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State-of-the-Art Review

Ten things to know about ten imaging studies: A preventive cardiology perspective ("ASPC top ten imaging")

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ABSTRACT

Knowing the patient's current cardiovascular disease (CVD) status, as well as the patient's current and future CVD risk, helps the clinician make more informed patient-centered management recommendations towards the goal of preventing future CVD events. Imaging tests that can assist the clinician with the diagnosis and prognosis of CVD include imaging studies of the heart and vascular system, as well as imaging studies of other body organs applicable to CVD risk. The American Society for Preventive Cardiology (ASPC) has published "Ten Things to Know About Ten Cardiovascular Disease Risk Factors." Similarly, this "ASPC Top Ten Imaging" summarizes ten things to know about ten imaging studies related to assessing CVD and CVD risk, listed in tabular form. The ten imaging studies herein include: (1) coronary artery calcium imaging (CAC), (2) coronary computed tomography angiography (CCTA), (3) cardiac ultrasound (echocardiography), (4) nuclear myocardial perfusion imaging (MPI), (5) cardiac magnetic resonance (CMR), (6) cardiac catheterization [with or without intravascular ultrasound (IVUS) or coronary optical coherence tomography (OCT)], (7) dual x-ray absorptiometry (DXA) body composition, (8) hepatic imaging [ultrasound of liver, vibration-controlled transient elastography (VCTE), CT, MRI proton density fat fraction (PDFF), magnetic resonance spectroscopy (MRS)], (9) peripheral artery / endothelial function imaging (e.g., carotid ultrasound, peripheral doppler imaging, ultrasound flow-mediated dilation, other tests of endothelial function and peripheral vascular imaging) and (10) images of other body organs applicable to preventive cardiology (brain, kidney, ovary). Many cardiologists perform cardiovascular-related imaging. Many non-cardiologists perform applicable non-cardiovascular imaging. Cardiologists and non-cardiologists alike may benefit from a working knowledge of imaging studies applicable to the diagnosis and prognosis of CVD and CVD risk – both important in preventive cardiology.

What is already known about this subject?

- The American Society for Preventive Cardiology (ASPC) has published "Ten Things to Know About Ten Cardiovascular Disease (CVD) Risk Factors," [1,2] which summarizes major CVD risk factors, accompanied by sentinel reviews or guidelines relative to ten important CVD risk factors.
- Assessing existing CVD and CVD risk through imaging is commonly used to stratify CVD risk and influence CVD prevention management. Diagnostic and prognostic imaging studies of the heart and other body organs help clinicians with management decisions to prevent future CVD events.

What are the new findings in this manuscript?

- The "ASPC Top Ten Imaging" summarizes ten things to know about ten important CVD-related imaging studies (listed in a tabular format).
- Non-cardiologists (e.g., primary care physicians, nurse practitioners, physician assistants, gynecologists, endocrinologists, obesity medicine specialists, lipidologists, diabetologists etc.) may benefit from an overview of CVD-related imaging studies commonly performed by cardiologists. Cardiologists may benefit from an overview of imaging studies beyond the heart, but applicable to global preventive cardiology – which are imaging studies often performed by non-cardiologists.

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- In addition to the "Top Ten" things to know about CVD imaging studies, citations are listed in the applicable tables to provide the reader more in-depth resources (e.g., illustrative guidelines and other references) pertaining to each imaging category.

