Journal of Clinical & Experimental Cardiology

Roubille et al., J Clin Exp Cardiolog 2014, 5:3
DOI: 10.4172/2155-9880.1000e135

Editorial Open Access

One Shot, Staged Procedures or Immediate Full Revascularization Strategy for Patients with Multivessel Disease Admitted for STEMI: Still a Bone of Contention

François Roubille*, Benoît Lattuca and Florence Leclercq

Department of Cardiology, Faculty of Medicine, University Montpellier, Montpellier cedex, Hospital Arnaud de Villeneuve, CHU Montpellier, France

***Corresponding author:** François Roubille, Cardiology Department, Hospital Arnaud de Villeneuve, CHU de Montpellier, UFR de Médecine, Université Montpellier 1, 371, avenue du Doyen Gaston Giraud, 34295 Montpellier cedex 05, France, Tel: 0033788014136; E-mail: francois.roubille@gmail.com

Rec date: Mar 03, 2014, **Acc date:** Apr 10, 2014, **Pub date:** Apr 18, 2014

In patients admitted for ST-segment sus-elevation myocardial infarction (STEMI), revascularization is the corner stone of the management, completing the medical treatments [1,2]. Although it is widely accepted and strongly recommended that the culprit lesion has to be treated during the Primary Percutaneous Coronary Intervention (PPCI), the better option regarding the other lesions in case of multivessel disease remains controversial. On the one hand, treating only the culprit lesion allows a shorter procedure with less renal impairment and lower risk of acute stent thrombosis. On the other hand, treating all the stenoses allow to shorten the hospitalization, stabilize the unstable plaques (See Table 1 for a detailed description of the advantages/disadvantages imbalance of the two sides of the medal). Importantly, this dilemma is not at all rare but should represent 30% to half of the patients admitted for STEMI [1,2].

	Advantages	Disadvantages
Culprit lesion only revascularization	The culprit lesion is treated and the more unstable plaque is treated The procedure is shorter Less contrast agent Less renal impairment Staff discussion is possible later Reevaluation of the lesions (-often overestimated during the emergency procedure, especially because of coronary spasms) Easier to obtain an informed consent, easier to inform the patient on different options and to take into account his preferences. opportunity to prove myocardial ischemia by functional test or FFR	Unstable plaques remaining are not treated Hemodynamic stenoses are not treated Longer hospitalization (in case of staged procedure) Requiring 2 arterial punctures
Full revascularization	All the significant lesions are stabilized and treated Shorter hospitalization Only one arterial puncture enhance of the collateral blood flow greater myocardial salvage achievement of a complete revascularization, factor that is associated with a better prognosis	peri-procedural complications More severe in case of stent thrombosis Longer procedure Hemodynamic instability during balloon inflations Vessel related complications (dissections, no-reflow) More contrast agent More renal impairment No staff discussion, no heart team

Table 1: Comparison of the two different options in case of multivessel disease revealed by a STEMI

A recent systemic review and metanalysis on this topic has just been published as well as an original work published in the leading medical journal [3,4]. In this important metanalysis, 26 studies with a total of 38,438 patients admitted for STEMI have been finally included [3]. The vast majority of them are not randomized (23 on 26). (See Table 2 for schematic description of the main features of the four prospective randomized trials available on this topic). The first three randomized trials have included only 339 patients. Among these three randomized trials, the multi-vessels PCI has been reported to be better than the culprit-only PCI as regards in hospital mortality (OR=0.24 (0.06-0.91), but only two small studies) and not in long-term mortality. Interestingly, among the non-randomized trials, it seems that the ideal timing of the revascularization is of great importance. As regards in-hospital mortality, immediate full revascularization is associated with poor outcomes (OR=1.35 (1.19-1.54)) whereas staged revascularization during the index hospitalization is associated with better outcomes (OR=0.35 (0.21-0.59). Similarly concerning the long term outcomes, immediate full revascularization is not statistically different from the culprit-only revascularization, but staged in hospital or later full revascularization is associated with better outcomes. Briefly, this work corroborates first that full revascularization, but perhaps not immediately during the index PCI, should be better that the culprit-only revascularization. Secondly, this analysis underlines that prospective randomized trials are mandatory.

