EuroIntervention 2012;8:423-425

Multivessel versus culprit-only revascularisation in ST elevation acute myocardial infarction: facts and criticism

Ran Kornowski, MD, FESC, FACC

Department of Cardiology, Institute of Interventional Cardiology, Rabin Medical Center, Petach Tikva and Tel Aviv University, Petah Tikva, Israel

Approximately 40-65% of patients with ST-elevation acute myocardial infarction (STEMI) have multivessel coronary artery disease, which is associated with worse outcomes compared with single-vessel disease. Proper management of non-culprit lesions in STEMI is a controversial topic. Current guidelines recommend only treating the culprit lesion unless the patient has cardiogenic shock[1,2]; however, there is no consensus about the best treatment strategy for this clinical syndrome[3,4].

Treating the culprit and non-culprit lesions together during STEMI has the following potential advantages: 1) acute multivessel PCI eliminates the need for a secondary procedure; 2) plaque instability may include non-culprit lesions, potentially triggering recurrent ischaemic events[5]; 3) complete coronary revascularisation is associated with improved cardiac function and better long-term prognosis[6]; and, 4) acute multivessel PCI may reduce treatment costs by diminishing the need for future hospitalisations and subsequent procedures.

In contrast, acute multivessel PCI may contribute to a higher risk of complications for the following reasons: 1) the increased thrombotic and inflammatory burden in STEMI is partly related to an increased incidence of stent thrombosis among patients treated with this strategy[7,8]; 2) the severity of non-culprit lesions in STEMI is frequently overestimated, resulting in unnecessary intervention of functionally insignificant lesions[9]; 3) greater radio-contrast is used, which may be poorly tolerated in STEMI, increasing the risk of contrast-induced nephropathy and worse prognosis[10]; and, 4) deferred treatment of non-culprit lesions allows further discussion of treatment options by the heart team based on the angiogram and non-invasive tests.

Multiple studies have addressed this topic and were recently reviewed[11]; here we will only mention a few studies. We previously reported on the results of culprit-vessel-only versus multivessel PCI during STEMI, from a *post hoc* analysis of the HORIZONS-AMI (Harmonising Outcomes with Revascularisation and Stents in Acute Myocardial Infarction) trial[12]. At one-year post-STEMI, patients undergoing multivessel PCI versus staged PCI (e.g., culprit-only PCI with later non-culprit intervention) had significantly greater rates of all-cause mortality (9.2% vs. 2.3%, p<0.0001) and cardiac mortality (6.2% vs. 2.0%, p=0.005). Additionally, acute multivessel PCI was associated with more stent thrombosis events. We found no outcome parameter in favour of acute multivessel PCI. Multivariable analysis showed that staged versus multivessel PCI strategy was independently associated with lower all-cause mortality at one-month and one-year post-STEMI. The 3-year extended outcomes of this study confirmed the prognostic superiority of staged PCI vs. one-time multivessel intervention during long-term follow-up[13].

Vlaar et al confirmed our results in their meta-analysis of four prospective and 14 retrospective studies involving more than 40,000 patients with STEMI[14]. Staged PCI aimed at completing the revascularisation was associated with lower short-term mortality rates compared with the culprit-vessel-alone PCI (odds ratio [OR]=3.03, p=0.005), and with the multivessel PCI group (OR=5.31, p=0.0001). Lower mortality rates were also associated with culprit-vessel-only versus multivessel PCI (OR=0.66, p=0.007). Lower long-term mortality rates were recorded in the staged PCI group. The rank-probability of the three therapeutic strategies was also investigated for short- and long-term mortality;

**Corresponding address: Cardiac Catheterization Laboratories, Department of Cardiology, Rabin Medical Center, Petah Tikva 49100, Israel. E-mail: ran.kornowski@gmail.com*

