Coronary Computed Tomography Angiography for Early Triage of Patients with Acute Coronary Syndrome

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Abstract: **It is unclear whether an evaluation incorporating coronary computed tomographic angiography (CCTA) is more effective than standard evaluation in the emergency department in patients with symptoms suggestive of acute coronary syndromes.**

Methods: In this single trial, we randomly assigned patients 20 to 75 years of age with symptoms suggestive of acute coronary syndromes but without ischemic electrocardiographic changes or an initial positive troponin test to early CCTA or to standard evaluation in the emergency department on Mondays and thusdays during daylight hours between(May 2014 to june 2015). The primary end point was length of stay in the hospital. Secondary end points included rates of discharge from the emergency department, major adverse cardiovascular events at 28 days, and cumulative costs. Safety end points were undetected acute coronary syndromes.

Results: The rate of acute coronary syndromes among 95 patients with a mean (±SD) age of 50.987±8 years (24.2% women), (75.8 % men).After early CCTA, as compared with standard evaluation, the mean length of stay in the hospital was reduced by 17 hours (P<0.0001) and more patients were discharged directly from the emergency department (P<0.0001). There were no undetected acute coronary syndromes and no significant differences in major adverse cardiovascular events at 28 days.

The total cumulative mean cost of care was less in the CCTA group as compared to the standard evaluation group (45000EP and71800 EP, respectively; P =<0.0001).

Conclusions: In patients in the emergency department with symptoms suggestive of acute coronary syndromes, incorporating CCTA into a triage strategy improved the efficiency of clinical decision making, as compared with a standard evaluation in the emergency department, with decrease in the overall costs of care.

Keywords: **coronary computed tomographic angiography (CCTA), electrocardiographic (ECG).**

1. INTRODUCTION

Treatment of patients with acute chest pain but an inconclusive initial evaluation with the use of biomarkers and electrocardiographic (ECG) testing is often diagnostically challenging and inefficient. The majority of patients with acute coronary syndromes have underlying coronary artery disease(1) Contrast-enhanced coronary computed tomographic angiography (CCTA) has high sensitivity and specificity for the detection of clinically significant coronary artery disease, as compared with invasive coronary angiography, in patients in stable condition with suspected or known coronary artery disease(2-5) Rule Out Myocardial Infarction/Ischemia Using Computer Assisted Tomography (ROMICAT-I), (6) a blinded observational study involving patients in the emergency department with suspected acute coronary syndromes, and other studies(7, 8) have shown that normal findings on CCTA have a very high negative predictive value for ruling out acute coronary syndromes during the index hospitalization and the occurrence of major adverse cardiovascular events over the next 2 years.(7, 9) The results of two previous randomized, multicenter trials(10, 11) suggest that CCTA may facilitate safe and earlier triage of low-risk patients and that CCTA can rule out coronary artery disease faster than stress

myocardial-perfusion imaging. However, imaging the coronary anatomy with CCTA can involve more procedures and greater costs than functional testing. (12) Thus, equipoise exists regarding the effectiveness of incorporating CCTA into an evaluation strategy in the emergency department. The objectives of this study were to compare the effectiveness of a CCTA-based evaluation strategy with that of standard evaluation in the emergency department for patients with symptoms suggestive of an acute coronary syndrome and to evaluate the downstream testing, cost, and radiation exposure associated with CCTA.

2. PATIENTS & METHODS

A total of 440 patients with a primary complaint of chest pain lasting> 15 minutes were screened during the enrollment period. Exclusion criteria were present in 345 patients (impaired renal function (n=100), history of CAD defined as previous stent placement or CABG (n=120), ECG diagnostic for myocardial ischemia or positive initial biomarkers (n=75), clinically unstable (n=45) and who refused participation or sign consent (n=5) Thus, the study cohort consisted of 95 patients .

Patients:

The study included 95 patients admitted to the National Heart Institute.

