Arteriosclerosis, Thrombosis, and Vascular Biology

BRIEF REVIEW

Recent Advances in Vascular Imaging

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ABSTRACT: Recent advances in vascular imaging have enabled us to uncover the underlying mechanisms of vascular diseases both ex vivo and in vivo. In the past decade, efforts have been made to establish various methodologies for evaluation of atherosclerotic plaque progression and vascular inflammatory changes in addition to biomarkers and clinical manifestations. Several recent publications in *Arteriosclerosis, Thrombosis, and Vascular Biology* highlighted the essential roles of in vivo and ex vivo vascular imaging, including magnetic resonance image, computed tomography, positron emission tomography/scintigraphy, ultrasonography, intravascular ultrasound, and most recently, optical coherence tomography, all of which can be used in bench and clinical studies at relative ease. With new methods proposed in several landmark studies, these clinically available imaging modalities will be used in the near future. Moreover, future development of intravascular imaging modalities, such as optical coherence tomography–intravascular ultrasound, optical coherence tomography–near-infrared autofluorescence, polarized-sensitive optical coherence tomography, and micro-optical coherence tomography, are anticipated for better management of patients with cardiovascular disease. In this review article, we will overview recent advances in vascular imaging and ongoing works for future developments.

Key Words: biomarkers ■ cardiovascular disease ■ magnetic resonance imaging ■ positron emission tomography ■ tomography

Recent advances in vascular imaging have enabled us to uncover the underlying mechanisms of vascular diseases both ex vivo and in vivo. In the last decade, efforts have been made to establish various methodologies for evaluation of atherosclerotic plaque progression and vascular inflammatory changes in addition to other biomarkers and clinical manifestations.[1] A number of recent publications in *Arteriosclerosis, Thrombosis, and Vascular Biology* highlighted the essential roles of in vivo and ex vivo vascular imaging, including magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET)/scintigraphy, ultrasonography, intravascular ultrasound (IVUS), and most recently, optical coherence tomography (OCT), all of which can be used in experimental and clinical studies. In this review article, we will review recent advances in vascular imaging and ongoing works for future developments from bench to bedside with a special emphasis given to recent publications in the Journal.

VASCULAR IMAGING (BASIC STUDIES)

Clinical studies that focused on the important roles of vascular imaging have increased its importance when extrapolating the findings from bench to bedside.[2–4] The challenge to develop a novel imaging approach always commences with basic studies so that the proposed approach can be well validated for future clinical use. We here overview some of landmark basic studies that depict the usefulness of conventional or novel approaches of vascular imaging.

Vasculature

Currently available MRI methods in cardiovascular field are hampered by insufficient predictive power to guide the individual patient needs.[2] Using albumin-based dynamic contrast-enhanced (DCE) cardiac MRI,[5] Leenders et al[6] examined how pleiotropic effects of statins impact on modulating vascular permeability due to endothelial dysfunction after myocardial infarction (MI) in C57BL/6, atherosclerotic ApoE$^{-/-}$ mice and statin-treated ApoE$^{-/-}$ mice. The albumin-based MRI technique allowed to measure healing processes after MI in mice in vivo and to assess vascular permeability when permeability surface area product or slope of concentration curve was normalized to

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For Sources of Funding and Disclosures, see page xxx.

Arterioscler Thromb Vasc Biol is available at www.ahajournals.org/journal/atvb

Nonstandard Abbreviations and Acronyms

CAD	coronary artery disease
CARE-II	Chinese Atherosclerosis Risk Evaluation
CCR2	C-C chemokine receptor type 2
CX_3CR1	C-X_3-C chemokine receptor 1
DCE	dynamic contrast-enhanced
DOTA	1,4,7,10-[tetraazacyclododecane-1,4,7,10-tetraacetic acid]-ECL1i [extracellular loop 1 inverso]
EDH	Endothelium-dependent hyperpolarization
FH	familial hypercholesterolemia
ISCHEMIA	International Study of Comparative Health Effectiveness With Medical and Invasive Approaches
JAM-A	junctional adhesion molecule A
LDL-C	low-density lipoprotein-cholesterol
MI	myocardial infarction
MVA	microvascular angina
NIRS	near-infrared spectroscopy
PVAT	perivascular adipose tissue
SEM	scanning electron microscopy
TG2	two transglutaminase isoenzymes
VSA	vasospastic angina

