Editorial – Special issue: Acute Coronary Syndromes

Classification and definition of acute coronary syndromes – A time for change?

Preamble. It is a great honor to be invited by the Czech Society of Cardiology to act as the guest editor of this special Cor et Vasa issue focused on acute coronary syndromes. Instead of the traditional opening editorial I decided to present a very interesting international discussion, which followed the publication of the provocative Czech position paper on acute coronary syndromes a year ago [1].

The original comments of distinguished international experts are presented below as their reaction on the Czech position statement. These comments were originally sent to me in the form of private e-mail communication. All colleagues cited below in the article approved the publication of their comments in this editorial article.

Introduction

The European Society of Cardiology (ESC) guidelines define acute coronary syndromes (ACS) based on their pathophysiology: “ACS in their clinical presentations share a widely common pathophysiological substrate. Pathological, imaging, and biological observations have demonstrated that atherosclerotic plaque rupture or erosion, with differing degrees of superimposed thrombosis and distal embolization, resulting in myocardial underperfusion, form the basic pathophysiological mechanisms in most conditions of ACS.” The classification of ACS is based on the electrocardiogram (ECG). Two categories of patients may be encountered: (1) Patients with acute chest pain and persistent (>20 min) ST-segment elevation. (2) Patients with acute chest pain but without persistent ST-segment elevation [2].

It is surprising that there is a detailed universal definition of acute myocardial infarction [3], but similar definition does not exist for acute coronary syndrome. In classical terms, acute coronary syndromes include ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (non-STEMI) and unstable angina pectoris (UAP). Thus, the definition of acute coronary syndrome should include the universal definition of myocardial infarction plus definition of unstable angina pectoris. And here is the key problem, today thanks to precise troponin measurements the group of patients classified as UAP includes two entirely different populations: (a) patients with significant coronary artery disease and unstable plaques causing chest pain, versus (b) patients with chest pain caused by non-coronary (and frequently even non-cardiac) problems. This problem is reflected in results of some large clinical trials – e.g. in the TRILOGY trial [4], showing different results for patients having their ACS confirmed by coronary angiography (prasugrel was effective in these patients) and for patients without such confirmation (prasugrel was ineffective in this subgroup, most likely due to the fact that some of these patients might suffer from other diseases, not related to thrombotic coronary obstruction).

The Czech Society of Cardiology published in 2013 a position statement [1] demonstrating some important limitations of the current classification and opening the question whether the above mentioned current classification of acute coronary syndromes (ACS) is still practical or whether it should be replaced by an updated one. This provocative article stimulated an interesting international discussion among experts from many countries. The summary of this discussion is presented below.

The summary of the Czech proposal for classification of acute coronary syndromes [1] is mentioned below:

(a) Acute coronary syndrome with ongoing myocardial ischemia (OMI) is defined as ongoing (or recurrent) clinical signs of acute myocardial ischemia (i.e. persistent chest pain and/or dyspnea at rest) plus at least one of the following:
1. ST segment elevations in ≥2 consecutive ECG leads (≥2 mm for leads V2–V3, ≥0.5 mm for leads V7–V9 and ≥1 mm for other leads).
2. New onset bundle branch block (right or left).
3. Persistent ST segment depressions in ≥2 consecutive ECG leads (≥2 mm for chest leads and ≥1 mm for extremity leads).
4. Cardiogenic shock or “pre-shock” type of hemodynamic instability (low-to-normal blood pressure + tachycardia + cool extremities) due to suspected ischemia.
5. Malignant arrhythmias including resuscitated cardiac arrest with return of spontaneous circulation.
6. Clinical signs of acute heart failure (Killip II–IV).
7. New onset of a wall motion abnormality on cardiac imaging.

(b) Acute coronary syndrome without ongoing myocardial ischemia (OMI) includes all other acute coronary syndromes. Specifically, these are patients with unstable angina and with small acute myocardial infarction (troponin elevation) not having the above-mentioned signs of ongoing ischemia at the time of first medical contact.

For further details see the full text of the original position statement [1].

We may face a new era in ACS diagnosis and this new era may be featured by two important modifications:

1) The classification of ACS needs update: either (a) unstable angina may merge with stable angina [5] and/or the true acute non-STEMI will merge with STEMI, or (b) ACS may be classified based on the presence or absence of ongoing myocardial ischemia (OMI) – the proposal is further discussed below in details.