Patient Population:

The study population of the study consisted of patients presented with chief complaint of acute chest pain lasting >15 minutes during the past 24 hours, normal initial cardiac enzymes and initial ECG without evidence of myocardial ischemia. In all patients, ED physicians had sufficient clinical suspicion for an ischemic origin of chest pain and admitted these patients to the hospital to rule out ACS.

The study was carried from 8am to 8pm on Monday and Thursday (May 2014 to june 2015).

Eligible patient were identified, provided written informed concent, and were randomly assigned at their intial evalution in the emergency department .patient were randomly assigned in a 1:1 ratio to either CCTA as part of the intial evalution in the emeregency department(group 1) or the standard evaluation strategy in the emeregency department(group 2).

Standered evalution included serial ECG (every 2 hours)and serial cardiac biomarker CKMB and troponin in addition to clinical follow up for 72 hours, those with negative results were assessed with maximal treadmeall excersice test using BRUCE protocol before discharge.

Inclusion Criteria:

1. Age > 20 years.

2. Greater than 15 minutes of chest pain within the previous 24 hours.

3. Admitted for rule out ACS through standard care protocols.

4. Sinus rhythm.

5. Ability to perform a breath hold of 10–15 seconds (in CCTA group).

Exclusion Criteria:

1. Elevated cardiac enzymes in the initial blood sample obtained in the ER.

2. New diagnostic ECG changes (ST-segment elevation or depression $\geq$ 1mm or T-wave inversion >4 mm in $\geq$2 anatomically contiguous leads.

3. Hemodynamic or clinical instability (systolic blood pressure <80 mmHg, clinically significant atrial or ventricular arrhythmias, persistent chest pain despite therapy).

4. Known allergy to iodinated contrast agent (for CCTA group).

5. Serum creatinine >1.3 mg/d(for CCTA group).

6. Inability to provide informed consent.

7. History of established CAD defined as stent implantation or coronary artery bypass grafting.

8. Valvular heart disease.

All patients in this study subjected to the following:

Methods 1. Full history taking: including:

- Personal History: as name age and sex.

- Analysis of chest pain: typical, non typical or non angina.

- Risk factors profile: as hypertension, diabetes mellitus, dyslipidemia, current smoking.

2. Physical Examination: including:

- Blood pressure, heart rate, respiratory rate, (Killip class).

3. Twelve leads ECG: For signs of ischemia as ST – T changes

4- Chest- X ray PA view.

5-Echodoppler study:

6- Laboratory investigations:

7. Coronary CTA (for the CCTA group):

Coronary angiography (CA) was done to all patients with significant coronary artery stenosis evidenced by CTA with probable revascularization. Using retrograde percutaneous transfemoral technique (Judkins technique).

Endpoints:

Primary end point:

- Length of hospital stay :-defined as the time from presentation to the emergency department to the time of discharge order. This end point was chosen because it reflects the summery of actions taken in response to clinical information and test results, as well as logistical, cost and medical consideration in medical Centre (udo, et al 2012)

- the time for diagnosis, defined as the time from presentation in the emergency room until the first diagnostic test that led to diagnosis of an acute coronary syndrome (udo, et al 2012)

- Resource utilization (the cost) was defined as resources used in emergency department or during hospitalization (udo, et al 2012)

Secondary end points:

Major Adverse CardiacEvents (MACE) during Follow-up.

A standardized follow up phone call was conducted one month after enrollment to determine the occurrence of MACE (death, MI, and coronary revascularization). In addition, we retrieved medical record for all patients to verify all events potentially corresponding to a MACE such as a report of recurrent symptoms resulting in medical consultation, diagnostic testing, or hospital admissions were subsequently validated by review of medical records

3. STATISTICAL ANALYSIS

Demographics, traditional risk factors, clinical events, and prevalence of plaque and stenosis as detected by coronary CTA are presented as mean ± standard deviation (SD) or medians and interquartile range for continuous variables, and percentages for categorical variables.

