

Implementation of the Third Universal Definition of Myocardial Infarction After Coronary Artery Bypass Grafting: A Survey Study in Western Europe

Dianne E. C. van Beek, MD; Bas van Zaane, MD, PhD; Marc P. Buijsrogge, MD, PhD; Wilton A. van Klei, MD, PhD

Background—Diagnosing a postoperative myocardial infarction in patients undergoing coronary artery bypass grafting is challenging, as the normally used criteria are more difficult to interpret. The rate of implementation of the consensus-based new diagnostic criteria for postoperative myocardial infarction proposed by the third universal definition of myocardial infarction is unknown. Therefore, the primary objective of this study was to address the implementation of the third universal definition of postoperative myocardial infarction following coronary artery bypass grafting.

Methods and Results—We conducted a web-based survey by sending 4 waves of invitations via e-mail to cardiothoracic surgeons in 12 Western European countries. Of the 302 participating cardiothoracic specialists, from 182 different centers, 213 (71%) were aware that troponin is the preferred biomarker and 112 (37%) knew that using a cut-off level of >10 times the 99th percentile is recommended. Overall, 90 (30%) participants (strongly) agreed with implementation of this cut-off level in their clinical practice. Troponin was used in clinical practice by 149 (49%) of the participants. In total, 117 (89%) of the 131 participants with a local guideline confirmed ECG changes as a diagnostic criterion in that guideline. ST segmental changes (75, 64%) were used more often for diagnosing postoperative myocardial infarction than Q waves (64, 55%) or new left bundle branch blocks (34, 29%).

Conclusions—Cardiac biomarkers and ECG changes were not used in concordance with the third universal definition, and only a minority had a positive attitude toward implementation of the proposed cut-off level for troponin in their clinical practice. (*J Am Heart Assoc.* 2015;4:e001401 doi: 10.1161/JAHA.114.001401)

Key Words: coronary artery bypass graft surgery • diagnosis • myocardial infarction • troponin

Approximately 1 million patients undergo cardiac surgery each year worldwide, and 7% to 15% of them will suffer from a postoperative myocardial infarction (PMI),^{1–3} mainly because of early graft failure.^{4,5} PMI after cardiac surgery is not only associated with an increased length of hospital stay, but also with a reduced short- and long-term survival.^{1–3} Diagnosing PMI in cardiac surgery patients is difficult, since

pain from the sternal wound and the prescribed opioids may mask the typical symptoms (eg, chest pain, shortness of breath). Furthermore, postoperative changes of the ECG are not uncommon due to direct myocardial damage from the surgery, and postoperative pericarditis.⁶ Cardiac-specific biomarkers, such as creatine-kinase M-band and troponin (Tn), are normally used to identify myocardial damage. However, biomarker levels after cardiac surgery can easily be above the cut-off value due to direct and indirect myocardial injury from the surgical trauma or from reperfusion injury after cardiopulmonary bypass without a true PMI being present.¹

The third universal definition of myocardial infarction provides, by arbitrary convention, diagnostic criteria for the different types of infarction. For PMI (ie, type 5 myocardial infarction associated with coronary artery bypass grafting [CABG]), the cornerstone for the diagnosis is the presence of a biomarker value of >10 times the 99th percentile of the upper reference limit.⁷ The preferred biomarker is Tn, because of its high sensitivity and specificity and because of its typical rise and fall pattern in myocardial infarction.⁷ The accuracy of

From the Departments of Anesthesiology (D.E.C.V.B., B.V.Z., W.A.V.K.) and Cardiothoracic Surgery (M.P.B.), University Medical Center, Utrecht, The Netherlands.

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Correspondence to: Dianne E. C. van Beek, MD, Division of Anesthesiology, Intensive Care and Emergency Care Medicine, Heidelberglaan 100, Post Office Box 85500, 3508 GA Utrecht, The Netherlands. E-mail: e.c.vanBeek-8@umcutrecht.nl

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the consensus-based cut-off level for this patient group is unclear, as is the ideal cut-off level for patients with an already elevated biomarker level preoperatively. More importantly, it is not clear whether PMI is always clinically relevant and when re-intervention is required. For these reasons, it cannot be expected that this definition is implemented in daily clinical practice without reservation.