2) The name acute CORONARY syndrome should be used only for patients with PROVEN CORONARY disease. In other words, to establish the final (not the working) diagnosis of ACS patients they should have either (a) an old known positive coronary angiography, or (b) a new – positive CAG or (c) at least a positive CT-coronary angiography. This would eliminate false positive diagnoses not only in trials, but also in clinical practice. Such approach (need to know coronary anatomy before establishing the final diagnosis) may facilitate early differential diagnosis with other illnesses (e.g. Tako-tsubo, acute myokarditis, gastroesophageal reflux, etc.).

The international comments to the original position statement paper [1] are grouped by their main message to six sections: (1) supportive comments to the “OMI” classification, (2) comments considering the proposal not suitable for many countries or regions, (3) request for more data to define the high risk group and to confirm the unstable angina pectoris (UAP) disappearance, (4) similar system is already in place, (5) change of classification may be difficult or impractical, and (6) potential problems with differential diagnosis of other illnesses.

Comments supporting the new “ACS–OMI” classification

This is a very thoughtful article and I believe that in Hamilton, Canada, we tend to follow this approach if feasible. Most patients with STEMI and within 12 hrs within the city go directly for primary PCI and those with non-STEMI elevation ACS + ongoing symptoms or those at high risk (e.g. the TIMACS) are sent if possible to the cath labs which operate 24/7. Patients from longer distances (or referral area can extend to about 120 Kms) may follow this, although at time the local doctors first give thrombolysis and then transfer immediately only those who appear to be unstable or those who have not evidence of reperfusion. Non ST elevation MI patients who are unstable or high risk can also be transferred within 24 hrs. Others may have stress testing after discharge and then get referred or sometimes get referred without stress test. So in our setting the principles that are outlined in your article are generally followed taking into account distance and access. (Saim Yusuf)

Our case from the last week supports your proposal without further words: the reason we went to the cath lab was: the patient still had pain! We have to do something for these patients, frequently having left circumflex or even left main lesions. (Menko-Jan DeBoer)

You have generated very robust and useful discussion on this important issue! I too am supportive of this initiative of addressing how to approach ACS definition and implications for early angiography. (Chris Granger)

This is an interesting and very pragmatic concept that deserves further discussion and validation. I am very supportive. (Jean-Pierre Bassand)

A selection of patients who present with non-STEMI should be treated ‘STEMI-like’, which is also common practice in many centers with 24/7 cath-facilities. The patients with left circumflex or left main occlusion or ischemia often present without ST elevation. A study randomizing this kind of high-risk non-STEMI patients to early vs late intervention would be unethical the moment the patient is still having chest pain or other signs of ongoing ischemia. The question is what to do with high-risk non-STEMI patients who present at a non-PCI center or at centers without 24/7 cath-facilities. Send them immediately to a PCI center? The recently presented and published ELISA-3 trial addressed this issue and it might be that patients presenting at a non-PCI center benefit from early intervention, although this was a subgroup analysis. To my opinion, we should no longer focus on the presence or absence of ST elevation as sole determinants of early angiography or reperfusion therapy and completely agree with your concept. (Arnoud van’t Hof, comment shared by Jeroen Bax)

Very interesting new classification, which seems to be more close to our clinical needs. I run a single center registry in ACS patients with long-term clinical follow-up and shall test the impact of this new classification on clinical outcome depending on the chosen strategy. (Kurt Huber)

I like this proposal a lot. That is exactly what we already do: “24/7” cath lab activation is not limited to ongoing “EGG” STEMI only because there are even more high risk patients with other ECG patterns/clinical conditions. If I just take an example of my last call 2 days ago: ST depression on V4–6, still mild chest pain despite initial therapy, we did immediate coronary angiography expecting “EGG-hidden” acute left circumflex as culprit. Instead, it was subtotal distal trifurcating left main combined with chronic total occlusion of the right coronary artery! Immediate intraaortic balloon pump (IABP) and urgent coronary artery bypass surgery (CABG), patient survived and currently is already out of intensive care unit (ICU). If this patient would enter non-PCI hospital, time-consuming risk stratification, long discussions about P2Y12 pretreatment, etc. ……. You can imagine what would happen by delaying time to right diagnosis (which can be established in such case only by angiography). I think what you suggested really is an “upgrade” of mature STEMI network to become “acute cardiac network”. It is therefore not probably for
I agree with you completely. (Deepak L. Bhatt)

The proposal is not suitable for many countries or regions where thrombolysis is still widely used

