

Acute, total occlusion of the left main stem: coronary intervention options, outcomes, and recommendations

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Abstract

Introduction: Acute, total occlusion of the unprotected left main stem (uLMo) in acute coronary syndrome (ACS) patients is a catastrophic event often accompanied by sudden cardiac death (SCD) and/or cardiogenic shock (CS) with high mortality rates and limited methods of successful treatment. Emergent, surgical and percutaneous revascularization has been reported before, yet comprehensive data remains scarce.

Aim: To examine emergency percutaneous coronary intervention (PCI) outcomes in ACS cases presenting with uLMo.

Material and methods: Data on 23 subjects undergoing primary PCI in uLMo cases were analyzed. The primary end-point was in-hospital death; secondary end-points were successful salvage of coronary anatomy and 90-day major cardiac adverse events (MACE).

Results: About 40% of LM occlusion cases presented following successful on-site cardio-pulmonary resuscitation (CPR). Of all patients arriving for treatment the occluded LM was successfully opened and stented in ~90% of cases. CS was present in > 85% of cases, and circulatory support in the form of intra-aortic balloon pump and/or extracorporeal membrane oxygenation systems was applied in every eligible case (~80%). The in-hospital death rate was 56%, mostly including individuals requiring prior CPR. At 6 months, additional MACE rates were low at 8.7%.

Conclusions: We found that uLMo ACS cases often present with preceding CPR and mostly in manifest CS. Coronary salvage is generally successful, yet uLMo even with optimal present day complex treatment yields quite high mortality rates. This is especially true for patients receiving prior CPR. In surviving patients, however, 6-month MACE rates are acceptable.

Key words: acute myocardial infarction/STEMI, left main coronary disease, coronary occlusion, percutaneous coronary intervention.

Summary

Unprotected left main stem occlusion in the setting of acute coronary syndrome is a catastrophic event with limited methods of successful treatment. Clinical presentation often includes sudden cardiac death with the need for cardiopulmonary resuscitation and manifest cardiogenic shock. Optimal treatment involves emergent percutaneous revascularization with circulatory augmentation. In-hospital mortality, even with complex care is quite high (~50%), despite overwhelmingly successful coronary salvage (~90%). Most important determining factor of primary survival is the need for resuscitation at any timepoint during care. In initial survivors, mid-term results are acceptable.

Introduction

Acute coronary syndrome (ACS) is one of the leading causes of acute chest pain, need for emergency care and eventual hospitalization. Invasive coronary anatomy assessment and revascularization of relevant coronary lesions are indicated according to current guidelines. Events involving the left main stem (LM) are of addition-

al clinical importance, as a significant percentage of the cardiac muscle mass is at ischemic risk. Treatment of such LM lesions is an issue of debate, as contemporary data from large population-based randomized controlled trials (RCTs) have shown that both coronary artery bypass grafting (CABG) surgery and percutaneous revascularization (PCI) may be considered [1–4]. Furthermore, although these studies have included ACS cases to some

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extent, mostly subjects with stable coronary artery disease and LM involvement were included.

Even in study populations considering ACS and LM lesions, however, RCTs have never included subjects with the gravest of coronary pathology circumstances: complete unprotected LM occlusion (uLMo). Only limited data has been published regarding true uLMo, in which the authors reported mostly fair results following either surgical or percutaneous emergency revascularization in such cases [5–7].

As of today, only one analysis has been published harnessing data from a nationwide electronic database, in the United Kingdom, using an event tagging algorithm. This, however, also included sub-occlusion cases in their uLMo definition [8]. Thus, to the best of our knowledge, no comprehensive data on true acute uLMo interventions have yet been published.

Aim

Therefore, we opted to gather information and report clinical findings and emergency PCI procedure outcomes in uLMo cases. Furthermore, we also included a summary of important recommendations for uLMo PCI, as these cases differ in many regards from everyday ACS interventions in both clinical presentation and the need for complex treatment in the catheterization laboratory.

