Can Imaging Improve Our Understanding of Cardiovascular Pathophysiology?

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Recent advances in noninvasive imaging technology now allow us to simultaneously investigate cardiovascular anatomy, soft tissue characteristics, and disease activity as pathological processes occur in the body. Moreover, this can be performed at different anatomical locations so that the interaction between different organ systems can be interrogated. This offers us a powerful tool with which to improve our understanding of the mechanisms underlying cardiovascular disease and the adverse events that ensue.

See Article by Figueroa et al

This is the focus of the article by Figueroa et al in this issue of Circulation: Cardiovascular Imaging, where the authors have used both anatomic computed tomography assessments and positron emission tomography (PET) measures of disease activity to investigate the relationship between visceral adiposity, vascular inflammation, and cardiovascular events. Recently, the view on adipose visceral tissue has evolved from a passive lipid storage compartment toward an active endocrine organ able to secrete large amounts of bioactive factors and proinflammatory cytokines, which might play a role in the progression of atherosclerosis. The current study is therefore both timely and of clinical relevance, especially given the worldwide epidemic in obesity rates and the acceptance that obesity represents a major modifiable risk factor for coronary artery disease.

The strength and originality of this work is that the authors have tested their hypothesis in a large cohort of >400 patients imaged with 18F-fluorodeoxyglucose (FDG) PET with a median follow-up of 4 years for the development of cardiovascular events. This builds on this research group’s extensive experience and expertise in evaluating vascular inflammation with FDG-PET that has provided a series of key pathological insights. Ultimately, they have here demonstrated that computed tomography measures of visceral fat demonstrate an association with vascular inflammation (the modest correlation is perhaps not unexpected given the multitude of factors with proinflammatory effects) and that patients with a combination of both elevated visceral fat and vascular inflammation have an increased rate of subsequent vascular events. Importantly, the imaging assessment of visceral fat provided incremental information to simpler and cheaper assessments, such as the body mass index, which did not demonstrate the same associations and predictive capability. This therefore adds credence to the growing argument that visceral fat is an important player in the progression of systemic atherosclerosis and worthy of study beyond more generalized measures of systemic adiposity. Moreover, it adds support to the expanding body of evidence, indicating that assessments of vascular inflammation with 18F-FDG are of prognostic value. The authors are to be congratulated on these 2 important additions to the literature.

Although such retrospective studies are of undoubted value in establishing potential pathological associations, there are limitations to the conclusions they allow us to draw. For example, the correlation between visceral adiposity and vascular inflammation cannot establish causality. Therefore, although it is interesting to speculate that visceral fat directly secretes factors that promote vascular inflammation, progression, and adverse events, this conclusion cannot be established directly from this data. Moreover, as the authors clearly acknowledge, the study of cancer patients will always be prone to referral bias, limiting generalizability. The major value of these retrospective observational data is therefore in generating novel hypotheses to then be tested in prospective and definitive mechanistic studies.

The design of definitive mechanistic imaging studies is challenging and has been limited by concerns regarding the radiation exposure associated with multiple time-point studies. Perhaps, the best model focuses on imaging a chosen parameter both before and after an intervention, allowing the effect of that intercession to be assessed in isolation. Indeed, this approach has been used by the authors’ research group and others to investigate the impact of drug therapy on atherosclerotic plaque anatomy and activity. Statins, for example, have been demonstrated to reduce both carotid atherosclerotic plaque burden and plaque composition on magnetic resonance (MR), as well as reducing vascular 18F-FDG uptake on PET. Other medications, such as cholesterol ester transfer protein inhibitors, have by comparison failed to reduce 18F-FDG activity mirroring the similarly disappointing effects of these drugs on clinical outcomes. The recent emergence of hybrid PET/MR systems offers major potential in this field, allowing combined, detailed assessment of large vessel plaque burden (MR), composition (MR), and activity (PET) at radiation doses considerably lower than possible...
with PET/computed tomography (3–4 mSv per scan). As a consequence, multiple time-point studies become feasible. How could this technology be used to build on the important study by Figueroa et al and further investigate the relationship between visceral fat and atherosclerosis? One possibility would be to image patients before and after gastric banding. This operation results in major weight loss in patients with obesity; of both MR11 and PET12 assessments, few patients would be required to demonstrate an effect, and depending on the timing of the scans, valuable insights might be gained into both the acute effects of surgery and the long-term effects of weight loss on systemic atherosclerosis. Large bore scanners would be preferential as ultimately would more specific markers of vascular inflammation than 18F-FDG. Moreover, it would be interesting to compare the activity of visceral fat with brown fat, the metabolic activity of which has also been studied using PET/18F-FDG activity. Given the excellent reproducibility of both MR11 and PET12 assessments, few patients would be required to demonstrate an effect, and depending on the timing of the scans, valuable insights might be gained into both the acute effects of surgery and the long-term effects of weight loss on systemic atherosclerosis. Large bore scanners would be preferential as ultimately would more specific markers of vascular inflammation than 18F-FDG. Moreover, it would be interesting to compare the activity of visceral fat with brown fat, the metabolic activity of which has also been studied using 18F-FDG. As we enter a new era of powerful noninvasive molecular imaging, the availability of imaging systems will increase as will the range of tracers at our disposal, costs will come down, and the scope for such studies will expand. There is therefore real excitement that noninvasive imaging can greatly contribute to our future understanding of cardiovascular disease in humans.

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None.

References

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