

NON-INVASIVE PREDICTORS AND PREVALENCE OF LEFT MAIN OR TRIPLE VESSEL DISEASE IN PATIENT WITH CORONARY ARTERY DISEASES

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ABSTRACT

BACKGROUND

Aim- Coronary artery disease is one of the common cause of death all over the world. There have been only few studies done regarding non-invasive predictors and prevalence of left main (LMD) or triple vessel disease (TVD) in patients with CAD. Uncertainties still exist about their prevalence and predictors in patients with CAD. Our aim was to detect non-invasive predictors, prevalence and clinical profiles of LMD/TVD patients.

MATERIALS AND METHODS

We collected data of 200 consecutive patients with CAD at our hospital (a tertiary care center). Selective coronary angiography in multiple views was performed by standard technique to define both the extent and severity of disease. Patients with LMD/TVD were included in the study and evaluated for their non-invasive predictors. Patients were divided into two groups-acute coronary syndrome (ACS) group and patients with stable coronary disease group (EA-Effort angina). Stable coronary disease group means TMT positive patients. A predefined proforma was completed in every patient with a detailed clinical history, physical examination, and investigation studies. The clinical history revealed information about age, gender, risk factors, modes of presentation, and duration of symptoms. The details of physical examination including anthropometric data, vital signs and complete systemic evaluation were recorded. The subjects were evaluated for conventional risk factors i.e. smoking, diabetes mellitus, systemic hypertension and family history of premature CAD.

RESULTS

Diabetes and dyslipidaemia was more common in ACS group compared to EA group and it was statistically significant. AWM was most common in ACS group. Low ejection fraction and high TIMI score was seen in ACS group and it was statistically significant. Incidence of TVD+LMD was 17%, only TVD 24% and only LMD was 9%, it is comparable with other study. ECG-aVR elevation was seen in 24% patients and it was statistically significant and it is comparable with other study. The most common predictors of TVD/LMD disease were heart failure at clinical presentation (reported in 44% of studies), degree of ST elevation in lead aVR (reported in 24% of cases) and high TIMI score (reported in 88% of cases) were the most powerful predictors, all of them were statistically significant.

CONCLUSION

We concluded that an ST↑aVR of 0.5 mm or greater predicted LMD/TVD and an independent predictor of prognosis during hospitalization period. Low ejection fraction and high TIMI score are also good noninvasive predictors of LMD /TVD. Prevalence of LMD and TVD in our study was 9% and 24% respectively.

KEYWORDS

CAD Coronary Artery Disease, Triple Vessel Disease, Left Main.

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BACKGROUND

Left main coronary disease (LMD) and three-vessel coronary disease (3VD) carry a high risk of death and adverse events in both stable and unstable clinical settings.^{1,2} This poor prognosis may be improved in selected patients by percutaneous or surgical revascularisation.^{1,3} but invasive interventions are often not carried out because of underestimation and poor definition of patient risk. In a large contemporary registry, percutaneous coronary intervention was performed in only 70% of patients with acute

myocardial infarction and 35% of patients with unstable angina.⁴

Clearly reliable and independent predictors of LMD/3VD could be helpful in order to focus resources and aggressive therapies to this high-risk subset of patients. A few studies have addressed these issues in various populations.^{5,6} early (i.e., before angiography), accurate, non-invasive identification of patients with LM/3VD in whom CABG is most likely to be indicated is thus a major clinical issue with important therapeutic implications.

