



“FUNCTIONAL STATUS OUTCOMES OF THE MANAGEMENT IN ACUTE CORONARY SYNDROMES (ACS) AMONG THE ELDERLY : A PROSPECTIVE STUDY AT A TERTIARY CARE CENTER IN KERALA, INDIA.”

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ABSTRACT Coronary artery disease is a major cause of death in the elderly all over the world and India. Even though evidence based therapies have improved the outcomes as a whole, outcomes in the elderly are equivocal. 228 consecutive cases of ACS (as per ACC/AHA guidelines) among the elderly admitted during a period of 6 months were enrolled in our study. Data was collected from EMR as well by personal interview using a semi-structured questionnaire and KPSS. After discharge, the patients were followed up at six months and one year. The mean of delta values of KPSS scores were computed each at 6 and 12 months of follow-up for both the management groups and Student's 't' test was applied for statistical analysis. 62.7% of cases were managed medically while the rest underwent interventions. The mortality in medically treated and those intervened at end of one year was 30%, 29.4% respectively. The mean delta of KPSS score after one year in medically treated and those underwent intervention were -0.9, 2.17 respectively. Elderly ACS patients receive less evidences based treatments. In our study we found that in elderly patients presenting with ACS, interventions including PTCA and CABG have almost similar nonetheless slightly better functional status outcomes compared to those managed medically over longterm.

KEYWORDS : ACS - Acute Coronary Syndrome, CAD - Coronary Artery Disease, KPSS - Karnofskys Performance Status Scale, NSTEMI - Non ST Elevation Myocardial Infarction, STEMI - ST Elevation Myocardial Infarction.

INTRODUCTION

Globally, the longevity of the population has increased, leading to a graying of population.

This has made the health care system focus on the emerging elderly population and hence the inception of Geriatric Medicine as an individual faculty in the practice of streamline medical departments.

With a growing geriatric population there exists a tremendous pressure on the health care delivery system too. It has now become evidently necessary to focus on geriatric problems.

In India, the proportion of geriatric population is showing an upward trend as demonstrated in the population and demographic studies conducted worldwide.

Of all the developing nations, India is going through the most rapid epidemiologic transition from communicable to non-communicable diseases which is characterized by high burden of atherothrombotic dominated non-communicable diseases.¹

Cardiovascular disease has emerged as a major health burden in developing countries. Coronary Artery Disease(CAD) constitutes the largest contributor to cardiovascular disease burden in India too. Cardiovascular risk factors for Ischemic Heart Disease and Acute Coronary Syndrome (ACS) are on the rise in people of Indian origin having a high burden of coronary artery disease and the later is now the leading cause of death.

India has the highest burden of Acute Coronary Syndrome (ACS) in the world. The CREATE registry provides contemporary data on 20,468 patients from 89 centers from 10 regions and 50 cities in India.² CAD is also found to occur in Indians 5–10 years earlier than in other populations around the world and the major reason of this peculiar phenomenon is the productive workforce of the country aged 35–65 years.³ It is predicted that more than half the worldwide cardiovascular disease risk burden will be borne by Indian sub continent in the next decade.⁴

There are significant differences in the prevalence of coronary artery disease with respect to gender, age and ethnicity as noted in various studies conducted pan-spectrum. India is currently experiencing an epidemic of Coronary Artery Disease (CAD). Statistics have shown that 20-25% of all medical admissions and 25% of all mortality is

attributed to CAD.¹⁰

The outcome of ACS are influenced by many factors viz, the level of health care or hospital setting, socio-demographic profile, comorbidities, education, financial status, premorbid functional status, etc. Age related inequalities in patient care, to a little extent can be explained by the higher incidence of atypical and delayed presentations alongwith underutilization of diagnostic procedures leading to a delay in the diagnosis of ACS.

Older patients represent a significant proportion of those presenting with ACS. However, they are under represented in clinical trial data owing to the fact that advanced age has been an exclusion criterion for the majority of studies done in the past. Elderly patients with an acute coronary syndrome (ACS) are less likely to be enrolled into randomized controlled trials or receive guideline-recommended therapies, because of a higher burden of comorbidity, including functional decline. And if included constitute a smaller subset of controlled population.

The selection of elderly patients for specific therapies and medication regimens still stays unanswered and even the reputed bodies of organizations seldom come up with clear guidelines.