The objective of this study was to address the clinical implementation of the third universal definition of PMI according to cardiothoracic surgeons in Western Europe. The focus of this survey was on the implementation of the consensus-based diagnostic criteria for biomarkers. The clinical implementation of other diagnostics mentioned in the universal definition, such as ECG changes, imaging, symptoms, and consultations, was also addressed.

Methods

Considering the nature of the study, the institutional review committee waived the requirement for medical ethical review committee approval and for informed consent (reference number WAG/om/14/005019).

Study Population

For this web-based survey, we invited cardiothoracic surgeons from a total of 12 Western European countries (Austria, Belgium, Denmark, France, Germany, Ireland, Luxembourg, Netherlands, Norway, Sweden, Switzerland, and the United Kingdom). We chose to include the 10 countries with the highest government expenditure on health care per capita, according to the most recent available data from Eurostat (2008–2010). The United Kingdom and Ireland were included as well. Even though no recent information on healthcare expenditure was available on Eurostat for these 2 countries, it is conceivable that their healthcare expenditure is in the top 10.

The 1627 cardiothoracic surgeons from the included countries were recruited for voluntary participation in this nonanonymous questionnaire using standardized e-mails. Cardiac centers and cardiothoracic surgeons were identified and e-mail addresses were retrieved by conducting a web-based search that was focused on the European cardiothoracic societies, national cardiothoracic societies, national registries for medical specialists, network websites, patient organizations, hospitals, and relevant publications. When the search did not result in identification of an e-mail address of a cardiothoracic surgeon, that person was excluded from participation ($n=291$; 18%), as it was considered not feasible to contact all cardiac centers throughout Europe to identify the missing e-mail addresses. The questionnaire was distributed to 1336 cardiac surgeons

in 4 waves to optimize the response rate. No incentives were given for participation.

Questionnaire

The questionnaire consisted of 16 questions (Data S1) and was validated by a focus group of colleagues from the University Medical Center Utrecht. Members of the group include a professor in intensive care medicine, a cardiac-anesthesiologist, and an epidemiologist. The questionnaire was evaluated by this focus group on 13 points (ie, 5 general points and 8 quality-related points) including the formulation of the questions, the construction of the survey, the layout, the user-friendliness, and time required to complete the survey. The quality of the content was addressed by validating the face validity (ie, a global evaluation on whether the survey measured what it should measure), and the content validity (ie, in-depth evaluation of whether the survey provided adequate coverage of the topic). The reliability of the survey was addressed on stability (whether repeated measurements on the same individual would yield similar results), equivalence (whether a measure interpreted by different investigators would yield similar results), and homogeneity (whether changing the operational definitions used would change the results).

Knowledge and Attitude

Voluntary implementation has to be supported by adequate knowledge. For successful implementation of the third universal definition for PMI regarding biomarkers, participants had to know about the proposed cut-off level and the preferred biomarker. Complete knowledge for implementation was defined in this study as the percentage of participants answering affirmatively to both “Were you aware that according to the third universal definition of myocardial infarction troponin is the preferred biomarker for the diagnosis of perioperative myocardial infarction?” and to “Were you aware that the third universal definition of myocardial infarction defines the cut-off level for troponin at >10 times the 99th percentile?”

Another prerequisite for successful voluntary implementation is a positive attitude toward the use of the medical guideline. In this study this was addressed by asking participants whether they agreed with the statement: “A cut-off level of troponin >10 times 99th percentile for diagnosis of perioperative myocardial infarction in patients undergoing CABG should be implemented in your local guideline.” Participants could answer on a 5-point Likert scale (strongly disagree, disagree, neutral, agree, and strongly agree). The answers “agree” or “strongly agree” were arbitrarily considered a positive attitude toward implementation.

Clinical Practice

The questionnaire addressed which participants had a local guideline concerning PMI and which diagnostic tools and criteria were mentioned in that local guideline. All participants were asked to rank the following diagnostic tools on importance for diagnosing PMI: biomarkers, consultation of other specialist, ECG changes, imaging, and symptoms.

