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STATE-OF-THE-ART REVIEW

Defining Staged Procedures for Percutaneous Coronary Intervention Trials

A Guidance Document

Ernest Spitzer, MD,[a,b] Eugène McFadden, MD,[a,c] Pascal Vranckx, MD, PhD,[d] Ton de Vries, MSc,[a] Ben Ren, MD, PhD,[a,b] Carlos Collet, MD,[e] Yoshinobu Onuma, MD, PhD,[a] Hector M. Garcia-Garcia, MD, PhD,[f] Renato D. Lopes, MD, PhD,[g] Gregg W. Stone, MD,[h] Donald E. Cutlip, MD,[i,j] Patrick W. Serruys, MD, PhD[k]

ABSTRACT

Patients in coronary intervention trials may require more than 1 procedure to complete the intended revascularization strategy. However, these staged interventions are not consistently defined. Standardized definitions are needed to allow meaningful comparisons of this outcome among trials. This document provides guidance on relevant parameters involving staged procedures, including minimum data collection and consistent classification of coronary procedures initially identified as staged; the aim is to achieve consistency among clinical trialists, sponsors, health authorities, and regulators. Definitions were developed jointly among representatives of academic institutions and clinical research organizations based on clinical trial experience and published literature. Reasons for staged procedures were identified and include baseline kidney function, contrast load and radiation exposure, lesion complexity, and patient or operator fatigue. Moreover, nonclinical reasons include procedure scheduling and reimbursement. Management of staged procedures should be a standalone section in clinical trial protocols and clinical events committee charters. These documents should clearly define a time window for staged procedures that allows latitude for local policies, while respecting accepted clinical guidelines, and consistency with study objectives. Investigators should document in the case report form the intent to stage a procedure, the lesions to be treated, and the reasons for staging, preferably before randomization. Ideally, all reinterventions, or at least all procedures performed after the recommended time window, those in which data suggest an anticipated procedure due to a worsening condition and those where a revascularization is attempted in the target vessel, should be reviewed by an independent clinical events committee. (J Am Coll Cardiol Intv 2018;11:823–32)

From the [a]Cardialysis Core Laboratories and Clinical Trial Management, Rotterdam, the Netherlands; [b]Department of Cardiology, Thoraxcenter, Erasmus University Medical Center, Rotterdam, the Netherlands; [c]Department of Cardiology, Cork University Hospital, Cork, Ireland; [d]Department of Cardiology and Critical Care Medicine, Hartcentrum Hasselt, Jessa Ziekenhuis, Faculty of Medicine and Life Sciences Hasselt University, Hasselt, Belgium; [e]Department of Cardiology, Academic Medical Center, Amsterdam, the Netherlands; [f]Department of Cardiology, MedStar Washington Hospital Center, Washington, DC; [g]Division of Cardiology, Duke University Medical Center/Duke Clinical Research Institute, Durham, North Carolina; [h]Clinical Trials Center, Cardiovascular Research Foundation and Division of Cardiology, Columbia University Medical Center, New York, New York; [i]Baim Institute for Clinical Research, Boston, Massachusetts; [j]Beth Israel Deaconess Medical Center, Boston, Massachusetts; and the [k]International Centre for Circulatory Health, NHLI, Imperial College London, London, United Kingdom. Dr. Onuma has been a member of an advisory board for Abbott Vascular. Dr. Garcia-Garcia has served as a consultant for Tryton; has received speaker fees from Volcano/Philips; and has received institutional grants from Biotronik, Medtronic, Infraredx, and Neovasc. Dr. Lopes has received personal fees for consulting from Bayer, Bristol-Myers Squibb, Daiichi Sankyo, GlaxoSmithKline, Merck & Co., Inc., Pfizer, Portola Pharmaceuticals, and Boehringer Ingelheim; and has received institutional grant support from Bristol-Myers Squibb, GlaxoSmithKline, Medtronic, and Pfizer. Prof. Serruys has served as a consultant to Abbott, AstraZeneca, Biotronik, Cardialysis, GLG Research, Medtronic, Sinomedical, Soc. Europa Dig. Publishing, Stentys, Svelte, Phillips/Volcano, St. Jude Medical, Qualimed, and Xeltis. Dr. Cutlip received research support from Celonova. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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ABBREVIATIONS AND ACRONYMS

ARC = Academic Research Consortium

CEC = clinical events committee

CTO = chronic total occlusion

LAD = left anterior descending coronary artery

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

Up to one-tenth of patients enrolled in coronary intervention trials require more than a single procedure to complete an intended percutaneous revascularization strategy due to multivessel disease (1,2). It would be ideal, both from patient and societal (health care economic) perspectives that all lesions requiring intervention could be treated in a single session. However, there are legitimate clinical and nonclinical reasons that may justify a staged procedure (3).