Many thanks for sharing this interesting and provocative proposal, which opens a necessary new debate regarding management of non-STEMI ACS. Your proposal is really well supported and very applicable to countries like the Czech Republic, where there is an excellent and uniform network for ACS management at a national level, which has abolished thrombolysis. However, I think that it is not applicable to the vast majority of countries, as most regional networks for STEMI management still consider pharmacoinvasive reperfusion with prehospital lysis as an alternative to primary PCI when it is not available or cannot be performed with an acceptable transfer delay. For instance, in Spain the current percentage of lysis varies between 20 and 40% of total reperfusion treatments. (Francisco Fernandez – Aviles)

The concept of new classification reflects the reality and potential needs in clinical practice of invasive treatment of ACS. In Poland similarly to your country very high number of cathlabs should enable timely interventions in STEMI and very high risk NSTE MI (ACS with OMI) patients. Unfortunately still the delays of primary PCI are substantial. Prehospital thrombolysis is a solution in certain regions and circumstances. In many countries the delays are unavoidable and prehospital thrombolysis is necessary. The proposed classification definitely warrants further debate. The results of ongoing studies regarding the efficacy and safety of very early interventions in NSTE MI with OMI may support your proposal. The role of prehospital fibrinolysis (when unavoidable delays of PCI) in NSTE MI with OMI is still not clear. Focusing early diagnosis in ACS on ongoing myocardial ischemia (OMI) is a great value of your publication. (Andrzej Budaj)

The message from Andrzej summarises my views too. I do like the acronym OMI. It is useful. A good initiative Petr. (Kenneth Dickstein)

The proposal is provocative, but the importance of defining ACS according to the initial ECG presentation still holds, because the urgency of PCI is certain in the presence of STEMI, while “to be defined case-by-case” in NSTE-ACS. In addition, thrombolysis is still an option in several areas of Europe, and I think it would be confusing to have two overlapping classifications running at the same time for the two different therapeutic options. (Raffaele De Caterina)

Utilizing the concept of “ongoing ischemia” as a strategy-driving factor is certainly very intuitive, reasonable, and already applied in many countries/regions; however its widespread applicability needs to be verified according to local settings. In addition, your new classification hints to new guidelines, but for that we do need some hard outcome data. (Germano Di Sciaccio)

Interesting concept which may well apply locally but not in countries or regions that still use the pharmacoinvasive strategy for some of our rural patients with longer transfer times despite helicopter use. It is simply a matter of geography including distance. The other issue relates to the data suggesting that most patients with non-STEMI ACS will not require primary PCI (the ABOARD trial) but no one would argue about emergency angiography for patients with persistent ongoing pain and/or ischemia. (Bernard Gersh)

I agree this is where the ACS is moving: further protocol-driven rational management. Earlier intervention in the non-STEMI population (“should non-STEMI be treated like STEMI”) in appropriate patients is probably the next paradigm. Indeed the DANCE trial in London has mobilised ambulances for non-STEMI management along such lines but it is difficult to prove it is advantageous. Also as has been suggested lysis is still being used worldwide (judging by the responses we are getting to the STREAM trial). In some systems (such as yours and ours) most if not all patients do go to the PCI centre expeditiously, but clearly in others delays can be incurred with worse outcomes. So taking on board all the other comments I believe that (1) Groups 1–5 per your classification go straight to the cath lab anyway as per the ESC Guidelines, (2) the others need to be assessed and discussed. There is little evidence having said that for any advantage for any of arrhythmic, “haemodynamically unstable” acute non-STEMI to be taken urgently to the cath lab, although that is what we do. I think the proposal misses two real issues: (a) the use of thrombolysis world wide and more importantly (b) there are patients who are not as hot as you indicate but who wait for 24–72 hours for their cath proceed. Giles Montalescot and myself are putting together a trial to see whether “very warm” patients do better with urgent intervention. I think it is fantastic that you have started a debate. (Anthony Gershlick)

Unfortunately not all the countries are Czech Republic. In my country (Italy), the latest nationwide data on the reperfusion treatment are the ones below. Fibrinolysis is still used in about 60% of the patients in centres without cath lab, in 28% of the cases in centres with cath lab available only in the working hours; only in the centres with cath lab 24/7 the use of fibrinolysis is negligible (but anyway existing). It is very important not to apply the beautiful data from the best STEMI networks published in the literature to the “real world” STEMI management in a whole country. Because fibrinolysis is applicable in STEMI but not in NSTE MI, the assumption of the Czech colleagues is not applicable in my country. The proposal could be applied in other countries, of course. (Marco Tubaro)

You have shook many trees…. In principal I agree, it may be feasible in Belgium, but real life depends on geography. (Josef Bartuneck)

More data are needed to define the high risk group and the disappearance of unstable angina