MATERIALS AND METHODS

Our aim was to detect non-invasive predictors, prevalence and clinical profiles of LMD/TVD patients. There have been only few studies done regarding non-invasive predictors and prevalence of left main (LMD) or triple vessel disease (TVD) in patients with CAD. Uncertainties still exist about their prevalence and predictors in patients with acute coronary syndrome (ACS) and also in patients with stable coronary disease. Left main disease (LMD) and three-vessel disease (3VD) have important prognostic value in patients with coronary artery disease.⁷

We collected data of 200 consecutive patients with CAD during 2013 at our hospital (a tertiary care center) out of which 100 patients were having either TVD or LMD disease were included in our study. Inclusion criteria was coronary angiography showing LMD/TVD. Exclusion criteria other conditions with ST-segment elevations in aVR lead in ECG (left or right bundle branch block, left ventricular hypertrophy, ventricular pacing, ventricular preexcitation, non-ischemic cardiomyopathy, or antiarrhythmic drugs)

Selective coronary angiography in multiple views was performed by standard technique to define both the extent and severity of disease. Significant CAD was defined as at least 50% reduction in the diameter of major epicardial coronary arteries. Patients with LMD/TVD were included in the study and evaluated for their non-invasive predictors. Patients were divided into two groups- acute coronary syndrome (ACS) group and patients with stable coronary disease group (EA-Effort angina). Stable coronary disease group means TMT positive patients.

A predefined proforma was completed in every patient with a detailed clinical history, physical examination, and investigation studies. The clinical history revealed information about age, gender, risk factors, modes of presentation, and duration of symptoms. The details of physical examination including anthropometric data, vital signs and complete systemic evaluation were recorded. The subjects were evaluated for conventional risk factors i.e. smoking, diabetes mellitus, systemic hypertension and family history of premature CAD.

Smoking was defined as regular smoking of cigarettes / beedies (a local type of tobacco). Patients who stopped smoking more than one year before the onset of disease were classified as ex-smokers. Diabetes mellitus was diagnosed on the basis of fasting blood glucose levels of >126 mg/dl or a patient already on anti-diabetic medications. Systemic hypertension was considered to be

present if the patient was taking anti-hypertensive treatment at the time of hospital admission or if blood pressure (BP) was recorded ≥ 140 mmHg systolic and/or ≥ 90 mmHg diastolic, at least twice on examination during admission

A positive family history of premature CAD was defined as any first degree relative that had documented CAD below the age of 55 years in males or 65 years in females. For lipid analysis, samples were obtained after an overnight fast at hospital admission. Samples were analysed for total cholesterol (TC), high density lipoprotein cholesterol (HDL-c), low density lipoprotein (LDL-c) and for triglyceride (TG). Dyslipidaemia was defined in accordance with the reports of the National Cholesterol Education Programme (Adult Treatment Panels II and III).^{8,9}

The diagnosis of CAD was made on the basis of clinical history (typical angina, history of MI), 12-lead standard electrocardiogram (ECG) and 2D-Echocardiography wherever necessary. Diagnosis of ACS was in accordance with the consensus paper from the ESC-ACC-AHA-WHF joint taskforce.¹⁰

Electrocardiographic Classification- ST-segment shifts were measured 80 ms after the J point for ST-segment depression and 20 ms after this point for ST-segment elevation, using the preceding TP segment as a baseline.¹¹ ST-segment elevation was considered present if elevation was more than 0.5 mm in aVR lead.

Statistical Analysis- Statistical analysis was primarily descriptive and focused on reporting the incidence of risk factors, clinical presentation and angiographic profile. Continuous variables have been summarized as mean with standard deviation.

RESULTS

	EA (n-20) (20%)	ACS (n-80) (80%)	P- value
Men	18	68	-
Arrhythmias	0 (0%)	2 (2.5%)	0.475
diabetes	6 (30%)	40 (50%)	0.108
hypertension	8 (40%)	56 (70%)	0.012*
dyslipidemia	2 (10%)	32 (40%)	0.011*
Smoking	10 (50%)	28 (35%)	0.216
Alcohol	4 (20%)	10 (12.5%)	0.387
Family history of IHD	6 (30%)	24 (30%)	1.000
EF-40-50	4 (20%)	40 (50%)	0.037
51-60	16 (80%)	40 (50%)	0.037

