LETTERS TO THE EDITOR

Percutaneous assist devices vs. intra-aortic balloon pump for cardiogenic shock: evidence under construction vs. expert opinion

With great interest, we read the meta-analysis by Cheng et al.1 The authors evaluated percutaneous left ventricular assist device (pLVAD) therapy vs. intra-aortic balloon pump (IABP) therapy in cardiogenic shock (CS). The authors found that pLVADs provided superior haemodynamic support when compared with the IABP. However, no benefit could be demonstrated with regard to 30-day mortality.

From the results of the present meta-analysis, the authors conclude that pLVAD therapy should not be the first choice of treatment in CS and it should not replace IABP therapy. These statements are in accordance with the current American and European ST-elevation myocardial infarction (STEMI) guidelines. However, some issues may need to be addressed with regard to these conclusions.

First of all, in a recently published meta-analysis of available evidence for IABP usage, both in the setting of high-risk STEMI and CS, no benefit could be demonstrated with regard to mortality or left ventricular function.2 In fact, more complications were observed in patients treated with IABP.

Another issue with respect to the current meta-analysis is the fact that two very different pLVADs are compared. The majority of patients (74 of 100) were randomized to TandemHeart vs. IABP. As emphasized by the authors, complication rate is high in TandemHeart-treated patients. Contrariwise, complication rate as reported in the current analysis is much lower with the Impella LP2.5, confirming previous safety and feasibility results.3

Finally, an important issue is the sample size of the current meta-analysis, as acknowledged by the authors. Although randomized trials are included in this meta-analysis, it is underpowered with regard to mortality. When including 100 patients, absolute mortality difference would have to be 28% to obtain significance. To detect an absolute 10% decrease in mortality, almost 800 patients would have to be included in a randomized trial when assuming 80% power and α = 0.05.

Several randomized trials are currently ongoing to evaluate mechanical circulatory support. One trial compares IABP support with medical therapy alone for STEMI with CS (www.clinicaltrials.gov NCT00491036). In another trial, the Impella LP2.5 is compared with IABP therapy in STEMI patients with cardiogenic pre-shock (www.trialregister.nl NTR 1079).

As stated by the authors, the currently available evidence shows that pLVADs provide superior haemodynamic support when compared with IABP, although there is no evidence for a beneficial effect on survival. Therefore, we agree with the authors that currently, pLVADs cannot be recommended for first line circulatory support. Nevertheless, this conclusion holds true for IABP usage as well.

Currently, there is no clinical evidence supporting the use of any mechanical device, including the IABP, in the setting of STEMI with haemodynamic compromise. Therefore, the use of any device may be considered on the basis of expert opinion while awaiting randomized evidence.

References

José P.S. Henriques
Department of Cardiology
Academic Medical Center
Meibergdreef 9, 1105 AZ Amsterdam
The Netherlands

Percutaneous assist devices vs. intra-aortic balloon pump for cardiogenic shock: evidence under construction vs. expert opinion: reply

We thank the colleagues from Amsterdam for their interest in our meta-analysis on the safety and efficacy of mechanical assist devices in cardiogenic shock.1 They raised some important issues, which we address below.

First, although current American and European ST-elevation myocardial infarction guidelines supported the use of IABP counterpulsation as method of first choice for mechanical assistance in cardiogenic shock, we agree with the authors that evidence supporting the use of IABP is somewhat fragile, as was demonstrated by their recent meta-analysis.2 This lack of evidence especially holds for patients with cardiogenic shock from acute myocardial infarction who undergo primary percutaneous coronary intervention. Our meta-analysis clearly showed that the use of a percutaneous LVAD provides superior haemodynamic support relative to IABP. However, the benefit on haemodynamics associated with the use of a percutaneous LVAD did not translate into improved 30-day survival, possibly by higher complication rates. Therefore, we concluded that, at the moment, percutaneous LVADs cannot be recommended for routine clinical practice. Because much more experience has been obtained using IABPs,3 and taking into account the very high costs of percutaneous LVADs, we argue to stick to the IABP in the time coming while awaiting further studies.

