Clinical Outcome of Acute Coronary Syndrome Patients with Left Main Intervention

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ABSTRACT

Objective: Acute coronary syndrome (ACS) is associated with adverse outcomes and is a common cause of death. Presence of left main (LM) disease in patients with ACS may increase the rate of morbidity and mortality. The purpose of the present study was to compare short-term outcomes as well as major adverse cardiovascular and cerebrovascular events (MACCE) at 30 days in ACS patients with LM disease treated percutaneously or surgically as compared to those with non-LM disease treated percutaneously. **Methods:** This is a prospective cross-sectional multicenter study carried out on 100 patients with ACS: Group (I): 50 patients with LM disease, Group (II): 50 patients without LM disease. The LM group was treated percutaneously or surgically and the non-LM group was treated percutaneously. The primary end point is the thirty-day incidence of MACCE. **Results:** Patients with LM disease who were treated with percutaneous coronary intervention (PCI) had more frequent repeat revascularization than those with LM disease who were treated with coronary artery bypass graft (CABG) (P=0.022). However, there was no significant statistical difference between LM patients who were treated with PCI and those who were treated with CABG regarding all other 30 days outcomes (P>0.05). **Conclusion:** Coronary revascularization of patients with LM disease in the acute setting provided similar outcomes in 30 days when compared to those without LM involvement. ACS patients with LM disease treated with PCI have similar 30 days outcomes in comparison with CABG. However, repeat revascularization was significantly more frequent in LM patients treated with PCI.

KEY WORDS: major adverse cardiovascular, acute coronary syndrome, left main, percutaneous coronary intervention, coronary artery bypass graft.

Introduction

Acute coronary syndrome (ACS) patients vary in terms of clinical appearance and the probability of death or non-fatal ischemic accidents in the short and long term [1]. About 6% of ACS patients who undergo coronary angiography have obstructive left main (LM) coronary artery disease, which provides 75–100% of the left ventricular myocardium. As a result, a severe LM stenosis may result in life-threatening complications [2].

Since patients with obstructive LM coronary artery disease have a greater chance of mortality and morbidity, coronary artery bypass graft (CABG) surgery has been regarded the standard of care for revascularization. There has been significant biomedical advances in the procedure of percutaneous coronary intervention (PCI) for the treatment of obstructive LM coronary artery disease over the last 20 years, including advancements in stent technologies, procedural procedures, and refinement [3] [4]. Several randomised controlled trials (RCTs) evaluating the possible therapeutic role of PCI as an alternative to regular CABG have shown that stenting achieves comparable rates of mortality and hard clinical endpoints, as well as a lower risk of stroke, though the rate of repeat revascularization is higher [5] [6].

There is scanty recent research in this field, so the aim of this study was to compare short-term outcomes as well as major adverse cardiovascular and cerebrovascular events (MACCE) at 30 days in ACS patients with LM disease treated percutaneously or surgically as compared to those with non-LM disease treated percutaneously.

Methods

Study design & patient selection

This is a prospective cross-sectional multicenter study carried out on patients with ACS attending to Benha University hospital and Zagazig General hospital from October 2018 to June 2020. The study included 100 ACS patients, divided into 2 groups according to the presence of LM disease: Group (I): 50 patients with LM disease, Group (II): 50 patients without LM disease. ACS patients were diagnosed by presence of typical chest pain $\geq$ 20 minute, electrocardiogram (ECG) finding as (ST segment deviation >1mm, inverted T wave, hyper acute T wave), cardiac enzymes and troponin elevation [7]. Inclusion criteria comprised patients of both genders, aged ≥18 years, referred for coronary angiography within 5 days after pain onset with a main diagnosis of ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), or unstable angina (UA). Exclusion criteria were defined as refusal to participate in the study or the presence of other significant heart disease (significant valvular dysfunction, cardiomyopathy, or pericardial disease) or non-cardiac disease that limits life expectancy. This study was approved by Benha Medical Institutional Review board (IRB) at Benha University and an informed consent was obtained from all patients.

Clinical and laboratory assessment

Patients were subjected to complete history taking including: age, sex and risk factors (hyperlipidemia, hypertension, diabetes mellitus, smoking and family history of coronary artery disease). Physical examination including: heart rate, blood pressure, body mass index (BMI), chest and cardiac examination and Killip class at presentation [8]. Cardiac creatine kinase MB, troponin I, random blood sugar, serum creatinine, serum Na and K were all done.

12-Lead Electrocardiogram:

Twelve-lead electrocardiogram was recorded to document absence or presence of ECG findings as (ST segment depression >1mm, inverted T wave) in non STE-ACS patients and to diagnose STEMI patients by the presence of new ST segment elevation at J-point in ≥2 contiguous leads of ≥2 mm in leads V1, V2 or V3 and ≥1 mm in other leads [9].

