيةCCTA وذلك لتحديد الدقة التشخيصية لتصوير الشرايين التاجية بواسطة الأشعة المقطعيةCCTA. بالنسبة للمعلومات النوعية تم جمعها من خلال 7 مقابلات شخصية مع مختلف الأخصائيين والذين يشاركون في عملية تصوير و تشخيص مرض الشريان التاجي وهم أخصائي القلب والأشعة المقطعية والتصوير الطبي.

تحليل البيانات

تم تحليل بيانات الدراسة باستخدام برنامج التحليل الإحصائي (SPSS) وقد تم عمل جداول توضح التحليل الوصفي لبيانات العينة وأيضاً تم عمل الفحوصات الإحصائية المختلفة لإيجاد علاقات بين المتغيرات.

تم استخدام نموذج رياضي يعتمد على Bayes' theorem ، وذلك لتقيّيم فعالية تكلفة الاستراتيجيات في التشخيص لمجموعات المرضى اعتمادا على مدى انتشار المرض.

تم تعريف فعالية الاختبارات التشخيصية بطريقتين ، الأولى معيار الفعالية هو قدرة اختبار تشخيصي لتحديد مرض الشريان التاجي بدقة ويمثل هذا التعريف نهجا مباشرا بافتراض أن الهدف الوحيد للاختبار هو إجراء تشخيص صحيح. والتعريف الثاني للفعالية هو تفسير النتائج الصحية المستقبلية للمرضى الذين يخضعون للاختبارات حيث من المفترض أن التشخيص الصحيح لمرض الشريان التاجي من شأنه تمكين المرضى من تلقي العلاج الأمثل مما يؤدي إلى تحسين البقاء على قيد الحياة بدون معاناة خلال فترة المتابعة.

تم استخدام برنامج اكسل (Excel) لحساب وتحليل التكلفة ومن ثم تم استخدام برنامج Origin pro 7.0 لرسم الأشكال البيانية التي توضح العلاقة بين التكلفة و الفعالية وذلك بهدف تحقيق أهداف الدراسة.

نتائج الدراسة

أظهرت الدراسة أن حساسية وخصوصية تصوير الشرايين التاجية بواسطة الأشعة المقطعية CCTA كانت 97.3٪ و 90.48٪ على التوالي .بالإضافة أن القيمة التنبؤية الإيجابية كانت 97.74 ٪ وكانت القيمة التنبؤية السلبية 95 ٪.

بالنسبة لتحليل التكلفة أظهرت الدراسة أن التكاليف المباشرة الإجمالية لإجراء القسطرة القلبية التشخيصية ICA (234.23 دولار) وهي تمثل حوالي 4.6 مرة أكثر من تكلفة إجراء تصوير الشرايين التاجية بواسطة الأشعة المقطعية CCTA (50.8 دولار). التكلفة الغير الضرورية للقسطرة القلبية التشخيصية ICA ظهرت بشكل ملموس في هذه الدراسة، حيث أن 43.6٪ من المرضى لم يستفيدوا من إجراء القسطرة القلبية التشخيصية ICA بسبب عدم وجود لمرض الشريان التاجي بشكل ذو أهمية و بتكلفة غير مبررة قدرها 26621 دولار للمرضى الذين خضعوا لهذا الفحص في هذه الدراسة.

تكلفة تصوير الشرايين التاجية بواسطة الأشعة المقطعية CCTA زادت كدالة خطية لانتشار لمرض الشريان التاجي . في المقابل ، فإن تكلفة القسطرة القلبية التشخيصية ICA لم تزيد بشكل كبير. على وجه التحديد، أظهرت الدراسة أن

تكلفة تصوير الشرايين التاجية بواسطة الأشعة المقطعية CCTA تكلفة أقل من تكلفة القسطرة القلبية التشخيصية ICA مع انتشار لمرض الشريان التاجي بنسبة اقل من ٪ 57 ولكن ارتفاع التكاليف مع انتشار اكثر من 57٪.

وفيما يتعلق بالفعالية من حيث التكلفة بالنسبة للتشخيص الصحيح لمرض الشريان التاجي ، يجدر الإشارة إلى أن كل من تصوير الشرايين التاجية بواسطة الأشعة المقطعية CCTA و تكلفة القسطرة القلبية التشخيصية ICA كانت فعالة بنسبة 448 دولار عند 55 ٪ انتشار لمرض الشريان التاجي.

ولكن أظهرت البيانات أن CCTA أكثر فعالية من حيث التكلفة في المرضى الذين يعانون من انتشار يصل إلى 54٪ مع تكلفة التشخيص الصحيح من CAD تتراوح بين 1139.1 دولار (10 ٪ انتشار لمرض الشريان التاجي) إلى 449.7 دولار (54 ٪ انتشار لمرض الشريان التاجي). في المقابل ، أظهرت القسطرة القلبية التشخيصية ICA فعالية أفضل من حيث التكلفة مع نسبة الانتشار اكثر من 55 ٪ مع تكلفة التشخيص الصحيح بين 436.13 دولار (56 ٪ انتشار لمرض الشريان التاجي) و 244.23 دولار (100 ٪ انتشار لمرض الشريان التاجي).

فيما يتعلق بتحسن عدد السنوات المصححة بجودة الحياة (ΔQALY) مع فعالية التكلفة ، كان هذا الاتجاه مماثلا فعندما كان معدل انتشار مرض الشريان التاجي بنسبة 55٪ كان كل من تصوير الشرايين التاجية بواسطة الأشعة المقطعية CCTA القسطرة القلبية التشخيصية ICA كانت فعالة بنفس القدر (150 دولار)

تصوير الشرايين التاجية بواسطة الأشعة المقطعية CCTA أكثر فعالية من حيث التكلفة بالنسبة لتحسن عدد السنوات المصححة بجودة الحياة ΔQALY يتراوح من 399.21 دولار (10 ٪ انتشار لمرض الشريان التاجي) إلى 128.06 دولار (54 ٪ انتشار لمرض الشريان التاجي). في المقابل ، يظهر بأن القسطرة القلبية التشخيصية ICA فعالية أفضل من حيث التكلفة من حيث نسبة الانتشار من 56 ٪ إلى 100٪ ، مع وجود تكلفة تتراوح بين 146.55 دولار (56 ٪ انتشار لمرض الشريان التاجي) و 81.79 دولار (100 ٪ انتشار لمرض الشريان التاجي).

التوصيات

توصي الدراسة بشدة بأن القسطرة القلبية التشخيصية ICA يجب أن يُنظر فيه للمرضى الذين يعانون من مرض الشريان التاجي والذين تشير خصائصهم السريرية إلى احتمالية عالية لوجود تضيق كبير وعندما تعتبر المنافع أكثر من الخطر .يجب أن يتلقى المرضى المشتبه في تعرضهم لمرض الشريان التاجي تاريخًا مرضيا شاملاً لتقييم احتمال لمرض الشريان التاجي قبل إجراء اختبارات تشخيصية إضافية. اضافة لذلك تصوير الشرايين التاجية بواسطة الأشعة المقطعية CCTA يمكن أن يكون مفيدا كاختبار بدرجة أولى لتقييم المخاطر في المرضى المشتبه في تعرضهم لمرض الشريان التاجي بدرجات معتدلة إلى متوسطة.