1. Introduction

The intent of the "American Society for Preventive Cardiology (ASPC) Top Ten Imaging" is to help primary care clinicians and cardiology specialists keep up with the ever-increasing pace of diagnostic and prognostic imaging studies applicable to preventive cardiology. Imaging studies focused on the heart are often performed by cardiologists and/or radiologists and help with diagnosis and prognosis. Other imaging studies may also help in CVD risk stratification, and include imaging studies of the peripheral vasculature, body fat, liver, brain, kidney, and ovary. The "ASPC Top Ten Imaging" summarizes ten things to know about ten CVD-related imaging studies, listed in tabular formats. These ten imaging studies include: (1) coronary artery calcium (CAC) imaging and scoring, (2) coronary computed tomography angiography (CCTA), (3) cardiac ultrasound (echocardiography), (4) nuclear myocardial perfusion imaging (MPI), (5) cardiac magnetic resonance (CMR), (6) cardiac catheterization [with or without intravascular ultrasound (IVUS) or coronary optical coherence tomography (OCT)], (7) dual x-ray absorptiometry (DXA) body composition, (8) hepatic imaging [ultrasound of liver, vibration-controlled transient elastography (VCTE), CT, MRI proton density fat fraction (PDFF), magnetic resonance spectroscopy (MRS)], (9) peripheral artery / endothelial function imaging (e.g., carotid ultrasound, peripheral doppler imaging, ultrasound flow-mediated dilation, other tests of endothelial function and peripheral vascular imaging) and (10) images of other body organs applicable to preventive cardiology (brain, kidney, ovary). (Fig. 1)

The intent is not to create a comprehensive discussion of all imaging studies applicable to CVD assessment. Nor is this document intended to be a comprehensive discussion of each imaging study. Rather, the intent is to focus on common imaging studies having implications for preventive cardiology. For a more in-depth discussion of these CVD imaging studies, this "ASPC Top Ten Imaging" provides updated guidelines and other selected references in the applicable tables.

2. Purpose of cardiac imaging

- Cardiac imaging helps assess the degree of CVD, which is important in stratifying current CVD risk and determining management strategies toward preventing future CVD events. CVD risk factor management is often more aggressive and often prioritized to patients most likely to benefit, which often includes those with diagnosed CVD or otherwise at increased CVD risk.
- Cardiac imaging may help further stratify patients at intermediate CVD risk, as otherwise determined by coronary heart disease (CHD) risk scores [1,3].
- Cardiac imaging results may help decide who to treat, what to treat, and when to treat, as well as how aggressively to treat atherosclerotic lesions (e.g., revascularization) and/or CVD risk factors (e.g., dyslipidemia, hypertension, hyperglycemia) – all for the purpose of helping prevent future CVD events.
- Extracardiac images of other body organs such as body composition (android and visceral fat) liver (hepatic fat), brain (cerebral vascular disease), kidney (vascular abnormalities), ovary (polycystic ovarian syndrome) and peripheral vasculature (endothelial dysfunction) can also provide insight regarding other CVD risk factors and need for potential treatment of these CVD risk factors.

