Children’s diet has changed dramatically in the last years, influenced by TV commercials and the convenience of fast food. Today, children consume too much fatty and processed food. Conversely, it has been demonstrated that high adherence to the traditional Mediterranean dietary pattern is associated with a lower prevalence of obesity in men and women in the Mediterranean population. This healthy dietary pattern is associated with a significant reduction in cardiovascular and cancer mortality. The main characteristics of this dietary pattern consist of a high consumption of plant-based foods and low and high intakes of meat and fish, respectively. Furthermore, high intakes of both low (e.g. vegetables and fruits) and high (e.g. olive oil and nuts) energy-dense food characterize the traditional Mediterranean diet. However, also the lack of exercise and the increased in access to sedentary recreation opportunities such as electronic games and computers may influence childhood obesity. Indeed, the American Academy of Pediatrics and the recent Australian Physical Activity Recommendations propose that children spend no more than 2 h/day watching TV and using other electronic entertainment media. Diet and exercise are extremely important to curb this escalating problem.

In our opinion, there is a need for a family-oriented approach to cardiovascular prevention. Parents must prefer for themselves and for their children healthy foods such as vegetables and cutting down fatty meals as well as encouraging regular exercise activities and limiting the time dedicated by their children to videogames.

References

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Endothelial progenitor cells and erectile dysfunction

Baumhäuser and coworkers have recently examined the levels of circulating CD34+KDR+ and CD133+ cells in patients with coronary artery disease (CAD), which were evaluated for the presence of erectile dysfunction (ED). They show that CD133+, but not CD34+KDR+, cell count negatively correlates with ED score and is independently associated with ED. Although this is an intriguing observation linking ED and CAD with depletion of progenitor cells, there are methodological issues that limit interpretation of this study. In describing flow cytometry, the authors have not indicated the antibodies used and have not specified whether direct or indirect staining was performed. Moreover, the number of events acquired for the analyses is far too low for a reliable enumeration of rare events, such as progenitor cell count. It is not clear why CD133+ cells were not studied for co-expression of CD34+ and KDR+. In fact, CD133 is a marker of immature haematopoietic stem cells, although, by definition, identification of endothelial progenitor cells (EPCs) relies on the co-expression of at least one endothelial marker, such as KDR. Additionally, CD133+KDR+ cells constitute a small fraction of the total EPC pool, and the count of CD133+KDR+ cells have not indicated the antibodies used and have not specified whether direct or indirect staining was performed. Moreover, the number of events acquired for the analyses is far too low for a reliable enumeration of rare events, such as progenitor cell count. It is not clear why CD133+ cells were not studied for co-expression of CD34+ and KDR+. In fact, CD133 is a marker of immature haematopoietic stem cells, although, by definition, identification of endothelial progenitor cells (EPCs) relies on the co-expression of at least one endothelial marker, such as KDR. Additionally, CD133+KDR+ cells constitute a small fraction of the total EPC pool.

In conclusion, there is a compelling need for a consensus on EPC definition and methods for their evaluation.

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Endothelial progenitor cells and erectile dysfunction: reply

Fadini et al. mention that antibodies used and staining performed in our study were not described. In order to condense the methods section, we referred to the publication of the EPCAD study (Circulating Endothelial Progenitor Cells and Cardiovascular Morbidity and Mortality in Patients with Coronary Artery Disease Study), in which the patients from our study were enrolled from. Flow cytometry and staining procedures were described in detail in this publication. This study demonstrated a clear and significant association of EPC and cardiovascular outcome in patients with coronary artery disease. Moreover, we could demonstrate that EPC are an independent risk factor for erectile dysfunction. Thus, in our opinion, event counts used in both studies are adequate, especially regarding the high number of patients included.

