Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/14087
DOI URL: http://dx.doi.org/10.21474/IJAR01/14087

*RESEARCH ARTICLE*

# TAKOTSUBO CARDIOMYOPATHY: A CASE SERIES FROM A CARDIAC CENTER IN RAJASTHAN AND REVIEW OF LITERATURE

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*Manuscript Info*

***Manuscript History***
Received: 15 November 2021
Final Accepted: 18 December 2021
Published: January 2022

*Abstract*



## Introduction:-

Takotsubo cardiomyopathy(TCM) is an acute cardiac condition that involves left ventricular apical ballooning, which occurs in the absence of significant coronary artery disease and mimics acute myocardial infarction [1].First, identified by Japanese scientists in 1991, this disorder was named for the distinctive echocardiogram's resemblance to traditional takotsubo, or octopus fishing pots, which is fishing jar with a narrow neck and wide base used to trap octopus. It is also known as 'Broken heart syndrome','ampullacardiomyopathy','stress induced cardiomyopathy' and 'apical ballooning syndrome'.

TCM patients present with symptoms of chest pain, ST- segment elevation on electrocardiogram(ECG), and elevation in cardiac biomarkers consistent with an acute coronary syndrome(ACS). However, angiography finds no significant coronary stenosis, and the LV apex is found to balloon, which usually resolves in weeks. The syndrome appears to be triggered by emotional or physical stress. TCM is being diagnosed more frequently, possibly because of increasingly stressful times and public attention to ACS. Incomplete understanding of its pathophysiology further complicates the diagnosis and management of Takotsubo cardiomyopathy. Currently there are three proposed mechanisms for dysfunction which include: coronary vasospasm, microvascular spasm,or catecholamine-induced neurogenic stunning of the myocardium [2-3].Although well known in cardiology, awareness of this entity is still developing in emergency medicine.It is important to consider this diagnosis, as patients may present to the emergency department.Initially believed to be a rare phenomenon, recent data suggests that the frequency of Takotsubo cardiomyopathy has been underestimated. It is now hypothesized that this dysfunction accounts for more than2% of all patients presenting with ST segment elevation and suspected acute coronary syndrome[4] To support this claim,we discuss six patients admitted to our center during last one year with chest pain, ECG changes and elevated cardiac biomarkers consistent with ACS, who were diagnosed with TCM. Aim of this discussion is to help clinicians better understand and manage this treatable condition.

**Case 1**

A 65-year-old female admitted to our hospital with complaints of sudden retrosternal chest pain radiating to both arms with shortness of breath. Her vitals were: pulse 80bpm,blood pressure of 130/82mmHg, respirations of 16breaths/min, oxygen saturation of 96%on room air. Her past medical history was not significant. Her son stated that his mother had been under extreme stress due to sudden death of her brother due to heart attack at the age of 50.ECG at presentation showed ST segment elevation in lead V1 to V6 suggestive of acute anterior wall myocardial infarction. Cardiac biomarkers were significantly elevated. Trans thoracic echocardiography showed apical

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ballooning with akinesia of left ventricular apex and hyperkinesia of basal LV part with residual ejection fraction was 25%. The patient had immediate cardiac catheterization that revealed no stenosis in coronary arteries. Left ventriculogram showed significant apical segment akinesis. Patient managed conservatively with angiotensin converting enzyme inhibitors(ACEI), diuretics, beta blockers. Follow-up echocardiogram 10 days later showed normal LV size and normal LV function with ejection fraction of 60%.

**Case 2**:
A 69-year-old female with a history of hypertension admitted to our hospital after complaining of chest pain with shortness of breath since last one day. Her vitals were:pulse 102 bpm,blood pressure of 140/80mmHg, respirations of 22 breaths/min, oxygen saturation of 96% on 2 liters/min via nasal cannula. She stated that she developed symptoms after heard about the sudden demise of her nephew in an accident. Initial ECG showed normal sinus rhythm, ST segment elevation in anterior precordial leads suggestive of anterior wall myocardial infarction. Cardiac biomarkers were significantly elevated. Echocardiogram showed apical ballooning of the entire distal lateral,septal,anterior and inferior walls with akinesis and hyperkinesia of basal segments with ejection fraction of 30%. Patient taken to cardiac Cath lab for coronary angiography. Coronary arteries were unremarkable. Patient managed with diuretics, ACEI, beta blockers and nitrates. Follow-up echocardiogram 15 days later showed normal LV ejection fraction.