DOI: 10.4244/EIJV8I4A66

staged PCI was the better strategy followed by culprit-vessel-only PCI (without subsequent revascularisation) and by multivessel PCI. However, the meta-analysis included studies that seemed to be in disagreement, and none of the prospective studies were large enough to show a significant between-group mortality difference. Hannan et al addressed the same topic retrospectively in a cohort of 4,024 STEMI patients with multivessel disease[15]. They found significantly lower in-hospital and long-term (42-month follow-up) mortality rates following culprit-vessel-only PCI group compared with acute multivessel PCI. At follow-up, mortality rates of staged multivessel PCI were lower than in the culprit-vessel-only PCI group, supporting completion of subsequent revascularisation in infarcted patients with multivessel coronary disease. Jensen et al retrospectively examined mortality according to timing of multivessel PCI in STEMI: acute procedure, staged procedures during the index hospitalisation or staged procedures performed within 60 days[16]. The study cohort consisted of 5,944 patients, of whom 4,770 had single-vessel disease and 1,174 had multivessel PCI within 60 days. For 354 (30.2%) patients with acute multivessel PCI, 194 (16.5%) patients with multivessel PCI during the index hospitalisation, and 626 (53.3%) patients with multivessel PCI within 60 days after the index hospitalisation, the adjusted hazards ratios (HRs) for one-year mortality were statistically significant at 1.53, 0.60, and 0.28, respectively, compared to patients with single-vessel disease. The investigators concluded that acute multivessel PCI in patients with STEMI was associated with increased mortality. Such cases should be treated in a staged fashion to complete the revascularisation, rather than at all at once.

Article, see page 456

Despite these data, I believe that a final conclusion cannot yet be drawn in this field of investigation. Most data addressing this question were derived from retrospective investigations or *post hoc* analyses. I was unable to find a properly designed and/or powered prospective randomised trial that examined multivessel PCI during STEMI; none were powered to explore all-cause mortality or cardiac mortality treatment effect as a primary endpoint. Furthermore, most reports described significant baseline differences between the two analysed groups, which may have influenced the clinical outcomes; age, pre-TIMI grades of flow and impaired left ventricular function sometimes differed between groups. Moreover, lesion and flow characteristics of non-culprit lesions were never described or specified. Thus, it is possible that patients treated with acute multivessel PCI were sicker and at greater cardiac risk regardless of the treatment strategy. More complex and lengthy procedures performed in tougher cases were likely associated with more periprocedural complications –such as contrast nephropathy, cardiac enzyme leaks, heart failure, and need to treat multiple culprit lesions.

Although some trials have attempted to correct for baseline differences using propensity controlled analysis, given the risk of residual confounding, a randomised trial is required to definitively address this issue. Until such a study is available, it can be argued that the results may be biased. The available studies lacked information about the operators' reasons for choosing one strategy over another; therefore, a potential bias in therapeutic decision might have influenced the observations. Additionally, the angiographic diagnosis of culprit versus non-culprit lesion in STEMI might sometimes be ambiguous, owing to the documented tendency to overestimate coronary artery disease severity in the context of STEMI due to coronary spasm and systemic vasoconstriction. Such a phenomenon may result in PCI treatment of non-significant\non-culprit lesions, adversely influencing the obtained results.

In summary, the results of the presently available studies strongly suggest that acute multivessel PCI in patients with STEMI may be associated with a greater risk of mortality compared to staged PCI. Furthermore, complete staged revascularisation remains the best therapeutic strategy in STEMI patients. Thus, pending the results of a properly designed randomised trial, a deferred angioplasty strategy of non-culprit lesions should remain the standard approach in patients with multivessel coronary artery disease and STEMI.

Conflict of interest statement

The author has no conflicts of interest to declare.

References

1. Kushner FG, Hand M, Smith SC Jr, King SB 3rd, Anderson JL, Antman EM, Bailey SR, Bates ER, Blankenship JC, Casey DE Jr, Green LA, Hochman JS, Jacobs AK, Krumholz HM, Morrison DA, Ornato JP, Pearle DL, Peterson ED, Sloan MA, Whitlow PL, Williams DO. 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.* 2009;54:2205-41.

2. Wijns W, KolhP, Danchin N, Di Mario C, Falk V, Folliguet T, Garg S, Huber K, James S, Knuuti J, Lopez-Sendon J, Marco J, Menicanti L, Ostojic M, Piepoli MF, Pirlet C, Pomar JL, Reifart N, Ribichini FL, Schalij MJ, Sergeant P, Serruys PW, Silber S, SousaUva M, Taggart D. Guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2010;31:2501-55.

3. Kornowski R. Completeness of revascularization in patients with ST-Elevation acute myocardial infarction. *Catheter Cardiovasc Interv.* 2008;72:934-6.

