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Review

Relationship Between the Current Definitions of Periprocedural Myocardial Infarction and Clinical Outcomes Following Percutaneous Coronary Revascularization

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Abstract

Since the beginning of the percutaneous coronary intervention (PCI) era, periprocedural myocardial infarction (PMI) has been recognized as a potential source of impaired outcomes in patients undergoing revascularization. Subsequently, several different definitions of PMI have been provided, coming from trial research groups or international consensus. Despite these efforts, the debate over the prognostic value or PMI in terms of mortality risk, as well as its role in defining composite ischemic endpoints in clinical investigations, has been extremely active. Currently, three international definitions of PMI are available: the Universal Definition of Myocardial Infarction (UDMI), the Academic Research Consortium (ARC)-2 definition, and the definition by the Society for Cardiovascular Angiography and Interventions (SCAI). These definitions differ significantly in terms of sensitivity and prognostic relevance, which has led to heterogeneous findings in clinical studies investigating this topic. Thus, this review aims to provide an overview of the main features of these definitions, their association with the risk of mortality, and how different definitions can influence the results of major investigations in the research setting.

Keywords: periprocedural myocardial infarction; percutaneous coronary intervention; coronary artery disease; coronary revascularization

1. Introduction

Recently, several studies have focused on defining the benefits and limitations of coronary revascularization in terms of major clinical outcomes [1–5]. Despite being effective in reducing future spontaneous myocardial infarctions (MIs) and re-interventions [6,7], percutaneous coronary intervention (PCI) is associated with procedural risks that can limit the prognostic value of this technique in terms of mortality. Since the early stages of PCI, periprocedural MI (PMI) has been recognized as a potential source of impaired outcomes following revascularization [8]. Several studies have been conducted to evaluate the relationship between PMI and mortality; however, these studies have been characterized by heterogeneity in their design, resulting in conflicting results [6,9–12].

A significant proportion of the heterogeneous findings on this topic derives from the different definitions of PMI that have been proposed over the years. While earlier studies often relied on protocol definitions, recently, international societies have made several efforts toward standardization [13]. Thus, three internationally recognized definitions of PMI are currently available: the Fourth Universal Definition of Myocardial Infarction (UDMI), the Academic Research Consortium (ARC)-2 definition, and the definition by the Society for Cardiovascular Angiography and Interventions (SCAI) [14–16]. These definitions have subsequently been adapted through various consensus documents [17,18] and differ significantly in terms of biomarker evaluation and the inclusion of ancillary criteria. Hence, this narrative review aims to synthesize the main features of each of the three available definitions of PMI and describe their dif-

ferent relationships with clinical outcomes following PCI, as per the available literature. Although PMI has significant implications in other scenarios, such as acute coronary syndromes (ACS) and cardiac surgery [19,20], this work will primarily focus on patients with stable coronary artery disease (CAD) treated with PCI, a setting that has been most extensively investigated previously.

2. Main Features of the International Definitions of PMI

The three definitions of PMI discussed in this paper are reported in Table 1. Similar to spontaneous MI [14], these definitions of PMI are characterized by two components: (1) biomarker elevation; (2) ancillary criteria. To date, the only biomarkers considered for detecting myocardial damage are cardiac troponin (cTn) and cardiac-specific creatine kinase myocardial band (CK-MB). Despite the purpose of this review, it is worth noting that these two enzymes exhibit different kinetic features, which can slightly influence the detection of myocardial damage [21,22]. In patients with normal baseline cTn values, the UDMI requires an elevation of at least 5× the upper rate limit (URL) for the used sampling assay; meanwhile, in patients with elevated baseline cTn values, a 20% variation must also be detected to define the occurrence of new myocardial damage [14]. Comparatively, the ARC-2 definition requires a cTn increase of 35× the URL, regardless of the baseline values [15]. Both these definitions also need the presence of at least one ancillary criterion to define a new PMI event. Unlike the UDMI and ARC-2 requirements, the SCAI definition of PMI primarily relies on CK-MB levels, while cTn is recommended only if the former is not available. SCAI-defined PMI requires a rise in CK-MB levels of 5× the URL or cTn of 35× the URL alongside one ancillary criterion. Alternatively, when no ancillary criteria are detected, isolated elevations in CK-MB levels of 10× the URL or cTn of 70× the URL are sufficient. These cut-offs are also valid in patients with elevated preprocedural biomarkers [16]. Notably, the use of CK-MB has decreased recently due to the lower diagnostic accuracy of this biomarker compared to cTn, while several centers no longer have the sampling assays required to measure CK-MB [23]. This may limit the application of the SCAI definition in real-world practice. Regarding the concerns about the type of ancillary criteria, both the UDMI and ARC-2 definitions include both electrocardiogram (ECG) and non-ECG features. Conversely, only ECG alterations are used in the SCAI definition. Moreover, while the UDMI considers various subtypes of possible ECG modification, the ARC-2 and the SCAI definitions emphasize the role of new Q-waves and left bundle branch block (LBBB) development.

3. Incidence of PMI According to the Different Definitions

The prevalence of any condition, including PMI, is influenced by a balance between the sensitivity of a specific diagnostic tool (e.g., cardiac enzymes) and the criteria required to meet a definition. Notably, the diagnostic accuracy for myocardial damage has significantly increased following the introduction of high-sensitivity (HS) cTn detection, resulting in a near elimination of the risk for false negatives [24]. Consequently, the type of definition applied and the clinical context in which the investigation is conducted are the main factors influencing the rates of PMI in the literature.