Echocardiography:

Echocardiography was done in the left lateral decubitus using the commercially available systems (Epiq 7, Philips ultrasound & Vivid S6, GE ultrasound, Horten, Norway). Images were obtained with a simultaneous ECG signal. Recordings and calculations of different parameters were performed according to the recommendations of the American Society of Echocardiography (ASE) [10].

Coronary angiography

Invasive coronary angiography was done during hospital stay either immediately on admission in STEMI patients and non STE-ACS patients with unstable hemodynamics caused by ischemic attacks and in whom ischemic attacks cannot be controlled by intensive drug treatment or within 5 days in stable patients. The SYNTAX score was calculated to assess the anatomical complexity of coronary artery disease (CAD) and the long-term mortality and morbidity after PCI. The patients were classified according to SYNTAX score severity into: Low SYNTAX score (0 – 22), intermediate SYNTAX score (23 – 32) and high SYNTAX score (≥33) [11].

Myocardial revascularization

The LM group was treated percutaneously or surgically and the non-LM group was treated percutaneously according to the 2018 European Society of Cardiology (ESC) guidelines [12]. The study end point was thirty-day incidence of MACCE defined as the composite of cardiac death, clinically indicated revascularization, transient ischemic attack (TIA), stroke, or myocardial infarction at 30 days.

Statistical analysis

All data were collected, statistically analyzed using statistical package for the social sciences (SPSS) program version 20 (SPSS, Chicago, IL, USA). Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as numbers and percentages. Independent samples Student's t-test was used to compare between two groups of normally distributed variables. While, Mann Whitney U test was used for non-normally distributed variables. Percent of categorical variables were compared using Chi-square test or Fisher's exact test when appropriate. All tests were two-sided. P value <0.05 was considered statistically significant (S), and p value ≥0.05 was considered statistically non-significant (NS).

Results

Demographic, clinical data and echocardiography among LM and non-LM groups:

Baseline demographic and clinical data are presented in (***table 1***). Patients with LM disease were older (63.54 ± 6.11 vs. 54.60 ± 9.23 years, P=0.006). However, there was no significant statistical difference between LM and non-LM groups regarding gender (P=0.34). In the present study, there was no significant statistical difference between LM and non-LM groups regarding HTN, DM, dyslipidemia, history of CAD and prior stroke (P=0.86, 0.62, 0.59, 0.09 and 1) respectively. In this study, there was no significant statistical difference in KILLIP class between LM and non-LM groups (P=0.62).

In the current study, LVEDV was significantly larger in non-LM group (P=0.013). While, LVESV was significantly larger in LM group (P=0.008). EF was significantly lower in LM group (P<0.001). While, WMSI was significantly higher in LM disease group (P<0.001). A wave velocity was significantly higher in LM disease group (P=0.039). There was no significant statistical difference between the two groups regarding E wave velocity (P=0.468). S wave velocity was significantly lower in LM disease group (P=0.003). There was no significant statistical difference between the two groups regarding E' wave velocity (P=0.07) and E/E' ratio (P=0.08).

Coronary angiography and 30 days outcomes among LM group versus non-LM group:

In the present study STEMI presentation was significantly more prevalent in non-LM group (P=0.001). While, NSTEMI presentation was significantly more prevalent in LM group (P=0.028). The presence of single vessel disease was significantly more prevalent in non-LM group (26 patients “52%” vs. 2 patients “4%”, P<0.001).

While, presence of three vessel disease was significantly more prevalent in LM group (35 patients “70%” vs. 12 patients “24%”, P<0.001). There was no significant statistical difference between the two groups regarding the presence of double vessel disease (13 patients “26%” vs. 12 patients “24%”, P=0.9) as shown in ***figure (1)***.

There was no significant difference between both groups regarding repeat revascularization (5 patients “10%” vs. 6 patients “12%”, P=0.418), reinfarction (2 patients “4%” vs. 3 patients “6%”, P=0.821), arrythmia (8 patients “16%” vs. 6 patients “12%”, P=0.612), bleeding (3 patients “6%” vs. 3 patients “6%”, P=1.00), stroke (2 patients “4%” vs. 2 patient “4%”, P=1.00) and death (6 patients “12%” vs. 4 patients “8%”, P=0.523) as shown in ***figure (2)***.

Demographic, clinical data and echocardiography among LM disease patients (PCI subgroup versus CABG subgroup):

There was no significant statistical difference between the two subgroups regarding age (P=0.271) and gender (P=0. 0.323). PCI subgroup included 16 male patients (76.19%) and 5 female patients (23.81%). While, CABG subgroup included 17 male patients (58.62%) and 12 female patients (41.38%) ***(table 2)***. In the present study, there was no significant statistical difference between PCI and CABG subgroups regarding HTN, DM, dyslipidemia, history of CAD and prior stroke (P=0.845, 0.634, 0.206, 0.352 and 1) respectively. In this study, there was no significant statistical difference in KILLIP class between PCI and CABG subgroups (P=0.956). In the present study, LVESV was significantly larger in PCI subgroup (P=0.019). While, EF was significantly lower in PCI subgroup (P=0.001).