Analysis

The results were analyzed using frequencies and proportions and presented graphically. Missing data due to unanswered questions can provide relevant information in implementation research and were therefore not excluded from the analysis. This is, because item nonresponse can be due to high sensitivity of the topic, not knowing the answer, or editing of the participant.⁸

The ranking scores for the importance of the different diagnostics were calculated per diagnostic as the sum of all the rankings from all the participants. When a diagnostic was ranked most important by a participant, 5 points were awarded, when it was ranked second 4 points were given, and so on.

Results

From the 1336 cardiac surgeons who were invited, there were 302 (23%) participants and 16 (1%) refusals. The time between the first and the last participation was 61 days. Participants represented 182 unique cardiac centers from all 12 countries included (Table 1). The participation rate per country was 29%, with a SD of 16%. The extremes in the participation rate were seen in countries where only a limited number of participants were invited. In total, 288 of the 302 participants were traced back to the invitation list. The 14 other respondents participated either anonymously or via an invitation from a colleague. The remaining 1048 cardiac surgeons were arbitrarily considered nonresponders. About half of the responders and the nonresponders were from an academic hospital (48% and 45%, respectively). Most participants were from centers performing 100 to 500 or 500 to 1000 CABG per year, and the majority indicated a PMI incidence of 0% to 3% in their hospital.

Knowledge, Attitude, and Clinical Practice

Of all 302 participants, 109 (36%) knew both the consensus-based cut-off level and that Tn is the preferred biomarker (Table 2). The majority of the 302 participants (213, 71%) knew that Tn is the preferred biomarker, and the proposed cut-off level was known by 112 participants (37%). Forty-nine

Table 1. Characteristics of the 302 Participants

	N (%)
Complete participation	257 (85)
Anonymous	14 (5)
Profession	
Cardiothoracic surgeon	278 (92)
Other	23 (8)
Missing data	1 (<1)
CABG per year in hospital of participant	
100 to 500	108 (36)
500 to 1000	122 (40)
Other	38 (13)
Missing data	34 (11)
Country	
Austria	9 (3)
Belgium	24 (8)
Denmark	14 (5)
Germany	99 (33)
France	16 (5)
Ireland	1 (<1)
Luxembourg	2 (1)
Netherlands	39 (13)
Norway	9 (3)
Sweden	13 (4)
Switzerland	24 (8)
United Kingdom	50 (17)

CABG indicates coronary artery bypass grafting.

participants (16%) had complete knowledge and also a positive attitude toward implementation. Overall, 90 (30%) participants agreed or strongly agreed with implementation of the cut-off level of >10 times the 99th percentile in their clinical practice. For 45 participants (15%) the data regarding knowledge and attitude were missing. In ranking the diagnostic criteria on importance, the most common order was biomarkers first, ECG changes second, and imaging third (37, 12%). Participants who had this order of ranking had less often a negative attitude toward implementation compared to participants with a different ranking order (Figure). The presence of a local guideline concerning PMI in CABG was reported by 131 (43%) participants.

Biomarkers

From the 131 participants with a local guideline, 120 (92%) mentioned the use of biomarkers for diagnosing PMI. Overall, 184 (61%) of all 302 participants determined biomarkers at least twice in all patients regardless of any symptoms, while

Table 2. Knowledge Regarding Biomarkers and Attitude Toward Implementation

Knows	Attitude		Total, N (%)
	(Strongly) Agrees With Implementation, N (%)	Does Not Agree With Implementation, N (%)	
1. Tn	29 (10)	75 (25)	104 (34)
2. Cut-off level	1 (<1)	2 (1)	3 (1)
3. Both Tn and cut-off level	49 (16)	60 (20)	109 (36)
4. Neither	11 (4)	30 (10)	41 (14)
Total	90 (30)	167 (55)	257 (85)*

The proportion of participants who either agreed or strongly agreed with implementation compared with the proportion that does not for 4 different groups. Group 1. Tn: participants who only knew that Tn is the preferred biomarker; Group 2. Cut-off: participants who only knew the cut-off level; Group 3. Both: participants who knew both that Tn is the preferred biomarker and the cut-off level; and Group 4. Neither: participants who knew neither that Tn is the preferred biomarker nor the cut-off level. Tn indicates troponin.