Second, we agree with the authors that complications rates of the TandemHeart should not be mixed up with those of the

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2009. For permissions please email: journals.permissions@oxfordjournals.org.
Cell survival: is not all about apoptosis

We have read with interest a recently appeared article by Biasucci et al.,1 the authors used two different protocols to assess apoptosis of PMNs and found that it was reduced and delayed among patients with unstable angina compared with subjects diagnosed with stable angina or healthy controls. On the basis of such findings, the authors hypothesized that prolonged PMN survival is a factor peculiar of UA contributing to enhanced inflammation and ultimately to coronary instability.

We agree on the importance of PMNs apoptosis as a regulatory mechanism of inflammation; however, we would like to emphasize that special care must be taken in the interpretation of these results for two main reasons.

First, because of significant differences between systemic and inflamed plaques environments, circulating cells might not accurately mirror the characteristics of the plaque-infiltrating counterpart. Such diversity can differentially promote or inhibit many cell processes including apoptosis. Secondly, reduced apoptotic rate per se does not necessarily translate into prolonged cell survival. Indeed, PMNs turnover results from the interplay of cell differentiation, mobilization, and death either by necrosis or by apoptosis. By different extent and timing, all those processes are greatly influenced by inflammation. Therefore, studying inflammatory cells half life rather than just a contributor of it (e.g. apoptosis) would be more informative, and apoptosis or necrosis or mobilization taken alone might reveal themselves somewhat misleading. Although studying cell turnover may be more informative, the quantification of necrotic cells is easy to assess and should be taken into consideration.

The flow cytometric analysis of Annexin V/propidium iodide staining used in Protocol 1 is unable to assess the overall extent of apoptosis undergoing in any given sample. Such method can be compared with a camera shooting a photo at the sample at the chosen time. The picture will show three categories of cells: (i) unstained healthy cells, (ii) cells stained by Annexin V only, undergoing early stages of apoptosis, and (iii) a third heterogeneous group stained by Annexin V and propidium iodide composed by both necrotic cells and cells undergoing late stages of apoptosis.1 Only cells falling into the second group can be univocally defined as apoptotic but they might likely represent just part of the total cells dying by apoptosis. This implies that one can face a picture showing massive death by necrosis with negligible apoptosis, where the small percentage of apoptotic cells obviously does not indicate prolonged cell survival. On the contrary, increased numbers of bona fide apoptotic cells can be present in the context of overall reduced cell death, thus implicating increased, rather than decreased cell survival.

Finally, because both apoptotic and necrotic cells are stained by Annexin V, the double staining with anti-CD16 antibody and Annexin V used in Protocol 2 is inadequate to quantify apoptosis.

In conclusion, extreme caution should be taken when inferring modifications of cell survival based on the study of apoptosis alone and in the choice of the experimental method to quantifying it.

References
3. Andrea la Sala
IRCCS San Raffaele Pisana
Rome
Italy
Email: andrea.lasala@sanraffaele.it

Giuseppe M.C. Rosano
IRCCS San Raffaele Pisana
Rome
Italy

doi:10.1093/eurheartj/ehp525
Online publish-ahead-of-print 1 December 2009

Cell survival: is not all about apoptosis: reply

We thank La Sala and Rosano for their interest in our work. We agree with them that neutrophil biology in the microenvironment of the atherosclerotic plaque is probably different of that in peripheral blood. Indeed, in the previous study, we found that neutrophils from unstable plaques but not from peripheral blood showed telomerase reactivation.1 Thus, the mechanisms of delayed neutrophil apoptosis in resident neutrophils and in peripheral neutrophils, as observed in the current study,2 are likely to be different indeed.

We also agree with them that the mechanisms of neutrophil survival are extremely complex. The measurement of neutrophil survival in man, however, is obviously unfeasible. Nevertheless, in the absence of overt inflammatory and infectious diseases, their production rate...