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Acute coronary syndromes due to culprit lesions located in unprotected left main coronary artery multifurcations

Short title: **ACS due to LMCA multifurcation lesions**

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Introduction

The presence of additional branches branching off from the left main coronary artery (LMCA) division is not a rare angiographic finding and may be as frequent as 53% according to a historical study [1]. Intuitively, in the case of atherosclerotic involvement of any left coronary branch, three or four left coronary branches may offer better protection against ischemia than two coronary branches, depending on the plaque location; however, this has not been studied so far.

Percutaneous coronary intervention (PCI) of unprotected LMCA trifurcation/quadrifurcation (multifurcation) presents a challenge, and coronary artery bypass grafting (CABG) seems to be a reasonable option. On the other hand, in the setting of acute coronary syndromes (ACS), surgical treatment is associated with a significantly increased perioperative risk, and therefore PCI is usually the method of choice in this group of patients [2]. However, this has only been proven for bifurcated LMCA, not for multifurcated LMCA. There is no comparison for the PCI outcome of the culprit lesion located in the bifurcated versus trifurcated LMCA in ACS-patients.

Aim

To evaluate the immediate and long-term outcomes of patients with ACS and culprit lesions located in unprotected LMCA multifurcation, treated with PCI or CABG.

Methods

Study Design: single-center retrospective observational study.

Patient Population: the hospital database was screened for PCI-treated patients with ACS and the culprit lesion located in the unprotected LMCA trifurcation-pentafurcation between January 2009 and September 2015. Inclusion criteria were: ACS presentation (ST-elevation myocardial infarction [STEMI], non-ST-elevation myocardial infarction [NSTEMI], and unstable angina [UA]), performed PCI, culprit lesion located in LMCA multifurcation. Patient clinical characteristics were collected in a dedicated database.

Angiography Analysis

A significant culprit lesion in the LMCA division was defined as lumen compromise of >50% in LMCA and/or >70% in any ostia of the proximal branches of LMCA multifurcation or presence of thrombus in the LMCA multifurcation in the setting of ongoing ischemia. A simple modification of the Medina classification designed for bifurcation lesions, extended for trifurcation or quadrifurcation lesions [3], was used to categorize the type of LMCA involvement. A binary value (1.0) was given to each of the consecutive segments of the LMCA division and branch ostia according to whether they were compromised or not. A true LMCA trifurcation lesion was defined as disease involvement of at least three of four LMCA division segments, and a true LMCA quadrifurcation lesion as involvement of at least four of five LMCA division segments. The SYNTAX score was used to calculate the extent of atherosclerosis complexity for the whole coronary tree (low-risk ≤ 22 , intermediate-risk 23–32, and high-risk ≥ 33).

Study Endpoints

The primary endpoint was a composite of major adverse cardiovascular events (MACE) defined as cardiac death, recurrent ACS, and target lesion revascularization (TLR) during the follow-up period. Clinical data on all-cause death, cardiac death, non-fatal ACS, stent thrombosis, TLR, were collected. Clinical information was obtained either from a review of the hospital records, by telephone interviews with the patients, family members, or by clinical visit. ACS

was defined as ischemic symptoms and/or ischemic changes on an electrocardiogram plus Troponin T elevation to twice the upper normal limit. TLR was defined as either repeated PCI or CABG due to restenosis within 5 mm proximal or distal of the carina of LMCA division. Statistical analysis was limited to the simple calculation of median patient's age and median follow-up period.

Results and discussion

Baseline patient characteristics, angiographic and treatment details as well as follow-up observations are shown in supplementary Table 1.

Eleven patients with ACS due to the culprit lesion located in the LMCA-multifurcation were identified (most of them LMCA-trifurcations). Among them, 7 patients were treated with PCI only, one patient was treated with PCI and delayed CABG and finally three patients were treated with CABG only. Median patient's age of the whole cohort was 68 years, inter-quartile range (IQR): 9.

