

## Long Term Follow up of CT Angiography in Low to Intermediate Risk Patients of Suspected Acute Coronary Syndrome (ACS)

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### ABSTRACT

**Objective:** To assess long term outcomes of CT Angiography in low to intermediate risk patients of suspected ACS and to assess if CT-angiography is a safe modality to discharge patients with clinically non-significant coronary artery disease.

**Study Design:** Descriptive cross-sectional study

**Place and Duration of Study:** Tertiary Cardiac Center in Rawalpindi, from Dec 2021 to Apr, 2022.

**Methodology:** A total of (n=600) patients who presented with ischemic sounding chest pain and suspicion of acute coronary syndrome (ACS) were selected via consecutive sampling technique and were followed up to 5-months. Patients' demographics, CT-Angiography findings and their outcomes were noted on data collection sheet. Data was analyzed by SPSS version-23. Descriptive statistics were run to present categorical data in frequencies and percentages. Chi-square and Fisher Exact Test was applied to find the association between study variables at 95% CI and 5% margin of error ( $\alpha=5\%$ ).

**Results:** Out of (n=600) suspected cases of acute coronary syndrome (ACS), n=352 (58.7%) were males and n=248 (42.3%) were females. As a result of follow-up of the patients, cases that represented in emergency department, readmission cases and re-vascularized cases were (n=10,4, 1;1.7%, 0.7%, & 0.2%) respectively. Frequency of ACS and STEMI patient was 0.0%. Mortality rate was 0.0%. There was significant association of comorbidities with CT-angiography findings and the findings with outcome variables ( $p<0.05$ ) except revascularization ( $p>0.05$ ).

**Conclusion:** In low to intermediate risk patients of suspected ACS, discharge decision from emergency department based on CT-angiography findings is safe and shows excellent long-term outcomes with no major adverse cardiac event (MACE) on long-term follow-up.

**Keywords:** Acute coronary syndrome, Coronary artery disease, CT-Angiography, Coronary angiography, Exercise tolerance test, Myocardial infarction.

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### INTRODUCTION

Acute coronary syndrome (ACS) is a condition comprising of signs and symptoms due to reduced coronary blood flow which leads to hypo perfusion and eventually myocardial ischemia. It is a medical emergency, which requires urgent intervention.<sup>1</sup> Coronary artery disease (CAD) is the manifestation of ACS and a global health problem of vast proportions. CAD is inflammatory in nature and is an atherosclerotic disease characterized by stable angina, unstable angina and Myocardial Infarction (MI) as well as sudden cardiac death.<sup>2</sup> Chest pain is the most common and typical symptom of acute myocardial infarction. Acute myocardial ischemia is the cause of morbidity and mortality in both genders worldwide. According to the American Heart Association (AHA), cardiovascular disease accounted for  $\geq 17.6$  million in 2016 and 17.5

million in 2014 deaths per year and the count is expected to be increased to  $\geq 23.6$  million by 2030. World Health Organization (WHO) has estimated 17.5 million deaths from cardiovascular diseases annually, demonstrating 31% of all global deaths. An estimated count of 7.4 million of these deaths, are due to CAD.<sup>3</sup>

Both developed and developing countries are targeted by the effects of CAD.<sup>4</sup> Patients suspected of ACS are often admitted in the hospital unnecessarily which poses a substantial burden on hospitals. Frequency of patients presenting to emergency department (ED) with chest pain and suspected ACS is fairly high. Most of these patients are found to have non cardiac chest pain. Thereby, to minimize the admissions in hospital and improve risk stratification, Coronary Computed Tomography Angiography (CCTA) is being used frequently in emergency departments in patients with chest pain who have low to intermediate risk of coronary artery disease. Numerous randomized control trials have been done recently which tested the

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CCTA rigorously as a method of triage for aptly selected patients who had the suspicion of acute coronary syndrome (ACS).<sup>5-7</sup> Several studies on CCTA-based discharge strategy have revealed dramatically reduced or similar cost and decreased disposal times in comparison to alternative standard of care along with excellent safety outcome.<sup>8-10</sup>

However, long term follow up of these patients has been a lesser studied entity. CT - angiography has high negative predicted value in detecting CAD, but its beneficial aspect in evaluating whether the patient's discharge from the emergency department is safe is not well studied.<sup>11</sup> Current study was aimed to assess the long term outcomes (ACS, death, readmission and revascularization) in low to intermediate risk patients of suspected ACS who get discharged after getting a CT angiography. It was also aimed to determine if CT angiography is a safe modality to discharge patients with clinically non-significant coronary artery disease.