We could demonstrate in our study that only CD133+/−, but not CD34+/−, cells correlate with erectile function. We discussed this finding in the paper, but explanations remain speculative. CD133+ cells are precursors of CD34+ cells with an increased potency for endothelial repair. This finding was clearly demonstrated by Friedrich et al. in vitro as well as in vivo in a mouse model and in humans. Hence, those experiments can be translated to the ex vivo determination of circulating EPC, particularly with flow cytometry, which is, at this time, the only and most validated method for EPC measurement. In the cardiovascular high-risk patients of our study, CD133+ cells might be upregulated because of the increased endothelial dysfunction. Hence, these increased CD133+ cell counts might allow to detect associations of CD133+ cells with target variables more reliably. In contrast, consumption of CD34+ cells into vascular lesion areas in these patients might result in decreased cell counts without the opportunity to detect distinct differences in our study population.

Fadini et al. criticize that EPC, in our study, was not further differentiated. We agree with this suggestion, but when the study was performed, detailed information about differentiation in CD133+/CD34+ or CD133+/CD34− cells were not yet available. Thus, we further agree with the conclusion of Fadini et al. that consensus on EPC definition and evaluation is needed.

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Acute coronary syndromes, response to clopidogrel, and worsened cardiovascular outcomes: the hen and the egg dilemma

I enjoyed reading the quality paper by Geisler et al. that tried to link low response to clopidogrel with the incidence of major cardiovascular events and death in a broad spectrum of post-stent patients. The team should be acknowledged for the effort, clean data, and the realistic assessment of the frequency of low response (5.8%) after loading with 600 mg clopidogrel. The major home-take message the authors try to deliver to the readership is that at 3 months after stenting the incidence of death and AMI was higher in the low clopidogrel responders. However, such conclusions are not fully supported by the presented evidence, and deserve at least some clarification, and/or adjustment.

The major limitation of the index analysis is the fact that almost all of the low responders (81.8%, or 18 out of 22 patients) underwent emergency revascularization, whereas only the minority (43.1%, or 147 out of 341 average responders) experienced acute coronary event (Table 1). In contrast, the majority of patients from the control group was subjected to the elective angioplasty and stenting, and did not suffer an acute event at the time of intervention. In short, low response cohort was not stable, experienced more myocardial damage, and probably worsened outcomes even before clopidogrel therapy. How fair and balanced is to declare low response to clopidogrel as a major risk factor to such harmful association remains to be seen, especially when patients were already at higher risk, and platelet glycoprotein IIb/IIIa inhibitors were not allowed. Although ISAR-REACT 2 trial revealed that addition of abciximab to 600 mg loading with clopidogrel improves cardiovascular outcomes in the troponin-elevated ACS patients, the index patients were deliberately denied the benefit, substantially limiting the practical value of the study. Obviously, the thrombotic burden in some patients with ACS exceeds the ability of even high dose loading with clopidogrel to prevent secondary events. However, it is not reasonable to generalize such clinical scenario, and blame clopidogrel’s low response for recurrent events, especially acknowledging that no-load 75 mg clopidogrel saved 119 lives and provided an absolute mortality benefit after AMI in the COMMIT trial.

Another critical baseline difference in the index study is the 14.6% less use of statins in the low responders group with highly significant (P = 0.001) hyperlipidaemia when compared with the average responders. Recent meta-analysis of 13 trials with almost 18 000 patients strongly suggests that statins reduce death and cardiovascular events after 4 months of treatment in ACS patients.

There are also certain shortcomings of the study design that limit our ability to adequately interpret the platelet data. Although the definition of low response, and lack of baseline platelet function assessment are questionable, but still acceptable, random non-pre-specified sample collection times cannot be advocated. Indeed, the single platelet test was performed after at least 6 h after clopidogrel loading, but with the broad mean of 34.8 ± 25.9 h after stenting. In common terms, it means that some patients were already treated with the maintenance clopidogrel dose for 1 or 2 days, and the data analysis should be adjusted accordingly. This is especially important because platelet activity after acute thrombotic events is not consistent, nor unchanged, but rather undergoing phasic changes, which in turn are dependent on the success of reperfusion. Therefore, single platelet aggregation test done randomly, not at the pre-specified time point after coronary intervention, may be