I like your approach to early invasive treatment of non-STE ACS. It will be important to obtain rigorous data that help to
define the high risk group. Attached is an article [5] on a related subject – the disappearance of unstable angina in the era of high sensitivity (hs) troponins. (Eugene Braunwald)

This is very interesting and correct approach from the pathophysiological point of view. Unfortunately, treatment strategies are at this stage difficult to match with this concept. Together we should, however, consider to discard in the future the diagnosis of “unstable angina”, because with hs troponins this is less justified. (Christian Hamm)

Your proposal merits full attention not only to the Czech acute cardiac care providers but to a more international platform as it is a clinical based approach that might facilitate and streamline acute management of ACS patients. The proposal implies a high PCI availability which is not guaranteed in many regions. In addition, the main difference in management will be in the group of patients that showed ischemia on admission and will be sent in your proposal directly to the cathlab, whereas in many situations non-STE ischemia will disappear after 30-60 minutes of anti-anginal drugs and those patients will get invasive evaluation 24–72 h after admission. It might be interesting to study first this “urgent invasive protocol” in this subpopulation. Your proposal is also an opportunity to critical evaluate the current ACS classification and to compare the advantage and the disadvantage of both classifications systems. (Marc Claeys)

I suspect we would all agree that the direction of travel is to accelerate treatment for high-risk non-STEMIs (and indeed all non-STE ACS cases). I think it is premature to consider losing the STEMI/NSTEMI classification. From responses there is still a lot of work to do internationally to get systems of healthcare to change to deliver primary PCI and pharmaco-invasive processes are still clearly used. So, although these are continuing challenges, the STEMI cohort in effect automatically fulfils the OMI classification. I suspect that most clinicians would investigate late-presenter STEMI cases (who fall outside of reperfusion windows) but who have on-going ischaemia at the earliest opportunity. The main issue then is to identify those non-STEMI cases where much earlier treatment provides benefit. Although any earlier treatment that minimises myocardial damage may prove effective in the longer-term, this is probably dependent on the degree of ischaemia, vulnerable territory, potentially for harm during procedures etc. One could argue that most non-STE ACS patients have ongoing ischaemia when they present to “first medical contact”, but we do not yet have sufficient evidence to suggest a primary PCI-like strategy for these cases. I personally am attracted to the ambulance services triaging cases to primary PCI-capable centres such that immediate, very early or next day angiography can be offered as deemed appropriate depending on individual patient characteristics. As long as the patient is in the right centre, the current guidelines allow for this. TIMACS has had an impact on some systems of care (but this is for earlier angiography – within 24 hours – rather than a primary PCI-like strategy), but many still believe that you need more than one piece of evidence to start changing national protocols. In many countries of course there is no such thing as a national protocol, and it is up to individual localities or regions to develop the most appropriate networks and pathways of care, which they do with the appropriate steer from the major international guideline groups. There are ongoing studies that will give us additional insight but I don’t think any are powered to give us definitive answers as yet, so perhaps Petr’s challenge is really a challenge to set up such a definitive large-scale international study. Sorting out the inclusion and exclusion criteria would be key to a successful trial. (Mark DeBelder)

Very interesting and provocative article. I do understand the interesting concept that you put across in this article of distinguishing ongoing myocardial ischaemia. I believe that our previous biomarker detection systems were insufficiently sensitive to identify some of the non-ST elevation myocardial infarctions from within the “unstable angina” cohort. I think we will be left with a small and heterogeneous number of “unstable angina” diagnoses overlapping with other causes of ECG abnormality – including non-cardiac causes. In my view it would be critical to distinguish type 1 myocardial infarction from type 2 (secondary causes for example following arrhythmia or heart failure) as these have different therapeutic implications. This distinction relies on the clinical context. The issue of ongoing “myocardial ischaemia” is complex as it implies that we can detect initial ischaemia and continuing ischaemia in all of these patients – I think this will be challenging. I think you have provoked a very interesting discussion and I am sure that a lot of valuable ideas may come out of this! (Keith Fox)

I agree that this is a forward-looking proposal, very interesting. Unfortunately, there is not as much data as I would like on the status of chest pain at the time patients have been taken to the cath lab versus treated medically in the prior non-STE ACS trials. This is certainly intuitive however, and future studies should collect this data. (Gregg Stone)