Nonetheless, conflicting data have been reported regarding the rates of PMI in the most recent registries, including all-comer patients undergoing PCI. Overall, current evidence suggests that PMI occurs in 10%–15% of cases when applying the UDMI [10,25–28], 5%–10% of cases when using the ARC-2 definition [10,25,27–29], and in 5% or fewer patients when the SCAI definition is applied [9,11,25,27,28,30,31]. These trends mainly reflect the minimal biomarker elevations required to meet each one of these definitions, which are progressively higher across the UDMI, the ARC-2, and the SCAI criteria. Therefore, while the UDMI criteria can be met even with minimal cTn elevations, the SCAI definition requires more extensive car-

Table 1. International definitions of periprocedural myocardial infarction.

	UDMI	ARC-2	SCAI
Biomarker			
cTn	5× URL	35× URL	35× or 70× URL
CK-MB	Not recommended	Not recommended	5× URL or 10× URL*
Ancillary criteria			
Mandatory	Yes	Yes	No
Ischemic ECG changes	Any	New Q wave	New Q wave or LBBB
Flow limiting angiographic complication	Yes	Yes	No
Loss of myocardial function	Yes	Yes	No

*CK-MB to be preferred over cTn. UDMI, Universal Definition of Myocardial Infarction; ARC-2, Academic Research Consortium-2; SCAI, Society for Cardiovascular Angiography and Interventions; cTn, cardiac troponin; CK-MB, creatine kinase myocardial band; ECG, electrocardiogram; URL, upper rate limit; LBBB, left bundle branch block.

diac damage, reducing its relative incidence. Other major influencers are represented by the complexity of coronary intervention and the amount of jeopardized myocardium involved during the revascularization, which both lead to a higher risk of PMI [32,33]. Moreover, patient-level clinical features can independently influence the incidence of PMI, such as age, chronic kidney disease, and diabetes [34]. Ultimately, methodological issues must also be considered. Specifically, there is notable heterogeneity in the designs of previous studies in terms of routine sampling of pre- and post-PCI biomarkers [10,11,25,35,36], systematic evaluation of ancillary criteria [9–11,26,27,35,36], or the use of non-HS cTn [25,28,29,31]. All these factors influence the capacity of those studies to detect PMI events and should be strictly considered when trying to infer its prevalence in patients undergoing PCI.

4. Relationship Between the Different Definitions of PMI and Mortality

Despite questioning the use of MI as a surrogate for all-cause and cardiovascular mortality in clinical investigations (mostly due to improvements in both interventional and medical treatment) [37], the association between spontaneous MI events and reduced survival remains relevant [38,39]. Conversely, conflicting evidence has been published regarding the relationship between PMI and the risk of death.

For UDMI, most studies have demonstrated a 1.5- to 2.0-fold increased risk of mortality following a PMI [11,27,30,40–42]. This association is progressively higher for the other two definitions, with a more than 2.0- and 3.0-fold increase for the ARC-2 [25,27,29,42] and the SCAI [9,25,27,29,31,36,40,42,43] definitions, respectively. Publication bias and selective reporting of positive findings are major issues when considering the prognostic relevance of a certain event that cannot be investigated through randomized studies, since these can inflate the conclusions derived from the available literature [44]. For the specific case of PMI, the significant number of positive studies is not sufficient to rule out this risk. In a dedicated sub-analysis of the "International Study of Comparative Health Effectiveness with Medical and Invasive Approaches" (ISCHEMIA) trial, neither the primary nor the secondary protocol definitions of PMI (which relied on CK-MB and cTn, respectively) were associated with mortality [6]. Similarly, the UDMI failed to show significant prognostic value in patients randomized to PCI in the "Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization" (EXCEL) trial [11]. Other negative reports have been published from observational cohorts [10,26,28,35]. The evidence from these investigations, combined with the risk of positive selective publishing, underscores the importance of a cautious approach when attempting to infer the mortality risk in patients experiencing PMI. Recently, we demonstrated that most of the death events reported in studies investigating this topic were of cardiac origin [42]. This supports the hypothesis that previous positive reports actually detected the presence of a true effect, but the risk that this association has been overestimated cannot be excluded.

Regarding concerns about the grade of this association, the increased prognostic relevance of the SCAI definition should support a higher threshold for biomarker elevation. Overall, a trend exists indicating an inverse relationship between each sensitivity definition and the subsequent prognostic relevance, with the UDMI and SCAI definitions being at opposite extremities of this balance [45]. Concordantly, recent studies have shown that the relative contribution of ancillary criteria to the association between PMI and mortality is progressively lower or even negligible when higher myocardial damage is identified, as indicated by biomarker sampling [27,42]. To date, whether a risk stratification model based solely on objective measurements of myocardial damage can be superior to traditional PMI definitions remains unclear. Despite some investigations demonstrating the reliability of this approach even in complex settings, such as acute coronary syndromes [19], others have reported that similar biomarker elevations in the context of PMI or spontaneous MI are associated with different prognostic relevance, suggesting that other factors are surely involved in the final mortality risk [46].

5. The Role of PMI Definitions in the Composite Outcomes of Clinical Trials

With the introduction of composite outcomes in cardiovascular research, the statistical power of trials investigating different aspects of coronary revascularization has become dependent on the relative rates of other clinical events, including MI [47]. Considering the major differences in incidence between these definitions, the choice of a specific PMI definition can lead to significant changes in the results of a certain study. While more sensitive definitions (such as the UDMI) can be useful for detecting even minor events and increasing the statistical power of a particular trial, the relatively limited association of these definitions with mortality raises questions about their prognostic relevance [45,48]. Opposite considerations could be applied to less sensitive definitions, such as the SCAI definition. This has been elegantly documented by Spitzer *et al.* [49], who reported how the MI events are by far the ones most exposed to heterogeneous definitions across contemporary coronary intervention trials.