4. RESULTS

Groups of the patient:

This study included 95 patients 72 males (75.8%) and 23 females (24.2%) with mean age of 50.987±8.983, patients were divided into 2 groups:

Group 1 (CT group): included 45 patient, 34 males(75.6%) and 11 female (24.4 %) with mean age of 50.978±7.744 years

Group 2(standard evaluation group): included 50 patients, 38 male (76%) and 12 female (24 %) with mean age.
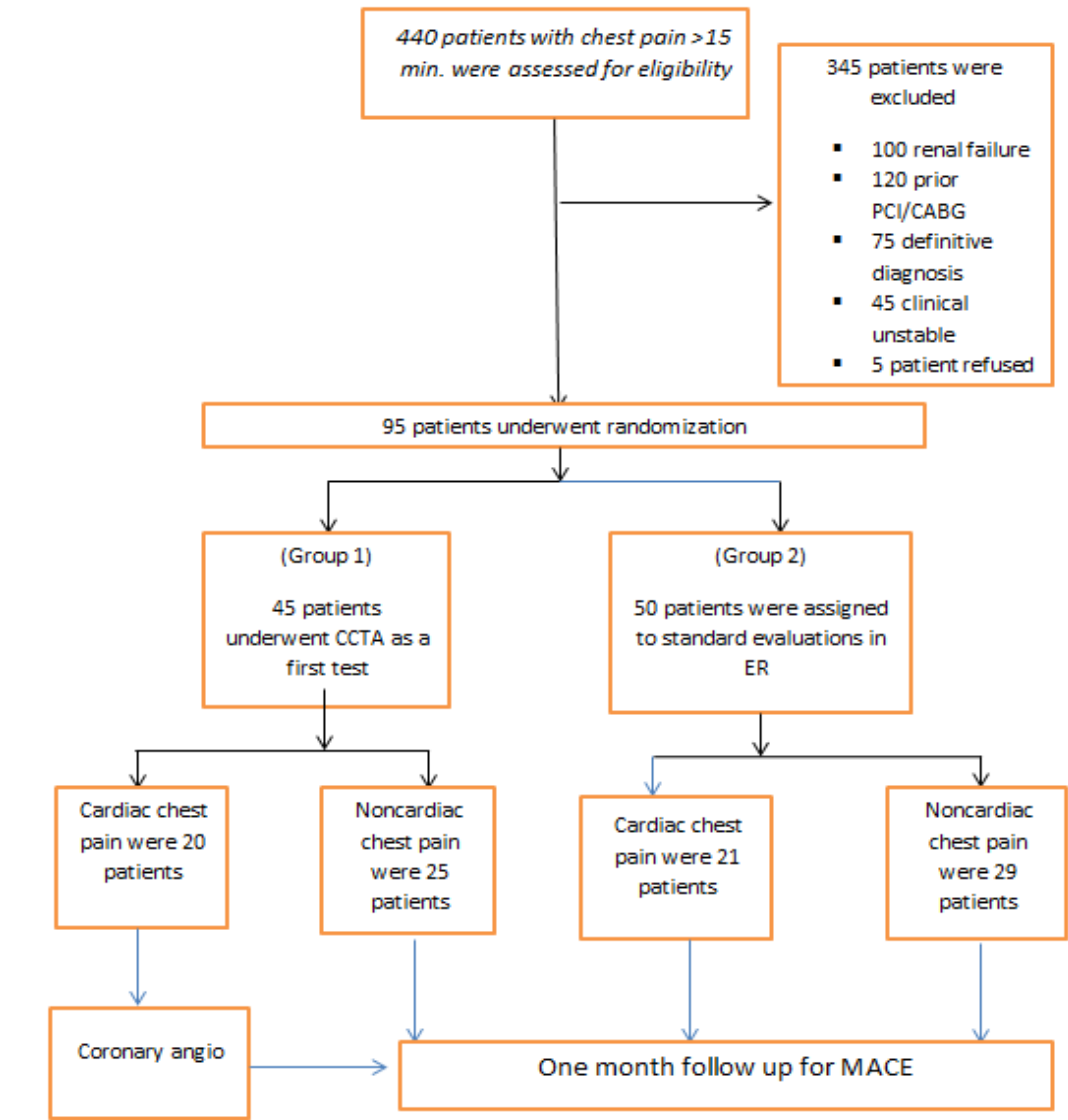
Fig.(1): Results of screening, randomization and follow up of the study patients