*Data missing from 45 participants (15%).

31 (10%) only determine biomarkers on indication, whereas 6 (2%) never determined biomarkers (Table 3).

The majority of 302 participants used a combination of more than 1 biomarker (174, 58%). The combination of creatine-kinase M-band and Tn was the most popular 1 (79, 45%). The majority did not use Tn but creatine-kinase M-band (149, 49% versus 202, 67%). Ten participants (3%) stated the use of liver function enzymes (eg, aspartate aminotransferases, alanine transaminase) in the comment space as other biomarker. Other biomarkers that were mentioned included myoglobin (4, 1%), total creatine kinase (2, 1%), and lactate dehydrogenase (1, <1%). Biomarkers were ranked as the most important diagnostic criterion by 122 (40%) of the 302 participants (Table 4).

Electrocardiography

A total of 117 (89%) of the 131 participants with a local guideline confirmed the presence of ECG criteria for PMI in that local guideline. ST segmental changes were used most often (75, 64%), followed by Q waves (64, 55%), new left bundle branch blocks (34, 29%), T-wave inversions (25, 21%), and new R-wave progression (12, 10%). Other criteria that were mentioned included ventricular arrhythmias (2, 2%), T-wave decrease (1, 1%), extrasystoles (1, 1%), and all ECG changes (1, 1%).

Other

Of the 131 participants with a local guideline, 85 (65%) included imaging. Transthoracic echocardiography (53, 62%),

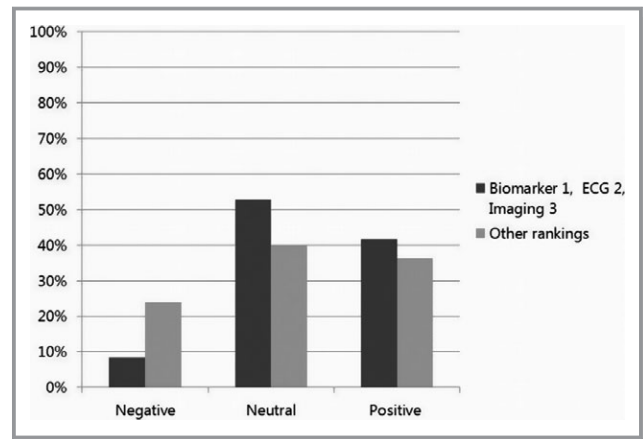


Figure. Ranking and attitude toward implementation. Responses in percentages to the question: “Do you agree with the following statement? A cut-off level of troponin >10x 99th percentile for diagnosis of perioperative myocardial infarction in patients undergoing CABG should be implemented in your local guideline.” The answers “strongly disagree” and “disagree” were considered a negative attitude and “agree” or “strongly agree” were considered a positive attitude. Comparison was made of the attitude toward implementation of participants who ranked biomarkers 1, ECG changes 2, and imaging 3 on importance as a diagnostic criterion to the participants who ranked the diagnostic criteria in any other order. ECG indicates electrocardiogram.

transesophageal echocardiography (43, 51%), and angiography (34, 40%) were used more commonly than magnetic resonance imaging scans (4, 5%) and computed tomography scans (3, 4%). Over 1 third (52, 40%) of the 131 local guidelines were reported to include symptoms for PMI, such as ischemic symptoms, hemodynamic instability, low cardiac output, and hypotension. Table 5 provides the definitions of these symptoms as defined by the participants in the comment space in the survey.

Consultation of another specialist was the criterion that was ranked most often as least important by the 302 participants (112, 37%) and it had the most missing data (95, 31%). Consultations of specialists were part of the diagnostic criteria in the local guidelines of 46 (35%) of the 131 participants with guidelines. Cardiologists (28, 61%), Cardiothoracic surgeons (24, 52%), and Intensive Care specialists (15, 33%) were the specialists of choice for consultations.