3. Appropriate use [4,5]

- The choice of cardiac imaging studies should be based upon established "Appropriate Use" criteria, [4,5] and individual patient presentation.
- Appropriate imaging studies are those where the clinical benefits and value in an individual patient exceed the risk (Reference Chart 1) and cost, through providing clinically meaningful information about CVD and CVD risk, beyond clinical judgment alone.
- Appropriate use of imaging studies includes procedures most likely to provide safe and definitive answers to the diagnostic questions raised, and least likely to prompt further imaging studies and invasive downstream procedures, irrespective of the initial imaging study results. In other words, in the interest of limiting the risks and costs of multiple imaging procedures, the choice of cardiac imaging procedure should focus on which procedure is likely to provide the greatest amount of actionable information applicable to the individual patient, in the safest manner possible.
- Clinicians should be cautious and judicious in cardiac imaging studies in patients at low CVD risk, especially for imaging studies that have low specificity in patients at low CVD risk. Low specificity cardiac imaging in low CVD risk patients may often lead to false positive results. False positive findings on cardiac imaging may needlessly prompt more invasive, more costly, and potentially unnecessary additional testing and/or procedures, resulting in more health risk than benefit.
- Selecting the most appropriate imaging test should take into consideration whether the patient is symptomatic or asymptomatic. Performing cardiac imaging studies with low selectivity in asymptomatic patients at low CVD risk has a higher risk of false positive findings than cardiac imaging studies with high selectivity in symptomatic patients at high CVD risk (Reference Chart 2).
- Procedures having the most robust evidence to support use in screening for coronary artery disease in asymptomatic individuals include family history assessment for premature CVD, CVD risk factor assessment, and CVD and CHD risk scores. [1,24] Additional diagnostic procedures having evidenced-based support in screening asymptomatic individuals include CAC scoring, with some suggestion that carotid artery ultrasound can assist with CVD risk stratification. [24] Little evidence supports the routine clinical use of cardiac resting or stress imaging testing in asymptomatic patients. Possible exceptions (albeit with lower level evidence as noted per guidelines) include coronary CTA among selected, asymptomatic individuals at high CVD risk, or stress electrocardiogram in physically inactive patients at higher CVD risk who plan to start a rigorous physical exercise program. [24]
- The selection of the most appropriate imaging test should be based upon the patient presentation. A common clinical scenario that directly impacts management directed at CVD prevention is the evaluation of chest pain, which typically involves various disease endotypes: (1) angina due to obstructive coronary artery disease (CAD) with fractional flow reserve ≤ 0.80; (2) microvascular angina with coronary flow reserve <2.0 and/or index of microvascular resistance >25); (3) microvascular angina due to small vessel spasm (which can be assessed by intracoronary acetylcholine administration); (4) vasospastic angina due to epicardial coronary spasm (which can be assessed by intracoronary acetylcholine administration); and (5) noncoronary etiology (i.e., patients found to have normal coronary anatomy and normal function via cardiac imaging). [6]
- While "ischemia and no obstructive coronary artery" (INOCA) disease can be assessed by the invasive coronary reactivity tests described above, common noninvasive cardiac imaging studies applicable to coronary microvascular disease include PET, CMR, and echocardiography, with invasive imaging studies including coronary flow reserve via coronary angiography. [7] Similarly, causes of "myocardial infarction with nonobstructive coronary arteries"

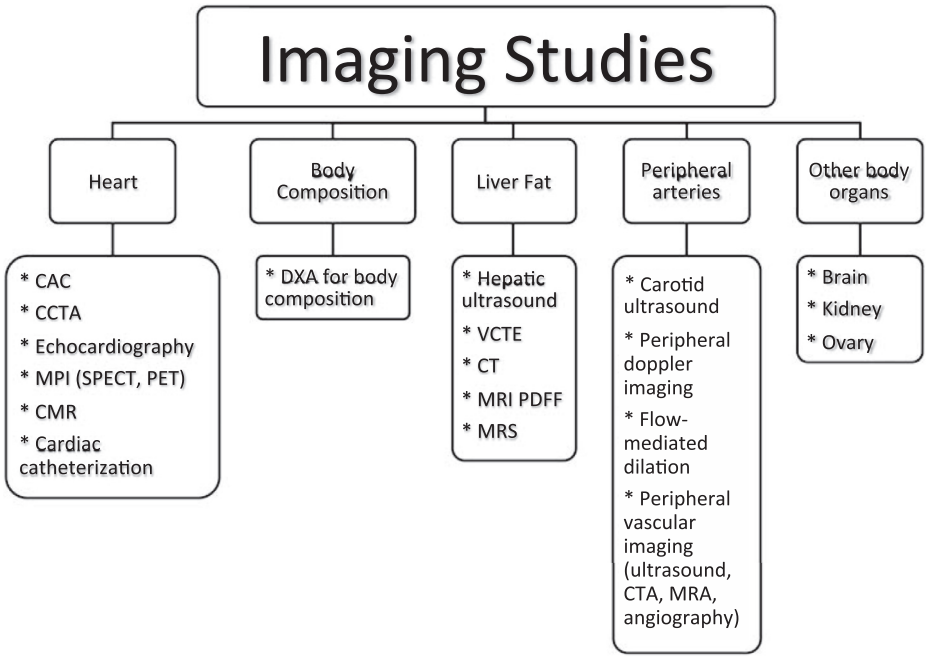

Fig. 1. Cardiac and other organ imaging relevant to preventive cardiology.