Hence, there is a growing need for randomized controlled trials and subsequent data to be more representative of elderly population and enrolling patients with multiple co-morbidities.⁴

Inequalities and variations in ACS care are very well recognised, more so in elderly patients with ACS.⁵ Furthermore, there is also limited statistical data on the intermediate and long-term outcomes of ACS in India. Few studies have looked at the mortality prevalence but not at the functional status and quality of life outcomes.

Current guidelines for the management of older adults are the same as for their younger counterparts, provided the treatments are personalised. These include an appreciation of premorbid functional status of the patient, comorbidities, ischaemic and bleeding risk as well as the physiological changes associated with ageing such as impaired renal function, financial and familial support etc to name a few. It thus signifies the need for clinical trials focused specifically at elderly cohorts, and quality-of-care programs that reinforce the use of such management options among these individuals to evaluate the outcomes of elderly patients after such above mentioned management

strategies are instituted.

So, here in this study we tried to determine the characteristics and functional status outcome of patients diagnosed with ACS based on their management options viz., conservative (medical) and interventional (including both PTCA and CABG). This study was performed at Amrita Institute of Medical Sciences and Hospital and Research Centre, a tertiary care centre in Kochi, India.

METHODS

I] Selection and description of Participants :

A longitudinal, cross sectional descriptive study done at Amrita Institute of Medical Sciences having a specialized cardiac centre with 21 bed coronary care unit (CCU), cardiac surgery facility and has 3 state-of-the art cardiac catheterization laboratories performing high volume percutaneous coronary interventions (PCI). It provides 24 h service including 24 h on-the-spot consultant coverage in the CCU and cardiac laboratory. The cases enrolled in the study were patients aged >60 years and admitted with a diagnosis of ACS. The inclusion criteria included newly diagnosed ACS defined using documented triad of characteristic, ischemic symptoms, ECG changes and cardiac biomarker (troponin I) status.⁸ STEMI was defined as characteristic angina symptoms and ST segment elevation of 1 mm in at least 2 adjacent limb leads or 2 mm in at least 2 contiguous precordial leads and/or presumed new onset left bundle branch block (LBBB) on initial 12-lead ECG and troponin level greater than hospital cut-off point of 0.012 ug/L. NSTEMI was diagnosed if there were angina symptoms with ST segment depression 1 mm or T wave abnormalities and elevated troponin I level above 0.012 ug/L. Unstable angina was defined as documented angina symptoms at rest with ST segment depression or T wave abnormalities without ST segment elevation or elevated troponin level below 0.012 ug/L.⁵ Patients with ST segment elevation following coronary artery bypass graft (CABG) or PCI were excluded. To summarise, elderly patients with non-ST-segment elevation and ST-segment elevation ACS according to the European Society of Cardiology guidelines were included in the study. Standard structured questionnaire was utilized to collect data on demography including age, gender and nationality. Cardiovascular risk factors including alcohol consumption and smoking were also recorded. Data regarding the comorbidities viz., Type 2 diabetes, Hypertension, Dyslipidaemia, COPD was obtained from the past medical records and EMR. Information on family history of CAD was obtained during interviewing the bystanders. Data on other laboratory investigations/procedures including haemoglobin values, renal biochemistry, ECHO findings. The treatment strategies including drug treatment, PCI and CABG as well as complications and the functional status outcomes at baseline, 6 and 12 months using Karnofsky Performance Status Scale (KPSS) were recorded. Whereas the exclusion criteria were patients with a previous history of ACS.

II] Technical Information :

The primary objective of this study was to study the functional status outcomes of Acute coronary syndrome interventions in elderly (>60 years), whereas the secondary objectives were to study the factors associated with it. The study period ranged from August 2015 to March 2017 (6 months of case enrolment with follow ups at 6 and 12 months interval). The data of elderly patients admitted with a diagnosis of ACS was collected from EMR as well by personal interview using a semi-structured questionnaire. The patients were followed up at 6 months and 12 months interval by telephone / in-person, whichever was logistically convenient. An informed and written consent was taken from every patient. Ethical clearance from the our Institutes Ethics Committee was also sought after presenting the study before the esteemed committee members.

III] Statistics :

Data analysis was done using Statistical Package for Social Sciences software (SPSS Inc Chicago, Illinois version 17.0). Continuous variables were expressed as mean and SD and compared using independent t-test (2-tailed). Discrete variables were presented as percentages (proportions) and compared using Chi square or Fisher's Exact test, as appropriate. Categorical variables were compared by Chi-square test and the continuous variables are presented as mean (\pm standard deviation) and were compared by unpaired t-test. P value < 0.05 was considered to be statistically significant.