There was no significant statistical difference between the two subgroups regarding LVEDV and WMSI (P=0.354 and P=0.189). E wave velocity was significantly higher in PCI subgroup (P<0.001). There was no significant statistical difference between the two subgroups regarding A wave velocity (P=0.917). E/E' ratio was significantly higher in PCI subgroup (P<0.001). There was no significant statistical difference between the two subgroups regarding E' wave velocity and S wave velocity (P=0.474 and P=0.292).

Coronary angiography and 30 days outcomes of LM disease patients (PCI subgroup versus CABG subgroup):

In the present study, STEMI presentation was significantly more prevalent in PCI subgroup (5 patients “20%” vs. 0 patient “0”%, P=0.024). There was no significant statistical difference between the two subgroups regarding NSTEMI and UA presentation. The presence of three vessel disease was significantly more prevalent in CABG subgroup (25 patients “86%” vs. 10 patients “50%”, P=0.023). There was no significant statistical difference between the two subgroups regarding the presence of single vessel disease and double vessel disease as shown in ***figure (3)***.

Repeat revascularization was significantly more frequent in PCI subgroup (5 patients “20%” vs. 0 patient “0%”, P=0.022). There was no significant statistical difference between the two subgroups regarding all other 30 days outcomes (P>0.05) as shown in ***figure (4)***

Table (1): Comparison between the two groups regarding demographic and clinical data.

Items	Studied groups		Test	P
	Group I (no=50) (LM disease)	**Group II (no=50) (No LM disease)**		
Age				
Mean ±SD				
Age per years	63.54 ± 6.11	54.60 ± 9.23	T = -2.628	**0.006 (S)**
Gender				
No (%)				
Males	38 (76%)	35 (70%)	X^2 = 1.221	0.34 (NS)
Females	12 (24%)	15 (30%)		
Risk factors				
No (%)				
HTN	24 (48%)	23 (46%)	X^2 = 0.041	0.86 (NS)
DM	31 (62%)	28 (56%)	X^2 = 0.371	0.62 (NS)
Dyslipidemia	22 (44%)	19 (38%)	X^2 = 0.48	0.59 (NS)
Smoking	23 (46%)	24 (48%)	X^2 = 0.382	0.89 (NS)
Prior CVA	2 (4%)	3 (6%)	F	1.0 (NS)
Prior CAD	34 (68%)	28 (56%)	X^2 = 3.281	0.09 (NS)
Family History	16 (32%)	12 (24%)	X^2 = 0.391	0.55 (NS)
Examination				
Mean ± SD				
BMI (Kg/m2)	31.60 ± 3.49	32.12 ± 3.19	T= 0.251	0.82 (NS)
SBP (mmHg)	124.00 ± 20.11	128.80 ± 22.79	T= 0.877	0.39 (NS)
DBP (mmHg)	80.24 ± 17.00	84.52 ± 13.64	T= 1.418	0.16 (NS)
Heart rate (Beat/min)	83.55 ± 15.23	85.89 ± 15.77	T= 0.719	0.51 (NS)
Killip class				
Median (Range)	1 (1-3)	1 (1-3)	MW= 1198.1	0.62 (NS)
No (%)				
I	40 (80%)	37 (74%)		
II	8 (16%)	12 (24%)		
III	2 (4%)	1 (2%)		

T: Student's T-test, χ^2: Chi-square test, F: Fisher exact test, MW: Mann-Whitney U test, NS: Non-significant, S: Significant, SD: Standard deviation, LM: Left main, HTN: Hypertension, DM: Diabetes mellites, CVA: Cerebrovascular accident, CAD: Coronary artery disease, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