Discussion

In this cross-sectional survey, we aimed to address the clinical implementation of the third universal definition of myocardial infarction after CABG according to cardiothoracic surgeons in Western Europe. We found that the majority of the 302 participating surgeons from 182 different cardiac centers used different biomarkers and different ECG criteria than

Table 3. Biomarker Use for Diagnosis PMI

How often are biomarkers determined? N (%)	
Never	6 (2%)
Only on indication	31 (10%)
1 time	0
2 times	0
>3 times	63 (21%)
Until decreasing	121 (40%)
Missing data	81 (27%)
Which biomarkers are used? N (%)	
CK-MB	202 (67%)
Tn	149 (49%)
HS-Tn	105 (35%)
Other	17 (6%)
Missing data	81 (27%)

The question how often biomarkers are determined standardly in all postoperative patients was a select 1 question (counts to 100%). The question about which biomarkers are used was a multiple-select question (counts to >100%). CK-MB indicates creatine-kinase MB; HS-Tn, high-sensitive troponin; PMI, postoperative myocardial infarction; Tn, troponin.

recommended by the third universal definition. In addition, most participants (55%) did not have a positive attitude toward the implementation of the third universal definition in their clinical practice.

Comparison With Literature

This is, to the best of our knowledge, the first study addressing the implementation of the third universal definition of myocardial infarction for diagnosing PMI after CABG. We found a self-reported implementation of knowledge and attitude of only 16%. A review evaluating clinical implementation of consensus-based guidelines found a physician self-reported implementation rate between 24% and 85%.⁹ The lack of implementation that we found might be due to the limited number of participants with sufficient knowledge

regarding this topic (36%). Our study showed that the proportion of participants who agreed with implementation of the Tn cut-off level was lower when the participants had insufficient knowledge compared to participants with sufficient knowledge (ie, knowledge about both Tn and the cut-off level). However, even in participants with sufficient knowledge, only a minority had a positive attitude toward implementation, indicating that there are probably more reasons for the lack of implementation demonstrated in this study. The first reason might be that the applicability of the consensus-based Tn cut-off level is inadequate. This is demonstrated by a recent study showing that patients with Tn levels >10 times the 99th percentile in combination with either specific ECG changes or echocardiographic criteria had an increased 30-day mortality.¹⁰ Although patients with an unstable preoperative Tn level were excluded in this study, still 93% had a Tn level >10 times the 99th percentile.¹⁰ So, if indeed >90% of the CABG patients meet this criterion, this could mean that the cut-off level, the cornerstone for the diagnosis, is not usable in clinical practice. Especially since the recent development of the high-sensitivity Tn tests, there is a general concern for the specificity of these new highly sensitive tests.¹¹ Therefore, some of the reluctance against implementation could be toward the consensus-based Tn criterion. Second, the diagnostics criteria that were implemented were not used as recommended by the third universal definition. For instance, the majority of the participants used local guidelines that mention the use of ST segmental changes as ECG criterion for the diagnosis of PMI (64%), while the third universal definition recommends using Q waves and/or new left bundle branch blocks. The use of ST segmental changes is remarkable, as ST-segment elevations are seen regularly after CABG in the absence of myocardial infarction and are not associated with the peak Tn level or adverse outcomes.⁶ A third reason for the lack of (correct) implementation can also be due to indifference toward diagnosing PMI. This can be the case if PMI is considered a standard or irrelevant complication. Indifference could explain the relatively high percentage of missing data (27%) on the

Table 4. Ranking Scores Diagnostic Criteria

	Ranking Score	Ranked #1, N (%)	Ranked #5, N (%)	Missing Data, N (%)
Biomarkers	1030	122 (40)	8 (3)	57 (19)
ECG	963	77 (25)	6 (2)	55 (18)
Imaging	681	23 (8)	32 (11)	66 (22)
Symptoms	562	26 (9)	48 (16)	81 (27)
Consultations	352	1 (<1)	112 (37)	95 (31)

Ranking score per diagnostic criterion and the proportion of participants who ranked a certain category as most important (ranked #1) and as least important (ranked #5). ECG indicates electrocardiogram.