Similar system is already in place

Your concept is very much matching the needs of your country and profiting from your experiences with even long distance transports of STEMI patients to tertiary centres for primary PCI. The logistic situation in Germany is very different. As you know, we have a large number of 24/7 cath-labs in Germany, so that any ACS should be directly admitted to those (STEMI-patients directly into the cath-lab). In addition, the German Cardiac Society has supported the implementation of chest pain units (CPU) all over the country, the current number of certified CPUs (certified by the German Cardiac Society) is 167 (see map of Germany with current CPU under http://cpu.dgk.org/index.php?id=376). In the ideal setting, any patient with ACS in Germany would be admitted to a hospital with PCI facility, many of them with additional certified CPUs providing the expertise to make rapid decisions also in patients with ACS without persistent ST-elevations according to the risk stratification of current ESC guidelines. Taking these considerations into account – at least in my view – your proposed new ACS classification would not help improving the current ACS-care in Germany. (Anselm Gitt)

Change of classification may be difficult or impractical

It is certainly an interesting concept. Practically it may be hard to change all of the terminology with which people are so
familiar. I remember how long it took to change from Q wave and non Q Wave to STEMI and NSTEMI. (David Holmes)

Conceptually a great and well described construct. Logistically may be hard to get people to change terminology. (Kenneth Mahaffey)

I agree that it is a great idea to open a discussion on ACS classification and treatment strategy. In Denmark we are lucky – like in your country we can provide PCI and do not use thrombolysis. Non-STEMI: we all agree that there is a small subgroup with on-going ischaemia that should be taken to cath acutely. The problem is how we handle the remaining 90–95%. We have discussed your proposal in our PCI team. The difficulty is to identify the high risk patients among the remaining ACS patients and secondly whether this high risk group will benefit from immediate cath. We are conducting a trial (NONSTEMI, principal investigator Christian Terkelsen) where high risk non-STEMI patients are randomized to immediate cath vs cath within 24/72 hour according to ESC guidelines. Personally after discussing implementation of STEMI networks with colleagues in many countries I realize that there are many different barriers and obstacles. The message that STEMI patients need urgent action is a simple one – the non-STEMI algorithm is more complex and the evidence is not so strong. It is important that we deliver simple messages to the health care providers. However, an academic discussion on a re-classification of ACS is important and appropriate. (Steen Dalby Kristensen)

The 2011 ESC non-STE ACS guidelines recommend “STEMI-like” management for very high-risk ACS patients who may have an “evolving MI” (i.e., refractory angina, severe heart failure, life-threatening ventricular arrhythmias, or hemodynamic instability), regardless of ECG or biomarker findings. I assume that “ongoing ischemia” (obviously in a patient without STEMI) imply persistence of pain (and/or ECG changes) following administration of standard initial treatment (antiplatelets/anticoagulants and if appropriate nitrates and/or betablockers). In the Geneva area, the first medical contact for chest pain patients who do call an ambulance is in the field. A physician writes an ECG and, in case of STEMI, activates an automatic alarm system (ALARME STEMI) and the cath lab team is “automatically” called-in. For the physician in the field (usually a resident) it may be difficult to wait for the response to the first treatment prior to decide whether the patient has indeed “therapy refractory” ongoing myocardial ischemia or not. This may lead either to an overuse of our alarm system or a delay in the transport. (Marco Roffi)

I like the concept and agree that it should, if generally implemented, improve outcome in patients with unrecognized LCX occlusions. However, I am afraid that the positive predictive value for groups 3–7 would be unacceptably low and that it would lead to many false negative cath lab activations and unnecessary shipping patients with prior MI and heart failure. I definitely think that your great idea should be tested prospectively in an observational study. (Stefan James)

Since in Poland the thrombolytic treatment is almost obsolete, your idea makes a lot of sense. It is simple, has important practical implications and does not impact on the final diagnosis. As pointed out by many responders, it will be difficult to have it accepted by medical community. (Michal Tendera)

Potential problems with differential diagnosis of other illnesses

Interesting suggestion that needs discussion. However, ST-Segment elevation may not always reflect ongoing ischemia. Indeed, Tako-Tsubo patients have this feature even after signs of ischemia have subsided clinically. We have now at least one patient per week. (Thomas F. Lüscher)

Summary

This interesting international discussion demonstrated wide variation of views. The current ACS classification is widely accepted and it is not certain whether it will undergo major changes in near future. However, as many contributors to this debate expressed, there are definite limitations and the new proposal has the potential to overcome these limitations.

The author of this editorial believes, that the future definition of acute coronary syndrome (as confirmed, in-hospital established diagnosis) should include knowledge of coronary anatomy as conditio sine qua non for the final (discharge) diagnosis (coronary syndrome should have a prove of coronary origin) and that the future classification should abandon the old separation between myocardial infarctions with and without ST segment elevation (which is poorly related to the severity of underlying disease and to clinical outcomes).

Conflict of interest

None.

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Ethical statement

Not needed.

REFERENCES