Material and methods

uLMo patients, endpoints

Due to the clinical features of uLMo occlusions, no prospective studies seem eligible in any reasonable time-frame. Thus, we opted to gather information from our heart catheterization database on all eligible uLMo ACS cases, encompassing more than 7 years (2009–2017) of statistics and including 23 patients. Demographics, clinical features, revascularization details and all occurring adverse events were assessed and evaluated. Patients with prior CABG or LM PCI were excluded from the study to preserve data integrity. Analyzed cases account for only ~0.2% of all ACS PCI procedures and ~0.1% of total PCI interventions during this time period. All subjects undergoing angiography at our institution were enrolled in a prospective registry after providing written consent, allowing us to gather information on procedures.

As a primary endpoint we examined in-hospital mortality of our patients. Procedural success (defined as successful implantation of an LM stent and restoration of at least a Thrombolysis In Myocardial Infarction (TIMI) flow of II in the left anterior descending (LAD) and left circumflex (LCX) branches) and major adverse cardiac events (MACE) encompassing all cause death, new onset myocardial infarction, target lesion failure and/or revascularization at 90 days were assessed as the secondary endpoint.

uLMo subject evaluation

All subjects presented via a direct route from the National Ambulance Service of Hungary. First medical contact (FMC) was initiated in every case by the medical doctor or paramedic of the ambulance service. ECGs mostly displayed typical anterior and aVR lead ST-segment elevations, and lateral ST-segment depressions showing signs of extensive transmural ischemia, easily recognizable by ambulance staff. Symptom onset to FMC times recorded by ambulance staff were markedly low (median 12 (interquartile range: 10–15) min) in our registry, mainly due to the severe clinical presentation of uLMo and immediate contact of emergency services. Ambulance transport times were also fairly short (20 (17–30) min), due to the fact that most subjects only required transportation within the bounds of Budapest. Sudden cardiac death (SCD), due to ventricular arrhythmias necessitating complex cardiopulmonary resuscitation (CPR) as the trigger event for the uLMo occurred in nine cases. Chest compressions were performed using the LUCAS system (Phisio-Control Inc. – Lund, Sweden) in seven of these cases. Eventually three more patients required CPR during revascularization therapy, where chest compressions were carried out manually. Altogether, 20 patients (~87%) presented in manifest cardiogenic shock (CS), defined as pulmonary edema along with systolic blood pressure under < 90 mm Hg with evidence of peripheral vasoconstriction (Killip IV state). Endotracheal intubation was performed on-site, in ~65% of cases.

uLMo patient PCI procedures

Coronary occlusion was defined as a stenosis of 100% with TIMI flow of 0 in the LM, with no bridging collaterals from the contralateral coronary circulation. Coronary dominance was also evaluated in each case. Intensive care specialist support was called for in every case to monitor patients' vital parameters and other support medication. The primary PCI operator focused on swift procedures, where all attention was fixated on restoring flow to the occluded LM as soon as possible. Hemodynamic supportive devices, such as intra-aortic balloon pumps (IABP) and venous-arterial extracorporeal membrane oxygenation (VA-ECMO) systems, were used at the discretion of the operator, patients' clinical and anatomical status, and availability of devices. Also, to minimize ischemic time and depressed circulation, whenever available, a second capable operator was introduced, his or her role being the rapid initiation of circulatory augmentation devices, simultaneously during LM PCI, from a different vascular approach. Door-to-balloon times were kept as short as possible (26 (22–30) min); arriving patients were advanced from the ambulance transport bed directly to the catheterization table. Prior to patients' hospital arrival staff arranged for fast and

effective instigation of invasive care. Thus with the combined efforts of the ambulance and hospital staff overall revascularization delay was kept as low as possible (63 (52–75) min).

Following PCI, optimal medical therapy, according to applicable guidelines, was initiated in every surviving patient.

Follow-up (FU) details

Follow-up of surviving patients was clinically driven, and all relevant data were collected via clinical outpatient contact or telephone calls. Records were verified using the Hungarian National Health Insurance database.