Coronary intervention trials aim to provide an unbiased comparison between a novel device and a predicate device, or to compare a percutaneous strategy with a surgical strategy. In trials designed to compare stent/scaffold platforms, consistency in the definition of reintervention is critical to ensure comparability among trials and to allow meaningful conclusions from pooled data and meta-analyses. This may be extended to trials comparing different percutaneous strategies (e.g., in the setting of ST-segment elevation myocardial infarction [STEMI]) or to those investigating combined percutaneous therapies (e.g., transcatheter aortic valve replacement and percutaneous coronary intervention [PCI]). The current absence of standardized definitions for staged procedures poses challenges for the interpretation of data among trials that involve staged interventions. Specifically, for 2 different studies, the same post-index intervention may be adjudicated as a staged procedure in one trial and as a re-intervention in another trial; with direct impact on the number of revascularizations that will be considered as an endpoint.

In the present document, we propose a standardized definition around data collection, and provide guidance for adjudicating staged procedures by clinical events committees (CECs). Clear guidance will also facilitate incorporation of trial data into clinical practice guidelines.

METHODS

Representatives of academic institutions and clinical research organizations jointly elaborated this guidance document based on clinical trial experience and published reports. A systematic review was performed independently by 2 authors to identify time windows and definitions used in selected coronary intervention randomized trials published between 2007 and 2017 in 5 major clinical journals that randomized at least 1,000 patients and for which information on staged procedures was available online. Details are provided in Online Tables 1 and 2, Online Figure 1.

CIRCUMSTANCES ASSOCIATED WITH STAGED PROCEDURES. In clinical trials, as well as in routine practice, staged procedures allow completion of an optimal coronary revascularization strategy, when this is not possible or preferred in a single coronary intervention procedure. Such circumstances include the clinical presentation (e.g., STEMI as compared with non-STEMI or stable angina) (4); the baseline angiographic characteristics (e.g., unanticipated procedural complexity with the need for ancillary techniques such as rotational atherectomy) (4); patient-related factors (e.g., renal impairment, contrast and radiation exposure); and in the setting of chronic total occlusions (CTOs), where a strategy that involves a second attempt may be prospectively defined by protocol (3). Furthermore, nonclinical reasons such as logistic issues (e.g., an on-call setting where another STEMI patient is en route) and rare scenarios such as equipment failure may also play a role. Finally, reimbursement practices may influence the decision to "stage" a procedure or, more likely, may affect the timing of "staged" procedures. More specifically, if a second procedure is scheduled within a specific time window, the procedure may or may not be reimbursed in some jurisdictions. This practice is not scientifically justified, and consideration should be given to only including centers/countries that can comply with protocol requirements. An overview of the situations that may result in an additional, planned procedure is provided in **Table 1**.

DEFINITION OF A STAGED PROCEDURE. Both the patient-orientated composite endpoint and the device-orientated composite endpoint, proposed by the Academic Research Consortium (ARC) have become widely accepted in coronary intervention trials (5) (**Central Illustration**). However, for both definitions, the consistent classification of any repeat intervention, after the index procedure, is necessary for the inherent validity of cross-trial comparisons (5). We propose to define a staged procedure as a planned intervention performed after the first catheterization when it fulfills the following requirements: 1) the intent to stage is documented, provisionally or definitely, before or within 24 h after completion of the first procedure (**Figure 1**); 2) the lesion(s) to be treated during the staged procedure should be defined upfront and should not involve the index vessel, except in specific study designs, such as trials for left main disease or CTOs; 3) the procedure should be performed within the protocol-defined time frame; and 4) stability of symptoms is required between the first and the subsequent procedure(s), because acute ischemia (including worsening of angina) would disqualify the