1] Mean and standard deviation of Karnofsky Performance Status

Scale was computed with respect to the treatment options utilized in the patients.

- 2] To test the statistical significance of the association of the difference in the functional status outcomes with respect to the management groups Student's 't' test was applied.
- 3] Data was prospectively entered in the MS Excel 2007 and an appropriate statistical test was applied.
- 4] A mean of delta values of KPSS scores were computed each at 6 and 12 months of follow-up for both the management groups and Student's 't' test was applied for further statistical analysis.

RESULTS

A total of 228 patients with acute coronary syndrome (ACS) were admitted during the 6 months case enrollment study period from August 2015 to January 2016.

The patients were aged 71.25 ± 7.4 years (range: 60-94 years, median 70.5 years).

The enrolled patients were categorized into 3 groups - a) 60-70 years b) 71-80 years c) 81 years and above.

The total number of male patients enrolled in the study were 159 (69.7%), whereas females were 69 (30.3%) of the total sample size of 228

Various comorbidities were noted in the patients enrolled in our study. Background history of 4 major comorbidities were recorded. 154 patients were diabetics, followed by 147 patients being hypertensives, 109 patients were dyslipidemics and 74 patients suffered from COPD. 161 cases were of NSTEMI whereas 67 cases were of STEMI type of ACS cases that were enrolled in the study. Since, Unstable Angina variant of cases were a mere few they were not included in the study for the sake of statistical convenience.

143 patients were enrolled for medical management, whereas remaining 77 underwent primary PTCA and 8 patients underwent CABG. The patients enrolled in my study were followed after 6 months and 12 months of enrollment.

Primarily, data regarding their current functional status was taken using the KPSS at the said intervals.

Patients were grouped into two main management groups –

- 1] those ACS patients managed Medically
- 2] those ACS patients who underwent Interventions (including both Coronary Artery Bypass Graft and Percutaneous Transluminal Coronary Angioplasty)

These KPSS scores were compared to their baseline scores noted pre-morbidly (before the development of ACS) 143 (62.7%) patients out of total 228 patients were medically managed whose mean KPSS Score was 81.33 (p-value 0.419) at the time of enrolment (pre-morbid functional status) whereas, remaining 85 (37.3%) patients were intervened (PTCA+CABG) whose mean KPSS Score was 82.71 (p-value 0.413) at the time of enrolment.

55 out of the 228 patients enrolled in the study were reported to be dead and lost to further follow up at the end of 6 months of their enrollment (35 and 20 each enrolled under medically managed and intervention group respectively). While an additional of 13 people (8 and 5 each enrolled under medically managed and intervention group respectively) died at 12 months follow up periods.

A follow-up of alive patients was done at 6 and 12 months interval with mean KPSS of medically managed/ intervention groups being 80.83 (p-value 0.732) / 81.5 (p-value 0.729) and 79.2 (p-value 0.011) / 84.26 (p-value 0.006) respectively.

For statistical superiority and for comparing between the management options used based on the functional status of the patients as per the KPSS score, a mean of delta values of these scores were computed each at 6 and 12 months of follow.

A Null hypothesis was defined as there existed no functional superiority between these two management groups whereas, an alternate hypothesis stated, intervention had functional outcome superiority compared to medically managed group.

Hence, intervention group patients (p-value 0.072) were found to have a slightly higher functional outcome superiority as documented by Karnofsky Performance Status Scale compared to medically managed patients (p-value 0.172) at the end of 12 months follow in elderly ACS patients as computed statistically by using student t test. Even though a statistically significant (p value < 0.05) was not observed in our study but a downward trend in p value was noted at the end of 12 months of follow up. Provided the study was carried forward and the sample sizes enrolled in both the management arms were more a statistical significant p value could have been achieved. It is a limitation of this study.

DISCUSSION

The prevalence of cardiovascular disease increases with age and cardiovascular disease is the leading cause of death in adults >75 years of age as has been noted in various studies done across the platform. However many trials have excluded older patients. So, we don't have randomized trials but only limited subgroup analysis or registries for older patients.

To quote, the indications for intervention and revascularization are not different in elderly patients. But complex co-morbidities, significant physical or cognitive disabilities can change our decision. In presence of complex coronary anatomy the complications procedure is higher in older patients.