Results

Demographic and clinical data

Table I displays all relevant demographic and clinical data of patients. Notable is the fact that patients were younger than expected (mean age: 63.7 ±10.8), with a relatively low incidence of relevant cardiovascular co-morbidities such as hypertension (65.2%, $n = 15$) and dyslipidemia (47.8%, $n = 11$). Diabetes (30.3%, $n = 7$) and smoking (52.2%, $n = 12$) were however more prevalent. Subjects who underwent prior (non-LM) PCI and multivessel disease cases were rare at 13% ($n = 3$) respectively. Also, the percentage of female patients ~43% ($n = 10$) was notably high in our study population.

Table I. Patients' clinical and demographic data ($n = 23$)

Patient data	Value
Age [years]	63.7 ±10.8
BMI [kg/m ²]	27.2 (26.1–31.5)
Male gender, n (%)	13 (56)
Cardiovascular risk factors, n (%):	
Hypertension	15 (65)
Diabetes mellitus	7 (30)
Dyslipidemia	11 (48)
Smoking	12 (52)
Prior ACS	6 (26)
Prior PCI (non-LM)	3 (13)
PAD	2 (9)
GFR [ml/min]	44.0 (31.0–57.5)
Ejection fraction (%)	30.0 (24.5–39.0)
Multivessel coronary disease, n (%)	3 (13)

Continuous parameters are expressed as median and interquartile range. ACS – acute coronary syndrome, BMI – body mass index, GFR – glomerular filtration rate, LM – left main, PAD – peripheral arterial disease, PCI – percutaneous coronary intervention.

Patients' procedural, adverse event and follow-up data

Table II contains detailed procedural data. Procedures with one main operator accounted for somewhat more than half (~56%) of the procedures. Dual operators performed ~43% of interventions. Angiography showed that predominantly right coronary artery dominant anatomy was registered, with a few cases of co-dominancy. No left dominant anatomy presented. With regards to interven-

Table II. Patients' procedural data ($n = 23$)

Parameter	Value
Symptom onset to FMC [min]	12 (10–15)
FMC to door (transport) time [min]	20 (17–30)
Door to balloon time [min]	26 (22–30)
Overall reperfusion time [min]	63 (52–75)
PCI performed with one operator, n (%)	13 (57)
PCI performed with dual operators, n (%)	10 (43)
Coronary dominance, n (%):	
Right	20 (87)
Left	0 (0)
Co-dominant	3 (13)
Procedure duration [min]	27 (22–33)
Contrast material expended [ml]	95 (87–182)
Radiation dose [mGy]	3551 (590–4141)
BMS/DES ratio	3 : 1
IABP use, n (%)	16 (70)
IABP duration [days]	1.7 ±0.7
VA-ECMO use, n (%)	3 (13)
VA-ECMO duration [days]	1.3 ±1.0
Procedural success, n (%) (defined as at least TIMI II flow in the LAD and LCX, following LM stent implantation)	21 (91)
Thrombectomy performed	9 (39)
Implanted stent width [mm]	3.3 ±0.3
Implanted stent length [mm]	22.2 ±7.1
Post-dilation carried out, n (%)	12 (52)
Shaft and/or ostial LM stenting, n (%)	9 (39)
LM-LAD directional stenting, n (%)	11 (48)
LM-LCX directional stenting, n (%)	3 (13)

Continuous parameters are expressed as median and interquartile range. BMS – bare metal stent, DES – drug-eluting stent, FMC – first medical contact, IABP – intra-aortic balloon pump, LAD – left anterior descending coronary, LCX – left circumflex coronary, LM – left main, PCI – percutaneous coronary intervention, TIMI – thrombolysis in myocardial infarction, VA-ECMO – veno-arterial extracorporeal membrane oxygenator.

tional techniques, single and multiple stent options were applied as operators saw fit in the clinical scenario, but mainly LM shaft/ostium or LM-LAD directional PCI was

Table III. Patients' adverse event and follow-up data (n = 23)

Parameter	Value
Cardiopulmonary resuscitation undertaken, n (%):	
Initialized prior to hospital admittance	9 (39)
Initialized during PCI	3 (13)
Combined	12 (52)
Cardiogenic shock at presentation, n (%)	20 (87)
IABP/VA-ECMO implantation complication, n (%)	0 (0)
In-hospital mortality, n (%):	
Total	13 (57)
Underwent CPR	12 (52)
No CPR	1 (4)
Additional MACE events during follow-up, n (%):	
Stent thrombosis (TLF)	1 (4)
New onset MI	1 (4)
Six-month total MACE rates, n (%)	15 (65)
Six-month total mortality, n (%)	15 (65)
Administered DAPT medication, n (%):	
Aspirin	23 (100)
Clopidogrel	20 (87)
Prasugrel	3 (13)