Table 1. Risk Factors in Patients with ACS

Age in Years	No. of Patients	Percentage
<40	4	4.0
41-50	12	12.0
51-60	46	46.0
61-70	30	30.0
>70	8	8.0
Total	100	100.0

Table 2. Age Distribution in Patients

Mean \pm SD: 57.38 \pm 9.68

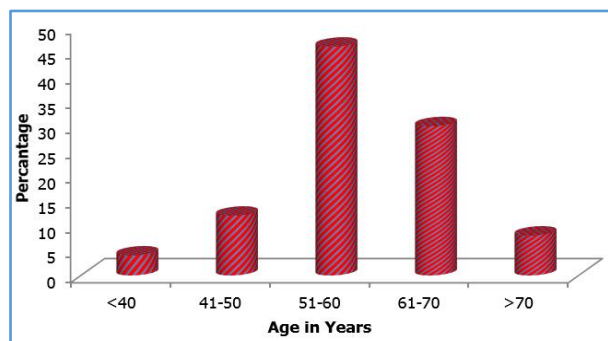


Chart 1. Mean Age of Our Patients was 57 Years

Mean age of our patients was 57 years.

Gender	No. of Patients	%
Female	14	14.0
Male	86	86.0
Total	100	100.0

Table 3. Gender Distribution of Patients Studied

Mode of Presentation	No. of Patients	%
Chest pain	64	64.0
Dyspnea	18	18.0
Fatigue	8	8.0
EA	8	8.0
Syncope	2	2.0
Total	100	100.0

Table 4. Mode of Presentation

Chestpain was most common mode of presentation.

	No. of Patients (n=100)	%
Arrhythmias	2	2.0
diabetes	46	46.0
hypertension	64	64.0
dyslipidemia	34	34.0
Smoking	38	38.0
Alcohol	14	14.0
Family history of IHD	30	30.0
Killip class	10	10.0

Table 5. Clinical Features of Patients Studied

Hypertension was most common comorbid condition followed by diabetes.

Type	No. of Patients (n=100)	%
AWMI	36	36.0
IWMI	28	28.0
LWMI	2	2.0
NSTEMI	10	10.0
UA	4	4.0

Table 6. Type of Acute Coronary Syndromes

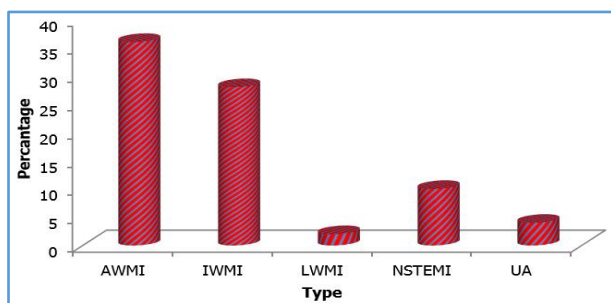


Chart 2. Type of MI

AWMI was most common MI.

Diagnosis	No. of patients	Percentage
EA	20	20.0
ACS	80	80.0
Total	100	100.0

Table 7. Diagnosis

Age in Years	EA	ACS	Total
<40	0 (0%)	4 (5%)	4 (4%)
41-50	4 (20%)	8 (10%)	12 (12%)
51-60	8 (40%)	38 (47.5%)	46 (46%)
61-70	6 (30%)	24 (30%)	30 (30%)
>70	2 (10%)	6 (7.5%)	8 (8%)
Total	20 (100%)	80 (100%)	100 (100%)

Table 8. Age Distribution of Patients Studied according to Type of ACS

P=0.011*, Significant, Fisher Exact test

Most of our patients were in age group of 51-60 years.

Gender	EA	ACS	Total
Female	2 (10%)	12 (15%)	14 (14%)
Male	18 (90%)	68 (85%)	86 (86%)
Total	20 (100%)	80 (100%)	100 (100%)

Table 9. Gender Distribution of Patients Studied according to Type of ACS

P=0.654, Not significant, Chi-Square test.

