European Heart Journal (2015) **36**, 323–324
doi:10.1093/eurheartj/ehu508

Acute coronary syndromes and coronary intervention

Thomas F. Lüscher

Editor-in-Chief, Zurich Heart House, Careum Campus, Moussonstrasse 4, 8091 Zurich, Switzerland

The current issue of the *European Heart Journal* is devoted to acute coronary syndromes (ACS) and coronary intervention. The editors were fortunate as prominent cardiologists from the Benelux countries (in close collaboration with the editors of our journal) agreed to summarize for 2014 the most important advances in these important subspecialties of cardiology together.

The European Society of Cardiology and the *European Heart Journal* recently emphasized the importance of this topic, publishing guidelines on revascularization,[1] those on the management of acute myocardial infarction in patients presenting with ST-segment elevation in 2012,[2] and a year earlier those on ACS in patients presenting without persistent ST-segment elevation.[3] Considerable progress has been made in the understanding and management of these syndromes. In particular, it appears that inflammatory changes may play an important role as the substrate and trigger of acute coronary events.[4,5] Furthermore, novel stents are currently under investigation as novel platforms and scaffolds.[6,7] In this issue of the *European Heart Journal* these developments are reviewed and novel data are presented relevant to the understanding and management of these conditions.

'The year in cardiology 2014 in acute coronary syndromes' has been thoughtfully reviewed by Frans Van de Werf and Filippo Crea from Leuven and Rome, respectively.[8] The authors provide an overview of the key findings published in 2014, and offer a perspective on future research on the pathophysiology, early diagnosis, prognosis, and acute and long-term treatment of ACS covering all types of non-ST-segment elevation and ST-segment-elevation myocardial infarction (NSTEMI and STEMI). Of note, few data have been provided on unstable angina patients in recent years due to the increasing use of high-sensitivity troponins (hsTns), which makes the diagnosis of unstable angina very difficult if not impossible.

Coronary intervention is closely linked to ACS, although it also encompasses the management of stable patients. **'The year in cardiology 2014 in coronary intervention'** has been summarized by Javaid Iqbal, Patrick W. Serruys, Felipe N. Albuquerque, and William Wijns from Manchester, Rotterdam, London, and Aalst, Belgium, respectively.[9] The authors note that 2014 has brought several innovations and new data from trials on myocardial revascularization, coronary stents and scaffolds, adjunctive pharmacological therapy, and treatment of coronary atherosclerosis and ACS. They review the most pertinent studies of 2014 and put their impact into clinical perspective.

In the first original research paper **'Genome-wide profiling of the cardiac transcriptome after myocardial infarction identifies novel heart-specific long non-coding RNAs'** Samir Ounzain *et al.* from Lausanne, Switzerland aimed to characterize the cardiac long non-coding transcriptome—truly novel regulators of gene expression—post-myocardial infarction and to elucidate their potential roles in cardiac homoeostasis.[10] James J. Januzzi from Massachusetts General Hospital provides an insightful **Editorial**.[11]

The authors annotated the mouse transcriptome after myocardial infarction using RNA sequencing and transcript reconstruction, and integrated genome-wide approaches to associate specific long non-coding RNAs (lncRNAs). Expression of specific lncRNAs strongly correlated with defined parameters of cardiac dimensions and function. Using chromatin maps to infer lncRNA function, they identified many that might be involved in cardiogenesis and pathological remodelling. The vast majority were associated with active cardiac-specific enhancers. Importantly, oligonucleotide-mediated knockdown implicated novel lncRNAs in controlling expression of key regulatory proteins involved in cardiogenesis. Finally, they identified hundreds of human orthologues and demonstrated that particular candidates were differentially modulated in human heart disease. They concluded that the hundreds of novel heart-specific lncRNAs with unique regulatory and functional characteristics relevant to maladaptive remodelling, cardiac function, and possibly cardiac regeneration may represent hitherho unrecognized potential therapeutic targets for cardiac disease.