blood concentration per minute. Vascular permeability expressed as permeability surface area product was significantly increased in ApoE$^{-/-}$ mice after MI as compared with C57BL/6 mice at day 3 (inflammatory phase), which was associated with left ventricular dilatation assessed by MRI volumetric analysis at day 21 (reparative phase). In contrast, hyperpermeability was ameliorated in statin-treated ApoE$^{-/-}$ mice. Tissue analysis showed that increased vascular permeability in ApoE$^{-/-}$ mice permitted invasion of leukocytes and inflammatory monocytes, which were also reversed with statin treatment. These results indicate that DCE-MRI for permeability mapping could help early prediction of high-risk MI patients who are developing heart failure. The approach with DCE-MRI was also chosen for a study focused on the roles of tissue TG2 (two transglutaminase isoenzyme) and Factor XIII that are essential in regulating vascular permeability and maternal angiogenesis during early pregnancy in mice.[7] DCE-MRI was helpful to measure vascular permeability expressed by permeability surface area and vessel densities defined as the volume fraction inside the capillary bed (fraction blood volume)[8] in mice carrying transgenic embryonic trophoblast cells with overexpression of TG2 or FXIII. Regarding alternative method for assessing endothelial function, Curaj et al[9] introduced JAM-A (junctional adhesion molecule A) as a target for molecular ultrasound imaging of early endothelial dysregulation under acute blood flow variations. JAM-A-targeted poly(n-butyl cyanoacrylate) microbubbles (JAM-A targeted poly(n-butyl cyanoacrylate) microbubbles) were used for a contrast agent for ultrasound imaging and were found to specifically bound to JAM-A on activated endothelium.[10] Thus, JAM-A targeted poly(n-butyl cyanoacrylate) microbubbles were useful to identify the location of vessel area with endothelial dysfunction.

Inflammation

PET has been emerging as a useful tool for evaluating vascular inflammation.[4,11] Li et al[12] examined the dynamic behavior of monocytes and macrophages in a newly developed murine model of cervical aortic arch transplantation. Before the study, the authors had developed the CCR2 (C-C chemokine receptor type 2)-targeted PET imaging with tail vein injection of ^{64}Cu-radiolabeled DOTA-ECL1i (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid-extracellular loop 1 inverso) conjugate that can serially and noninvasively monitor monocyte-related inflammation.[13] Atherosclerotic aortic arch grafts from ApoE$^{-/-}$ donors were transplanted into syngeneic CX_3CR1 (C-X_3-C chemokine receptor 1) GFP (green fluorescent protein) reporter mice and were imaged by intravital 2-photon microscopy and PET.[12] Plaques at the graft showed profound regression after transplantation. Progressive decreases in CX_3CR1^+ monocytic cells or CCR2$^+$ cells were detected on both 2-photon microscopy and PET.[12]

VASCULAR IMAGING (CLINICAL STUDIES)

Magnetic Resonance Imaging

Most of the recent studies using MRI focused on carotid artery morphology in pursuit of its clinical significance.[2,14] Watase et al[15] evaluated atherosclerotic changes at the common carotid artery, bifurcation, and internal carotid artery with MRI in 525 subjects without history of cardiovascular disease. Remodeling pattern at the common carotid artery was characterized by positive remodeling while bifurcation by negative remodeling. The internal carotid artery showed a mixture of positive and negative remodeling patterns. Using MRI for the carotid artery, a cross-sectional, observational, multicenter study of CARE-II (Chinese Atherosclerosis Risk Evaluation) reported that diabetic patients with cerebral ischemic symptoms in anterior cerebral circulation showed more advanced atherosclerotic changes with calcification and lipid-rich necrotic core as compared with nondiabetic patients[16] and that an incomplete circle of the Willis ring was independently associated with intraplaque hemorrhage of carotid atherosclerotic plaques.[17] The authors speculated

that with the absence of the anterior communicating artery, it is difficult to effectively regulate blood pressure in stenotic carotid artery. Augmented blood pressure would then increase the maximum principal stress and occurrence of intraplaque hemorrhage as a consequence of rupture of neovessels. Of note, Hippe et al[18] showed that even after the intensive LDL-C (low-density lipoprotein-cholesterol)–lowering therapy <70 mg/dL, atherosclerotic lesions in the carotid artery on MRI continued to progress, for which lipoprotaein (a), an LDL variant containing apolipoprotein (a), could be an independent predictor.