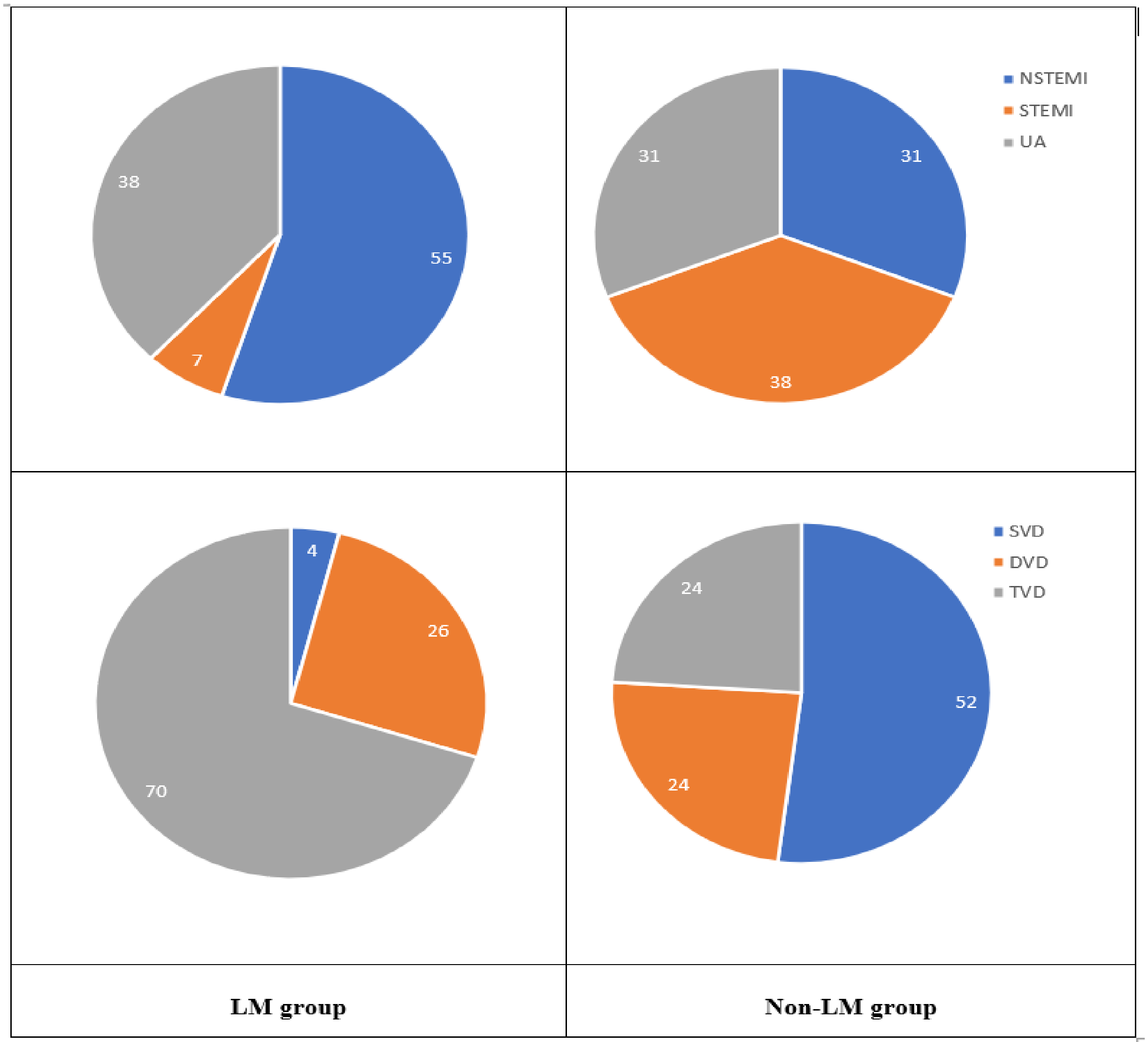


Figure (1): Comparison between LM and Non-LM groups regarding types of acute coronary syndrome and number of vessels affected on coronary angiography.