CPR – cardiopulmonary resuscitation, DAPT – dual-antiplatelet therapy, IABP – intra-aortic balloon pump, MACE – major adverse cardiovascular events, MI – myocardial infarction, PCI – percutaneous coronary intervention, TLF – target lesion failure, VA-ECMO – veno-arterial extracorporeal membrane oxygenator.

carried out. Device parameters (length and width) were chosen according to best visual estimation. The PCI success rate was over 90%. IABP and VA-ECMO use rates were ~70% and 13%, respectively. Additional complications in conjunction with IABP and VA-ECMO implantation did not occur in our registry.

Table III shows encountered adverse events, follow-up and medication data. In-hospital mortality totaled ~56% or 13 patients. Out of all 13 fatalities, 12 individuals required prior CRP. Thus, in-hospital mortality only showed an association with the need for CPR at any time during care (relative risk = 9.2, 95% CI: 1.4–59.6, p = 0.016). Figure 1 shows CS and CPR subjects in relation and displays in-hospital mortality according to these parameters. Only the remaining 10 patients (~43%) left the hospital alive. Six-month follow-up yielded additional MACE events by two subjects, both proving fatal. One subject suffered an acute stent thrombosis, the other a new onset myocardial infarction. Thus, the summed mortality rate at 6 months FU amounted to ~65%, with 15 patients deceased at this time point. Dual-antiplatelet medication was administered to every patient in the form of aspirin and a P2Y₁₂ inhibitor, mainly clopidogrel. Prasugrel was given in a minority of cases (3 patients, ~13%).

Analysis according to CS and CPR

Table IV shows procedural and survival parameters in relation to CS and CPR requirements in our patient population. The use of one or multiple stent techniques and post-implantation further stent manipulations (kissing balloon post-dilation and/or proximal optimization technique) shows no relevant differences in the patient populations. We can see, however, that the non-CS population's procedure times were shorter, although, due to the low size of this sub-group statistical comparison was not valid (26 and 33 vs. 21 and 15 min). Intra-aortic

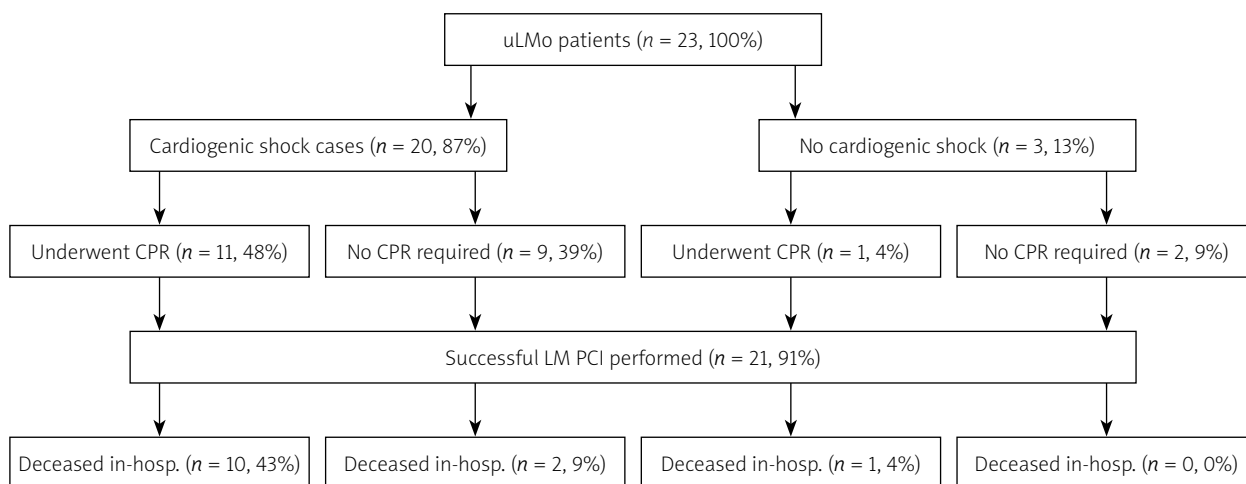


Figure 1. Flow diagram showing the relation of cardiogenic shock to CPR and correlation with patient mortality of each sub-group

CPR – cardio-pulmonary resuscitation, LM – left main stem, PCI – percutaneous coronary intervention, uLMo – unprotected left main stem occlusion.