Several examples of the complex heterogeneity resulting from these different definitions can be proposed. Within trials comparing PCI against coronary artery bypass grafting (CABG) in left main or multivessel disease, protocol-defined PMI [50–52], the SCAI definition [53,54], the UDMI [55], or no definition [56] have all been used previously [57]. The influence of each definition on the overall findings of those studies has been largely debated.

In a renowned editorial by Serruys *et al*. [57], the authors demonstrated how the application of different ways to define PMI could dramatically change the 5-year results of the "TAXUS Drug-Eluting Stent Versus Coronary Artery Bypass Surgery for the Treatment of Narrowed Arteries" (SYNTAX) trial. Specifically, when the protocol definition or the UDMI was applied, the composite endpoint of major cardiac and cerebrovascular events was reduced by a CABG strategy. On the other hand, when the SCAI definition was used, PCI appeared not to be inferior to a surgical approach [57]. Resembling results were reported in a pooled analysis of trials comparing PCI and CABG in patients with left main disease [58]. Notably, this issue is not limited to studies comparing different revascularization strategies; similar heterogeneities can also be found in trials investigating medical therapy versus revascularization [1,4,59], intracoronary physiology [60–62], intracoronary imaging [63–66], and other areas [67]. The debate on how to define PMI events in major clinical trials has been active for several years. While the use of more prognostically relevant definitions may result in a more appealing approach to detect larger MI with a higher risk of mortality [45,46], evidence has been published showing that even minor myocardial damage can have a clinical value [42]. Alternative solutions to the rigid application of one specific definition have been proposed. In the ISCHEMIA trial, two different definitions of PMI were contemporarily applied [4,6]. A similar approach has been used in a post hoc analysis of the EXCEL trial [11]. This strategy can facilitate different interpretations of the study findings, thereby reducing the risk of drawing misleading conclusions based on pre-specified outcome definitions. To perform such analyses, the routine and standardized collection of post-PCI biomarker elevation (ideally two samplings at 8 h and 16 h) together with the systematic assessment of ancillary criteria within the first 48 hours is mandatory [49]. A significant example in this regard can be provided by the three "A Clinical Trial Comparing Cangrelor to Clopidogrel Standard Therapy in Subjects Who Require Percutaneous Coronary Intervention" (CHAMPION) studies, which compared P2Y12 inhibition with cangrelor against clopidogrel following PCI in different clinical settings [68–70]. While the two earlier trials relied on a protocol-defined PMI (CHAMPION-PCI and CHAMPION-PLATFORM), the CHAMPION-PHOENIX trial implemented the UDMI criteria. Despite this major difference, the routine assessment of post-PCI biomarker elevations and ancillary criteria allowed for homogenizing the PMI definition on the UDMI in a subsequent pooled analysis of those three studies, which showed that cangrelor could actually be associated with a periprocedural benefit in terms of ischemic events [67].

Another possible strategy to overcome the limitations associated with a rigid application of a single PMI definition may be the use of hierarchical/weighted composite endpoints, which are designed to tailor the results of a specific study according to the clinical relevance of each isolated component of the primary outcome. These techniques are becoming increasingly popular in cardiovascular research, primarily because they preserve the benefits of composite endpoints in terms of study power while providing prognostically robust results [71]. In the case of PMI, it has been proposed to locate such events immediately below spontaneous MI [72]. Despite their appeal, these outcomes have been utilized in only a few coronary intervention studies, primarily as retrospective analyses of previously published trials. Therefore, it remains unclear whether hierarchical/weighted outcomes will replace classical time-to-event composite endpoints in the future [73,74].

6. Future Perspectives

The quest for the perfect definition of PMI has been a years-long journey, which has led to the generation of sev-

Table 2. Main strengths and limitations of the current international definitions of PMI.

	Strengths	Limitations
UDMI	(1) High sensitivity (2) Simulate the international definition for spontaneous MI (3) Largely investigated in major studies	(1) Low prognostic value (2) Alternative definition for patients with ACS and undergoing CABG (3) Relying on both biomarkers and ancillary criteria evaluation
ARC-2	(1) Moderate sensitivity and prognostic value (2) Do not provide alternative definitions for patients with ACS or undergoing CABG	(1) Rarely investigated in major studies (2) Relying on both biomarkers and ancillary criteria evaluation
SCAI	(1) High prognostic value (2) Provide an alternate definition relying solely on biomarker evaluation (3) Largely investigated in major studies (4) Do not provide alternative definitions for patients with ACS or undergoing CABG	(1) Low sensitivity

MI, myocardial infarction; ACS, acute coronary syndromes; CABG, coronary artery bypass grafting.

eral international recommendations and significant debate within the cardiovascular scientific community [45,49,57,75]. Each one of the available PMI definitions shows specific strengths and limitations, not only in terms of the ratio between sensitivity and prognostic power, but also in terms of generalizability in complex settings, such as acute coronary syndromes and CABG (Table 2) [15,42]. While a definition of PMI is surely needed when conducting a specific investigation, it is our opinion that those limitations should be strictly accounted for. Considering that the UDMI, ARC-2, and SCAI definitions encompass a broad spectrum of biomarker elevations and subtypes of ancillary criteria, we believe it is unlikely that a revised definition of PMI could overcome the limitations found in the existing ones. If we accept the hypothesis that including MI events in the composite endpoints of clinical trials is a way to infer cardiac mortality risk, then we should also acknowledge that this relationship is not dichotomous but reflects a continuous association between the amount of cardiac damage and the consequent prognosis. Unlike spontaneous MI, whose objective quantification can be hindered by non-predictable factors, such as the time comprised between myocardial ischemia and coronary revascularization [76], PMI can only occur in a fully controllable setting. Previous studies have suggested that a detailed collection of biomarkers following coronary revascularization can provide an accurate representation of the subsequent mortality risk [20,27,77–80]. Accordingly, a detailed depiction of post-PCI myocardial damage based on reporting objective cTn/CK-MB elevations at specific time points could be more informative compared to the use of a dichotomic outcome. This approach could provide a quantitative and continuous assessment of these adverse events, allowing for tailored future analyses. Eventually, if combined with routine evaluation of ancillary criteria, a similar strategy could enable a global estimation of the clinical risk, independent of the limitations of a specific definition of PMI. Despite this, it is worth noting that a systematic assessment of post-PCI myocardial injury in clinical practice would require significant efforts in terms of patient care, time, and costs. Moreover, the use of multiple assays to estimate cardiac biomarkers could limit the comparability of sampling data obtained from various centers in a hypothetical research setting. Presently, no studies have been conducted to evaluate the feasibility of this approach and to compare it with the strategies traditionally used to detect PMI. Therefore, this hypothesis should be considered only speculative, and dedicated investigations are needed to address the clinical and research validity of the hypothesis.