Table (1) Comparison between group 1 & group 2 as regard demographic data and baseline characteristics and risk factors

	Group 1 45pts.		Group 2 50 pts.		P value
Age Mean±SD	50.987±8.983		49.78 y±8.983.		>0.05
	Count	%	Count	%	
smoking	30	66.6%	35	70 %	0.726
Dyslipidemia	21	46%	23	46%	0.9442
D.M.	12	26.6%	14	28%.	0.8807
HTN	34		35	70%	0.9442
Family history	12	26.6%	17	34%	0.4413
No. of risk factor					
0-1 risk factor	7	15.5%	6	12%	>0.05
2-3 risk factor	34	75.5%	36	72%	
More than 4 risk factors	4	9%	8	16%	

HTN =hypertension

- Mean age of both groups was older than fifty years old. In group 1 mean age (50.978y ± 7.445) and in group 2 mean age (49.78 y ± 8.983). This showed that patients of group 1 were little older than those of group 2.
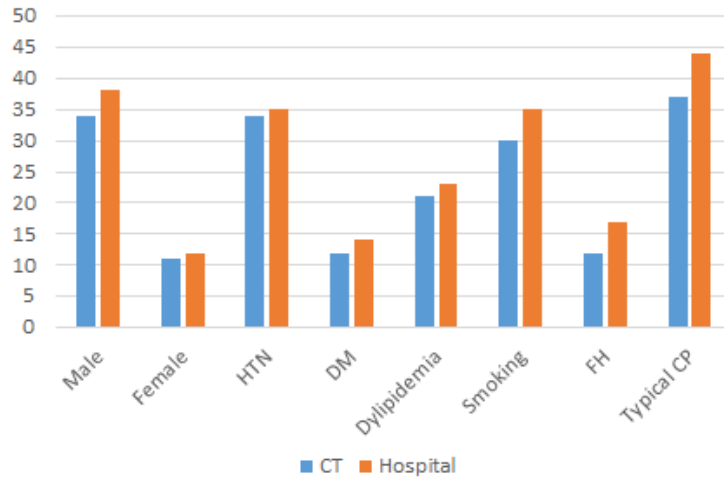

Figure (2) Comparison between group 1 & group 2 as regard demographic data and baseline characteristics and risk factors

- Table (1) and figure (2) shows that there were no significant difference between the studied groups as regard demographic and baseline criteria.

Table (2) Clinical presentation of the patients:

		Group 1 45pts.		Group 2 50 pts.		P value
		Count	%	Count	%	
Clinical presentation	Typical chest pain	38	84.4%	43	86%	0.42952
	Atypical chest pain	7	15.6%	7	14%	0.83366

Cardiac chest pain was defined by either +ve CCTA(group1) or +ve serial enzymes, serial ECG changes or positive treadmill test in (group 2)

Non cardiac chest pain was defined as -ve CCTA in(group1) and normal ECG, laboratory or negative stress test in (group 2)

As regard clinical presentation (table 2), 34 patients out of the 45 patients in group 1 were presented with typical chest pain and 7 patients presented with atypical chest pain . Forty three patients out of 50 patients in group 2 were presented with typical chest pain and and 7 patients presented with atypical chest pain.This reflects that the most of patients in both groups presented with typical chest pain and Statistical analysis showed non a significant difference between both groups as regard clinical presentation.