Ejection fraction	Type of ACS		Total
	EA	ACS	
40-50	4 (20%)	40 (50%)	44 (44%)
51-60	16 (80%)	40 (50%)	56 (56%)
Total	20 (100%)	80 (100%)	100 (100%)

Table 10. Clinical Features According to Type of ACS

Features	EA (n=20)	ACS (n=80)	Total (n=100)	P value
Arrhythmias	0 (0%)	2 (2.5%)	2 (2%)	0.475
diabetes	6 (30%)	40 (50%)	46 (46%)	0.108
Hypertension	8 (40%)	56 (70%)	64 (64%)	0.012*
dyslipidemia	2 (10%)	32 (40%)	34 (34%)	0.011*
Smoking	10 (50%)	28 (35%)	38 (38%)	0.216
Alcohol	4 (20%)	10 (12.5%)	14 (14%)	0.387
Family history of IHD	6 (30%)	24 (30%)	30 (30%)	1.000

Table 11. Ejection Fraction According to type of ACS

P= 0.037*, Significant, Chi-Square test.

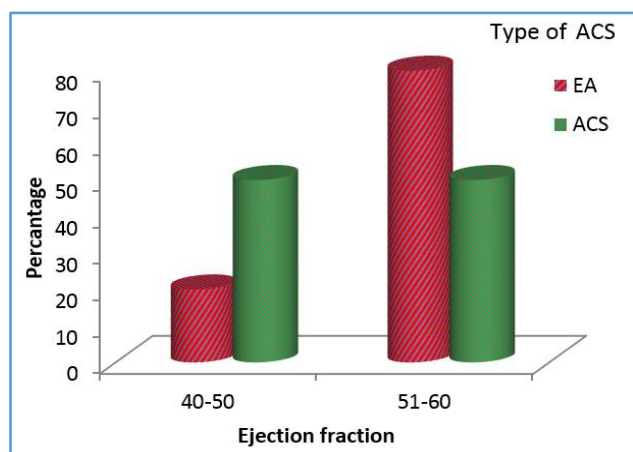


Chart 3. Ejection Fraction in Two Groups of Patients

	EA (n=20)	ACS (n=80)	Total (n=100)	P value
Renal dysfunction				
• No	16 (80%)	52 (65%)	68 (68%)	0.198
• Yes	4 (20%)	28 (35%)	32 (32%)	
Total occlusion				
• No total occlusion	20 (100%)	78 (97.5%)	98 (98%)	0.475
Total occlusion	0 (0%)	2 (2.5%)	2 (2%)	
Thrombus				
• No	14 (70%)	62 (77.5%)	76 (76%)	0.482
• Yes	6 (30%)	18 (22.5%)	24 (24%)	
Hypothyroidism				
• No	16 (80%)	58 (72.5%)	74 (74%)	0.494
• Yes	4 (20%)	22 (27.5%)	26 (26%)	
Carotid Doppler				
• No Stenosis	16 (80%)	48 (60%)	64 (64%)	0.096+
• Stenosis present	4 (20%)	32 (40%)	36 (36%)	
TIMI score				
• <4	8 (40%)	2 (2.5%)	10 (10%)	<0.001**
• 4-8	12 (60%)	76 (95%)	88 (88%)	
• >8	0 (0%)	2 (2.5%)	2 (2%)	
Table 12. Renal Dysfunction, Total Occlusion, Thrombus, Hypothyroidism, Carotid Doppler, TIMI Score According to Type of ACS				