## METHODOLOGY

The given study was prospective cross sectional study conducted at tertiary care cardiac center from December 2021 to April 2022.

**Sample Size:** Non-probability consecutive sampling technique was used to collect data from the patients (n=600) who fulfilled the inclusion criteria of the study.

**Inclusion Criteria:** Patients who presented with ischemic type chest pain, negative highly sensitive Troponin-I, mild (25 to 49%) to moderate (50% to 69%) clinically non-significant CAD on CT-angiography were included in our study.

**Exclusion Criteria:** Patients with history of renal impairment, previous myocardial infarction and severe CAD i.e., >70% on CT angiography were excluded. Study's approval was taken from IERB (letter # 26/10/R&D/2021/119) and written informed consent was taken from the patients prior to data collection. Patients' demographics comorbid and outcomes were noted on data proforma. Data was analyzed by using SPSS version-23. Descriptive data was presented in frequency and percentage. Chi-square test was applied to find out the association of co-morbid and CT-angiography findings and subsequently with outcome of CT-angiography for the variables whose expected count of 80% cell was above 5 otherwise Fisher exact test was used (for those having more than 20% cells with expected count less than.<sup>5</sup>

Patients presenting with chest pain at emergency department were approached, symptoms were

assessed and if their symptoms sounded ischemic in nature, they were advised a highly sensitive Trop I test. Patients with moderate CAD on CT angiography had two sets of Hs-Trop I to make sure moderate disease didn't represent unstable plaque. All the patients with mild-moderate disease in CT-angiography and negative Trop-I test were discharged. Patients with moderate CAD on CT-angiography were given early appointments for Exercise Tolerance Test (ETT) with plan to refer for urgent coronary angiography in case ETT was positive. Patients with negative ETT were followed up with all other patients to determine the long term outcomes of CT angiography. Follow-up of the patients (study participants) was 100% completed as they were contacted via calls to note down the desired outcomes.

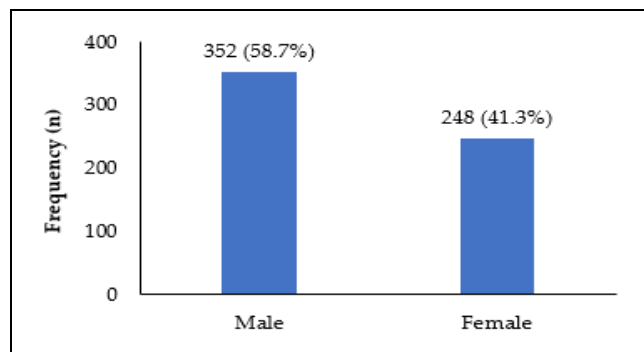
Outcome of the CT angiography comprised of major adverse cardiac events (MACE) in discharged patients such as ST elevation Myocardial infarction (STEMI), Non-ST elevation MI (NSTEMI), readmission, revascularization and death. Patients with normal and mild to moderate, clinically non-significant CAD on CT angiography were characterized as low to intermediate risk patients of ACS. Suspected ACS cases were the patients presenting at emergency department with history of chest pain with clinical suspicion of ACS warranting highly sensitive Troponin I (HS-Trop I). CT-Angiography findings were divided into different categories; normal findings meant no visible plaque buildup in coronary arteries based on based cardiac scan; mild findings meant less than 30% blockage in one to two coronary arteries; moderate findings meant 30-49% blockage in one to coronary arteries and severe findings meant narrowing of 1-2 vessels >50% or three-coronary arteries moderately blocked. Very severe disease included left main stem involvement and >50% blockage of four or more vessels.<sup>12</sup>