Subgroup treated with PCI

Three patients presented with STEMI, three patients with NSTEMI, and one with UA. Among 6 LMCA trifurcations and single LMCA quadrifurcation, true LMCA division involvement by a significant lesion (see definition above) was diagnosed in 3 cases (all of them LMCA trifurcations). Treatment strategy was mainly based on the patient's hemodynamic stability and the type and extent of coronary artery disease. There were two in-hospital deaths (28.5%). The median follow-up of patients treated with PCI after hospital discharge was 41 months, (IQR 28), during which four deaths occurred (57.1%). The median ACS-death interval was 41.5 months, (IQR 13.2).

In summary, PCI was undertaken in five different scenarios. It was a part of a hybrid approach (patient no 2), was forced by the patient's instability/cardiogenic shock (patients no 3, 5, 7), or excessive surgical risk related to redo (patient no 6). Finally, favorable coronary anatomy in the settings of STEMI (patient no 8) or relative safety of opening of chronic total occlusion (patient no 4) promoted PCI over CABG.

No systematic study of ACS-patients due to culprit lesions located at LMCA dividing into more than two branches exists. The first and probably the only case of an ACS-patient with LMCA trifurcation treated with PCI was reported by Can et al. so far [4]. The novelty of this

retrospective study is the periprocedural outcome as well as the midterm observation of ACS patients due to such an anatomical scenario, who were treated percutaneously.

Surgical treatment seems to be the gold standard for such lesion location in stable patients. However, ACS, especially complicated by hemodynamic instability and unacceptable surgical risk, may force the operator to perform PCI. The goal of PCI in the settings of ACS may not necessarily be the complete percutaneous revascularization, but only the first stage of coronary and hemodynamic stabilization, before the second, hybrid approach (see patient no 2).

The type of stenting and procedural success of PCI depends largely on the type of LMCA lesion involvement and concomitant coronary narrowings. The retrospective observation of Chen et al. suggests that in analogy to PCI of LMCA bifurcation lesion, a one-stent technique may lead to better long-term results compared to a two-stent technique for LMCA trifurcation lesion [5]. Additionally, the utility of the SYNTAX score has been questioned for the LMCA trifurcation subgroup of patients. The benefit of a one-stent strategy was supported by another group [6]. As opposed to CABG, the in-hospital and follow-up outcome of ACS patients treated with LMCA trifurcation PCI remains unknown.

EuroSCORE in ACS

The predictive value of Euroscore for LMCA PCI outcome in the settings of ACS is unclear, and for LMCA trifurcation remains unknown. In the study of 200 ACS patients treated with PCI of unprotected LMCA, elevated EuroSCORE value and pre-procedural hemodynamic instability were the strongest predictors of target lesion failure [7]. A multicenter prospective registry of 138 patients with severely narrowed, unprotected LMCA disease and NSTEMI revealed that Euroscore >5 (and surgical revascularization) were the independent risk factors increasing early mortality, while a Euroscore >6 was the independent predictor of late mortality [2].

Long-term outcome

Tamburino et al. reported long-term outcomes after elective PCI for LMCA trifurcation in just 11 patients. Up to 32 months, three patients (27%) experienced clinically-driven TLR. No stent thrombosis was observed [8]. In the study by Kubo et al. [6], the incidence of TLR at 3 years was 14.5%, and it was significantly higher in the multi-stent group (31.3%), than in the one-stent group. Further, in the largest registry of patients with LMCA trifurcation disease treated with PCI, the only independent predictor of MACE at follow-up was the presence of true trifurcation disease [9]. Finally, data from LMCA bifurcation disease treated with PCI indicate

that involvement of the LCx ostium per se does not necessarily adversely affect long-term outcomes [10]. It is unknown however, if such observations would be proven for LCx and/or IM involvement in LMCA trifurcation.

Study Limitations

This is a retrospective, descriptive, and single-center study. The small and heterogeneous sample size precludes any statistical comparison.

Conclusions

The treatment of choice for culprit lesions located at LMCA multifurcation is surgical revascularization in most cases. However, in very selected ACS patients, especially in unstable hemodynamic conditions, immediate PCI may be required. Careful follow-up observation of patients after such treatment should be considered.