Computed Tomography

A number of studies with CT or CTA (CT angiography) have been reported for clinical vascular imaging.[3] Kim et al[19] reported that cardiovascular health metrics defined according to the American Heart Association Life Simple 7 factors[20] successfully stratified the risk for 5-year progression of coronary arterial calcium deposition among apparently healthy adults. A CTA study performed by Chiva-Blanch et al[21] quantified circulating extracellular microvesicles in patients with asymptomatic heterozygous familial hypercholesterolemia (FH) by using flow cytometry for annexin V and cell surface–specific antibodies,[22] correlated them with atherosclerotic plaque characterization and Agatston coronary calcium score[23] and plaque composition sum calculations performed by CTA. They found that FH patients with coronary atherosclerotic plaque had higher levels of circulating extracellular microvesicles as compared to those without atherosclerotic plaque. It was indicated that the cluster of platelet-, granulocyte-, neutrophil-, and endothelial-derived circulating extracellular microvesicles had an additive predictive value to the specific risk equation for plaque presence in patients with FH.[21]

Regarding noncardiac CT studies, Gade et al[24] examined the correlation between calcification and intracranial aneurysms obtained during surgery. As opposed to the knowledge for calcification outside the brain, in situ imaging analysis performed with a high-resolution micro-CT showed that ruptured intracranial aneurysms had significantly lower calcification fraction as compared to unruptured ones and only displayed nonatherosclerotic calcifications. This study suggested a different role of calcification between intracranial and coronary atherosclerosis. Another CT study by Parker et al[25] examined morphology and hemodynamics in isolated common iliac artery aneurysms. The study enrolled 23 patients with 25 isolated common iliac artery aneurysms. Computational fluid dynamics were analyzed on CTA, showing that all subjects exhibited abnormal flow. Using hypothetical aorto-iliac geometries in silico with varying abdominal aortic deflection and aortic bifurcation angles, lower wall shear stress at isolated common iliac artery aneurysm was associated with its progression and disruption, whereas altered blood flow could promote abdominal aortic remodeling, with adaptive lateral deflection of the aorta towards the aneurysmal side. Interestingly, Thomas et al[26] showed the association of thoracic aorta calcification with noncardiovascular disease morbidity and mortality. Briefly, highest tertile of thoracic aorta calcification volume was associated with higher risk of noncardiovascular disease mortality (hazard ratio [HR], 1.56 [95% CI, 1.23–1.97]), as well as morbidities of hip fracture (HR, 2.14 [95% CI, 1.03–4.46]), chronic obstructive pulmonary disease (HR, 2.06 [95% CI, 1.29–3.29]), and pneumonia (HR, 1.79 [95% CI, 1.30–2.45]). Importantly, magnitude of noncardiovascular disease risks of thoracic aorta calcification was larger than that for coronary artery calcium.

PET/Scintigraphy

^{18}F-fluorodeoxyglucose (^{18}FDG) PET has been regarded as a useful tool for its ability to precisely evaluate the extent of vascular inflammation in vivo.[4,11] Briefly, FDG enters inside cells predominantly through glucose transporter protein receptors, becomes phosphorylated into FDG-6-phosphate, and accumulates within cells in direct proportion to their metabolic activity.[4] FDG uptake detected by PET reflects the average metabolic activity of cells in the region. Using pig models with coronary adventitial inflammation induced by drug-eluting stents with nonbiocompatible polymers, we performed a histopathologic validation study with ^{18}FDG-PET for perivascular adipose tissue (PVAT) inflammation.[27] First, we obtained ^{18}FDG-PET images of the coronary arteries ex vivo and in vivo. Then, we quantified target-to-background ratio for coronary PVAT by ^{18}FDG-PET, which well correlated with PVAT inflammatory changes in histology. The approach with ^{18}F-sodium fluoride for calcification could identify the culprit lesions of patients with acute coronary syndrome, particularly in areas of growing hydroxyapatite.[28] Raggi et al. explored the potential role of ^{18}F-sodium fluoride for risk stratification in ambulatory patients with diabetes mellitus.[29] In 88 patients with diabetes mellitus, coronary artery plaques with high-^{18}F-sodium fluoride uptake were noted in only 15% of patients, a much lower rate than expected. Thus, the authors concluded that further study with follow-up data is needed to determine whether ^{18}F-sodium fluoride PET/CT is useful for screening high-risk plaques. Plasma levels of ceramides have been emerging as a novel marker associated with major adverse cardiovascular events (MACE) in patients with coronary artery disease (CAD).[30] Mantovani et al[31] reported that plasma levels of ceramides are correlated with post-stress myocardial perfusion scintigraphy, suggesting that plasma levels of ceramides are useful to identify patients with CAD.