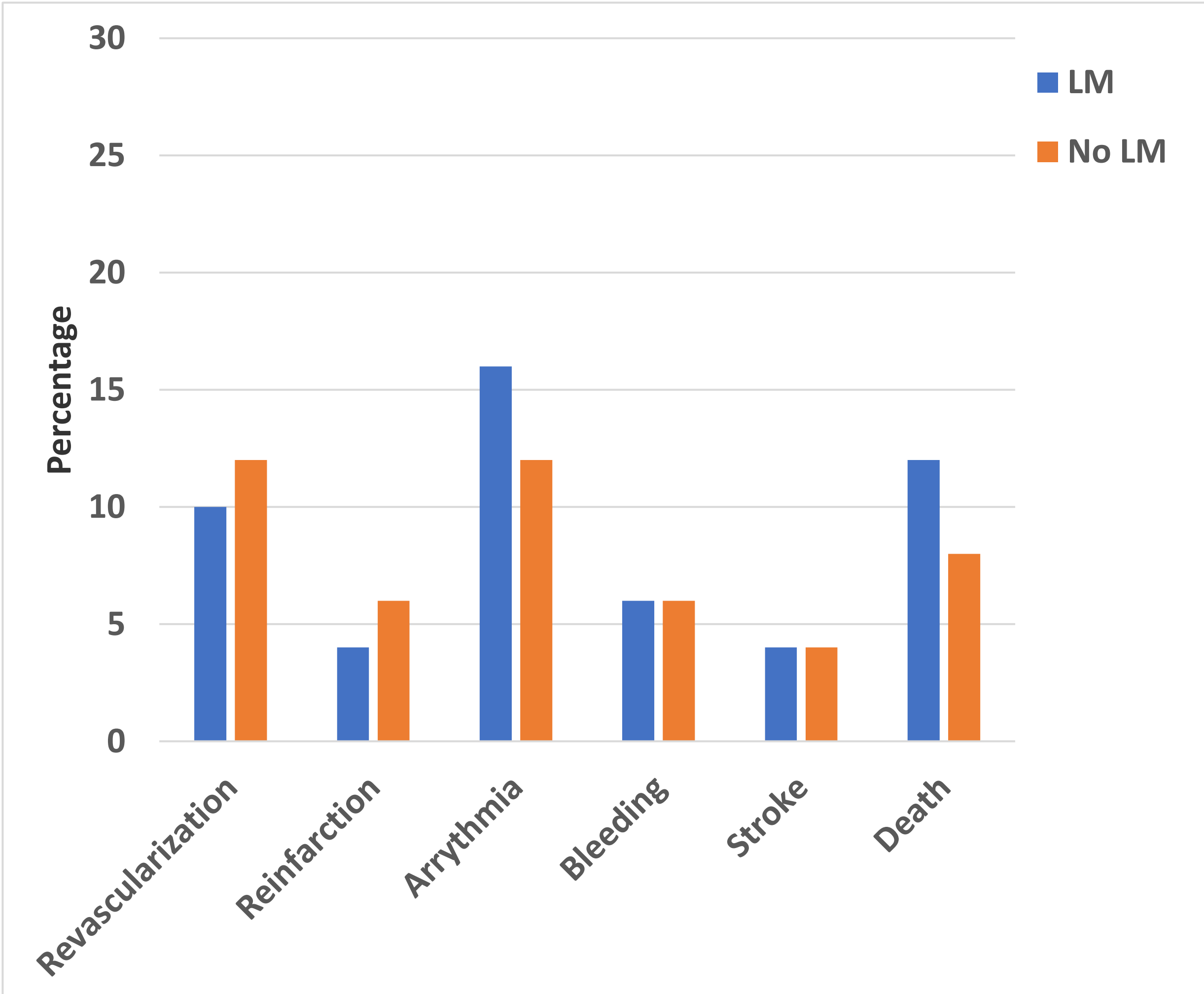
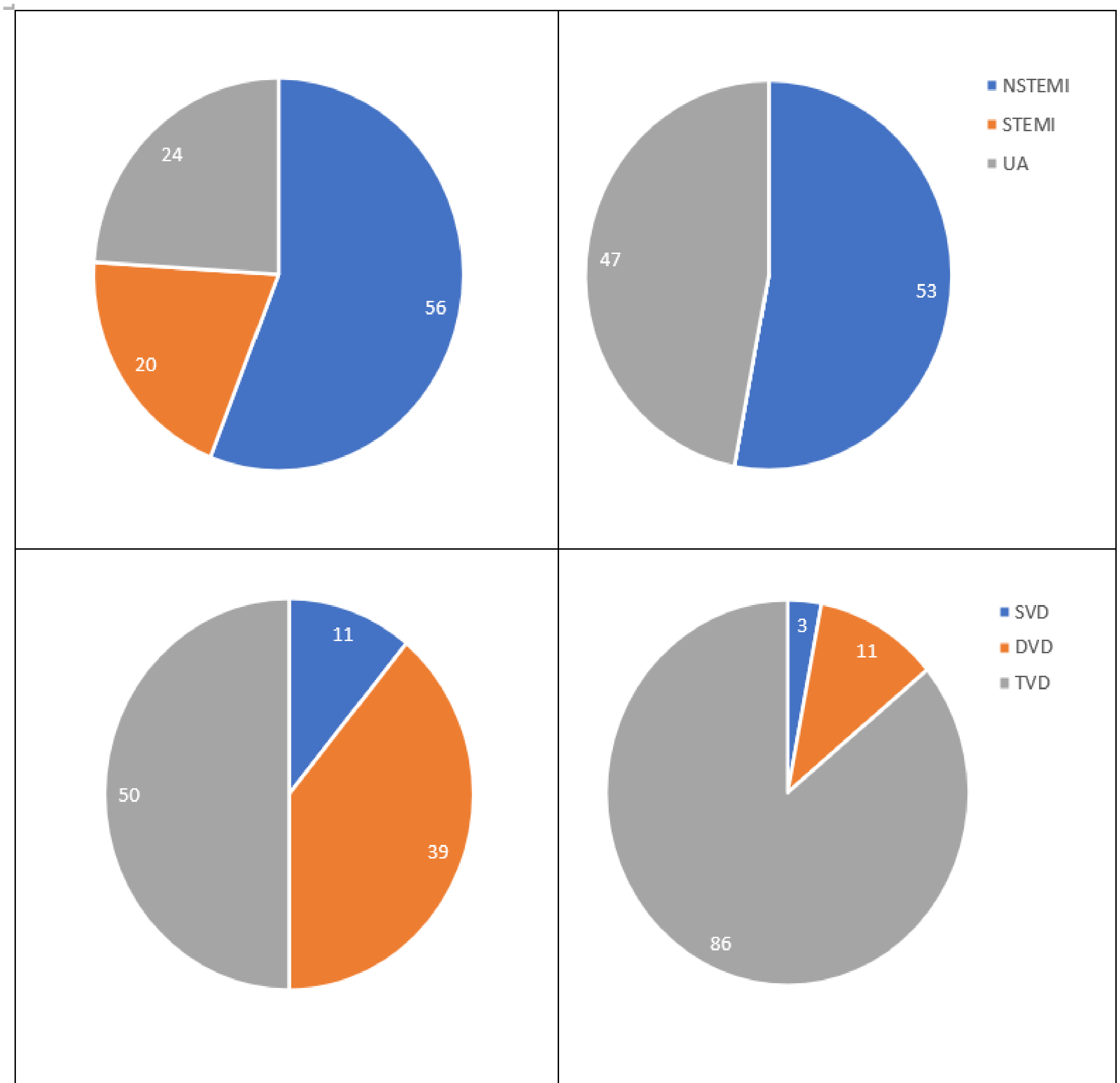