Article information

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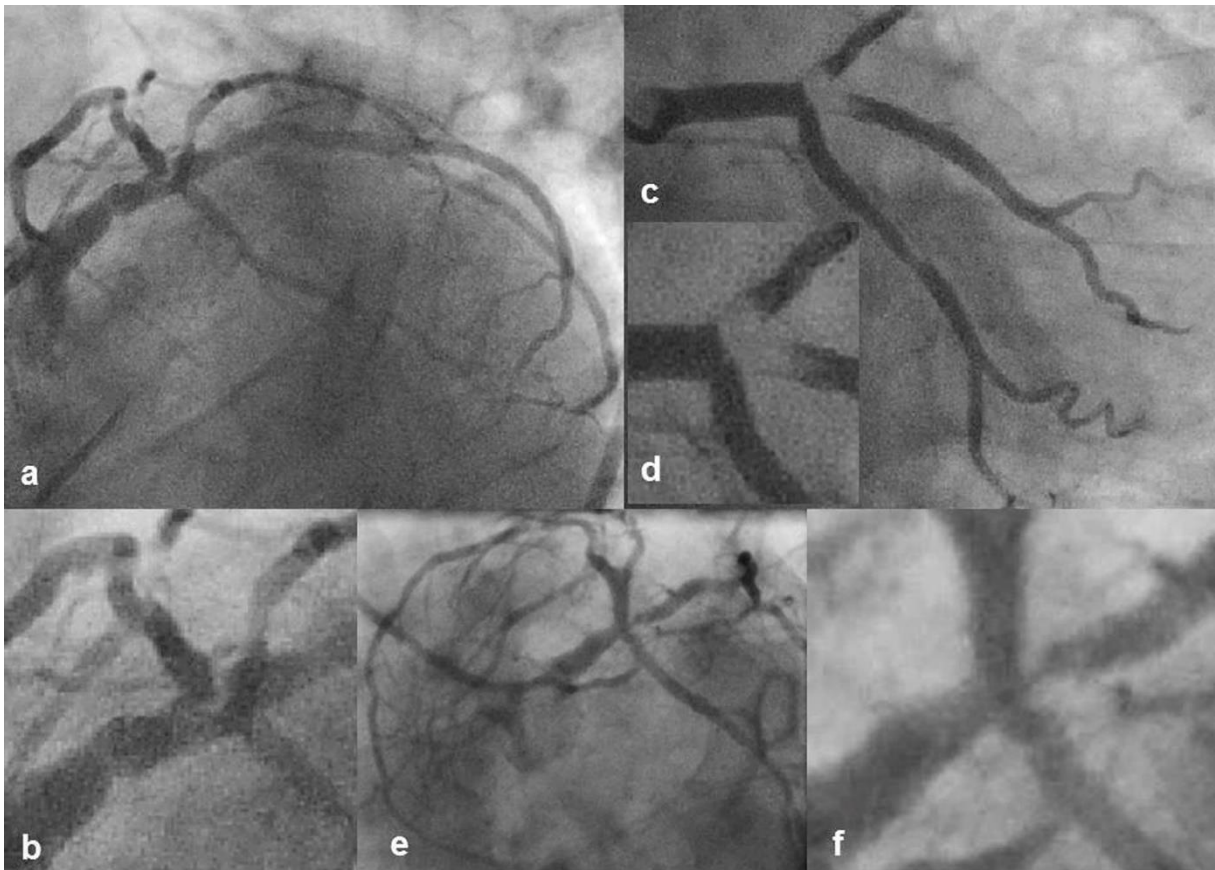


Figure 1a–f. Examples of the left main coronary artery division involvement by atherosclerotic plaque or thrombus.

a — left main coronary artery quadrifurcation with significant stenosis of the distal left main coronary artery. The patient was treated percutaneously; b — magnification of the image “a”; c — large thrombus located at the ostia of the left anterior descending coronary artery and the intermediate branch. Unsuccessful percutaneous treatment with thrombectomy was performed; d — magnification of the image “c”; e — critical ostial stenosis of the intermediate branch. The patient was treated conservatively; f — magnification of the image "e".