Table (3) Discharge diagnosis

Discharge diagnosis	Group 1 45 pts.		Group 2 50 pts.	
	Number	%	Number	%
Cardiac chest pain	20	44.4 %	21	42%
Non cardiac chest pain	25	55.6%	29	58%

As regard discharge, table (3) shows that 20 (44.4 %) patients out of the 45 patients in group 1 were diagnosed with cardiac pain and 25 (55.6%) patients diagnosed as non-cardiac chest pain . Twenty one patients (42%)out of 50 patients in group 2 were diagnosed as cardiac chest pain and and 29 (58%) patients diagnosed as non-cardiac chest pain. This reflects that about half of the patients in both groups discharged with non-cardiac chest pain.

Primary end points:

<p style="text-align:center">**Table (4) Primary end point**</p>

	Group 1 45 pts.		Group 2 50 pts.		P value
	mean	median	mean	median	
Time to diagnosis (in hours)	9.133±1.7914	9	26.72± 8.3643	27	<0.0001
Length of hospital stay (in hours)	33.667±24.6429	30	55.38±17.3168	47	<0.0001

This table shows highly significant difference between group (1) and group (2) as regard time to diagnosis.The average length of the hospital stay in the group of randomly assigned to CCTA group (1)was decreased by 17 hrs as compared to with the group randomly assigned to the standard evalution group (2) (p<0.0001).

As regard time to diagnosis it was significantly decreased in the group 1(group of randomly assigned to CCTA) by 18 hrs as compared to group 2(the group randomly assigned to the standard evalution) (p<0.0001).
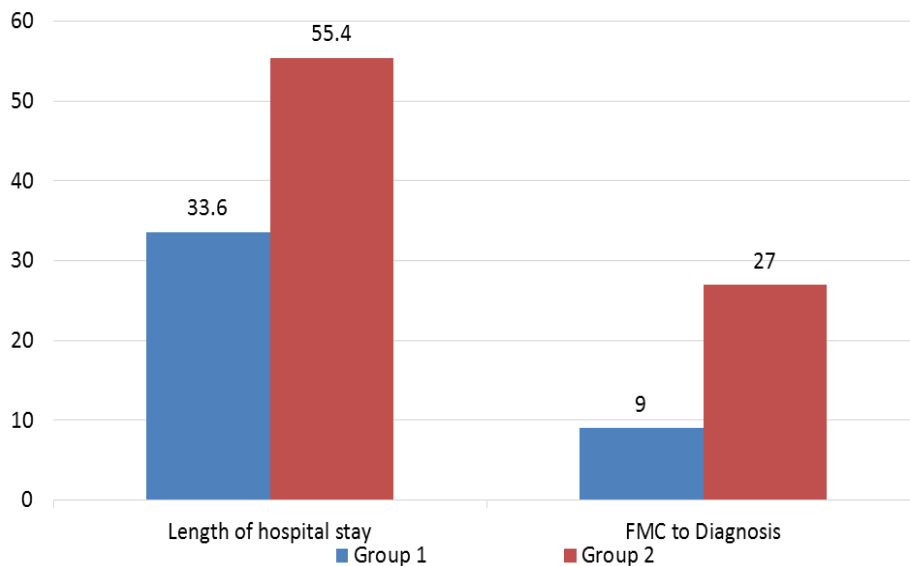

<p style="text-align:center">**Figure (3) Primary end point**</p>

Coronary CT angio and cost effectiveness:

<p style="text-align:center">**Table (5) Hospital cost**</p>

	Group1 25pts.	Group 2 29 pts.	P value
Hospital cost for single patient.	1800	2564.29±44.840	<0.0001
Hospital cost for all patient	45.000	71, 800	<0.0001

In hospital cost we compare hospital cost of the patients with no cardiac chest pain in both groups, there was a highly significant difference (p value<0.0001) between both group.