7. Conclusions

The three current international definitions of post-PCI PMI dramatically differ in terms of sensitivity and prognostic relevance. Therefore, this narrative review aimed to synthesize the main strengths and limitations of these studies, as well as their potential influence on the results obtained from the available literature. Notably, the PMI definitions have not remained constant over the years, but rather reflect the ongoing efforts of scientific societies to address the clinical and research needs of the cardiovascular community. While future dedicated studies are needed to address this topic, a dynamic and comprehensive approach to estimating post-PCI myocardial damage should be recommended to improve the risk stratification of these patients in real-world practice [13].

This review has several limitations that should be taken into consideration. Due to its narrative nature, the lack of systematic research on studies investigating the relationship between PMI and adverse events may have influenced the conclusions of our work. Moreover, the quality of the reported studies has not been critically evaluated using standardized methods. This, together with the significant heterogeneity of those reports and their mostly observational nature, limits the generalizability of those findings. Ultimately, the reported perspectives and conclusions on this topic reflect the opinions of the authors, which are not supported by dedicated research.

Author Contributions

LP and GN conceptualized the study; LP, GN, ML, and GO searched for references and studies related to the topic; FM, RV, IC, CB, DG and FDF revised the selected references and the review's design and were all involved in the critical review of significant concepts. Specifically, they proposed the concept of using a comprehensive assessment of absolute troponin values to better detect myocardial injury following PCI. Moreover, their expertise was required to critically comment on the issue of PMI definitions in the cited trials on coronary revascularization (SYNERGY, EXCEL, CHAMPIONS and so on). CM contributed to conceptualizing and drafting two paragraphs of the review. LP, GN, ML, FM and CM drafted the first version of the manuscript. All authors critically revised and approved the final submitted version of the review, checking its integrity and accuracy. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest. Carlo Briguori is serving as one of the Editorial Board members of this journal. We declare that Carlo Briguori had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Yong Peng.

References

[1] Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, *et al*. Optimal medical therapy with or without PCI for stable coronary disease. The New England Journal of Medicine. 2007; 356: 1503–1516. https://doi.org/10.1056/NEJMoa070829.

[2] Velazquez EJ, Lee KL, Deja MA, Jain A, Sopko G, Marchenko A, *et al*. Coronary-artery bypass surgery in patients with left ventricular dysfunction. The New England Journal of Medicine. 2011; 364: 1607–1616. https://doi.org/10.1056/NEJMoa1100356.

[3] Mehta SR, Wood DA, Storey RF, Mehran R, Bainey KR, Nguyen H, *et al*. Complete Revascularization with Multivessel PCI for Myocardial Infarction. The New England Journal of Medicine. 2019; 381: 1411–1421. https://doi.org/10.1056/NEJMoa1907775.

[4] Maron DJ, Hochman JS, Reynolds HR, Bangalore S, O'Brien SM, Boden WE, *et al*. Initial Invasive or Conservative Strategy for Stable Coronary Disease. The New England Journal of Medicine. 2020; 382: 1395–1407. https://doi.org/10.1056/NEJMoa1915922.

[5] Perera D, Clayton T, O'Kane PD, Greenwood JP, Weerackody R, Ryan M, *et al*. Percutaneous Revascularization for Ischemic Left Ventricular Dysfunction. The New England Journal of Medicine. 2022; 387: 1351–1360. https://doi.org/10.1056/NEJMoa2206606.

[6] Chaitman BR, Alexander KP, Cyr DD, Berger JS, Reynolds HR, Bangalore S, *et al*. Myocardial Infarction in the ISCHEMIA Trial: Impact of Different Definitions on Incidence, Prognosis, and Treatment Comparisons. Circulation. 2021; 143: 790–804. https://doi.org/10.1161/CIRCULATIONAHA.120.047987.

[7] De Bruyne B, Pijls NHJ, Kalesan B, Barbato E, Tonino PAL, Piroth Z, *et al*. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. The New England Journal of Medicine. 2012; 367: 991–1001. https://doi.org/10.1056/NEJMoa1205361.

[8] Lansky AJ, Stone GW. Periprocedural myocardial infarction: prevalence, prognosis, and prevention. Circulation. Cardiovascular Interventions. 2010; 3: 602–610. https://doi.org/10.1161/CIRCINTERVENTIONS.110.959080.

[9] Hara H, Serruys PW, Takahashi K, Kawashima H, Ono M, Gao C, *et al*. Impact of Peri-Procedural Myocardial Infarction on Outcomes After Revascularization. Journal of the American College of Cardiology. 2020; 76: 1622–1639. https://doi.org/10.1016/j.jacc.2020.08.009.

[10] Paolucci L, Mangiacapra F, Viscusi MM, Ungaro S, Cocchia F, Piccirillo F, *et al*. Relationship Between the Completeness of Revascularization and Myocardial Injury in Patients Treated With Percutaneous Coronary Intervention. Cardiovascular Revascularization Medicine: Including Molecular Interventions. 2023; 48: 15–20. https://doi.org/10.1016/j.carrev.2022.10.006.