References	Publication date	Design and intervention	Number of patients and randomisation	Inclusion criteria	Exclusion criteria	Delay of revascularization	Primary (1) and secondary (2) endpoints	Main results
Dambrink et al. [5]	2010	Culprit PPCI + medical treatment (conservative group) vs culprit PPCI + FFR in vessels with a significant stenosis (PCI performed if FFR < 0.75 or directly for severe lesions >90%) (invasive group)	121 patients: - 80 patients in invasive group - 41 patients in conservative group	STEMI with >50% stenosis in ≥ 2 arteries	- > 80 years - CTO of non IRA - Prior CABG - Left main significant stenosis -In-stent restenosis -Chronic AF	Invasive group: during index hospitalization or electively during the 3 weeks following (mean 7.5 days (5-20))	1) LVEF at 6 months 2) MACE at 6 months	1) No LVEF difference: 59+/-9% in invasive group and 57+/-9% in conservative group: p=0.362 2) No difference in MACE : 21% in invasive group and 22% in conservative group : p=0.929
Di Mario et al. [6]	2004	Culprit PPCI with additional revascularization at the investigators discretion (need and timing decided according to clinical status, evidence of ischemia in non-invasive tests or angiographic severity) vs complete revascularization during index catheterization Study using only one or more heparin coated stents (HepaCoat stents)	69 patients: - 17 patients inculprit lesion treatment only group - 52 patients in complete revascularization group	STEMI < 12h with MVD with 1-3 lesions in non IRA	- Lesion in vein and arterial grafts -In-stent restenosis -Chronictotal occlusion -Thrombolysis -Cardiogenic shock -Leftmain significant stenosis	Not specified for culprit lesion treatment only group	1) 12-month incidence of any repeat revascularization 2)(a) Composite with in hospital repeat revascularization, reinfarction and death (b) total 12-month cost	1) No significant difference in the incidence of new revascularization at 12 months: 35.3% in the culprit treatment group vs 17.3% in complete revascularization group, p= 0.174) 2) (a) Similar incidence of in-hospital MACE in the 2 groups: 0 and 3.8% in culprit and multivessel treatment, p=0.164) (b)No difference in total cost at 12-months : Euro 22,330 +/- Euro 13,653 in culprit treatment group vs Euro 20,382 +/- Euro 11,671 in complete revascularization group, p= 0.323).
Politi et al. [7]	2010	3 strategies - Culprit PPCI only -Full revascularization during index catheterization -Full revascularization during staged procedure	214 patients: - 84 patients in the culprit PPCI only group, - 65 patients in the complete revascularization group - 65 patients in the staged revascularization group	STEMI < 12-h with > 70% stenosis in ≥ 2 arteries	-Cardiogenic shock -Left main significant stenosis -Previous CABG -Severe valvular disease -Unsuccessful procedure	56.9 ± 12.9 days after the primary PCI for the staged revascularization group	1) MACE at 2.5 years 2) (a)Each event of MACE assessed individually (b)Survival free of MACE (c)Survival (d)Multivariate analyses	1) MACE occurred in 42 patients (50%) in the culprit only revascularization group, in 13 patients (20%) in the staged revascularization group and in 15 patients (23.1%) in the complete revascularization group (p<0.001). 2) (a) The incidence of in hospital death, repeat revascularization and re-hospitalization was significantly higher in the culprit only revascularization group (all p<0.05). No significant difference in re-infarction among the three groups. (b) Survival free of MACE was worse in the culprit only revascularization group compared with both the complete revascularization group (p=0.002) and the staged revascularization group (p=0.001), No difference between the complete and staged

								revascularization groups (p=0.815). (c) Tendency for a worse overall survival in the culprit only revascularization group compared with the other two groups (p=0.151).
Wald et al. [4]	2013	Complete revascularization vs.culprit PPCI + subsequent PCI only for refractory angina with objective evidence of ischemia	465 patients: - 234 patients in preventive PCI group (complete revascularization) - 231 patients in no preventive PCI group (culprit PPCI only)	STEMI < 12-h with Stenosis ≥ 50% in one or more coronary arteries other than the IRA and cardiologist consider that both infarct artery-only PCI and preventive PCI would be acceptable treatment options.	- Cardiogenic shock - Previous CABG - Left main stenosis > 50% - Chronic Total Occlusion	Number and timing of requiring subsequent PCI in no preventive PCI group were not specified	1) composite endpoint of cardiac death, non fatal myocardial infarction and refractory angina at 36 months 2)(a)Each item of composite endpoint assessed individually (b)Non cardiac death (c)Repeat revascularization	Trial prematurely stopped 1) Significant reduction of composite endpoint in preventive PCI group with 21 patients (9%) vs 53 patients (22.9%) in no preventive PCI group (p<0.001) 2)(a) No difference for death from cardiac causes : 4 patients in preventive PCI group and 10 in no preventive PCI group (p=0.07) but significant reduction for myocardial infarction (7 vs. 20 patients, p=0;009) and refractory angina (12 vs. 30 patients, p=0.002) respectively in preventive PCI group and no preventive PCI group (b)No difference between the 2 groups for non cardiac death (p=0.86) (c)Significant reduction of repeat revascularization in preventive PCI group (p<0.001)