**Case3:**
A 59-year-old female admitted to our hospital with chest pain, perspiration and vomiting from last 8 hours. Her vitals were:pulse 90bpm,blood pressure of 110/82mmHg, respirations of 18breaths/min, oxygen saturation of 96% on room air. No significant past medical history. Her daughter stated that her mother had been under extreme stress due to sudden death of her son in an accident 5 days ago. Her initial ECG showed ST segment elevation in lead V1 toV4 and ST depression in inferior leads.Echocardiogram showed apical ballooning with akinesia of LV apex and hyperkinesia of basal segments with ejection fraction of 25%. Cardiac enzymes were elevated. Patient had cardiac catheterization with left ventriculography, which showed mid-anterior and apical akinesia with preserved anterobasal and posterobasal function. Coronary arteries showing non obstructive disease. Patient was managed with ACEI, beta-blockers,heparin and nitrates. Follow-up echocardiogram 7 days later showed normal LV ejection fraction.

**Case 4:**
A 60-year-old female with no known past medical history admitted to our hospital with chest pain, shortness of breath and perspiration from last 3 days. Her vitals were:pulse 102bpm,blood pressure of 110/70mmHg, respirations of 20breaths/min, oxygen saturation of 90% on room air. When asked about family history for any heart disease,she stated that the day before onset of symptoms,her younger sister had died of a massive heart attack at age 58. Her initial ECG showed poor R wave progression and non-specific ST changes in precordial leads. Echocardiogram showed apical ballooning with akinesia of LV apex with ejection fraction of 20%. Cardiac enzymes were elevated. Patient taken to cardiac cath lab, coronary angiography revealed non obstructive disease. Patient was managed with diuretics,ACEI, beta-blockers,heparin and nitrates. Follow-up echocardiogram 10 days later showed normal LV ejection fraction.

**Case 5:**
A 56-year-old female admitted to our hospital with 6 hours history of chest pain and perspiration. She had just been informed that one of her sons had died in an accident. She had no past medical history. Her vitals were:pulse 110bpm,blood pressure of 150/70mmHg, respirations of 18breaths/min, oxygen saturation of 92% on room air. Her initial ECG showed ST segment elevation in V1 toV6 leads.Cardiac enzymes were elevated . Echocardiogram showed apical ballooning with akinesia of LV apex with ejection fraction of 25%. Emergent cardiac catheterization revealed normal coronary arteries. Patient was managed with ACEI, beta-blockers, and nitrates. Follow-up echocardiogram 7 days later showed normal LV ejection fraction.

**Case 6:**
A 28-year-old female with a history of her first cesarean delivery 10 days previously was admitted to our hospital with 3 hours history of chest pain and perspiration. She had no previous medical problems and no significant family history. Her vitals were:pulse 120bpm,blood pressure of 120/70mmHg, respirations of 18breaths/min, oxygen saturation of 96% on room air. Her initial ECG showed ST segment elevation in V1 toV4 leads.Cardiac enzymes were slightly elevated. Echocardiogram revealed regional systolic dysfunction of the left ventricular walls with

akinesia of the mid apical segments and hyperkinesis of the basal segments with LV ejection fraction of 35%.She underwent cardiac catheterization, which revealed normal coronary arteries.She was managed conservatively and her symptoms resolved.A follow-up transthoracic echocardiogram performed 15 days later revealed resolution of the wall motion abnormalities with LV ejection fraction of 55%.

## Discussion And Review Of Literature:-

In 1991, Dote et al, first identified Takotsubo cardiomyopathy in five patients[5]. For many years, this pathology was believed to be specific to eastern Asian population. Prevalence of the syndrome is unknown, although various researchers have reported that 1.7%-2.2% of patients with suspected ACS at their institutions are diagnosed with TCM [4,6-8]. Multiple studies have found that most presentations of TCM occur in postmenopausal women between the ages of 60 and 75. Our case series identified six women, with average age of 59.16 years, which fits between the stereotypical ages as described in previous publications [9-10].

Although the clinical presentation of TCM may be identical to ACS, the suspected pathogenesis of TCM and ACS differ greatly. An emotional or physical stressor frequently precedes the development of symptoms (26.8% and 37.8% respectively[1]. These stressors have included: death of a loved one, bad financial news, legal problems, car accidents, surgery and other medical problems [11-12]. Five patients in our series had loss of a family member as a major stressor, sixth patient had a history of cesarean 10 days prior to symptoms.