[11] Gregson J, Stone GW, Ben-Yehuda O, Redfors B, Kandzari DE, Morice MC, *et al*. Implications of Alternative Definitions of Peri-Procedural Myocardial Infarction After Coronary Revascularization. Journal of the American College of Cardiology. 2020; 76: 1609–1621. https://doi.org/10.1016/j.jacc.2020.08.016.

[12] Silvain J, Zeitouni M, Paradies V, Zheng HL, Ndrepepa G, Cavallini C, *et al*. Procedural myocardial injury, infarction and mortality in patients undergoing elective PCI: a pooled analysis of patient-level data. European Heart Journal. 2021; 42: 323–334. https://doi.org/10.1093/eurheartj/ehaa885.

[13] Bulluck H, Paradies V, Barbato E, Baumbach A, Bøtker HE, Capodanno D, *et al*. Prognostically relevant periprocedural myocardial injury and infarction associated with percutaneous coronary interventions: a Consensus Document of the ESC Working Group on Cellular Biology of the Heart and European Association of Percutaneous Cardiovascular Interventions (EAPCI). European Heart Journal. 2021; 42: 2630–2642. https://doi.org/10.1093/eurheartj/ehab271.

[14] Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, *et al*. Fourth universal definition of myocardial infarction (2018). European Heart Journal. 2019; 40: 237–269. https://doi.org/10.1093/eurheartj/ehy462.

[15] Garcia-Garcia HM, McFadden EP, Farb A, Mehran R, Stone GW, Spertus J, *et al*. Standardized End Point Definitions for Coronary Intervention Trials: The Academic Research Consortium-2 Consensus Document. Circulation. 2018; 137: 2635–2650. https://doi.org/10.1161/CIRCULATIONAHA.117.029289.

[16] Moussa ID, Klein LW, Shah B, Mehran R, Mack MJ, Brilakis ES, *et al*. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus document from the Society for Cardiovascular Angiography and Interventions (SCAI). Journal of the American College of Cardiology. 2013; 62: 1563–1570. https://doi.org/10.1016/j.jacc.2013.08.720.

[17] Thygesen K, Alpert JS, White HD, Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction, Jaffe AS, Apple FS, *et al*. Universal definition of myocardial infarction. Circulation. 2007; 116: 2634–2653. https://doi.org/10.1161/CIRCULATIONAHA.107.187397.

[18] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, *et al*. Third universal definition of myocardial infarction. European Heart Journal. 2012; 33: 2551–2567. https://doi.org/10.1093/eurheartj/ehs184.

[19] Armillotta M, Bergamaschi L, Paolisso P, Belmonte M, Angeli F, Sansonetti A, *et al*. Prognostic Relevance of Type 4a Myocardial Infarction and Periprocedural Myocardial Injury in Patients With Non-ST-Segment-Elevation Myocardial Infarction. Circulation. 2025; 151: 760–772. https://doi.org/10.1161/CIRCULATIONAHA.124.070729.

[20] Devereaux PJ, Lamy A, Chan MTV, Allard RV, Lomivorotov VV, Landoni G, *et al*. High-Sensitivity Troponin I after Cardiac Surgery and 30-Day Mortality. The New England Journal of Medicine. 2022; 386: 827–836. https://doi.org/10.1056/NEJMoa2000803.

[21] Chia S, Senatore F, Raffel OC, Lee H, Wackers FJT, Jang IK. Utility of cardiac biomarkers in predicting infarct size, left ventricular function, and clinical outcome after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. JACC. Cardiovascular Interventions. 2008; 1: 415–423. https://doi.org/10.1016/j.jcin.2008.04.010.

[22] Kristensen JH, Hasselbalch RB, Strandkjær N, Jørgensen N, Østergaard M, Møller-Sørensen PH, *et al*. Half-Life and Clearance of Cardiac Troponin I and Troponin T in Humans. Circulation. 2024; 150: 1187–1198. https://doi.org/10.1161/CIRCULATIONAHA.123.066565.

[23] Volz KA, Horowitz GL, McGillicuddy DC, Grossman SA, Sanchez LD. Should creatine kinase-MB index be eliminated

in patients with indeterminate troponins in the ED? The American Journal of Emergency Medicine. 2012; 30: 1574–1576. https://doi.org/10.1016/j.ajem.2011.08.017.

[24] Raber I, McCarthy CP, Januzzi JL, Jr. A Test in Context: Interpretation of High-Sensitivity Cardiac Troponin Assays in Different Clinical Settings. Journal of the American College of Cardiology. 2021; 77: 1357–1367. https://doi.org/10.1016/j.jacc.2021.01.011.

[25] Wang HY, Xu B, Dou K, Guan C, Song L, Huang Y, *et al*. Effect of Periprocedural Myocardial Infarction After Initial Revascularization With Left Main PCI in Patients With Recent Myocardial Infarction. Journal of the Society for Cardiovascular Angiography & Interventions. 2023; 2: 100576. https://doi.org/10.1016/j.jscai.2022.100576.

[26] Zhou Y, Chen Z, Chen A, Ma J, Dai C, Lu D, *et al*. Association between the magnitude of periprocedural myocardial injury and prognosis in patients undergoing elective percutaneous coronary intervention. European Heart Journal. Quality of Care & Clinical Outcomes. 2022; 8: 871–880. https://doi.org/10.1093/ehjqcco/qcab103.

[27] Ueki Y, Otsuka T, Bär S, Koskinas KC, Heg D, Häner J, *et al*. Frequency and Outcomes of Periprocedural MI in Patients With Chronic Coronary Syndromes Undergoing PCI. Journal of the American College of Cardiology. 2022; 79: 513–526. https://doi.org/10.1016/j.jacc.2021.11.047.