## RESULTS

The current descriptive cross-sectional study was an effort to find out the long term outcomes of CT-angiography and its safety. It had enrolled (n=600) patients meeting the inclusion and exclusion criteria as outlined above. Out of n=600 study participants enrolled in study, majority were the males (n=352; 58.7%), while 41.3% (n=248) were females as depicted in Figure-1, with mean age of 41.56±11.64 years (Table-I).

n=600; H/O IHD=History of Ischemic Heart Disease; ETT=Exercise Tolerance Test; ED=Emergency department; ACS=Acute Coronary Syndrome; STEMI= ST-Elevation Myocardial Infarction.

## Acute Coronary Syndrome



**Figure-1: Gender Distribution of Study Population**

In light of statistics given in Table-I, a sound number of study participants had family history of Ischemic heart Disease (n=318; 53.0).

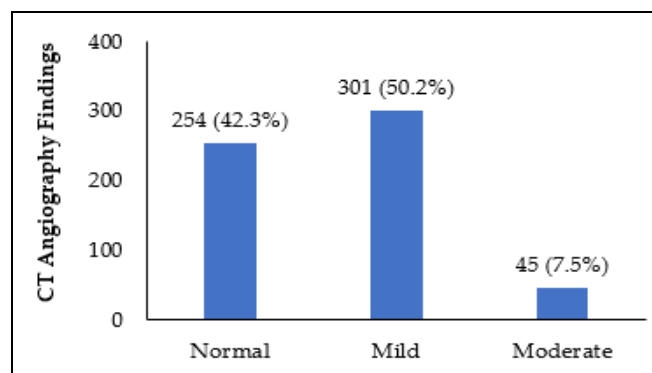
**Table-I: Descriptive Statistics of Study Variables**

| Patient Variable             |                         | Mean±SD     |            |
|------------------------------|-------------------------|-------------|------------|
| Age (years)                  |                         | 40.56±11.64 |            |
| Variables                    |                         | Yes n(%)    | No n(%)    |
| Co-Morbid                    | Diabetes Mellitus       | 119(19.8)   | 481(80.2)  |
|                              | Hypertension            | 261(43.5)   | 339(56.5)  |
|                              | Family H/O IHD          | 318(53.0)   | 282(47.0)  |
|                              | Smoking                 | 140(23.3)   | 460(76.7)  |
|                              | Obesity                 | 151(25.2)   | 449(74.8)  |
| CT-Angiography Findings n(%) | Normal-No Plaque        |             | 254(42.3)  |
|                              | Mild Stenosis           |             | 301(50.2)  |
|                              | Moderate Stenosis       |             | 45(7.5)    |
| ETT n(%)                     | Done                    |             | 45(7.5)    |
|                              | Not Done                |             | 555(92.5)  |
|                              |                         | Yes n(%)    | No n(%)    |
| Outcomes                     | Representation in ED    | 10(1.7)     | 590(98.3)  |
|                              | Readmission             | 4(0.7)      | 596(99.3)  |
|                              | Acute Coronary Syndrome | -           | 600(100.0) |
|                              | STEMI                   | -           | 600(100.0) |
|                              | Revascularization       | 1(0.2)      | 599(99.8)  |
|                              | Mortality               | -           | 600(100.0) |

n=600; H/O IHD=History of Ischemic Heart Disease; ETT= Exercise Tolerance Test; ED=Emergency department; ACS=Acute Coronary Syndrome; STEMI=ST-Elevation Myocardial Infarction

Other comorbidities such as diabetes mellitus, hypertension, smoking and obesity also existed in different proportions. CT-angiography findings revealed normal results in 42.3% (n=254), mild stenosis was in 50.2% (n=301) study participants, while moderate stenosis was noted in n=45 (7.5%), who subsequently underwent ETT. Outcomes of our study showed that patients who represented in ED, had readmission in

hospital and had revascularization were only (n=10, 4 & 1; 1.7%, 0.7% & 0.2%). ACS and STEMI were 0.0% (n=0). Mortality rate was also nil (n=0; 0%). Frequency of CT-angiography findings presented in Figure-2 highlighting the maximum cases with mild findings n=301 (50.2%).