Figure (2): Comparison between the two groups regarding 30 days outcomes.

Table (2): Comparison between the two subgroups regarding demographic and clinical data.

Items	Studied groups		Test	P
	Group IA (no=21) (PCI subgroup)	Group IB (no=29) (CABG subgroup)		
		Age		
Mean ±SD				
Age per years	61.45 ± 6.34	62.78 ± 5.84	T = -1.131	0.271 (NS)
		Gender		
No (%)				
Males	16 (76.19%)	17 (58.62%)	X^2 = 1.512	0.323 (NS)
Females	5 (23.81%)	12 (41.38%)		
		Risk factors		
No (%)				
HTN	11 (52.38%)	12 (41.38%)	X^2 = 0.046	0.845 (NS)
DM	14 (66.66%)	15 (51.72%)	X^2 = 0.311	0.634 (NS)
Dyslipidemia	10 (47.61%)	10 (34.48%)	X^2 = 1.574	0.206 (NS)
Smoking	8 (38.09%)	12 (41.38%)	X^2 = 2.845	0.102 (NS)
CVA	1 (4.76%)	1 (3.45%)	F	1.000 (NS)
CAD	16 (76.19%)	17 (58.62%)	X^2 = 0.912	0.352 (NS)
Family History	8 (38.1%)	10 (34.48%)	X^2 = 0.328	0.603 (NS)
		Examination		
Mean ± SD				
BMI (Kg/m2)	30.15 ± 3.22	29.32 ± 3.29	T= 1.085	0.297 (NS)
SBP (mmHg)	127.65 ± 28.3	123.26 ± 24.4	T= 0.821	0.510 (NS)
DBP (mmHg)	82.55 ± 18.28	79.33 ± 15.47	T= 0.693	0.552 (NS)
Heart rate (Beat/min)	87.38 ± 18.77	85.43 ± 16.63	T= 0.299	0.811 (NS)
Killip class				
Median (Range)	1 (1-3)	1 (1-3)	MW= 301	0.956 (NS)
No (%)				
I	17 (81%)	23 (79%)		
II	3 (14%)	4 (14%)		
III	1 (5%)	2 (7%)		

T: Student's T-test, χ^2: Chi-square test, F: Fisher exact test, MW: Mann-Whitney U test, NS: Non-significant, SD: Standard deviation, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass graft, HTN: Hypertension, DM: Diabetes mellites, CVA: Cerebrovascular accident, CAD: Coronary artery disease, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.



PCI subgroup	**CABG subgroup**

Figure (3): Comparison among LM diseases patients (PCI subgroup and CABG subgroup) regarding types of acute coronary syndromes and number of vessels affected on coronary angiography.