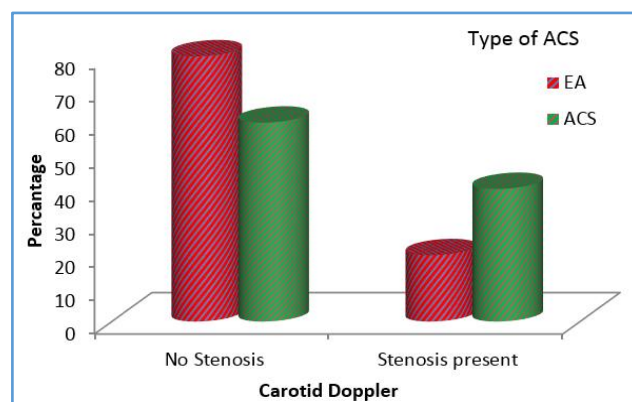


Chart 4. Carotid Doppler Finding in Two Group of Patients

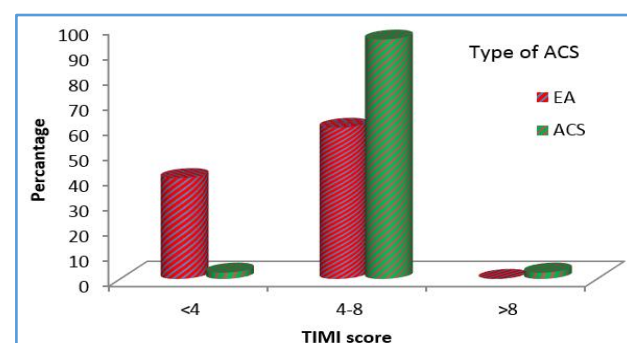


Chart 5. Comparison of TIMI Scores ACS Patients

Variables	Type		Total (n=100)	P value
	EA (n=20)	ACS (n=80)		
CAG of 200 patients				
• TVD+ LMCA	10 (5%)	24 (12%)	34 (17%)	0.212
• ONLY TVD	8 (4%)	40 (20%)	48 (24%)	
• ONLY LMCA	2 (1%)	16 (8%)	18 (9%)	
ECG-AVR elevation-For 200 patients				
• No	18 (90%)	34 (42.5%)	52 (52%)	<0.001**
• Yes	2 (1%)	46 (23%)	48 (24%)	
Table 13. CAG, ECG-AVR Elevation, According to type of ACS				