Table IV. Specifics of cardiogenic shock and CPR in the patient population ($n = 23$)

Variable	Cardiogenic shock			Non-cardiogenic shock		
	Required CPR ($n = 11$)	No CPR ($n = 9$)	Total ($n = 20$)	Required CPR ($n = 1$)	No CPR ($n = 2$)	Total ($n = 3$)
One stent technique used for LM PCI ($n/\%$ of total):	6/26	4/17	10/50	–	1/4	1/4
POT undertaken ($n/\%$ of total)*	2/9	2/9	4/18	–	–	–
KBI undertaken ($n/\%$ of total)*	1/4	1/4	2/9	–	–	–
Multiple stent technique used for LM PCI ($n/\%$ of total):	5/22	5/22	10/50	1/4	1/4	2/9
TAP technique used ($n/\%$ of total)	3/13	2/9	5/22	1/4	2/9	3/13
Culotte technique used ($n/\%$ of total)	2/9	3/13	5/22	–	–	–
POT undertaken ($n/\%$ of total)*	4/17	4/17	8/35	1/4	1/4	2/9
KBI undertaken ($n/\%$ of total)*	2/9	2/9	4/18	–	1/4	1/4
Procedural time [min]	26 (14–40)	33 (17–50)	29 (14–50)	21	15	18
Expended contrast material [ml]	112 (84–196)	100 (94–194)	106 (84–194)	108	149	129
TIMI III flow in LAD and LCX ($n/\%$ of total)	7/30	7/30	14/60	1/4	2/9	3/13
IABP used ($n/\%$ of total)	7/30	7/30	14/60	1/4	1/4	2/9
VA-ECMO used ($n/\%$ of total)	3/13	–	3/13	–	–	–
Initial hospital survival ($n/\%$ of total)	1/4	7/30	8/35	–	1/4	1/4
Follow-up additional mortality ($n/\%$ of total)	1/4	1/4	2/9	–	–	–

Continuous parameters are expressed as median and interquartile range. CPR – cardio-pulmonary resuscitation, IABP – intra-aortic balloon pump, KBI – kissing balloon inflation, LAD – left anterior descending coronary, LCX – left circumflex coronary, POT – proximal optimization technique, TAP – T-stent and protrusion, TIMI – thrombolysis in myocardial infarction, VA-ECMO – veno-arterial extracorporeal membrane oxygenator. *Several patients received both KBI and POT manipulations.

balloon pumps use showed a homogeneous distribution, but VA-ECMO systems were only used in CS patients who required CPR. The availability of the VA-ECMO system however differed throughout the study, as it only became available in later years of our registry (from 2013).

Conclusions

MACE and mortality implications

Results after uLMo PCI prove that survival following this catastrophic event is fair at most, with less than half of subjects surviving hospitalization, although restoration of coronary flow is mostly successful. The use of DES devices may seem underrepresented in this unique patient population, but due to the fact that numerous patients underwent salvage PCI following initial CPR and in manifest, often irreversible CS, long-term survival was less likely. Thus, BMS devices were more commonly used. Noteworthy is also the fact that we encountered no left-coronary dominant type anatomy, as presumably this leads to imminent death upon uLMo.

In-hospital death rates far outweigh any other form of ACS. Prior published, similar data concur with these findings [8]. Also, the fact that in conjunction with the uLMo event more than half of the subjects treated re-

quired CPR at some time point further complicates the clinical situation. Our data show that the need for CPR leads to very poor procedure outcomes and strongly correlates with hospital mortality. Initial CPR survivors in ACS display especially poor outcomes even if treated according to current guidelines [9–12].