The etiology of TCM remains speculative. Proposed mechanisms include: multi vessel coronary artery spasm, impaired cardiac microvascular function and endogenous catecholamine induced myocardial stunning. Lacy et al [13] have shown that during a mental stressor of simulated public speaking patients have decrease in coronary artery diameter, which returned to baseline after five minutes. Physicians who originally reported on and named 'Takotsubo cardiomyopathy' have also shown that approximately 70% of TCM patients had coronary artery spasm during a provocation test[14]They suggested that either multi vessel coronary artery spasm or microvascular spasm may contribute to the onset.

Sadamatsu et al[15] reported two cases of patients with apical wall motion abnormalities with reduced coronary flow reserve not due to coronary artery stenosis. They postulated that this reduction in reserve may be due to microvascular dysfunction. Other studies have also shown that mental stress may cause endothelial dysfunction, further supporting the idea that coronary microcirculation may play a role in the etiology [16-17]. The most commonly discussed mechanism for this condition is stress induced catecholamine release. They may cause a direct toxic effect on the myocardiumby changing autonomin tone, enhancing lipid mobility, calcium overload, free radical production, or increased sarcolemmal permeability [18]. Akashi et al[19] suggested that neurogenetically mediated myocardial stunning due to autonomic imbalance may be the cause of LV wall motion abnormalities. Wittstein et al[20] showed that stress-induced cardiomyopathy patients have statistically higher levels of catecholamines than patients with myocardial infarction.

The diagnosis of TCM can be challenging because there is significant variation in the clinical presentation of this disorder. Affected patients most often complain of chest pain and dyspnea [10] and exhibit electrocardiographic changes. Common electrocardiographic abnormalities at the time of presentation include ST segment elevation, most often in the precordial leads during acute phase, followed by T wave inversion [1,21-22].ECG changes tend to be transient and resolve within two to four months[23]. Few studies have shown minor ECG differences between patients with TCM and ACS [21]. Cardiac markers are usually elevated. However, the levels tend to be lower and normalize sooner than with ACS patients [1]. Coronary angiography is required for diagnosis, as there is no accurate way to reliably distinguish TCM from ACS using ECG or cardiac markers.

Presently, the cardiac echocardiogram is the clinician's most valuable diagnostic tool for TCM. Wall dyskinesis extending beyond the distribution of a single coronary artery is nearly pathognomic for this dysfunction [3,9]. We were able to identify sufficient dyskinesis in all of our cases to make a diagnosis of this condition. During the acute phase left ventricular dysfunction and apical dyskinesis or akinesis with apical ballooning. Mean ejection fraction(EF) for these patients range from 20-49% [1]. LV basal hyperkinesis also occurs, and one systematic review reported 16% with transient LV outflow tract obstruction(LVOT) due to this hyperkinesis [1]. Coronary arteries are either normal or show mild stenosis(< 50% luminal stenosis) [1,22] On follow -up studies, patients show rapid improvement in wall motion and restoration of LV function with improved EF of 60-76% [1].

Acute complications occur in approximately 20% of TCM cases and include cardiogenic shock, left sided heart failure with or without pulmonary edema, tachy- and bradyarrhythmias, LV thrombus formation or free wall rupture, and death [1,8,22,24].

Currently, there is no established therapy to treat patients with this cardiomyopathy. Initially, individuals are treated for myocardial infarction until this diagnosis has been disproven [3]. Following a diagnosis of TCM, treatment is primarily focused on monitoring and supportive care. Guidelines published by American Heart Association and American College of Cardiology in 2014 suggest that patients should be treated with typical medications, including ACE inhibitors, beta blockers, aspirin, and diuretics as tolerated by the patient's hemodynamic status [25] Intra-aortic balloon pump has been shown to be successful in severe cases by reversing left ventricular outflow obstruction when the degree of hypokinesis is sufficiently severe to require exogenous catecholamines to maintain hemodynamic stability [26].