In the second original research paper **'Early discharge using single cardiac troponin and copeptin testing in patients with suspected acute coronary syndrome: a randomized, controlled clinical process study'** Martin Möckel *et al.*[12] report on a European muliticentre, randomized controlled trial evaluating whether an approach using single combined testing of copeptin and troponin at admission in patients with low to intermediate risk and suspected ACS might not lead to a higher proportion of major adverse cardiac events (MACE) than the current standard process using a non-inferiority design. To that end, they randomized a total of 902 patients and assigned them to standard care or the copeptin group where patients with negative troponin and copeptin values at admission were eligible for discharge after final clinical assessment. The proportion of MACE at 30 days was similar and ~5% in both the standard group and the copeptin group. In the per protocol analysis, MACE was 5.3% in the standard group and 3% in the copeptin group.

Patients discharged with copeptin-negative results had an event rate of 0.6%. Thus, although these results need to be corroborated in a larger cohort in the future, it appears that after clinical work-up and single combined testing of troponin and copeptin to rule out ACS, early discharge of low to intermediate risk patients appears to be safe and may shorten length of stay.

In the third paper on **'The effect of interleukin-1 receptor antagonist therapy on markers of inflammation in non-ST elevation acute coronary syndromes'** Allison C. Morton *et al.*[13] report, on behalf of a UK-based group of investigators, the results of the MRC-ILA Heart Study. Charles Dinarello from the University of Colorado provides excellent comments in an accompanying **Editorial**.[14] Morton *et al.* hypothesized that if interleukin-1 (IL-1) is a driving influence of inflammation in NSTE-ACS, IL-1 inhibition would reduce the inflammatory response at the time of ACS. In a phase II, double-blind, randomized, placebo-controlled study they recruited 182 patients with NSTE-ACS, presenting <48 h from onset of chest pain. They allocated patients to daily, subcutaneous IL-1 receptor antagonist (IL-1ra) or placebo for 14 days. The primary endpoint was the area under the curve for C-reactive protein over the first 7 days. This value was 22 mg day/L in the IL-1ra group and significantly lower than in the placebo group (43.5 mg day/L). In the IL-1ra group, 14-day achieved high-sensitive C-reactive protein and IL-6 levels were significantly lower than on day 1. The authors concluded that IL-1 drives C-reactive protein elevation at the time of NSTE-ACS. Following 14 days IL-1ra treatment, these inflammatory markers were reduced. These results suggest that IL-1 might represent a novel therapeutic target in ACS, although certainly additional studies are required.

In the last original research paper **'Applying novel methods to assess clinical outcomes: insights from the TRILOGY ACS trial'** Jeffrey A. Bakal *et al.* assessed on behalf of the TRILOGY ACS investigators[15] conventional and novel methods for the definition of clinical trial composite endpoints. In that study, also discussed in an **Editorial** by Rickey Carter from the Mayo Clinic in Rochester,[16] the traditional time-to-first-event, Andersen–Gill recurrent events method, win ratio, and a weighted composite endpoint (WCE) were compared using the randomized, active-control TRILOGY ACS trial that had randomized 9326 patients managed without coronary revascularization within 10 days of their ACS to receive either prasugrel or clopidogrel. Interestingly, the traditional composite, win ratio, and WCE demonstrated no significant survival advantage for prasugrel, whereas the Andersen–Gill method demonstrated a statistical advantage for prasugrel. The traditional composite used 73% of total patient events; 40% of these were derived from the death events. The win ratio used 66% of total events; deaths comprised 57% of these. Both Andersen–Gill and WCE methods used all events in all participants; however, with the Andersen–Gill method, death comprised 41% of the proportion of events, whereas with the WCE method, death comprised 64% of events. Thus, the methods accounting for all events, in particular those incorporating their clinical relevance, appear most advantageous, and may be useful in interpreting future trials. The authors stress the fact that this clinical and statistical advantage is especially evident with long-term follow-up where multiple non-fatal events are more common.

The editors hope that this issue on an important topic of cardiology will be of interest to our readers.