[28] Wang HY, Xu B, Dou K, Guan C, Song L, Huang Y, *et al*. Implications of Periprocedural Myocardial Biomarker Elevations and Commonly Used MI Definitions After Left Main PCI. JACC. Cardiovascular Interventions. 2021; 14: 1623–1634. https://doi.org/10.1016/j.jcin.2021.05.006.

[29] Song L, Wang Y, Guan C, Zou T, Sun Z, Xie L, *et al*. Impact of Periprocedural Myocardial Injury and Infarction Definitions on Long-Term Mortality After Chronic Total Occlusion Percutaneous Coronary Intervention. Circulation. Cardiovascular Interventions. 2021; 14: e010923. https://doi.org/10.1161/CIRCINTERVENTIONS.121.010923.

[30] Cho MS, Ahn JM, Lee CH, Kang DY, Lee JB, Lee PH, *et al*. Differential Rates and Clinical Significance of Periprocedural Myocardial Infarction After Stenting or Bypass Surgery for Multivessel Coronary Disease According to Various Definitions. JACC. Cardiovascular Interventions. 2017; 10: 1498–1507. https://doi.org/10.1016/j.jcin.2017.05.051.

[31] Erriquez A, Pavasini R, Biscaglia S, Tebaldi M, Tonet E, Maietti E, *et al*. The impact of periprocedural myocardial infarction on mortality in older adults with non-ST-segment elevation acute coronary syndrome: a pooled analysis of the FRASER and HULK studies. Journal of Cardiovascular Medicine (Hagerstown, Md.). 2021; 22: 546–552. https://doi.org/10.2459/JCM.0000000000001146.

[32] Mangiacapra F, Rinaldi R, Colaiori I, Sticchi A, Viscusi MM, Paolucci L, *et al*. Prediction of type 4a myocardial infarction with the angiography-derived hemodynamic (ADDED) index. Heart and Vessels. 2022; 37: 1471–1477. https://doi.org/10.1007/s00380-022-02050-x.

[33] Błaszkiewicz M, Florek K, Zimoch W, Reczuch K. Response to a letter on the article "Predictors of periprocedural myocardial infarction after rotational atherectomy". Postepy W Kardiologii Interwencyjnej = Advances in Interventional Cardiology. 2024; 20: 243. https://doi.org/10.5114/aic.2024.140858.

[34] Ueki Y, Kuwahara K. Periprocedural myocardial infarction in patients undergoing percutaneous coronary intervention. Journal of Cardiology. 2023; 81: 364–372. https://doi.org/10.1016/j.jjcc.2022.11.005.

[35] Jaguszewski M, Gilis-Malinowska N, Gutierrez-Chico JL, Chmielecki M, Skarzynski P, Burakowski S, *et al*. Periprocedural Myocardial Injury After Recanalization of Single Chronic Coronary Occlusion - A Propensity Score Analysis Comparing Long-Term Clinical Outcomes. The Journal of Invasive Cardiology. 2017; 29: 63–67.

[36] Garcia-Garcia HM, McFadden EP, von Birgelen C, Rademaker-Havinga T, Spitzer E, Kleiman NS, *et al*. Impact of Periprocedural Myocardial Biomarker Elevation on Mortality Following Elective Percutaneous Coronary Intervention. JACC. Cardiovascular Interventions. 2019; 12: 1954–1962. https://doi.org/10.1016/j.jcin.2019.07.014.

[37] O'Fee K, Deych E, Ciani O, Brown DL. Assessment of Nonfatal Myocardial Infarction as a Surrogate for All-Cause and Cardiovascular Mortality in Treatment or Prevention of Coronary Artery Disease: A Meta-analysis of Randomized Clinical Trials. JAMA Internal Medicine. 2021; 181: 1575–1587. https://doi.org/10.1001/jamainternmed.2021.5726.

[38] Yeh RW, Sidney S, Chandra M, Sorel M, Selby JV, Go AS. Population trends in the incidence and outcomes of acute myocardial infarction. The New England Journal of Medicine. 2010; 362: 2155–2165. https://doi.org/10.1056/NEJMoa0908610.

[39] Szummer K, Wallentin L, Lindhagen L, Alfredsson J, Erlinge D, Held C, *et al*. Improved outcomes in patients with ST-elevation myocardial infarction during the last 20 years are related to implementation of evidence-based treatments: experiences from the SWEDEHEART registry 1995-2014. European Heart Journal. 2017; 38: 3056–3065. https://doi.org/10.1093/eurheartj/ehx515.

[40] Tricoci P, Newby LK, Clare RM, Leonardi S, Gibson CM, Giugliano RP, *et al*. Prognostic and Practical Validation of Current Definitions of Myocardial Infarction Associated With Percutaneous Coronary Intervention. JACC. Cardiovascular Interventions. 2018; 11: 856–864. https://doi.org/10.1016/j.jcin.2018.02.006.

[41] Toma A, Stähli BE, Gebhard C, Gick M, Minners J, Mashayekhi K, *et al*. Clinical implications of periprocedural myocardial injury in patients undergoing percutaneous coronary intervention for chronic total occlusion: role of antegrade and retrograde crossing techniques. EuroIntervention: Journal of EuroPCR in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2018; 13: 2051–2059. https://doi.org/10.4244/EIJ-D-17-00338.

[42] Paolucci L, Mangiacapra F, Sergio S, Nusca A, Briguori C, Barbato E, *et al*. Periprocedural myocardial infarction after percutaneous coronary intervention and long-term mortality: a meta-analysis. European Heart Journal. 2024; 45: 3018–3027. https://doi.org/10.1093/eurheartj/ehae266.