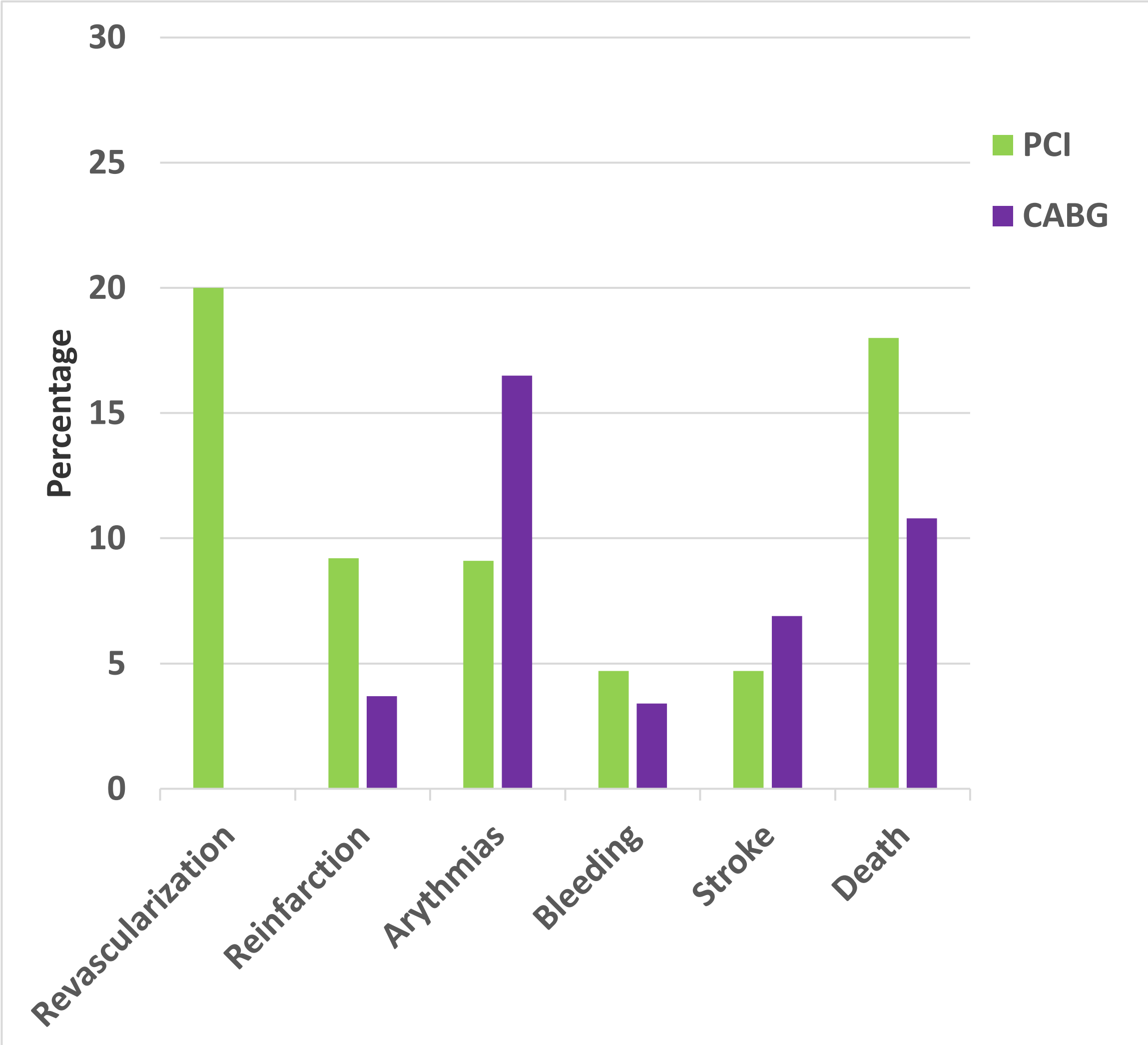


Figure (4): Comparison between the two subgroups regarding 30 days outcomes.

Discussion

About five percent of patients receiving coronary angiography have significant left major coronary artery disease [13]. Patients who have a left primary coronary artery stenosis revascularized are at a high risk of having a heart attack or stroke. For LM stenosis, CABG was thought to be the gold standard [14]. However, as stent technology has improved and operator expertise has grown, the number of percutaneous coronary procedures to treat LM stenosis has increased [15]. The purpose of the present study was also to compare short-term outcomes as well as MACCE at 30 days in acute coronary syndrome patients with LM disease that were treated percutaneously or surgically as compared to those with non-LM disease that were treated percutaneously in a group of Egyptian patients enrolled from two centers (double-centered study), it included 100 patients with acute coronary syndrome, divided into 2 groups according to the presence of LM disease: Group (I): 50 patients with ACS and LM disease and Group (II): 50 patients with ACS without LM disease.

In this study, there was no significant difference between both groups regarding 30 days outcomes including repeat revascularization, re-infarction, arrythmia, bleeding, stroke and death (P=0.428, 0.835, 0.578, 1.00, 1.00 and 0.689) respectively. This was in agreement with ***Obeid et al.*** who reported that there was no significant statistical difference between LM and non-LM groups regarding 30 days net adverse clinical events including death, myocardial infarction, cerebrovascular accident and bleeding (P=0.1) [16].