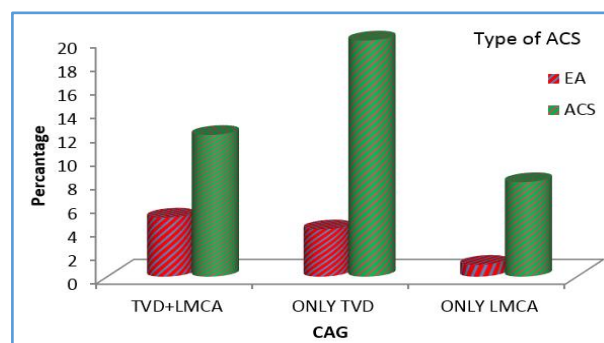


Chart 6. Angiography Finding in Two Groups

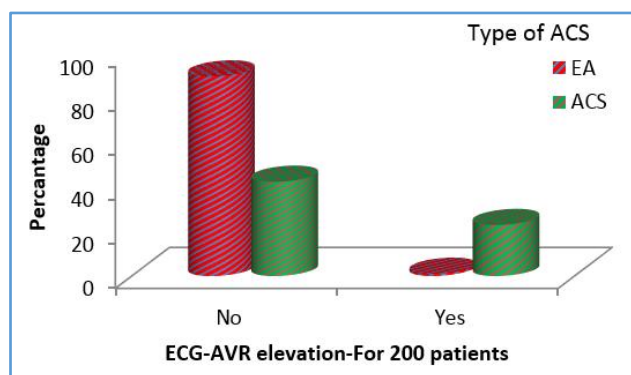


Chart 7. ECG-AVR Changes in Two Groups

	ECG-AVR elevation		Total (n=100)	P value
	Not Elevated (n=52)	Elevated (n=48)		
Renal dysfunction				
• No	42 (80.8%)	26 (54.2%)	68 (68%)	0.004**
• Yes	10 (19.2%)	22 (45.8%)	32 (32%)	
Total occlusion				
• No total occlusion	52 (100%)	46 (95.8%)	98 (98%)	0.228
• Total occlusion	0 (0%)	2 (4.2%)	2 (2%)	
Thrombus				
• No	38 (73.1%)	38 (79.2%)	76 (76%)	0.476
• Yes	14 (26.9%)	10 (20.8%)	24 (24%)	
Hypothyroidism				
• No	42 (80.8%)	32 (66.7%)	74 (74%)	0.108
• Yes	10 (19.2%)	16 (33.3%)	26 (26%)	
Carotid Doppler				
• No Stenosis	34 (65.4%)	30 (62.5%)	64 (64%)	0.764
• Stenosis present	18 (34.6%)	18 (37.5%)	36 (36%)	
TIMI score				
• <4	8 (15.4%)	2 (4.2%)	10 (10%)	0.066+
• 4-8	44 (84.6%)	44 (91.7%)	88 (88%)	
• >8	0 (0%)	2 (4.2%)	2 (2%)	
Table 14a. Renal Dysfunction, Total Occlusion, Thrombus, Hypothyroidism, Carotid Doppler, TIMI Score According to Type of ECG				

Table 14a. Renal Dysfunction, Total Occlusion, Thrombus, Hypothyroidism, Carotid Doppler, TIMI Score According to Type of ECG

CAG	ECG		Total (n=100)
	Not Elevated (n=52)	Elevated (n=48)	
TVD + LMCA	10 (5%)	24 (12%)	34 (17%)
Only TVD	32 (16%)	16 (8%)	48 (24%)
• Only LMCA	10 (5%)	8 (4%)	18 (9%)

Table 14b. CAG According to Type of ECG

P=0.004**, Significant, Chi-square test.

Ejection fraction	ECG		Total
	Not Elevated	Elevated	
40-50	18 (34.6%)	26 (54.2%)	44 (44%)
51-60	34 (65.4%)	22 (45.8%)	56 (56%)
Total	52 (100%)	48 (100%)	100 (100%)

Table 15. Ejection Fraction According to ECG

P=0.049*, Significant, Chi-Square test.

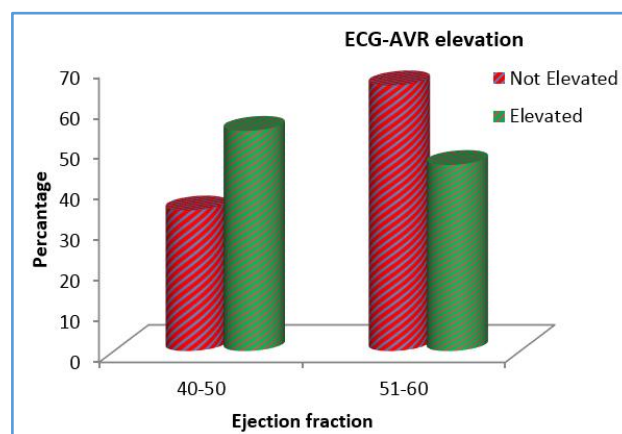


Chart 8. Comparing Ejection Fraction in Patients with and Without ST Elevation in Lead AVR

Statistical Methods- Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean \pm SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions- 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant Figures-

+Suggestive significance (P value: 0.05 <P <0.10)* Moderately significant (P value: 0.01 <P \leq 0.05)** Strongly significant (P value : P \leq 0.01)

Statistical Software-

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Out of 200 patients studied 100 patients were having either TVD or LMD disease. Clinical and angiographic profile of these 100 patients is as follows. 80 patients presented as ACS and 20 as EA.