Recommendations for uLMo PCI

As a clinical notion, we gathered key points during uLMo PCI which may facilitate patient care if this catastrophic event is indeed encountered.

1. Fast procedures: First and foremost, we have to state that speedy procedures targeted at opening the LM stem as soon as possible are key to restoring flow to the left coronary branches. Procedure times (measured from lidocaine injection to guiding catheter pullout) were under 30 min for every case we undertook. Unless critical downstream lesions (> 90%) are present we do not recommend ad hoc extended PCI of branches other than the LM. If, however, secondary stenoses are present, we recommend a late staged procedure during a second hospitalization. Nevertheless, our data also showed that most patients had one-vessel disease, defined as plaque of the LM-ostial LAD-ostial LCX complex, so it was not necessary

to expand revascularization beyond this in any of our cases. Operators focused on opening the occluded artery via thrombectomy or balloon pre-dilation and stented the lesion according to pathological LM status (see Tables II and IV). If readily available and applicable, intravascular ultrasound (IVUS) imaging may also improve outcomes and is recommended especially in cases when the LM bifurcation was involved.

2. Dual operators: If two capable operators are available for such interventions, we recommend that both interventionalists take part in care. The first operator should focus all attention on salvaging the coronary status, while the second operator should begin implementation of circulatory support devices. Valuable time is saved via this method and circulatory augmentation can also commence earlier, leading to possibly better outcomes [13].
3. Circulation augmentation: Unsurprisingly, almost 90% of subjects presented with manifest CS, necessitating the need for circulatory support. If dual operators are unavailable for simultaneous treatment, circulatory support initiation should commence only after the occluded LM has successfully been opened. In this scenario we recommend at least restoring blood flow to the left coronary branch prior to circulatory support initiation. Finishing, stenting and optimizing LM treatment may commence at a later time point when circulation is already amplified. Intra-aortic balloon pumps devices and especially VA-ECMO augmentation are very much indicated and endorsed. Of the two devices, IABP is the more accessible one, available in nearly all laboratories, yet its clinical benefit has been disputed [14]. VA-ECMO, on the other hand, although usually requiring on-site cardio-thoracic surgery, is certainly an overall better alternative [13, 15]. Due to the relatively small number of VA-ECMO implantations however, our database can provide no solid numbers in this regard. Nonetheless, percutaneous VA-ECMO implantation and system initialization, preferably under 20 min from initial puncture, provides the best alternative for circulatory support to date in CS ACS cases and our patients more than fit into this group [16, 17]. However, this above scenario is only feasible if devices are readily available pre-assembled with on-site staff as required for VA-ECMO activation.
4. Further care and follow-up: Surviving patients require complete intensive care after PCI, preferably in a hospital with intensive care specialists on site. In patients following SCD guidelines recommended post-resuscitation care is needed [9, 18]. If VA-ECMO support has been initiated, this requires further attention and may even require eventual conversion to mid-term circulatory augmentation devices, according to patients' clinical status. Patient care should be

guided via regular Heart Team meetings, also involving an intensive care specialist. Secondary prevention medication along with aspirin and a P2Y₁₂ inhibitor and further cardiological care are mandatory for each such surviving patient, as most patients require dedicated heart failure therapy in the medium and long term.

Feasibility of uLMo procedures

Unprotected LM occlusion, although the most severe form of ACS, is relatively scarce and seldom encountered in the catheterization laboratory. However, knowledge of this clinical scenario is important as interventionalists need to act fast to give patients any chance of survival. Percutaneous revascularization approaches, bearing in mind the uLMo case-specific recommendations discussed above, seem the only viable salvage option, as surgical forms of revascularization are unfeasible mostly due to the clinical presentation of subjects, especially in the most severe cases: initial SCD survivors. Nonetheless, without prompt reperfusion therapy and circulatory support, survival of such patients is virtually non-existent.

Limitations of the study

The main limitation of our work is that our study group was limited to 23 subjects and our study population was not correlated with a control group. Furthermore, no IVUS imaging was performed in our registry.

Conflict of interest

The authors declare no conflict of interest.

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