**Figure-2: Grades of Stenosis on CT-Angiography Findings**

Chi-square test was applied to find out the association between co-morbidities and CT-angiography findings (Table-II) for the variables whose expected count of 80% cell was above 5, otherwise Fisher exact test was used (having more than 20% cells with expected count less than 5). It was noted that there existed a statistically significant and strong association ( $p < 0.01$ ) between all the co-morbidities (DM, HTN, Family history of IHD, Smoking and Obesity) and CT-angiography findings at CI=95% with 5% margin of error.

**Table-II: Cross Tabulation of Co-Morbidities with CT-Angiography Findings of Study Participants (n=600)**

| Co-Morbidities |        | CT- Angiography Findings |      |          | p-value |
|----------------|--------|--------------------------|------|----------|---------|
|                |        | Normal                   | Mild | Moderate |         |
| Gender         | Male   | 200                      | 120  | 32       | <0.01   |
|                | Female | 54                       | 181  | 13       |         |
| DM             | Yes    | 18                       | 60   | 41       | <0.01   |
|                | No     | 236                      | 241  | 4        |         |
| HTN            | Yes    | 26                       | 191  | 44       | <0.01   |
|                | No     | 228                      | 110  | 1        |         |
| Family H/O IHD | Yes    | 55                       | 221  | 42       | <0.01   |
|                | No     | 199                      | 80   | 3        |         |
| Obesity        | Yes    | 31                       | 95   | 25       | <0.01   |
|                | No     | 223                      | 206  | 20       |         |

DM=Diabetes Mellitus; HTN= Hypertension; H/O IHD=History of Ischemic Heart Disease. n=600; p-value significant; ED=Emergency department; ACS=Acute Coronary Syndrome; STEMI=ST-Elevation Myocardial Infarction.

Association of CT-angiography findings with outcomes after a long-term follow-up of the patients revealed good results with least morbidity and no mortality and there was statistically significant

association ( $p < 0.01$ ) of CT-angiography findings with representation of patients to ED and readmission to hospital, while insignificant association was noted with revascularization as presented in Table-III. None of the cases reported with ACS, STEMI and mortality. Thus it was concluded that CT-angiography is a good diagnostic tool to safely discharge the patients from ED with excellent long term outcome.

**Table-III: Cross Tabulation of CT-Angiography Findings with Outcome of the Study Participants (n=600)**

| Outcome              |     | CT- Angiography Findings |      |          | p-value |
|----------------------|-----|--------------------------|------|----------|---------|
|                      |     | Normal                   | Mild | Moderate |         |
| Representation in ED | Yes | 3                        | 3    | 4        | 0.008*  |
|                      | No  | 251                      | 298  | 41       |         |
| Readmission          | Yes | 0                        | 0    | 4        | <0.01*  |
|                      | No  | 254                      | 301  | 41       |         |
| Revascularization    | Yes | 0                        | 0    | 1        | 0.075   |
|                      | No  | 254                      | 301  | 44       |         |

\*=p-value significant; ED=Emergency department; ACS=Acute Coronary Syndrome; STEMI=ST-Elevation Myocardial Infarction Note: There were no cases of ACS, STEMI and death were found in study sample during the follow-up of 6-months (n=0; 0.0%)

## DISCUSSION

The given cross-sectional study on patients presenting with typical ischemic chest pain and suspicion of ACS (low to intermediate risk of ACS), revealed their CT-angiography findings and its long term outcomes. It was found that CT-angiographic based algorithm guided ED discharge of the patients with only 1.7% (n=10) represented cases to ED, 0.7% (n=4) readmission cases and 0.2% (n=1) revascularized cases. There was no case with ACS and STEMI (n=0; 0.0%). Mortality rate also 0.0% (n=0). Patients with no stenosis or plaque, mild stenosis and moderate stenosis were 42.3%, 50.2% and 7.5% respectively. However, significant association was found out between comorbidities and outcomes of CT-angiography findings ( $p$ -value<0.01) except coronary revascularization ( $p$ -value>0.05). Thus the 5-months follow-up outcomes revealed that discharge decision based on CT-angiography findings is safe for low to intermediate risk patients of suspected ACS and shows excellent long term outcomes with no MACE on long term follow up.