Table 5. Criteria Used to Define Symptoms

Ischemic symptoms (N=36)
(Chest) pain
ECG changes
New wall-motion abnormalities
Hemodynamic instability (N=32)
Catecholamine use
Low blood pressure
Tachycardia/rhythm disturbances
Impaired renal function/oliguria
Low cardiac output (N=22)
Low cardiac index
Low (systolic) blood pressure
Low mean arterial pressure
(Chest) pain
Hypotension (N=10)
Low (systolic) blood pressure
Catecholamine use

Participants who indicated to use either ischemic symptoms, hemodynamic instability, low cardiac output, and/or hypotension as a diagnostic criterion were asked the follow-up (open text) question on how they defined these criteria. In this table, the most commonly given response in the open text field on how participants defined ischemic symptoms, hemodynamic instability, low cardiac output, and hypotension is given. ECG indicates electrocardiogram.

questions regarding the type of biomarker used and the frequency of taking lab samples. Since it is possible that participants with indifference are more likely to not know the answers to these questions, not knowing the answer to a question can result in missing data.⁸ Finally, for a successful implementation program it is crucial that knowledge be increased, attitudes be changed positively (physicians have to agree with the implementation), behavior be changed, and the patient outcome be affected.¹² The effect on outcome of this new guideline specifically and of diagnosing PMI in general is not clear yet, which means that currently there is not a solid foundation for implementation.

Limitations

Our study has limitations. First, potential participants were identified by conducting a web-based search. When contact information was not available on the website of the hospital, e-mail addresses were searched in scientific publications. This could result in overestimation of the implementation of knowledge, as it is possible that researchers are more exposed to publications regarding the third universal definition. Second, despite sufficient efforts the final participation rate was 23%. In a recent web-based survey study aimed at

cardiothoracic surgeons, the final response rate was 16%,¹³ indicating that our response rate is ample. The risk of a low response rate is nonresponse bias, and it is unknown which participation rate is minimally required in web-based surveys to avoid it. Web-based surveys with a low response rate (<35%) were shown to be representative.¹⁴ In this study, we reduced the risk of nonresponse bias by selecting multiple participants per cardiac center and by recruiting participants from 182 different cardiac centers. The lower risk of nonresponse bias makes the participation rate of 23% acceptable. Third, directive “yes” or “no” questions were used to assess knowledge, making the survey vulnerable to participants providing sought-after answers. The use of these lead-in questions could have resulted in bias. Moreover, participating in the survey resulted in a learning effect and the survey was not protected against editing previous answers, also allowing for an overestimation of the implementation of knowledge. However, the results demonstrated a large difference between the knowledge regarding the cut-off level and Tn as the preferred biomarker (37% versus 71%); therefore, it is unlikely that participants were editing or giving sought-after answers. Fourth, applicable participants were asked in an open text question how they defined ischemic symptoms, hemodynamic instability, low cardiac output, and/or hypotension as a diagnostic criterion for PMI. This open text question likely resulted in bias due to under-reporting.

Clinical Implications

The results of this study can be used as a first step toward designing an implementation program. However, for effective implementation of a clinical guideline, either the quality of care or patient outcome needs to be improved.¹² Although PMI is associated with an adverse outcome,^{1–3} it is not clear whether improving diagnostics by using the third universal definition will positively affect patient care or outcome. Therefore, further research, focused on patient outcome, seems to be required first to provide a solid foundation for successful implementation. Such a study will need to investigate not only the added diagnostic value of the third universal definition, but also the clinical significance of using this definition in routine practice. In addition, it would be relevant to study the use of the third universal definition in research, as the results of such a study would allow for the comparison of the implementation in research and clinical practice.

This was a cross-sectional, survey-based study, including 302 cardiothoracic surgeons from 182 European cardiac centers. The implementation of the third universal definition for PMI in Western Europe is limited. In clinical practice, different ECG criteria and different (combinations of) biomarkers are used for the diagnosis of a PMI following CABG.

In addition, less than 1 third of the participants agreed with implementation of the cut-off level for cardiac biomarkers as defined in the third universal definition, indicating that there currently does not seem to be consensus for the implementation of the third universal definition regarding biomarker use for diagnosing PMI.

Disclosures

None.

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