In patients who diagnosed as non-coronary chest pain the cost for single patient was 1800 EP in comparison with single patient in standard evaluation which was 2564 EP.

Table (5) and figure (4) shows that in comparison of total cost of patients of both groups, the total cost of patients with non-coronary chest pain in CT group was 45, 000EP and 71, 800EP for patients with non-coronary chest pain in patients in group 2.

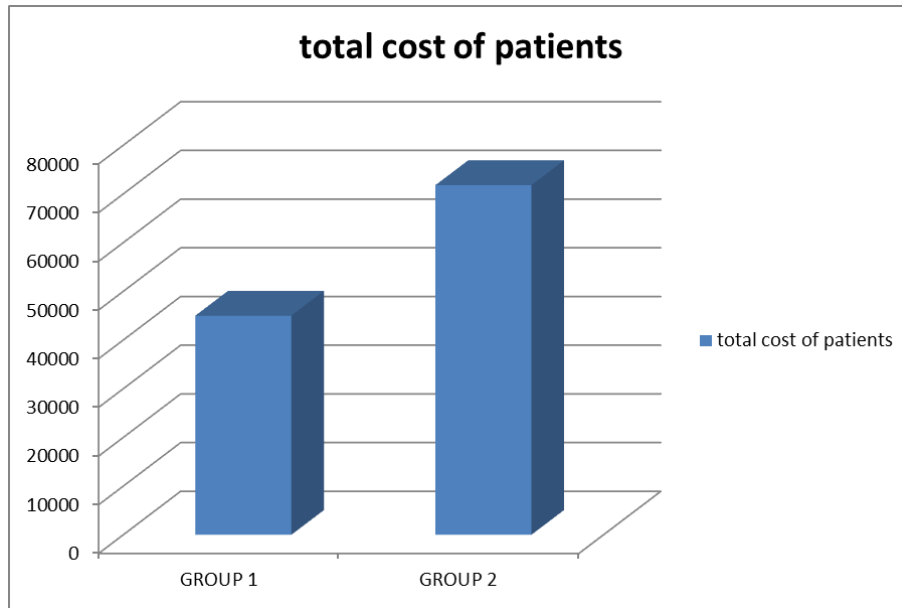Statistical analysis showed highly significant difference between both groups (p value<0.0001).

Figure (4) total cost of the patients with non-cardiac chest pain

Secondary end point:

Table (6) Follow up for recurrent chest pain within one month

	Group 1 45pts.		Group 2 50 pts.		P value
	Count	*%*	*Count*	*%*	
Repeat visit to ER	1	2.2%	4	8%	0.2333
Repeat hospitalization	1	2.2%	3	4%	0.1222

Regarding follow up of patient in group 1, there is one paient presented to the ER with chest pain, admitted to the hospital and coronary angio was done and show right coronary artery spasm and patient diagnosed as having vasospastic angina .

In group 2, four patients presented to ER with chest pain, one patient showed -ve test for ischemia and was discharged and three patient was admitted to the hospital and angio was done and showed non-significant lesion in two patients and coronary spasm in one patient
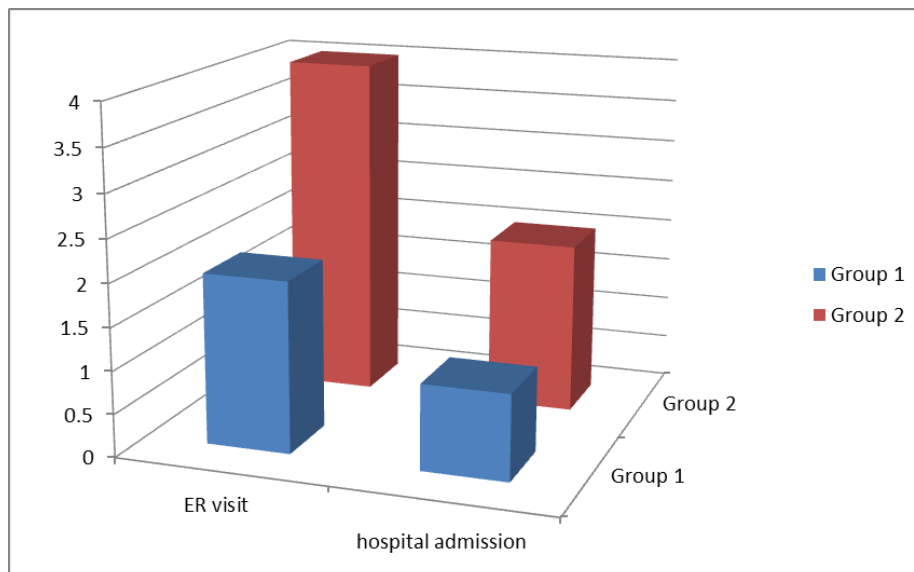

