

The real question isn't whether Inclisiran reduces LDL cholesterol - but whether Inclisiran reduces coronary artery disease. Re: UK deal over inclisiran

The real answer about the benefit of Inclisiran, or any lipid-lowering drug - or for that matter any dietary recommendation(s) made for LowCarb-Keto, Vegan, AHA or other dietary proposals – isn't whether the drug or diet lowers LDL cholesterol or triglyceride levels, or increases HDL cholesterol levels, or lowers CRP.

The real question to be answered is whether these drugs or diets have an impact at the tissue level – i.e. the coronary arteries; where the inflammatory process impairs coronary blood flow [1] eventually resulting in angina [2] and ultimately myocardial infarction and death.

More than two decades after first presenting the "Inflammation and Heart Disease" and "Angina" Theories [1-4], the discussion of the treatment of coronary artery disease continues to revolve around blood tests and weight loss. When the expected or desired changes in blood tests do not occur, purported pundits merely declare that cholesterol and saturated fat are a myth – demonstrating either a complete lack of understanding of the Inflammation Theory itself [3] or a failure to actually read it. Reminding us of the adage "I can teach it to you but I cannot understand it for you."

Mere measurement of these blood tests is only mildly to moderately "correlated" with actual changes in coronary artery disease (CAD) itself [5], and the resulting change in physiologic function [1] responsible for the symptomatic development of angina [1-4].

We would agree that a well designed study on the effect of Inclisiran – or again any drug or diet, which proposes that the impact of the drug or diet on CAD is a reduction in CAD – is needed. Such a study; however, must quantify the effect upon the coronary arteries themselves [6,7] and not merely look at blood tests, changes in weight or some qualitative interpretation [7,8]. Anything less is merely guesstimating [7].

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Richard M Fleming

Physicist-Cardiologist

Matthew R Fleming, BS, NRP (FHHI-OI-Camelot); Tapan K. Chaudhuri, MD (Eastern Virginia Medical School) FHHI-OI-Camelot
Los Angeles, CA

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References:

1. Fleming RM. Chapter 29. Atherosclerosis: Understanding the relationship between coronary artery disease and stenosis flow reserve. Textbook of Angiology. John C. Chang Editor, Springer-Verlag, New York, NY. 1999. pp. 381-387.
2. Fleming RM., Boyd L., Forster M. Angina is Caused by Regional Blood Flow Differences - Proof of a Physiologic (Not Anatomic) Narrowing, Joint Session of the European Society of Cardiology and the American College of Cardiology, Annual American College of Cardiology Scientific Sessions, Anaheim, California, USA, 12 March 2000, 49th (Placed on internet www.prousonline.com for physician training and CME credit, April 2000.)
3. Fleming RM. Chapter 64. The Pathogenesis of Vascular Disease. Textbook of Angiology. John C. Chang Editor, Springer-Verlag New York, NY. 1999, pp. 787-798.
4. Fleming RM. Angina and coronary Ischemia are the result of coronary regional Blood Flow Differences. J Amer Coll Angiol 2003;1:127-42.
5. Fleming RM, Harrington GM. What is the Relationship between Myocardial Perfusion Imaging and Coronary Artery Disease Risk Factors and Markers of Inflammation? Angiology 2008;59:16-25.
6. The Fleming Method for Tissue and Vascular Differentiation and Metabolism (FMTVDM) using same state single or sequential quantification comparisons. Patent Number 9566037. Issued 02/14/2017.
7. Fleming RM, Fleming MR, Dooley WC, Chaudhuri TK. Invited Editorial. The Importance of Differentiating Between Qualitative, Semi-Quantitative and Quantitative Imaging – Close Only Counts in Horseshoes. Eur J Nucl Med Mol Imaging. DOI:10.1007/s00259-019-04668-y. Published online 17 January 2020 <https://link.springer.com/article/10.1007/s00259-019-04668-y>
8. Fleming RM., Kirkeeide RL, Smalling RW, Gould KL. Patterns in Visual Interpretation of Coronary Arteriograms as Detected by Quantitative Coronary Arteriography. J Am Coll. Cardiol. 1991;18:945- 951.

Competing interests: FMTVDM is issued to first author. First author, authored the "Inflammation and Heart Disease" and "Angina" Theories.