In this study, patients with LM disease were divided into 2 subgroups according to the procedure, the first subgroup underwent PCI and the second one underwent CABG. There was no significant statistical difference between the two subgroups regarding age (P=0.271) and gender (P=0.323). There was also no significant statistical difference between the PCI and CABG subgroups regarding hypertension, diabetes, dyslipidemia, smoking, history of previous cerebrovascular accident, history of previous CAD, family history of CAD and BMI (0.845, 0.634, 0.206, 0.102, 1.000, 0.352, 0.603 and 0.297) respectively. This was in agreement with ***Buszman et al.*** who reported that there was no significant statistical difference between the two groups regarding age, gender, hypertension, diabetes, dyslipidemia and history of previous CAD (P=0.69, 0.13, 0.78, 0.80, 0.78 and 0.60) respectively [17]. Similar results are reported by ***Boudriot et al.*** who reported that there was no significant statistical difference between the two groups regarding hypertension, diabetes, dyslipidemia, smoking, history of previous cerebrovascular accident, history of previous CAD and BMI (P=0.88, 0.35, 0.89, 0.34, 0.51, 0.43 and 0.31) respectively [18]. Also, similar results were reported by ***Ahn et al.*** who found that there was no significant statistical difference between the two groups regarding diabetes (P=0.66) [19]. ***Holm et al.***

also found that there was no significant statistical difference between the two groups regarding age, gender, and BMI (P= 0.37, 0.22, and 0.45), respectively [20]. In the present study, LVESV was significantly larger in PCI subgroup (P=0.019). While, EF was significantly lower in PCI subgroup (P=0.001). There was no significant statistical difference between the two subgroups regarding LVEDV and WMSI (P=0.354 and P=0.189). On the contrary, ***Boudriot et al.*** found no significant statistical difference between the two groups regarding EF (P=0.86) [18]. The disagreement between our results and those reported by ***Boudriot et al.*** may be due to the different patient presentations and selection. In the present study, 20% and 56% of the patients of PCI subgroup had STEMI & NSTEMI respectively. While, patients with myocardial infarction were excluded in their study [18].

In the current study, there was no significant statistical difference between the two subgroups regarding the presence of single vessel disease and double vessel disease (P=0.634 and 0.11) respectively. However, in our work, three vessel disease was significantly more prevalent in CABG subgroup (P=0.023). In the study of ***Buszman et al.*** they reported that there was no significant statistical difference between the two groups regarding the presence of single vessel disease, double vessel disease and three vessel disease (P= 0.17, 0.32 and 0.08) respectively [17]. This difference regarding three vessel disease can be attributed to the different characteristics of our patients; where in our study patients who underwent CABG had a higher SYNTAX score (P=0.002). Current 2018 European Society of Cardiology (ESC) guidelines have adopted SYNTAX score to aid in selection of the appropriate revascularization strategy for LM coronary artery stenosis, and clinical practice in Egypt usually follows these guidelines [12]. This was in contrast to ***Ahn et al.*** who found no significant statistical difference between the two groups regarding SYNTAX score (P=0.49) as in their study, done in Asan Medical Centre, Seoul, South Korea, SYNTAX score did not discriminate the more appropriate strategy between treatments [19].

In the current study, repeat revascularization at 30 days was significantly more frequent in PCI subgroup (P=0.022). This was in contrast with ***Buszman et al.*** who found that there was no significant statistical difference between the two groups regarding repeat revascularization at 30 days. This discrepancy might be attributed to larger sample volume included in their study [17]. Also, results reported by ***Boudriot et al.*** showed that PCI was noninferior to CABG regarding repeat revascularization at 30 days (P<0.001). This discrepancy might be attributed to larger sample size of their study [18]. This was in agreement with ***Buszman et al.*** who found that repeat revascularization at 1 year was significantly more frequent in PCI group (P=0.01) [17]. In our work, there was no significant statistical difference between the two subgroups regarding other 30 days outcomes including reinfarction, arrythmia, bleeding, stroke and death (P=0.635, 0.715, 1.00, 1.00 and 0.597). This was in agreement with ***Buszman et al.*** who found that there was no significant statistical difference between the two groups regarding 30 days outcomes including reinfarction, arrythmia, bleeding, stroke and death [17]. Also, similar results are reported by ***Boudriot et al.*** who found that PCI was noninferior to CABG regarding reinfarction at 30 days (P=0.002) [18].

The limitations of our study included the relatively limited number of patients and lack of longer-term follow-up. Moreover, our study was applied on ACS patients only; excluding those with chronic coronary syndromes undergoing coronary revascularization. The choice of treatment strategy, vascular access, type of stent, and concomitant medications in our study might have reflected individual physician's preferences.

Finally, we conclude that coronary revascularization of patients with LM disease in the acute setting provided similar outcomes in 30 days when compared to those without LM involvement. ACS patients with LM disease treated with PCI have similar 30 days outcomes in comparison with CABG. However, repeat revascularization was significantly more frequent in LM patients who where treated with PCI.

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