newer Impella LP2.5. However, in our opinion, more safety data on the latter device are urgently needed and we encourage the group from Amsterdam to present these data in the near future.

Finally, we clearly explained in the article that limited sample size was not an important shortcoming of our study. On the basis of the post hoc analyses, we described that the probability for Type II error did not exceed 12%. We refer to the Discussion section of our meta-analysis.

In conclusion, until further evidence will be available, we recommend IABP counterpulsulation as first choice mechanical circulatory assistance in the treatment of cardiogenic shock patients who do not respond sufficiently to pharmacological therapy alone. In our opinion, a percutaneous LVAD may only be a valuable alternative in specific cases when IABP counterpulsation provides unsatisfactory circulatory support.

References

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Cell survival: is not all about apoptosis

We have read with interest a recently appeared article by Biasucci et al., 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 unfeasible in humans, 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. 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

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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. Thus, the mechanisms of delayed neutrophil apoptosis in resident neutrophils and in peripheral neutrophils, as observed in the current study, 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

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