Reviewer's report

Title: Epicardial adipose excision slows the progression of porcine coronary atherosclerosis.

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Reviewer: Gianluca Iacobellis

Reviewer's report:

This is an interest experimental study with a very complex design. Authors sought to address a key topic, such whether and how epicardial fat plays a direct role in CAD.

I appreciate the aim and the complexity of the study.

Authors suggest selective resection of coronary epicardial fat to improve or prevent the progression of CAD.

My major concern is how and whether we may translate this experimental data obtained from experimental pigs to humans.

LDL (>500 mg/dl) and Glucose levels (peaks of 800 mg/dl) from the pigs that were fed with an atherogenic diet were incredibly high and uncommonly high for humans.

This animal model may not apply to patients, even those with poor lipid and glucose profile.

The finding that LAD segment underneath the adipectomy did not increase (actually there was not statistically difference between before and after adipectomy) is of potential interest. However, it is not sufficient to conclude that selective coronary epicardial fat surgical removal may help in reducing CAD progression and should be therefore implemented.

Although it is certainly accurate, IVUS may underestimate the total calcified plaque cross-sectional area by 40%. Also IVUS is unable to detect plaque inflammation which is a key factor in complications of atherosclerotic plaques.

Whilst this study may provide some interesting insights in understanding the pathophysiological role of segmental epicardial fat in causing segmental CAD, I do not see a clinical application.

Should we recommend cardiac surgery and then coronary adipectomy in our high risk patients? If we would perform this procedure in patients routine undergoing cardiac surgery for established CAD, this may be considered secondary prevention. However, we would need much more solid evidences than just a no statistically significant difference.

I would certainly suggest clinical interventions targeting the epicardial fat and
aiming to reduce its size and revert it to its physiological role rather than completely remove it.

Epicardial fat has physiological and protective effects to the coronary arteries. Its surgical resection may cause important mechanical changes to the underlying coronary arteries.

Finally, several studies performed in humans showed the effect of weight loss interventions on epicardial fat and the consequent improvement in cardiac and metabolic profile following epicardial fat reduction. These studies are not or only minimally cited by the authors.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I have no conflict of interest