References

1. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jüni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A; Authors/Task Force members. 2014 ESC/EACTS Guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2014;**35**:2541–2619.
2. Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, Di Mario C, Dickstein K, Ducrocq G, Fernandez-Aviles F, Gershlick AH, Giannuzzi P, Halvorsen S, Huber K, Juni P, Kastrati A, Knuuti J, Lenzen MJ, Mahaffey KW, Valgimigli M, van't Hof A, Widimsky P, Zahger D. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012;**33**:2569–2619.
3. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, Caso P, Dudek D, Gielen S, Huber K, Ohman M, Petrie MC, Sonntag F, Uva MS, Storey RF, Wijns W, Zahger D; ESC Committee for Practice Guidelines. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: the Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2011;**32**:2999–3054.
4. Ridker PM, Lüscher TF. Anti-inflammatory therapies for cardiovascular disease. *Eur Heart J* 2014;**35**:1782–1791.
5. Wyss CA, Neidhart M, Altwegg L, Spanaus KS, Yonekawa K, Wischnewsky MB, Corti R, Kucher N, Roffi M, Eberli FR, Amann-Vesti B, Gay S, von Eckardstein A, Lüscher TF, Maier W. Cellular actors, Toll-like receptors, and local cytokine profile in acute coronary syndromes. *Eur Heart J* 2010;**31**:1457–1469.
6. Kočka V, Malý M, Toušek P, Buděšínský T, Lisa L, Prodanov P, Jarkovský J, Widimský P. Bioresorbable vascular scaffolds in acute ST-segment elevation myocardial infarction: a prospective multicentre study 'Prague 19'. *Eur Heart J* 2014;**35**:787–794.
7. Head SJ, Davierwala PM, Serruys PW, Redwood SR, Colombo A, Mack MJ, Morice MC, Holmes DR Jr, Feldman TE, Ståhle E, Underwood P, Dawkins KD, Kappetein AP, Mohr FW. Coronary artery bypass grafting vs. percutaneous coronary intervention for patients with three-vessel disease: final five-year follow-up of the SYNTAX trial. *Eur Heart J* 2014;**35**:2821–2830.
8. Van de Werf F, Crea F. The year in cardiology 2014: acute coronary syndromes. *Eur Heart J* 2015;**36**:342–346.
9. Iqbal J, Serruys PW, Albuquerque FN, Wijns W. The year in cardiology 2014: coronary intervention. *Eur Heart J* 2015;**36**:347–352.
10. Ounzain S, Micheletti R, Beckmann T, Schroen B, Alexanian M, Pezzuto I, Crippa S, Nemir M, Sarre A, Johnson R, Dauvillier J, Burdet F, Ibberson M, Guigó R, Xenarios I, Heymans S, Pedrazzini T. Genome-wide profiling of the cardiac transcriptome after myocardial infarction identifies novel heart-specific long non-coding RNAs. *Eur Heart J* 2015;**36**:353–368.
11. Gandhi PU, Januzzi Jr JL. Can copeptin emerge fromthe growing shadow of the troponins? *Eur Heart J* 2015;**36**:333–336.
12. Möckel M, Searle J, Hamm C, Slagman A, Blankenberg S, Huber K, Katus H, Liebetrau C, Müller C, Muller R, Peitsmeyer P, von Recum J, Tajsic M, Vollert JO, Giannitsis E. Early discharge using single cardiac troponin and copeptin testing in patients with suspected acute coronary syndrome (ACS): a randomized, controlled clinical process study. *Eur Heart J* 2015;**36**:369–376.
13. Morton AC, Rothman AMK, Greenwood JP, Gunn J, Chase A, Clarke B, Hall AS, Fox K, Foley C, Banya W, Wang D, Flather MD, Crossman DC. The effect of interleukin-1 receptor antagonist therapy on markers of inflammation in non-ST elevation acute coronary syndromes: the MRC-ILA Heart Study. *Eur Heart J* 2015;**36**:377–384.
14. Abbate A, Dinarello CA. Anti-inflammatory therapies in acute coronary syndromes: is IL-1 blockade a solution? *Eur Heart J* 2015;**36**:337–339.
15. Bakal JA, Roe MT, Ohman EM, Goodman SG, Fox KAA, Zheng Y, Westerhout CM, Hochman JS, Lokhnygina Y, Brown EB, Armstrong PW. Applying novel methods to assess clinical outcomes: insights from the TRILOGY ACS trial. *Eur Heart J* 2015;**36**:385–392.
16. Ciolino JD, Carter RE. Reanalysis or redefinition of the hypothesis? *Eur Heart J* 2015;**36**:340–341.