4. Dangas GD, George JC, Weintraub W, Popma JJ. Timing of staged percutaneous coronary intervention in multivessel coronary artery disease. *JACC Cardiovasc Interv.* 2010;3:1096-9.

5. Ambrose JA. In search of the "vulnerable plaque": can it be localized and will focal regional therapy ever be an option for cardiac prevention? *J Am Coll Cardiol* 2008;51:1539-42.

6. Kalarus Z, Lenarczyk R, Kowalczyk J, Kowalski O, Gasior M, Was T, Zebik T, Krupa H, Chodór P, Poloński L, Zembala M. Importance of complete revascularization in patients with acute

myocardial infarction treated with percutaneous coronary intervention. *Am Heart J.* 2007;153:304-12.

7. Chan MY, Andreotti F, Becker RC. Hypercoagulable states in cardiovascular disease. *Circulation.* 2008;118:2286-97.

8. Arbab-Zadeh A, Nakano M, Virmani R, Fuster V. Acute coronary events. *Circulation.* 2012;125:1147-56.

9. Hanratty CG, Koyama Y, Rasmussen HH, Nelson GI, Hansen PS, Ward MR. Exaggeration of nonculprit stenosis during acute myocardial infarction: implication for immediate multivessel revascularization. *J Am Coll Cardiol.* 2002;40:911-6.

10. Assali AR, Brosh D, Ben-Dor I, Solodky A, Fuchs S, Teplitsky I, Kornowski R. The impact of renal insufficiency on patients outcomes in emergent angioplasty for acute myocardial infarction. *Cathet Cardiovasc Interv.* 2007;69:395-400.

11. Codner P, Kornowski R. Multivessel Versus Culprit-Only Revascularization: One Time Versus Staged Procedures for the ACS Population. *Curr Cardiol Rep.* April 25, 2012 [Epub ahead of print].

12. Kornowski R, Mehran R, Dangas G, Nikolsky E, Assali A, Claessen BE, Gersh BJ, Wong SC, Witzenbichler B, Guagliumi G, Dudek D, Fahy M, Lansky AJ, Stone GW; HORIZONS-AMI Trial Investigators. Prognostic impact of staged versus "one-time" multivessel percutaneous interventions in acute myocardial infarction: analysis from the HORIZONS-AMI trial. *J Am Coll Cardiol.* 2011;58:704-11.

13. Kornowski R, Mehran R, Dangas G, Assali A, Nikolsky E, Claessen BE, Gersh BJ, Wong SC, Witzenbichler B, Guagliumi G, Dudek D, Fahy M, Lansky AJ, Stone GW; HORIZONS-AMI Trial Investigators. Prognostic Impact of Staged versus "One-Time" Multivessel PCI in Acute ST Elevation Myocardial Infarction: Long-Term Analysis from the HORIZONS-AMI Trial. Am Coll Cardiol Annual Meeting, April 2011 [Oral Abstract Presentation].

14. Vlaar PJ, Mahmoud KD, Holmes DR Jr, van Valkenhoef G, Hillege HL, van der Horst IC, Zijlstra F, de Smet BJ. Culprit Vessel Only Versus Multivesseland staged Percutaneous Coronary Interventionfor Multivessel Disease in Patients PresentingWith ST-Segment Elevation Myocardial Infarction. *J Am Coll Cardiol.* 2011;58:692-703.

15. Hannan EL, Samadashvili Z, Walford G, Holmes DR Jr, Jacobs AK, Stamato NJ,Venditti FJ, Sharma S, King SB 3rd. Culprit vessel percutaneous coronary intervention versus multivessel and staged percutaneous coronary intervention for ST- segment elevation myocardial infarction patients with multivessel disease. *J Am Coll Cardiol Intv.* 2010;3:22-31.

16. Jensen LO, Thayssen P, KörmendinéFarkas D, Hougaard M, Terkelsen CJ, Tilsted HH, Maeng M, Junker A,Lassen JF, Puho E, Sørensen HT, Thuesen L. Culprit Only or Multivessel Percutaneous Coronary Intervention in Patients with ST-Segment Elevation Myocardial Infarction and Multivessel Disease. *EuroIntervention* 2012;8:456-64.