Recent Transient Ischemic Attack or Ischemic Stroke (MATCH) trial also raises serious concerns about the safety of combining aspirin and clopidogrel long-term. In MATCH, clopidogrel and aspirin (n = 3797) were compared with clopidogrel alone (n = 3802) after an ischaemic stroke or transient ischaemic attack. There was a non-significant 0.73% absolute risk reduction in the composite of cardiovascular death, myocardial infarction or ischaemic stroke during 18 months of follow-up in patients receiving both aspirin and clopidogrel, compared with those receiving clopidogrel only. However, the absolute risk of life-threatening or major bleedings increased by 2.6% in patients who were given both aspirin and clopidogrel (p < 0.001). Accordingly, the number needed to harm was only around 38.

Obviously, further study is needed to determine the risks and benefits of combining aspirin and clopidogrel for more than a few months in patients with atherothrombotic disease, including those receiving a drug-eluting stent. Remember Voltaire’s bright reflection: “The best may be the enemy of the good”.

References

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Cardiovascular disease, periodontitis, and the monocyte relationship

To the Editor

One investigative approach to linking periodontal disease to atherosclerotic cardiovascular disorders is demonstrating a shared risk factor with the potential for actually mediating cardiovascular disease. In this regard, the Buhlin et al., report comparing cardiovascular risk factors between patients with severe periodontal disease (without known history of cardiovascular disorders) and healthy individuals suggests discovery of an important relationship. Their meticulous and innovative investigation discloses that a unique haematological index, the peripheral blood monocyte count, associates strongly with severe periodontal disease. Yet the investigators dismiss any potential for clinical relevance of this finding on the stated ground that the monocyte levels were within the “normal” range, and consequently they excluded this variable from their reported multivariable models and analyses.

The discovery of novel risk factors in exploratory studies like the Buhlin study requires entertaining scenarios beyond the entrenched paradigms. Moreover, several bases do exist to support an inference that peripheral blood monocyte indices, within today’s reference range, may in fact operate to confer substantial cardiovascular disease risk. The true healthy range for peripheral blood monocyte levels vis-à-vis cardiovascular disease is not known. This conundrum persists because an appropriate reference population cannot be constituted. Present day technology does not enable physicians to validate the absence of underlying atherosclerosis. Therefore the statistical approach used today to define the reference range, for example, as two standard deviations above and below the mean is problematic in that it relies on a group of apparently healthy individuals. However a more meaningful approach, defining abnormal values as those associated with adverse physiological or clinical consequences, is feasible. Several initial developments in this direction are reported. First, the available longitudinal epidemiological studies indicate that minor increments in monocyte counts and proportions (that fall well within their reference ranges) do convey long-range predictive value for clinical cardiovascular disease and mortality. Second, the available longitudinal clinical imaging studies show that minor incremental differences in monocyte counts or proportions within today’s reference range associate with near-term augmentation in rates of atherosclerotic vascular lesion progressions. The putative atherogenic effect of circulating monocytes manifests at native lesions in non-manipulated arteries as well as at iatrogenically triggered lesions such as restenosis after angioplasty or endovascular stent placement.

In summary, this cumulative evidence enables the conclusion that it is both valid scientifically and clinically relevant for investigators to pursue evaluating monocyte levels in future risk factor analyses of cardiovascular disease. This logic is germane to the aim of the Buhlin study seeking to identify independent risk factors for periodontal disease that might be shared with cardiovascular diseases. Therefore the inclusion of peripheral blood monocyte indices (absolute count and relative proportion) as variables into their multivariate models is warranted. This more comprehensive modelling might also serve to illuminate interactions between circulating monocytes and the inflammatory mediators and biomarkers discussed (e.g., C-reactive protein, TNF-α receptor 1, IL-6), where such physiological relationships in vivo have yet to be articulated.

References
To the Editor

specific conclusions in our published article we felt unable to draw any

Given these equivocal findings and the lack of significant differences in monocyte counts be observed in this study, then we would, in light of Dr. Otis and her colleagues' suggestion, certainly re-evaluate the relationship between monocyte counts and the risk of CVD, particularly in individuals with periodontitis.

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Cardiovascular disease, periodontitis and the monocyte relationship: Reply

To the Editor

Dr. Otis and her colleagues raise an important and interesting issue regarding our recently observed association between elevated monocyte counts and periodontitis,1 given the potential influence of monocytes on the development and progression of cardiovascular disease (CVD). As they state, studies have reported a relationship between circulating monocyte numbers and the risk of developing CVD,2-3 and increased monocyte activity is known to play a role in the restenosis process.4-5 However, data on increased monocyte counts in subjects with periodontitis are inconclusive, as a Dutch study has found no significant differences in monocyte counts between patients with periodontitis and controls. In fact, in this study monocyte counts tended to be higher in the control group (0.48 × 10^3/L vs. 0.46 × 10^3/L).6

Given these equivocal findings and the limited amount of data that are available in this area we felt unable to draw any specific conclusions in our published study.7 Our finding that monocyte counts are elevated in individuals with periodontitis could be circumstantial and the validity of this finding must be tested in larger studies.

The observed relationships between oral health, particularly periodontitis, and general health are intriguing, however much remains unknown. Our findings1 indicate a potential link between the periodontitis and CVD, and provide a possible explanation for the nature of this association. However, CVD is a complex, multifactorial group of diseases and further studies are clearly warranted. We are currently undertaking a larger intervention study, the aim of which is to assess whether treatment of periodontal disease reduces the levels of serological markers of CVD risk. Should differences/changes in monocyte counts be observed in this study, then we would, in light of Dr. Otis and her colleagues' suggestion, certainly re-evaluate the relationship between monocyte counts and the risk of CVD, particularly in individuals with periodontitis.

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Direct epicardial mapping predicts the recovery of left ventricular dysfunction in chronic ischaemic myocardium

We read with interest the article of Vahlhau et al.,1 concerning epicardial mapping to predict the recovery of left ventricular dysfunction in chronic ischaemic myocardium. This study has been based on bi-polar voltage mapping criteria during surgery for the diagnosis of myocardial hibernation.

The authors report that there is a great overlap between groups of viable and non-viable myocardial segments found in a grey zone of 5.4–12.3 mV. They also state that the data provided by their study is obviously obtained too late to help in pre-operative decision making, but that bi-polar voltage may be useful to understand the pathophysiology of chronic ischaemic dysfunction. They also admit that it is not the aim of the present study to implement direct electrical mapping for clinical use.

Our criticism of this study is that their method was different from that generally used for electromechanical mapping, namely the combined bi-polar voltage criteria and local linear shortening.2 The recognition of myocardial viability should be based not only on voltage measurement (electrical reserve) but also on local linear shortening (contractility reserve). The method advocated in clinical use is the endocardial electromechanical NOGA mapping (Biosens Webster Cordis, Johnson Johnson, Diamond Bar, CA, USA). The NOGA segmental quantitative analysis is performed after transformation of the three dimensional map into a polar map, with 12 segments from the apical, the mid and basal location. Myocardial viability is present when the voltage is more than 6 mV (Nle value of 15 mV) and linear shortening is more than 7% (Nle value of 15 mV) and local linear shortening is more than 5.4–12.3 mV. They also state that the data provided by their study is obviously obtained too late to help in pre-operative decision making, but that bi-polar voltage may be useful to understand the pathophysiology of chronic ischaemic dysfunction. They also admit that it is not the aim of the present study to implement direct electrical mapping for clinical use.

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