Literature review revealed somehow similar results. A study done by Hollander *et al.*<sup>13</sup> on a sample of (n=481) presenting to ED with typical chest pain, did follow-up of 1-year and stated a very low incidence of major adverse cardiac events (MACE) (0.2%). A 4-year follow-up study included a count of n=585 consecutive patients (mean age 58±11 years; Male=58%), revealed no stenosis or coronary plaque in 34%

participants, non-obstructive plaque in only 49%, 4% with moderate stenosis and 13% cases with severe stenosis. There were consistent findings of readmission cases (95% CI; 1%) for the chest pain and 0.0% (at CI=95%) rate of revascularization of coronary vessels, ACS and death. Only 2% cases represented in ED.<sup>14</sup> Moreover, the investigations<sup>15</sup> of Rule Out Myocardial Infarction-Computer Assisted Tomography (ROMICAT) on n=333 patients with a follow-up period of 2-years demonstrated some of the outcomes inline to our study's findings such as 0.0% mortality rate of patients presented with acute chest pain at ED while inconsistent findings with respect to MI (3.6%). Amsterdam *et al.*, reported the use of invasive angiography remained a standard of care in diagnosing and treating the ACS patients and subsequently reduced re-infarction, refractory angina, morbidity and mortality because of the timely identification of obstructive CAD.<sup>16</sup> But CT-angiography further improved such outcomes in long-term follow-up along with reduction in cost as well as resource utilization. Because of such improvements, CT-angiography in ACS patients also gained importance during the COVID-19 era, 2019.<sup>17-19</sup> Thus It was concluded that CT-angiography has an incremental prognostic value on the clinical evaluations in ACS patients.

In another prospective and observational research done in the past, relatively good outcomes of CT-angiography were reported in discharged patients who presented with ischemic type chest pain and had a suspicion of ACS. They noted that CT-angiography is a good diagnostic tool for the rapid assessment in suspected patients of ACS.<sup>20</sup> This is further supporting and assuring that CT-angiography is a safe long term diagnostic strategy. The significant strengths of current study are the use of standard diagnostic protocols of CT-angiography in all study participants along with 100% completed long term follow-up.

## LIMITATIONS OF STUDY

Existing study's findings can not be generalized as it was a single center study. It also excluded the patients with severe CAD on CT-angiography who were admitted in the hospital and we didn't follow-up them as the study's primary focus was to follow-up low to intermediate risk patients of suspected ACS who were discharged from the ED.

## CONCLUSION

Our study concluded that in low to intermediate risk patients of suspected ACS, discharge decision from emergency department based on CT-angiography findings is safe and shows excellent long-term outcomes with no major adverse cardiac event (MACE) on long-term follow-up. Thus,

CT-angiography has an incremental prognostic value on the clinical evaluations in ACS patients. This is not only supporting the clinical utility of CT-angiography but also a cost-effective strategy due to low rate of succeeding investigations followed by hospital readmissions.

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**Conflict of Interest:** None.

### Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

FR: Manuscript writing, drafting and editing

MS: Intellectual contribution, concept and final approval

MBS: Proof reading, Intellectual contribution, final approval

SIS: Study design, concept and critical review

MAV: Data collection

SAK: Data collection, data entry and review of article

ZA: Data management, data collection & manuscript writing

NA: Analysis, result interpretation, review of article and formatting

SS: Data collection, data entry and review of article

MA: Proof reading, data collection, final approval

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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