Table 2: Main features of the four available prospective randomized trials on various strategies for PCI in patients admitted with STEMI and multivessel disease

PPCI : Primary Percutaneous Coronary Intervention; STEMI : ST segment sus-elevation myocardial infarction; FFR : Flow Fraction Reserve; CTO : Chronic Total Occlusion; IRA : Infarction Related Artery; CABG : Coronary Artery Bypass Graft; AF : Atrial Fibrillation; MVD : MultiVessel Disease; LVEF : Left Ventricular Ejection Fraction; MACE : Major Adverse Cardiac Events

Recently, the important PRAMI trial was published [4]. In this prospective randomized trial, 465 patients with STEMI were treated by PCI (culprit lesion) and then randomly assigned either to preventive PCI or no preventive PCI. This trial has been largely discussed (at least 8 comments following the publication) on several points. The main concern is the choice to revascularize all stenoses>50% (and not 70% as usually recommended, except as regards the main left trunk). This full revascularization was performed at one time. In spite of all the concerns mentioned, this trial established for the first time a large prospective trial corroborating that full revascularization could be safe and better than the culprit-lesion only revascularization (the primary endpoint was a clinical composite endpoint; hazard ratio 0.35 (0.21-0.58).

Here, Dahud et al. (paper to quote by the editorial office) report a retrospective trial including 491 patients admitted for STEMI and presenting a multiple vessel disease. 69.5% of the patients were treated with immediate full revascularization during the index PCI, whereas 30.5% were treated only on the culprit lesion and treated later for the other lesions. Importantly, these two different procedures don't evaluate the culprit only versus the full revascularization, but compare the ideal timing for the full revascularization: either immediate or staged full revascularization. This trial is a large retrospective study, corroborating that immediate full revascularization could be interesting, with a significantly shorter hospitalization, less MACEs, although by contrast, transient renal dysfunction was more frequent. Many limitations are to rise. Beyond the retrospective design, the long duration for inclusions (procedures have evolved and stents or antiplatelet agents have changed for instance), one important concern is how the patients had been allocated to each group? The more severe patients are likely to have been allocated to the more simple procedure first. If true, the results are a very good surprise. As regards methods, the regression models could be more detailed (especially the impact of the different operators). On ethical point of view, informed consent and preferences of the patients are obviously difficult to obtain in the onetime full revascularization procedures. As no surgical back-up is available in this centre, heart team discussion is difficult.

In spite of all these limitations, the authors provide interesting real-life data, underlining that this question is not solved. On contrary, several trials currently on going are precisely addressing this issue as briefly presented in Table 3.

In conclusion, a systematic approach is difficult to recommend. Two schematic situations are to be considered. On the one hand, a young patient with two critical stenoses on the RCA and on the LDA. The culprit lesion is clearly the LDA. In case the revascularization of the LDA should be easy and quick, it seems then reasonable to treat the other lesion during the same procedure (immediate full

revascularization). On the other hand, an old patient, with severe multiple stenoses, unknown (but likely impaired) renal function. In case the revascularization of the LDA should be long and difficult, it is obviously preferable to propose the angioplasty of the RCA later (staged procedure). The ideal delay, how to evaluate the stenosis, remain under debate. An individually tailored strategy should be the best option, but the best parameters to take into account are to be defined through prospective randomized trials currently on going (See Table 4 for some propositions presently taken into consideration routinely).