The patients in our case series were treated with diurecics,ACE inhibitors, beta blockers exhibited favorable outcomes. Furthermore, treatment of other preexisting or underlying physical conditions has also been helpful in rapidly reversing the Takotsubo pathology. Prognosis for patients with TCM is good for those who survive the acute episode. Mortality rates have been reported by Gianni etal[1] and Donohue and Movahed[11] at 1% and 3.2%, respectively. Recovery time for TCM patients is generally rapid. Marked improvement in ECG findings, cardiac markers, and EF can be seen within days [20,7,27,28]. Complete recovery of LV usually occurs within 1-4 weeks, although some have taken up to a year. Recurrence appears to be rare at 2-3% [1].

The emergency department deals with the consequences of natural disasters, and emergency physicians should be aware that this syndrome might present during or soon afterward. The syndrome may also occur in younger patients without cardiac risk factors. Some anxious or emotionally distraught patients with chest pain may be more complicated than simple anxiety disorder, and may develop dysrhythmias or shock.

The emotional distress and chest pain of family members after death notification are sometimes dismissed or managed with anxiolytics, benzodiazepines and social counselling. Emergency physicians should consider TCM in the differential diagnosis of chest pain following death notification. Increased awareness of this entity will contribute to timely diagnosis and appropriate treatment.

## Conclusion:-

Takotsubo cardiomyopathy(TCM) is a rare but potentially fatal condition, initially indistinguishable from acute coronary syndrome, thus diagnosis of this entity is often missed or delayed. Therefore, the physician should maintain a high index of suspicion for Takotsubo cardiomyopathy, especially in patients with chest pain and a recent stressful event, especially in elderly females.