Figure (5) Follow up for recurrent chest pain within one month

Table (7) prevalence of coronary risk factors between patient with normal CCTA angio finding and patient with obstructive CHD (in group 1)

		Normal CCTA finding 25		Obstructive CCTA finding.20		P value
		Count	%	Count	%	
sex	M	19	76%	15	75%	
	F	6	24%	5	25%	
smoking		13	52%	17	85%	(p<0.0001).
Dyslipidemia		6	24%	15	75%	(p<0.0001).
D.M.		4	16%	8	40%	(p<0.0001).
HTN		16	64%	18	90%	(p<0.0001).
Family history		7	28%	5	25%	>0.05

This table shows that patients with obstructive CCTA findings had significantly higher prevelance of coronary risk factors, smocking, hypertension, hypercholestelomia, diabeters and hypertension compared to those with normal coronary arteries in CCTA. However there were no significant difference between them as regard age, sex and family history of CAD.Figure (6) prevalence of coronary risk factors between patient with normal ct angio finding and patient with obstructive CHD (in group 1)

5. DISCUSSION

Evaluation of chest pain in the ED is a public health issue of great consequence. According to the available health statistics report from the Centers for Disease Control and Prevention, evaluation of acute chest pain and related symptoms was the second most common reason for a visit to the ED by a female adult and the most common reason by a male adult in 2006 *(13)*.

Specialist in the field of emergency medicine can utilize a number of methods to diagnose chest pain, however in significant number of cases .these tests are insufficient in identifying a cause.

Specialist after resort to repetition of the some tests which lead to mismanagement of time and resources resulting in an expensive investigation which often delay the initiation of appropriate treatment and for the patients .

Strategies that explicitly incorporate assessment of chest pain symptoms need to be evaluated (.Coronary CT angiography emerge as an reliable test, then may effectively triage patients with undiagnosed chest pain in the ED(14).

Our study was randomized, comparing a coronary CTA-based strategy with traditional approaches for low-to-intermediate-risk patients presenting to the emergency department with chest pain and possible acute coronary syndrome.

This prospective, trial was designed primarily to assess whether coronary CTA, incorporated early into an evaluation strategy for patients presenting to an emergency department with chest pain suggestive of an acute coronary syndrome, safely improves the efficiency of clinical decision making, as compared with a standard evaluation in the emergency department.

Our study includes 95 patients with a primary complaint of chest pain lasting 15 >minutes were screened during the enrollment period. The whole populations were 55.6±16.51 years with minimal age of 20 and maximum of 70 years.

The aim of this study is to assess the usefulness of coronary CTA in patients with acute chest pain who are being admitted with low to intermediate risk for ACS.

In the presented work, 20 patients out of the 45 patients in(group 1) were diagnosed with cardiac chest pain (44.4%) and 25 (55.6%)of the patients diagnosed as non-cardiac chest pain .

In(group 2), 21 patient out of 50 patients (42%) were diagnosed as cardiac chest pain and 29 patients (58%)patients diagnosed as non cardiac chest pain.