Long term mortality is similar in patients treated with Coronary artery bypass graft surgery or percutaneous coronary intervention, but re-intervention is higher in coronary intervention group.

Invasive approach is found to be superior to conservative treatment even in very elderly patients with acute coronary syndrome. Having mentioned that, we need more randomized trials who include mainly older patients in these times.¹

We analysed data from various registries of patients with acute coronary syndromes from India and abroad. The main studies used by me as references were CREATE Registry India, Global Registry of Acute Coronary Syndromes.

Various variables like characteristics of patients, practice patterns, and the rates of major outcomes from a range of hospitals in different regions of India and abroad were noted.

By contrast with data from developed countries, we recorded more cases of STEMI than non-STEMI or unstable angina, different practice patterns and outcomes.

The types of acute coronary syndromes in my study differed from those recorded in developed countries.

About 30% of patients who we assessed had STEMI, whereas in reports from developed countries, including the European Heart Surveys fewer than 40% had STEMI the findings of whose are similar to my study. This suggests that patients admitted to Indian hospitals with acute coronary syndromes are likely to have worse prognoses than those in other countries.

So also, data from the developed countries and my study record more cases of NSTEMI than STEMI or unstable angina in the elderly.

Heart disease is the lethal cause of death more common in adult male & smoking is the major risk factor. In the present study maximum no. of cases of ACS were in the age group 61 to 70 (50%) the cases were predominately male (69.7%) suggesting that it is predominately a disease of men as noted in other studies. The present study also shows that with increasing age the preponderance of male patients admitted with ACS decreases and sex ratio becomes smaller.

This possibly reflects a higher percentage of female and elderly population and more equal distribution of risk factors for ACS in both genders at high age group.

Even after the age 60 as a group more females are prone to CAD the number of female patients are less was strikingly as noted in my study. Alcohol consumption was the leading risk factors (131 out of 228) followed by smoking and presence of coronary disease in the family.

Male preponderance and smoking being the major risk factor as seen in Yusuf S et al.⁷ Diabetes alone was a risk factor in 154 out of 228 and hypertension in of the total enrolled cases 147 cases alone. Diabetes mellitus is well known to have and adverse influence on the prognosis of patients with ACS as noted in Hasdai D et al study.⁸

Elderly patients suffer from various comorbidities as we have mentioned in our study viz., Type 2 Diabetes Mellitus, Systemic Hypertension, Dyslipidemia, Chronic Obstructive Pulmonary Disease. A special mention about the incidence of anaemia and development of ACS in elderly also has to be noted. In my study we see a lot of elderly patients were enrolled to have anaemia from, with a mean Hb of 11.039. a total of 102 cases had haemoglobin below 12.5 that were enrolled in the study. Anaemia was more common in the elderly 40.4%, similar data was noted in my study with anaemia being present in 44.73% of patients. However, the prognostic impact of anaemia in the elderly with acute coronary syndromes has not been specifically analysed, and little information exists about causes of mortality in this setting. The association between anaemia in elderly with ACS and mortality was not analysed in our study.

Data from the study by Huerre also indicate that functional decline does occur quiet frequently in elderly patients presenting with an ACS and does not alter the hospital therapeutic management of these patients significantly. They also add that functional decline could be considered as a marker of poor prognosis in ACS management.⁸ In addition to other comorbid conditions, altered functional and cognitive status associated with ageing reduces activity and is therefore likely to reduce life expectancy after an ACS.⁸

The reason for opting medical management in the elderly in the context of Indian setting is varied. To quote a few, financial burden of intervention procedures, patients desire, patients medically ineligible for PCI/ CABG, notion of medical therapy being safe and unharmed, lack of supportive evidence, late presentation to the hospital due to unawareness about health issues in the elderly and delay in diagnosis. The mean duration for which the patient stayed in AIMS as noted in our study was 9 days.

The policy of discharging AMI patients earlier (in fewer than 4 days) without any interdisciplinary intervention by health care providers while they are on admission is claimed to be cost-saving. However, in the long run, the quality of life of these patients will be compromised. On the other hand, longer stays may allow more time for clinical pharmacists and concerned physicians to practise pharmaceutical care interventions, medication counselling and therapeutic agents optimisation which have been associated with improved long-term prognoses.¹⁰

As noted in the study by Isezuo et al.¹¹ pharmacotherapy mainly dual-antiplatelet treatment which included clopidogrel was used at a rate quite higher than many previous reports from India and comparable to the developed nations was noted in unison with our study in which 62.7% cases of ACS were managed medically.