**Figure Legends:**

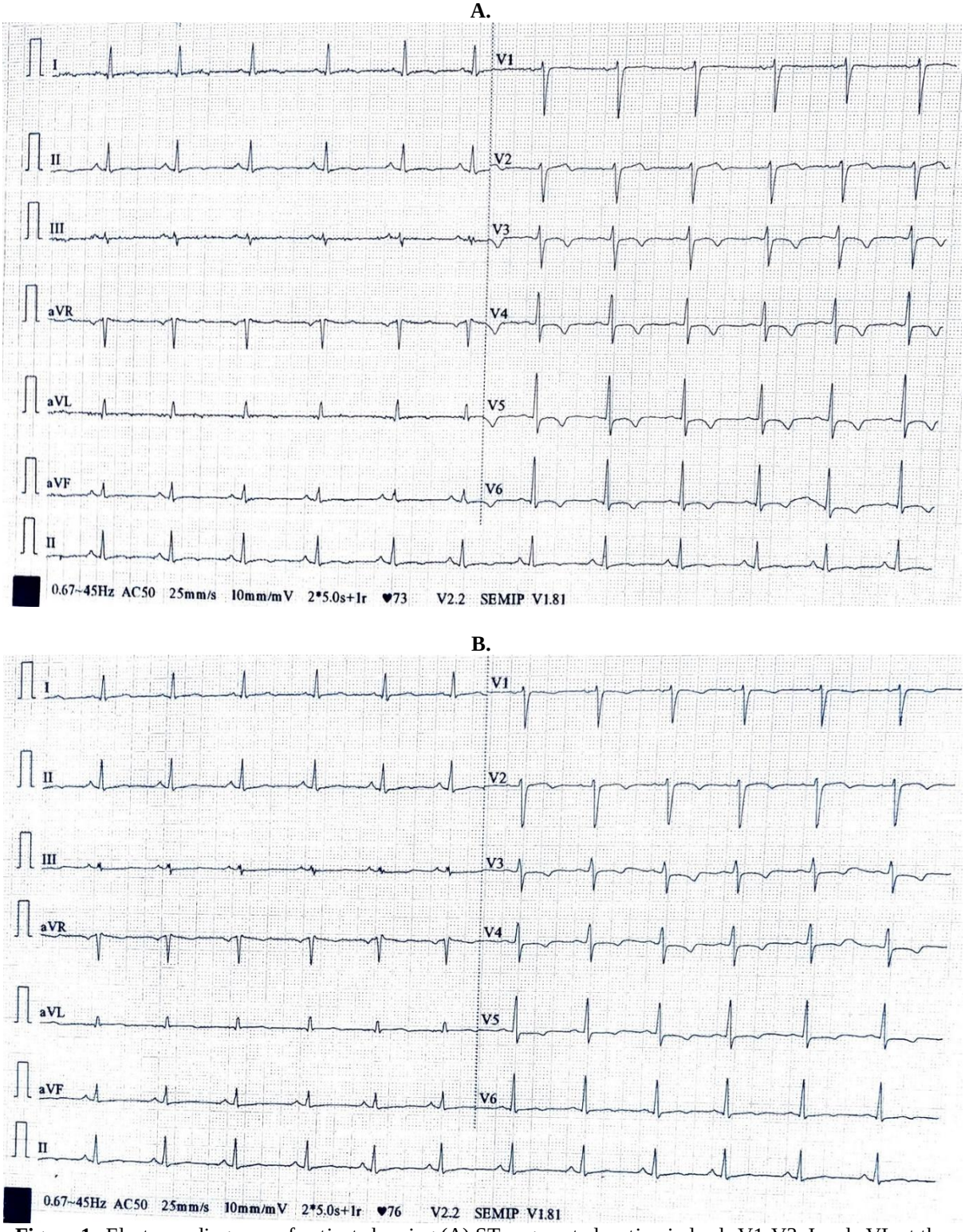


**Figure 1:**-Electrocardiograms of patient showing (A) ST-segment elevation in leads V1-V3, I and aVL at the presentation, (B) improvement of the T-wave inversion and normalization of ST-elevation at four days after presentation.

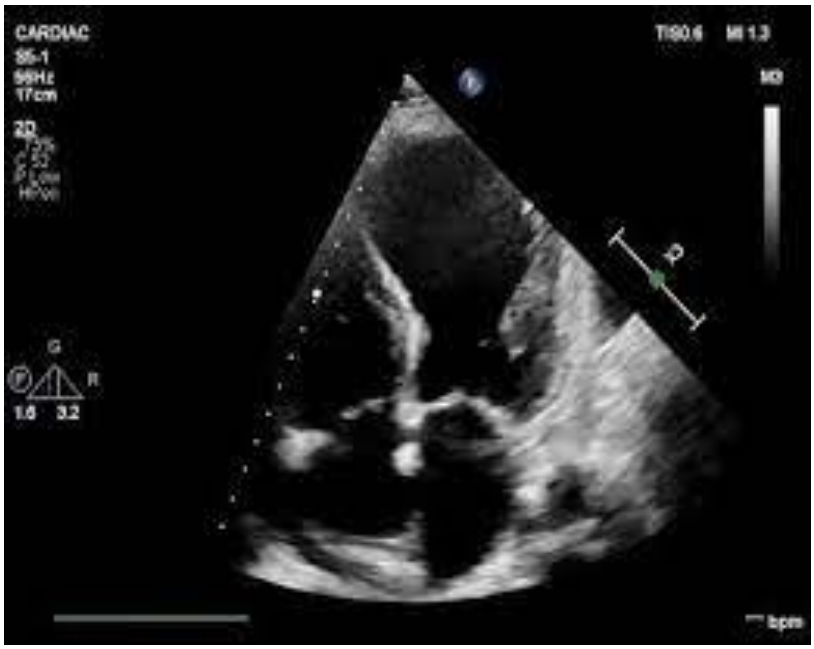


**Figure 2:-**Transthoracsic echocardiogram showing severely hypokinetic left ventricular anteroapical wall and mid to distal septum during systole.