[43] Koskinas KC, Ndrepepa G, Räber L, Karagiannis A, Kufner S, Zanchin T, *et al*. Prognostic Impact of Periprocedural Myocardial Infarction in Patients Undergoing Elective Percutaneous Coronary Interventions. Circulation. Cardiovascular Interventions. 2018; 11: e006752. https://doi.org/10.1161/CIRCINTERVENTIONS.118.006752.

[44] Joober R, Schmitz N, Annable L, Boksa P. Publication bias: what are the challenges and can they be overcome? Journal of Psychiatry & Neuroscience: JPN. 2012; 37: 149–152. https://doi.org/10.1503/jpn.120065.

[45] Ahmad Y, Lansky AJ. Periprocedural myocardial infarction: thresholds of (in)significance. European Heart Journal. 2024; 45: 3028–3030. https://doi.org/10.1093/eurheartj/ehae451.

[46] Spirito A, Sartori S, Koshy AN, Feng Y, Vogel B, Baber U, *et al*. Mortality After Procedural or Spontaneous Myocardial Infarction. Journal of the American College of Cardiology. 2024; 84: 467–477. https://doi.org/10.1016/j.jacc.2024.04.061.

[47] Braunwald E, Cannon CP, McCabe CH. Use of composite endpoints in thrombolysis trials of acute myocardial infarction. The American Journal of Cardiology. 1993; 72: 3G–12G. https://doi.org/10.1016/0002-9149(93)90101-h.

[48] Spagnolo M, Occhipinti G, Laudani C, Greco A, Capodanno D. Periprocedural myocardial infarction and injury. European Heart Journal. Acute Cardiovascular Care. 2024; 13: 433–445. https://doi.org/10.1093/ehjacc/zuae014.
[49] Spitzer E, McFadden E, Vranckx P, Garcia-Garcia HM, Seltzer JH, Held C, *et al*. Critical Appraisal of Contemporary Clinical Endpoint Definitions in Coronary Intervention Trials: A Guidance Document. JACC. Cardiovascular Interventions. 2019; 12: 805–819. https://doi.org/10.1016/j.jcin.2018.12.031.
[50] Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, *et al*. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. The New England Journal of Medicine. 2009; 360: 961–972. https://doi.org/10.1056/NEJMoa0804626.
[51] Park SJ, Kim YH, Park DW, Yun SC, Ahn JM, Song HG, *et al*. Randomized trial of stents versus bypass surgery for left main coronary artery disease. The New England Journal of Medicine. 2011; 364: 1718–1727. https://doi.org/10.1056/NEJMoa1100452.
[52] Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, *et al*. Strategies for multivessel revascularization in patients with diabetes. The New England Journal of Medicine. 2012; 367: 2375–2384. https://doi.org/10.1056/NEJMoa1211585.
[53] Stone GW, Sabik JF, Serruys PW, Simonton CA, Généreux P, Puskas J, *et al*. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease. The New England Journal of Medicine. 2016; 375: 2223–2235. https://doi.org/10.1056/NEJMoa1610227.
[54] Park SJ, Ahn JM, Kim YH, Park DW, Yun SC, Lee JY, *et al*. Trial of everolimus-eluting stents or bypass surgery for coronary disease. The New England Journal of Medicine. 2015; 372: 1204–1212. https://doi.org/10.1056/NEJMoa1415447.
[55] Fearon WF, Zimmermann FM, De Bruyne B, Piroth Z, van Straten AHM, Szekely L, *et al*. Fractional Flow Reserve-Guided PCI as Compared with Coronary Bypass Surgery. The New England Journal of Medicine. 2022; 386: 128–137. https://doi.org/10.1056/NEJMoa2112299.
[56] Mäkikallio T, Holm NR, Lindsay M, Spence MS, Erglis A, Menown IBA, *et al*. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial. Lancet (London, England). 2016; 388: 2743–2752. https://doi.org/10.1016/S0140-6736(16)32052-9.
[57] Serruys PW, Hara H, Garg S, Onuma Y. Have We Overdefined Periprocedural Myocardial Infarction to the Point of Extinction? JACC. Cardiovascular Interventions. 2021; 14: 1635–1638. https://doi.org/10.1016/j.jcin.2021.06.006.
[58] Sabatine MS, Bergmark BA, Murphy SA, O'Gara PT, Smith PK, Serruys PW, *et al*. Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis. Lancet (London, England). 2021; 398: 2247–2257. https://doi.org/10.1016/S0140-6736(21)02334-5.
[59] BARI 2D Study Group, Frye RL, August P, Brooks MM, Hardison RM, Kelsey SF, *et al*. A randomized trial of therapies for type 2 diabetes and coronary artery disease. The New England Journal of Medicine. 2009; 360: 2503–2515. https://doi.org/10.1056/NEJMoa0805796.
[60] Tonino PAL, De Bruyne B, Pijls NHJ, Siebert U, Ikeno F, van' t Veer M, *et al*. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. The New England Journal of Medicine. 2009; 360: 213–224. https://doi.org/10.1056/NEJMoa0807611.
[61] Rioufol G, Dérimay F, Roubille F, Perret T, Motreff P, Angoulvant D, *et al*. Fractional Flow Reserve to Guide Treatment of Patients With Multivessel Coronary Artery Disease. Journal of the American College of Cardiology. 2021; 78: 1875–1885. https://doi.org/10.1016/j.jacc.2021.08.061.
[62] Stables RH, Mullen LJ, Elguindy M, Nicholas Z, Aboul-Enien YH, Kemp I, *et al*. Routine Pressure Wire Assessment Versus Conventional Angiography in the Management of Patients With Coronary Artery Disease: The RIPCORD 2 Trial. Circulation. 2022; 146: 687–698. https://doi.org/10.1161/CIRCULATIONAHA.121.057793.
[63] Ali ZA, Landmesser U, Maehara A, Matsumura M, Shlofmitz RA, Guagliumi G, *et al*. Optical Coherence Tomography-Guided versus Angiography-Guided PCI. The New England Journal of Medicine. 2023; 389: 1466–1476. https://doi.org/10.1056/NEJMoa2305861.
[64] Lee JM, Choi KH, Song YB, Lee JY, Lee SJ, Lee SY, *et al*. Intravascular Imaging-Guided or Angiography-Guided Complex PCI. The New England Journal of Medicine. 2023; 388: 1668–1679. https://doi.org/10.1056/NEJMoa2216607.
[65] Hong SJ, Lee SJ, Lee SH, Lee JY, Cho DK, Kim JW, *et al*. Optical coherence tomography-guided versus angiography-guided percutaneous coronary intervention for patients with complex lesions (OCCUPI): an investigator-initiated, multicentre, randomised, open-label, superiority trial in South Korea. Lancet (London, England). 2024; 404: 1029–1039. https://doi.org/10.1016/S0140-6736(24)01454-5.
[66] Holm NR, Andreasen LN, Neghabat O, Laanmets P, Kumsars I, Bennett J, *et al*. OCT or Angiography Guidance for PCI in Complex Bifurcation Lesions. The New England Journal of Medicine. 2023; 389: 1477–1487. https://doi.org/10.1056/NEJMoa2307770.
[67] Steg PG, Bhatt DL, Hamm CW, Stone GW, Gibson CM, Mahaffey KW, *et al*. Effect of cangrelor on periprocedural outcomes in percutaneous coronary interventions: a pooled analysis of patient-level data. Lancet (London, England). 2013; 382: 1981–1992. https://doi.org/10.1016/S0140-6736(13)61615-3.
[68] Harrington RA, Stone GW, McNulty S, White HD, Lincoff AM, Gibson CM, *et al*. Platelet inhibition with cangrelor in patients undergoing PCI. The New England Journal of Medicine. 2009; 361: 2318–2329. https://doi.org/10.1056/NEJMoa0908628.
[69] Bhatt DL, Lincoff AM, Gibson CM, Stone GW, McNulty S, Montalescot G, *et al*. Intravenous platelet blockade with cangrelor during PCI. The New England Journal of Medicine. 2009; 361: 2330–2341. https://doi.org/10.1056/NEJMoa0908629.
[70] Bhatt DL, Stone GW, Mahaffey KW, Gibson CM, Steg PG, Hamm CW, *et al*. Effect of platelet inhibition with cangrelor during PCI on ischemic events. The New England Journal of Medicine. 2013; 368: 1303–1313. https://doi.org/10.1056/NEJMoa1300815.
[71] Pocock SJ, Gregson J, Collier TJ, Ferreira JP, Stone GW. The win ratio in cardiology trials: lessons learnt, new developments, and wise future use. European Heart Journal. 2024; 45: 4684–4699. https://doi.org/10.1093/eurheartj/ehae647.
[72] McCarthy CP, Januzzi JL, Jr. Periprocedural MI as an Endpoint in Clinical Trials: A Proposed Path Forward. Journal of the American College of Cardiology. 2022; 79: 527–529. https://doi.org/10.1016/j.jacc.2021.11.046.
[73] Milojevic M, Head SJ, Andrinopoulou ER, Serruys PW, Mohr FW, Tijssen JG, *et al*. Hierarchical testing of composite endpoints: applying the win ratio to percutaneous coronary intervention versus coronary artery bypass grafting in the SYNTAX trial. EuroIntervention: Journal of EuroPCR in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2017; 13: 106–114. https://doi.org/10.4244/EIJ-D-16-00745.
[74] Hara H, van Klaveren D, Takahashi K, Kogame N, Chichareon P, Modolo R, *et al*. Comparative Methodological Assessment