Noninvasive Ultrasonography

In recent studies, ultrasonography was applied for noninvasive functional assessment of the peripheral artery.[32] Stein et al[33] used novel processing methods of ultrasound, namely gray level difference statistic-contrast and entropy values, for evaluating subclinical brachial arterial injury in patients with HIV which activities were suppressed with low-dose methotrexate. These arterial texture changes determined by gray level difference statistic-contrast or entropy on ultrasound were inversely correlated with changes in markers of both inflammation ($CD4^+$ T cells) and coagulation (D dimer levels) for cardiovascular risks in patients with HIV. This result indicates favorable changes in arterial texture after treatment with low-dose methotrexate, suggesting the usefulness of advanced arterial ultrasound grayscale analysis as clinical markers. Hashimoto et al[34] reported that carotid flow augmentation index expressed as the ratio of late/early systolic velocity amplitude has a good association with cerebral white matter hyperintensities determined by MRI as compared to aortic pressure augmentation index, a known parameter, indicating microcerebrovascular injury through augmented cerebral flow pulsations. Most recently, we have demonstrated the impairment of endothelial functions in peripheral circulation of patients with vasospastic angina (VSA) or microvascular angina (MVA).[35] Heretofore, our group has revealed that NO plays a dominant role in conduit arteries and endothelium-dependent hyperpolarization in resistance vessels in normal condition.[36,37] In this study,[35] we evaluated endothelium-dependent vasodilatations of the brachial artery to intraarterial infusion of bradykinin before and after oral aspirin and intraarterial infusion of NG-monomethyl-L-arginine by ultrasonography and those of fingertip arterioles by peripheral arterial tonometry in patients with VSA alone, MVA alone, or VSA+MVA. Surprisingly, digital vasodilatations to bradykinin were almost absent in MVA group and VSA+MVA group as compared with those with VSA alone, and NO-mediated and endothelium-dependent hyperpolarization–mediated digital vasodilatations were markedly impaired in patients with MVA alone. In contrast, endothelium-independent vasodilatations to sublingual nitroglycerin were comparable among the 3 groups. These results indicate for the first time that a considerable subset of patients with MVA with impaired microvascular dilatation are complicated with systemic small artery disease affecting both NO-mediated and endothelium-dependent hyperpolarization–mediated vasodilatations.[35]

Intravascular Imaging

Clinically available intravascular imaging includes IVUS[38] and intravascular OCT.[39,40] The former is currently the most widely utilized imaging for guidance of percutaneous coronary intervention. Besides its clinical usefulness, IVUS has also been used for research purposes. Accumulated evidence has suggested that intramural or adventitial inflammatory changes[41–43] or allergic responses[44,45] play important roles in the development of CAD. In a series of basic studies, we demonstrated that chronic adventitial inflammatory changes cause coronary arteriosclerotic lesions where coronary artery spasm can be induced by vascular smooth muscle hypercontraction through Rho-kinase activation.[46–48] Others demonstrated the roles of degranulation of adventitial mast cells in diverse CAD and a link between serum IgE levels and CAD.[44,45,49,50] Wilson et al[51] conducted a clinical IVUS study to examine the relationship between type 2 immunity and IVUS-delineated CAD development, with a special reference to mammalian oligosaccharide α-Gal (galactose-α-1,3-galactose) as a foreign epitope. α-Gal is regularly consumed as glycolipids and a subset of the population has a different type of immune response.[52] This result suggests the association of IgE sensitization to α-Gal with IVUS-derived plaque burden.