The reason of deaths were not studied in our study as the patients were only followed up at timely intervals of 6th and 12th month after enrollment in the study.

37.3% cases underwent intervention. This finding also is at par with the previously reported in India^{2,11} and comparable with the findings in the developed nations.^{4,11} The PCI rate was also higher than previously reported in India. Patients' choice of treatment strategy, disease severity, financial difficulties, family decision and old age might have influenced PCI rate in the current report.

This study provides information on epidemiology, practice patterns and outcomes of patients with ACS in a specialized cardiac centre in South India. We observed similar demographic

and CAD risk profiles to the previous reports from Indian and some other developing nations.¹¹

It is a need of the time to start thinking out of the box for the long term. A new shift in paradigm is required for the management of old and very old patients with ACS, in which evaluation of outcomes traditionally ignored by cardiologists should be considered, including parameters

such as independence, return to usual life place, and quality of life and functional status.¹²

STRENGTHS AND LIMITATIONS :

Our study estimates and compares the functional status outcomes between the two main management options for the elderly with ACS. Hence, helps in guiding physicians to choose between the management option for which no strong evidence based guidelines are available. However, a better assessment of quality of life, frailty, nutritional, functional and cognitive status, is necessary to better separate age-related health issues from ACS-related risk. These secondary outcomes could be better studied at follow up studies.

CONCLUSION :

Prognosis of elderly ACS patients remains clearly severe. Functional decline is frequently noted in this setting and emerges as single most vital predictor of poor outcome in these older patients. There is a lack of evidence-based guidelines and protocols for the management of these ACS types in the elder population. Functional decline seems to portend poor prognosis in elderly ACS patients. Larger, community-based studies are needed to confirm these findings in a multivariable model. In conclusion, elderly patients with acute coronary syndromes in India tend to have a higher rate of NSTEMI as is seen among patients in developed countries. In our study we found that, elderly patients presenting with ACS, the intervention management strategies including PTCA and CABG (p value 0.072) have almost similar nonetheless slightly better outcomes in elderly patients developing ACS managed medically (p value 0.172). A bigger cohort of similar patients is required to be enrolled and studied to statistically and significantly conclude above mentioned findings.

TABLE 1 - Cases enrolled and followed under the ACS Management Arms

	NO OF CASES(n)	
	MEDICAL	INTERVENTION
AT BASELINE	143	85
AT 6 MONTHS	108	60
AT 12 MONTHS	100	55

TABLE 2 - Comparison between delta values at 6th and 12th months among ACS management types

Delta Values	Types of Managements	No. of Patients (n)	Mean	SD	t - Test Value	p - value	Significance
At 6 th Month (n=173)	Medical	108	1.11	14.09	1.371	0.172	> 0.05
	Intervention	65	-2.15	16.81			
At 12 th Month (n=160)	Medical	100	-0.90	9.85	-1.808	0.072	> 0.05
	Intervention	60	2.17	11.21			

TABLE 3 - Comparison of acute coronary syndromes in developed and developing countries

STUDY	ACS TYPE(%)		MEAN AGE (years)
	STEMI	NSTEMI	
1] OUR STUDY	29.4	70.6	71.25
2] CREATE27	61	39	57
3] Global Registry of Acute Coronary Syndromes28	30-40	60-70	64-69
4] European Heart Surveys29	42	51	63

FIGURE 1 - Pattern of gender distribution in our study

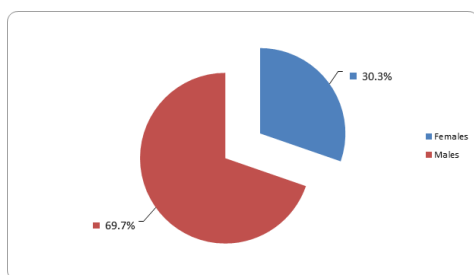
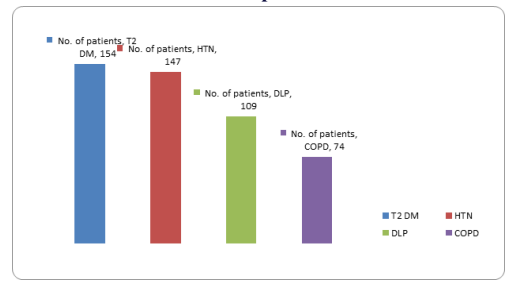


FIGURE 2 - Comorbidities in the patients enrolled in our study



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