of the Randomized GLOBAL LEADERS Trial Using Total Ischemic and Bleeding Events. Circulation. Cardiovascular Quality and Outcomes. 2020; 13: e006660. https://doi.org/10.1161/CIRCOUTCOMES.120.006660.

[75] Stone GW. How should procedure-related myocardial infarction be defined, and does it matter? (Spoiler alert - it does!). EuroIntervention: Journal of EuroPCR in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2020; 15: 1393–1396. https://doi.org/10.4244/EIJV15I16A253.

[76] Park J, Choi KH, Lee JM, Kim HK, Hwang D, Rhee TM, *et al*. Prognostic Implications of Door-to-Balloon Time and Onset-to-Door Time on Mortality in Patients With ST -Segment-Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention. Journal of the American Heart Association. 2019; 8: e012188. https://doi.org/10.1161/JAHA.119.012188.

[77] Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, *et al*. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. The New England Journal of Medicine. 1996; 335: 1342–1349. https://doi.org/10.1056/NEJM199610313351802.

[78] McEvoy JW, Daya N, Tang O, Fang M, Ndumele CE, Coresh J, *et al*. High-sensitivity troponins and mortality in the general population. European Heart Journal. 2023; 44: 2595–2605. https://doi.org/10.1093/eurheartj/ehad328.

[79] Schindler M, Stöckli F, Brütsch R, Jakob P, Holy E, Michel J, *et al*. Postprocedural Troponin Elevation and Mortality After Transcatheter Aortic Valve Implantation. Journal of the American Heart Association. 2021; 10: e020739. https://doi.org/10.1161/JAHA.120.020739.

[80] Ndrepepa G, Colleran R, Braun S, Cassese S, Hieber J, Fusaro M, *et al*. High-Sensitivity Troponin T and Mortality After Elective Percutaneous Coronary Intervention. Journal of the American College of Cardiology. 2016; 68: 2259–2268. https://doi.org/10.1016/j.jacc.2016.08.059.