With regard to translational study of intravascular imaging, Hoogendoorn et al[53] reported that a pig model of FH with homozygous LDL-receptor R84C mutation showed mild to advanced atherosclerotic coronary arteries delineated by both IVUS and OCT. Pigs with advanced coronary plaques exhibited normal size of LDL that contained more cholesterol than those with mild plaques, whereas larger LDL was also found to contain more sphingosine-1-phosphate, ceramides, and sphingomyelins. Importantly, this was also the case in patients with homozygous FH.[53] Plasma levels of ceramides and sphingomyelins were implicated in the development of CAD[54] and MACE.[30] Since increases in the levels were noted early after the initiation of atherogenic diet, abnormal LDL profile may be a useful biomarker for early detection of atherosclerotic plaque progression.[53] On the basis of the lower, the better theory, the current clinical guidelines for management of dyslipidemia[55] offer more intensive care toward lipid-lowering therapy than ever before, and side by side novel biomarkers to predict future atherosclerosis development are needed. Near-infrared spectroscopy combined with IVUS has been emerging as an intravascular imaging tool for early detection of lipid deposition to the coronary artery with high predictive value for future MACE.[56] Near-infrared spectroscopy–IVUS offers a novel prognostic marker of a lipid core burden index for MACE, which is calculated for the total length of the region of interest and 4 mm segment with the maximum lipid core burden index, is appreciated for the prognostic marker.[56] A recent study demonstrated that Near-infrared spectroscopy–IVUS–derived 4 mm segment with the maximum lipid core burden index >400 is a useful marker for MACE (HR, 3.39 [95% CI, 1.85–6.20]; $P<0.0001$).[57]

OCT excels at an excellent resolution of 10 μm[39,58] that is an order of magnitude higher than IVUS. OCT allows the clear delineation of borders of 3 arterial layers and

the measurement for fibrous cap thickness at the lipid-rich or necrotic core lesions.[59] Kurihara et al[60] correlated OCT-derived thin-capped fibro-atheromatous plaques in stable CAD patients with postprandial lipid profiles. The authors found a marked increase in remnant-like particle cholesterol, Apo CIII, changes in apo B48 during the meal tolerance testing in patients with thin-capped fibro-atheromatous plaques as compared with those without it. Besides its high accuracy for coronary plaque-type categorization and feasibility for coronary intervention, OCT enables to elucidate underlying mechanisms of CAD development by identification of coronary arterial components at nearly cellular levels, such as cholesterol crystals deposition[61] and macrophage infiltrations beneath the surface.[62] Furthermore, we demonstrated the ability of OCT to identify nutrient blood vessels harbored by the coronary adventitia, termed vasa vasorum.[63] Adventitial vasa vasorum is thought to function as a conduit for inflammatory cells and cytokines communicating the outside and inside arterial wall, and internal vasa vasorum arising from the adventitia is likely to disrupt at the necrotic coronary lesions[64] and cause intraplaque hemorrhage, helping rapid plaque progression and occasionally plaque rapture.[65] By referring to the previous study that proposed a role of adventitial vasa vasorum associated with coronary spasm as a trigger of the coronary plaque rapture,[66] it is important to examine the behavior of adventitial vasa vasorum in patients in vivo. With the novel OCT approach, we were able to elucidate the enhanced adventitial vasa vasorum formation in patients with VSA.[67] The usefulness of OCT for elucidating the clinicopathological mechanisms of VSA was also reported by Tanaka et al.[68] They demonstrated that the spastic coronary segments during pharmacological provocation testing were characterized by intimal bump due to thickened medial wall.[68]

The current consensus for the major causes of acute coronary syndrome is that plaque rapture accounts for 44%, plaque erosion 31%, and calcified nodule 8%.[69] In the past few years, much attention has been paid to coronary plaque erosion as a second leading cause of acute coronary syndrome because the erosion has different mechanisms and clinical manifestation from plaque rapture.[70,71] Furthermore, a recent clinical study by Katayama et al. demonstrated that invading cholesterol crystals detected by OCT could be a plausible cause of plaque rupture because of their potential to protrude towards plaque surface.[72] Taken together, OCT appears to have an additive value both in the guidance of percutaneous coronary intervention[73] and clinical research.

FUTURE PERSPECTIVES OF VASCULAR IMAGING

Recently, the ISCHEMIA trial (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) has convincingly demonstrated that coronary revascularization strategy with percutaneous coronary intervention or coronary bypass surgery does not improve long-term prognosis of patients with stable CAD.[74] Also, it was previously demonstrated that diagnostic coronary angiography has low diagnostic yield for estimating myocardial ischemia and future MACE.[75] Thus, it is important to seek more effective approach that can detect myocardial ischemia and predict future MACE. In this regard, DCE-MRI may be attractive as it better corresponds to myocardial ischemia than conventional modalities.[76] Because coronary microvascular dysfunction has been shown to increase mortality rate in several clinical cohorts,[77,78] imaging approaches for coronary microvascular dysfunction may hold promise in the future.