Mean age of our patients was 57 years. 86% our patients were males. Chest pain was most common

presentation. 64% our patients were hypertensives, 46% diabetic and 34% dyslipidemic. Diabetes and dyslipidemia was more common in ACS group compared to EA group and it was statistically significant. AWWMI was most common in ACS group. Low ejection fraction and high TIMI score was seen in ACS group and it was statistically significant. Hypothyroidism was seen in 26% patients. Carotid artery stenosis was seen in 36% patients.

Incidence of TVD+LMCA was 17%, only TVD 24% and only LMCA was 9%, it is comparable with other study.¹²

ECG-aVR elevation was seen in 24% patients and it was statistically significant and it is comparable with other study.¹² Patients were also divided into ECG-aVR elevation group and non-elevation. ECG-aVR elevation was seen more commonly with TVD+LMCA patients, it was statistically significant, and it is comparable with other study. ECG-aVR elevation group of patients had low ejection fraction, high TIMI score and renal dysfunction, it was statistically significant.

The most common predictors of TVD/LMCA disease were heart failure at clinical presentation (reported in 44% of studies), degree of ST elevation in lead aVR (reported in 24% of cases) and high TIMI score (reported in 88% of cases) were the most powerful predictors, all of them were statistically significant.

DISCUSSION

The key findings of our study are: (a) LMD and TVD are common clinical conditions, more common than generally expected, in both stable and unstable coronary disease; (b) simple, inexpensive and readily available clinical and laboratory tests may be helpful for screening patients with these high-risk conditions to enable them to receive optimal treatment.

Patients with TVD and LMD have been the subject of several investigations to assess the best revascularization procedure.¹² For this reason, it is useful to know tools that could quickly identify this condition or raise a strong clinical suspicion

Incidence of TVD+LMCA was 17%, only TVD was 24% and only LMCA was 9%, it is comparable with other study. The most powerful predictors of LMCA or TVD were degree of ST elevation in lead aVR and heart failure. Our percentage of LMCA is slightly higher than literature data of 4.7% to 9%.^{13,14,15} In our analysis, 25% patients with ACS were affected by TVD; this rate is higher than reported in data extrapolated from CADILLAC (15.6%) and Stent-PAMI I (13.18%) study.^{16,17} COURAGE study show incidence of TVD was 25%.¹⁶

Another important aspect to consider is that we found the most powerful predictors of TVD and LMD to be ST elevation in lead aVR, high TIMI score and a clinical finding of heart failure. It is important to emphasise this finding because it means that clinical examination and the 'plain old 12-lead ECG' are still among the top predictors in the evaluation of ACS, even though new technologies are assuming an increasing role.¹⁸⁻²⁰ Moreover, this could be very useful in the clinical evaluation of unstable disease: if

LMD is suspected, ergometric tests should be avoided because of potential risk, and an invasive diagnostic study should be performed. Several clinical studies have shown that ST elevation in lead aVR was not only helpful in identifying severe coronary artery disease but could also be a predictor of adverse outcome in ACS. Similar considerations can be made about heart failure and ACS. In fact, the GRACE study group has amply shown that Killip class is a powerful predictor of in-hospital and 6-month mortality in ACS. A correlation between extent of coronary artery disease and heart failure was underlined by Haim et al.²²

Limitations

Study was performed at a single center and involved a small number of patients.

Clinical Implications

A standard 12-lead ECG on admission is the initial and most widely used method for early risk stratification in patients with CAD. Our study showed that ST-segment elevation in lead aVR on admission is useful for predicting LMD/TVD and can thereby facilitate decision-making, that is, patients likely to have LMD/TVD should promptly undergo an angiography and not to receive clopidogrel therapy to allow early CABG.

CONCLUSION

We concluded that an ST \uparrow aVR of 0.5 mm or greater predicted LMD /TVD and an independent predictor of prognosis during hospitalization period. Low ejection fraction and high TIMI score are also good noninvasive predictors of LMD /TVD. Prevalence of LMD in our study was 9%.

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