This reflect that more than half of the patients in both groups discharged with noncoronary chest pain .This reflect the burden of unnecessary admission in form of extra hospital cost, overload on medical staff and unnecessary utilization of hospital resources.

In TIMI registry, the mean cost of admission and length of hospital stay for patients with nonspecific chest pain are significant with annual cost estimated at a proximally 71 million dollars with unnecessary hospital admission .Consuming 73, 000 bed days per year (15)

In the present work the average length of the hospital stay in the group of randomly assigned to CCTA was decreased by 17 hrs. as compared to with the group randomly assigned to the standard evaluation(p<0.0001).

This result was consistent with the result of ROMIC 11study as among thousand patients enrolled, 501 patients were randomized to ACCT and 499 patients to slandered protocol. Patient undergoing CCTA had significant reduction in length of hospital stay. (16)

Additionally the ACRIN-RA(**17**) showed that 83% of patient did CCTA did not have CHD and discharged directly from ER, compared to standard evaluation protocol resulting in reduction of hospital stay .

In the present study as regard time to diagnosis it was significantly decreased in the group 1(group of randomly assigned to CCTA) by 18 hrs. as compared to group 2(the group randomly assigned to the standard evaluation) (p<0.0001) table . This result was consistent with ROMIC 11study(16) which assessed time to diagnoses and reported that Patient underwent CCTA had significant reduction 15 hours in time to diagnosis as compared to those with standard evaluation.

As regard the in hospital costs of both groups in the present work there was a significant difference (p value<0.0001). Between both group. IN patients who diagnosed as non-coronary chest pain the cost for single patient was 1800 EP in group (1) in comparison with single patient in standard evaluation(group 2) which was 2564 EP.In comparison of total cost of patients of both groups, the total cost of patients with non-coronary chest pain in CT group was 45, 000EP and 71, 800EP for patients with non-coronary chest pain in patient in group 2(standard evaluation group).Statistical analysis showed significant difference between both groups with p value<0.0001

Additionally, cury et al, (2008) and Goldstein et al (2008) concluded that In the evaluation of acute chest pain, coronary CTA can reliably exclude coronary artery disease and its use reduces diagnostic time and cost compared with more traditional approaches *(18)*

In the present study, earlier discharge in the CCTA group (those with non-cardiac chest pain)was not associated with increased rate of undetected acute coronary syndrome or increased adverse events compared to group 2during the period of follow up after hospital discharge in group 1, there is one patient presented to the ER with recurrent chest pain, admitted to the hospital with chest pain and coronary angio was done and show right coronary artery spasm and patient diagnosed as having vasospastic angina .

In group 2, four patients presented to ER with chest pain, one patient was discharged and three patient was admitted to the hospital .angio was done and shows non-significant lesion in two patient and coronary spasm in one patient .

In both groups no evedience of fatal or non-fatal myocardial infarction were recorded amoning patients diagnosed as having non cardiac chest pain on hospital discharge .

So in the present study, the clinical adverse events were infrequent in this trial as compared to ROMIC 11 study(16) in which there was eight major cardiovascular events during 28 days follow up :six after slandered evaluation protocol (four myocardial infarction and two unstable angina)and two after CCTA (one myocardial infarction and one unstable angina)

Limitations of the study:

- Small number of the studied population
- Short term follow up
- Patient hazards of radiation and contrast agents use were not involved in the present study
- It is single centre trial

6.   CONCLUSIONS AND RECOMMENDATION

In the evaluation of acute chest pain, coronary CT angio can reliably exclude or early detect CAD in ED and its use reduces diagnostic time and cost compared with standard approach.

So, CCTA may be appropriate for patients triage in the ED who presents with undiagnosed etiology of their chest pain.

Larger caliber studies recruiting more patients in a larger number of centres are recommended to highlight the results of the present study in Egypt.

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