Letter to the Editor

Nitrate-Induced Headache May Have Confounding Factors

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Dear Editor

We have read the article of Erkan et al. entitled 'Relationship between nitrate-induced headache and coronary artery lesion complexity' [1] with great interest. The authors concluded that nitrate-induced headache (NIH) was inversely associated with the SYNTAX score which identified the complexity of coronary artery disease.

Indeed, the clinical application of the SYNTAX score has been widening. It was basically developed to guide the cardiologists to decide the revascularization option: coronary artery bypass grafting or percutaneous coronary intervention [2]. Moreover, the SYNTAX score system has been upgraded by the addition of various clinical variables (age, creatinine clearance, and left ventricle ejection fraction) or invasive parameters (such as fractional flow reserve), and the clinical SYNTAX score, logistic clinical SYNTAX score, SYNTAX score II, and functional SYNTAX score were developed. Since the SYNTAX score is derived from numerous parameters such as dominance, number of lesions, segments involved per lesion, lesion characteristics, total occlusion (number of segments involved, age of total occlusion, blunt stump, bridging collaterals, side branch involvement), trifurcation (number of diseased segments), bifurcation (type, angulation between distal main vessel and side branch), aorto-ostial lesion, severe tortuosity, length >20 mm, thrombus, or diffuse disease/small vessels (number of diffuse disease/small vessels) [3], the authors could have described those parameters and the method of SYNTAX score calculation in the Material and Method section. Additionally, which types or characteristics of lesions predominated and were associated with the absence of NIH could have been presented. Additionally Gensini and CASS scoring systems are the most widely used angiographic coronary artery disease burden scoring systems and correlated better with the intravascular ultrasound plaque burden than the SYNTAX score [4]. This issue could have been stated in the Discussion.

Additionally, since vasodilatory effects of nitrates may be blunted by the volume expansion and activated renin-angiotensin-aldosterone system due to heart failure [5], whether patients with heart failure or lower ejection fraction were excluded from the study or not should be stated in the study. Since carotid artery disease or peripheral artery disease is accompanied with endothelial dysfunction [6] and can influence NIH, the presence of overt or subclinical carotid atherosclerosis in patients with higher SYNTAX scores could have been discussed as a confounding factor for irresponsiveness to nitrate.

At last NIH can be used as a clinical variable to predict the complexity or burden of coronary atherosclerosis in patients with stable angina pectoris. However, it should not be used as a test method in patients with acute coronary syndrome, because new onset angina could have been developed due to a thrombotic lesion on a fissured or ruptured non-critically stenotic coronary artery plaque located at a single coronary artery or only at one arterial segment.

In conclusion, the relationship of NIH and features of coronary atherosclerosis has many confounding factors and may be influenced by many clinical and pathophysiological factors. Furthermore, the results are promising and may be used to provide a novel clinical tool if it is developed or integrated in a scoring system.

Editor's Note

The corresponding author of 'Relationship between nitrate-induced headache and coronary artery lesion complexity' was invited to respond to this letter but he declined to do so.

References

1 Erkan H, Kırış G, Korkmaz L, et al: Relationship between nitrate-induced headache and coronary artery lesion complexity. Med Princ Pract 2015; 24:560–564.
2 Farooq V, Head SJ, Kappetein AP, et al: Widening clinical applications of the SYNTAX score. Heart 2014;100:276–287.
3 Metzler B, Winkler B: SYNTAX, STS and EuroSCORE – how good are they for risk estimation in atherosclerotic heart disease? Thromb Haemost 2012;108:1065–1071.
4 Neeland IJ, Patel RS, Eshtehardi P, et al: Coronary angiographic scoring systems: an evaluation of their equivalence and validity. Am Heart J 2012; 164:547–552.
5 Sivri N, Tekin G, Erbay AR, et al: Headache response to nitrate in patients with coronary artery disease and systolic heart failure. Int J Cardiol 2012; 26:158:453–454.
6 Chan SY, Mancini GB, Kuramoto L, et al: The prognostic importance of endothelial dysfunction and carotid atheroma burden in patients with coronary artery disease. J Am Coll Cardiol 2003;42:1037–1043.

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