Although thin-capped fibro-atheromatous plaques have been proposed as a rupture-prone morphology feature,[59,79] the resolution of OCT may not be enough for perfect delineation of thin-capped fibro-atheromatous plaques.[80] Thus, it is possible that there are unknown atherosclerotic or vulnerable features in diseased coronary arteries. Further development of imaging modalities should overcome these limitations. For instance, the combination of OCT and IVUS imaging was found to work properly in human coronary atherosclerotic plaque and stented arterial segments in vivo, and will soon be commercially available (Figure).[81] This multimodality imaging approach offers the high resolution of OCT while retaining the deeper penetration advantage of IVUS. OCT combined with near-infrared autofluorescence provides detailed information on intraplaque hemorrhage due to leaky vasa vasorum invading into the necrotic core.[84] One big advantage of OCT–near-infrared autofluorescence is that it requires no exogenous molecular agents and is not be compromised with ethical issues. Recently, Otsuka et al[85] performed a clinical feasibility study with polarization-sensitive OCT for predicting plaque vulnerability by measuring the polarization or depolarization signals from coronary plaques. This study underlined that an increase in depolarization detected by polarization-sensitive OCT was noted in the fibrous cap over the necrotic core region.[85] It is known that coronary endothelium has a thickness of a few μm and that endothelial dysfunction is the first step of atherosclerosis.[82] A new mode of OCT, termed micro-OCT with a 1 to 2 μm spatial resolution, is able to identify the thin layer of endothelium, and by 3-dimensional volume rendering, micro-OCT allowed clear delineation of endothelial pavementing, just like scanned electron microscopy (Figure).[82] Micro-OCT has already been implemented in a catheter-based clinical system,[86] and the micro-OCT catheter would be helpful in pursuit of natural history of coronary atherosclerosis in the very near future (Figure).

In addition to the role of adventitial vasa vasorum, we demonstrated the important roles of other adventitial components, such as sympathetic nervous system, PVAT inflammation, and lymphatic vessels in the pathogenesis of