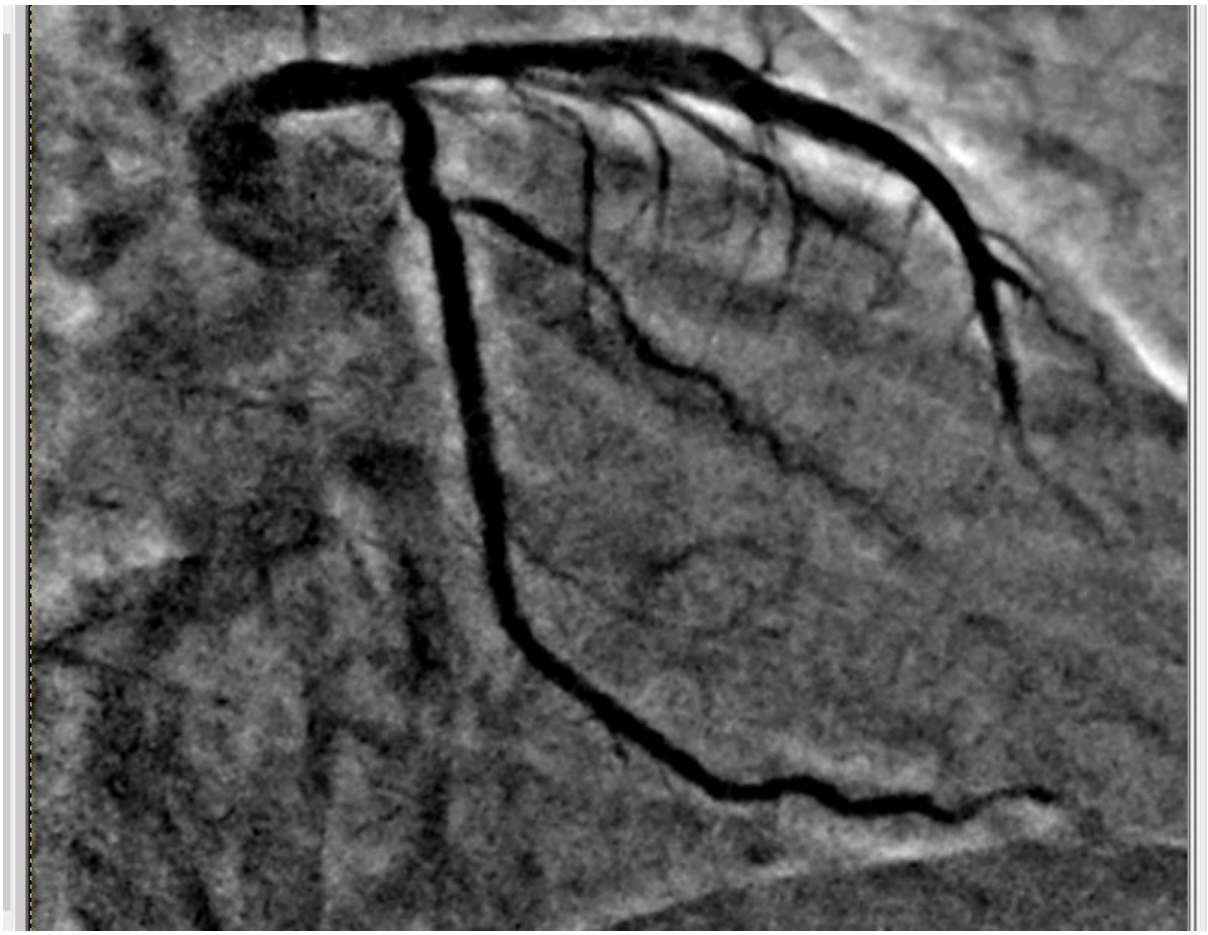

**Figure 3:-**Coronary angiogram showing normal coronary arteries.

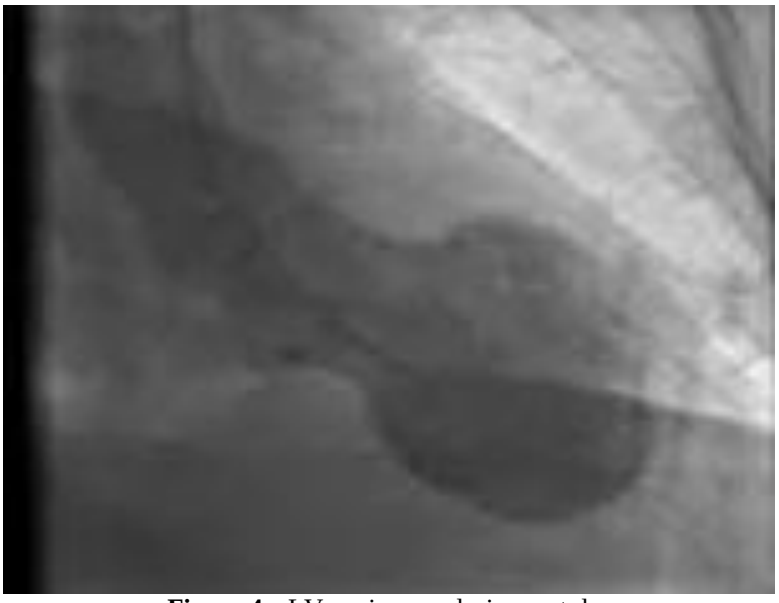

**Figure 4:-** LV angiogram during systole.

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