Country	Endpoint	Number of patients Planned to enroll	Design Randomization between two distinct PCI strategies	Delay for the full revascularization	NCT number
Spain	Clinical composite endpoint	400	Randomization 1) Full revascularization in a staged procedure during the index admission 2) Stress echocardiography and revascularization if required	1) During the initial hospitalization 2) Delayed (delay not provided)	NCT01179126
Denmark	Clinical composite endpoint	650	Randomization 1) Full revascularization guided by Fractional Flow Reserve (FFR) in a separate procedure within the index hospitalization 2) Culprit lesion revascularization only	1) During the initial hospitalization 2) Not applicable	NCT01960933
Korea	target vessel related major adverse cardiac events	646	Randomization 1) Complete revascularization : one time 2) Culprit revascularization : PCI of only the culprit lesion and staged nonculprit PCI at a later date	Immediate full revascularization versus later (delay not provided)	NCT01180218
Canada	Infarct size by CMR	250	Randomization 1) Full revascularization during the index PCI 2) IRA only PCI with planned staging for non-IRA lesions	1) Immediate 2) Delayed (delay not detailed)	NCT01818960
International	Clinical composite endpoint	885	Randomization 1) Full revascularization guided by FFR 2) Evaluation by FFR and referred to the cardiologist for further management	1) Same procedure (or delayed if necessary) 2) Delayed if any (delay not provided)	NCT01399736
Russia	Clinical composite endpoint	120	Randomized 1) one-time PCI of the culprit and nonculprit lesions 2) PCI of only the culprit lesion and staged nonculprit PCI at a later date (3-15 days) With Zotarolimus-eluting coronary stents	1) One time 2) 3-15 days	NCT01781715
Czech Republic	Clinical composite endpoint	400	Randomized 1) complete revascularization of significant stenoses of "non-infarct" coronary arteries (PCI or surgery; 3rd-40th day after primary PCI) 2) conservative management standard guideline-based medical therapy	1) Day 3-40 2) Not applicable	NCT01332591
Germany	30-day mortality and/or severe renal failure (Only patients with cardiogenic shock are included)	706	Randomization 1) immediate full revascularization 2) culprit lesion only and other revascularization later following guidelines	1) Immediate 2) Delayed (delay not provided)	NCT01927549

Table 3: Prospective randomized clinical trials currently registered dealing with STEMI and various PCI strategies for the management of patients with multiple vessel disease.

Only trials comparing full revascularization to culprit-only revascularization are compared, not trials comparing for instance two different stents. Research with the keyword "multivessel disease", March 19th, 2014 on the clinicaltrials.gov site

NCT: National Clinical Trial, FFR: Fractional Flow Reserve; PPCI: Primary Percutaneous Coronary Intervention; IRA: Infarct-Related Artery

The clinical presentation (including cardiogenic shock)
The clinical background (including renal function and other comorbidities)
The anatomy of the lesions (dedicated scores)
The thrombotic context (thrombus, drugs…)
The lesion severity: significant or critical?
The initial result on the culprit lesion (opportunity to check the result later)
ECG +/- echography parameters
The arterial access (in case of difficult access, it seems reasonable to prefer one time full revascularization)
The duration of the procedure
The necessity for heart team /staff discussion
The necessity for multiple operators procedure
The local facilities

Table 4: How could we decide to continue or to stop the procedure?

Acknowledgments

This is an editorial on the article "Infarct related artery only versus multivessel revascularization during primary PCI for STEMI" published in the Journal of Clinical & Experimental Cardiology.

The authors would like to acknowledge Drs Jean-Christophe MACIA, Richard GERVASONI and Thien-Tri CUNG (Montpellier University Hospital, France) for their suggestions and improvement of this manuscript.

References

1. Steg PG, James SK, Atar D, Badano LP, Blomstrom-Lundqvist C, et al. (2012) Esc guidelines for the management of acute myocardial infarction in patients presenting with st-segment elevation. Eur Heart J 33: 2569-2619.
2. Kushner FG, Hand M, Smith SC Jr., King SB 3rd, Anderson JL, et al. (2009) 2009 focused updates: Acc/aha guidelines for the management of patients with st-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and acc/aha/scai guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update) a report of the american college of cardiology foundation/american heart association task force on practice guidelines. J Am Coll Cardiol 54: 2205-2241.
3. Bainey KR, Mehta SR, Lai T, Welsh RC (2014) Complete vs culprit-only revascularization for patients with multivessel disease undergoing primary percutaneous coronary intervention for st-segment elevation myocardial infarction: A systematic review and meta-analysis. Am Heart J 167: 1-14.
4. Wald DS, Morris JK, Wald NJ, Chase AJ, Edwards RJ, et al. (2013) Randomized trial of preventive angioplasty in myocardial infarction. N Engl J Med 369: 1115-1123.
5. Dambrink JH, Debrauwere JP, van 't Hof AW, Ottervanger JP, Gosselink AT, et al. (2010) Non-culprit lesions detected during primary PCI: treat invasively or follow the guidelines? EuroIntervention 5: 968-975.
6. Di Mario C, Mara S, Flavio A, Imad S, Antonio M, et al. (2004) Single vs multivessel treatment during primary angioplasty: results of the multicentre randomised HEpacoat for cuLPrit or multivessel stenting for Acute Myocardial Infarction (HELP AMI) Study. Int J Cardiovasc Intervent 6: 128-133.
7. Politi L, Sgura F, Rossi R, Monopoli D, Guerri E, et al. (2010) A randomised trial of target-vessel versus multi-vessel revascularisation in ST-elevation myocardial infarction: major adverse cardiac events during long-term follow-up. Heart 96: 662-667.