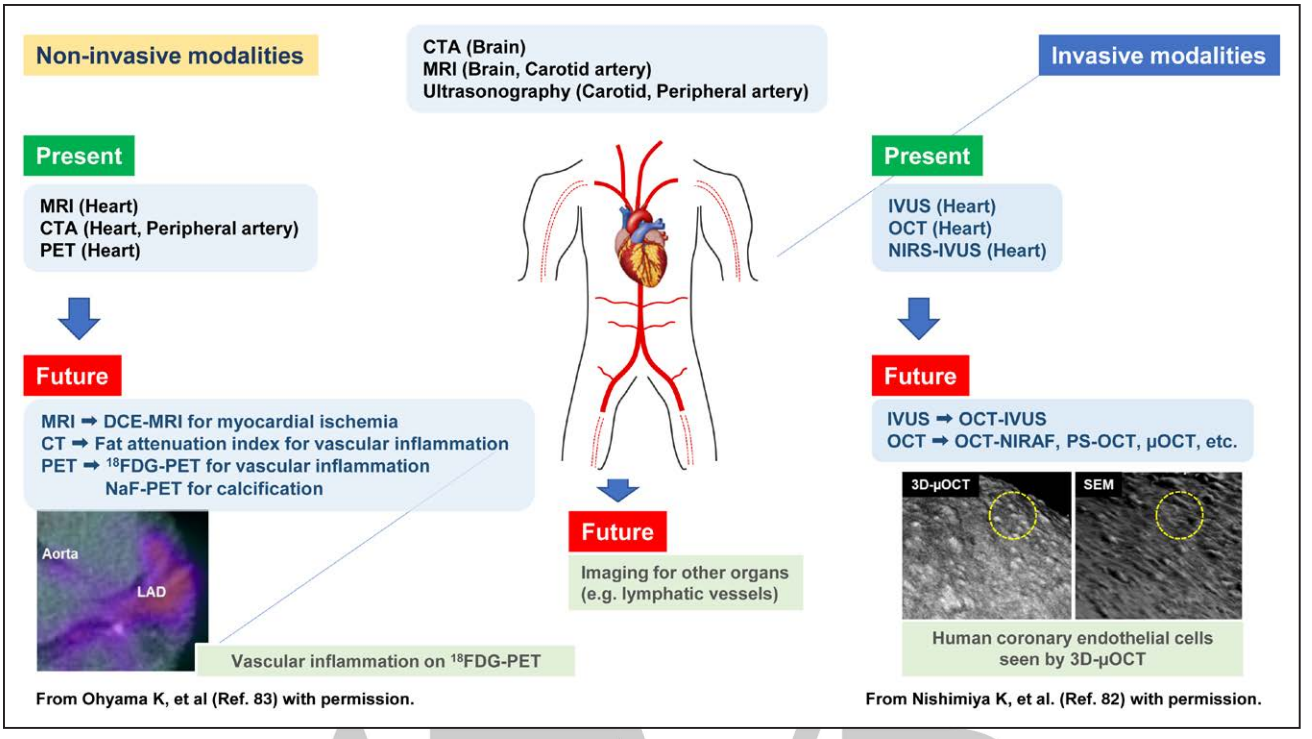

Figure. Current status and future perspectives in vascular imaging.
Currently, both invasive and noninvasive imaging modalities are available for diagnosis and treatment of patients with cardiovascular disease, including magnetic resonance imaging (MRI), computed tomography angiography (CTA), positron emission tomography (PET), ultrasonography, intravascular ultrasound (IVUS), and near-infrared spectroscopy (NIRS)–IVUS. In the near future, several novel modalities will be available, including dynamic contrast-enhanced (DCE)–MRI, optical coherence tomography (OCT)-IVUS, OCT-NIRAF, polarization-sensitive (PS)-OCT, and micro-optical coherence tomography (μOCT). 3D indicates 3-dimensional; ^{18}FDG, ^{18}fluorodeoxyglucose; LAD, left anterior descending coronary artery; NaF, ^{18}F-sodium fluoride; NIRAF, near-infrared autofluorescence; and SEM, scanning electron microscopy. **Left**, Reprinted from Ohyama et al[83] with permission. Copyright ©2019, Elsevier. **Right**, Reprinted from Nishimiya et al[82] with permission. Copyright ©2018, Elsevier.

CAD.[83,87,88] We demonstrated that sympathetic renal denervation therapy ameliorates coronary hyperconstricting responses by inhibiting the inflammatory changes and sympathetic nerve activities in the coronary adventitia through the renal-brain-heart axis after drug-eluting stent implantation in pigs in vivo.[87] In this study, autoradiogram with [^{3}H] rauwolscine, a specific radioligand for α_2-adrenoceptor binding sites, helped revealing the renal-brain-heart axis in the enhanced coronary vasoconstricting responses.[87] Our histopathologic validation study with ^{18}FDG-PET for PVAT inflammation[27] was followed by the perivascular fat attenuation index that can be evaluated by coronary CTA.[89] With the approach of ^{18}FDG-PET, we were able to demonstrate enhanced PVAT inflammation in patients with VSA in vivo (Figure).[83] Finally, we have recently demonstrated that lymphatic vessel dysfunction is associated with adventitial inflammatory changes since inflammatory cells/cytokines drainage through lymphatic vessels was sorely disturbed.[88] In this study, cardiac lymphatic vessels were imaged by the photodynamic eye near-infrared camera system during injection of indocyanine green.[88] In this regard, Karlsen et al[90] developed a PET/CT method for lymph flow assessment in mouse muscles by injecting human serum albumin labeled with ^{124}I into a thigh muscle. However, the roles of lymphatic vessels[91,92] still remain to be fully elucidated. Clinically available imaging technology is warranted for resolving cardiac and systemic lymphatic system.

SUMMARY

The widespread utilization of invasive and noninvasive vascular imaging has opened up a new window for the field of vascular biology in multiple ways. Recent publications in the Journal hold promise to consider the use of commercially available imaging techniques to elucidate underlying mechanisms of diverse vascular diseases in animals and patients in vivo (Figure).[93] Future developments of vascular imaging are anticipated for better management of patients with cardiovascular disease.

ARTICLE INFORMATION

Received May 10, 2020; accepted May 15, 2020.

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Sources of Funding

This work was supported, in part, by the Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology, Tokyo, Japan (16K19384 and 19K17511).

Disclosures

None.

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