CAC = Coronary artery calcium imaging and scoring
CCTA = Coronary computed tomography angiography
CMR = Cardiac magnetic resonance
CT = Computerized tomography
CCTA = Coronary CT angiography
DXA = Dual X-ray absorptiometry
MRA = Magnetic resonance angiography
MPI = Nuclear myocardial perfusion imaging (SPECT, PET, MUGA)
MRI = Magnetic resonance imaging
MRI-PDFF = MRI proton density fat fraction
MRS = Magnetic resonance spectroscopy
MUGA = Multiple-gated acquisition scan
PET = Positron emission tomography
SPECT = Single-photon emission computerized tomography
VCTE = Vibration-controlled transient elastography

(MINOCA) include cardiac microvascular disease (i.e., microvascular plaque, thrombosis), coronary vasospasm, and coronary artery dissection. [8] Imaging studies to assess MINOCA include coronary angiography with or without intravascular ultrasound or optical coherence tomography, as well as possibly intracoronary acetylcholine if coronary spasm is suspected. [9,8,10] Yet other cardiac imaging studies to help assess MINOCA include echocardiography, [10] with PET and CMR useful to assess coronary microvascular dysfunction. [11,12]

- Most instances of coronary artery disease involve macrovascular disease leading to obstruction and often clinically manifest by angina and myocardial infarction. Even among patients with coronary microvascular disease, most such patients also have macrovessel atherosclerosis. [7] However, a sole focus on coronary macrovascular disease may underdiagnose cardiac disease in patients with coronary microvascular disease as often occurs in women. [7] Therefore, selecting the most appropriate imaging study is best determined by the patient presentation, and the information reasonably derived by the imaging study performed on an individual patient.
  - Coronary anatomy can be assessed by CAC, CCTA, CMR and cardiac catheterization. [13]
  - Cardiac diastolic dysfunction can be evaluated by echocardiogram and CMR. [14,15]
  - Myocardial perfusion can be assessed by SPECT, PET, and CMR. [16,17]
  - Cardiomyocyte injury and fibrosis can be evaluated by CMR and CTA. [18,19]
  - Microvascular dysfunction can be evaluated by PET and CMR. [12]
  - Hybrid imaging includes:
    - PET/CT and PET/MRI: Assesses perfusion, cardiac viability, and atherosclerosis [20,21]
    - CT- Fractional Flow Reserve (FFR): Provides anatomic (i.e. luminal and plaque) and physiologic/functional imaging data to assess obstructive CAD [22,23]
    - Cardiac catheterization and FFR: Provides (invasive) anatomic and functional assessment of CAD [24]
- CAC added to SPECT or PET may help further identify coronary artery plaque and better stratify risk [25,26]
- CCTA added to CAC scoring may help improve the assessment of total plaque burden and better discriminate risk of death and/or myocardial infarction among symptomatic patients with suspected coronary artery disease. [27,28]
- Although it may have low specificity, CAC scoring is illustrative of a cardiac imaging study of high sensitivity, limited invasiveness, and low radiation exposure (Reference Charts 1 & 2). CAC is often performed in asymptomatic patients to help stratify CVD risk (see Section 1 and Table 1 below). [10,7]

Reference Chart 1
Invasiveness and patient radiation exposure regarding various imaging procedures. Radiation exposure for some procedures may be less than listed via use of ultra-low dose radiation protocols involving stress-only imaging. Some common diagnostic procedures are listed at the bottom of the table for reference/illustrative purposes. [37, 38].

Procedure	Invasiveness	Patient radiation exposure*
Contemporary coronary artery calcium CT (CAC)	Noninvasive, no contrast	~ 1 mSv [39, 40, 41]
Contemporary coronary CT angiography (CCTA)	Requires injection of contrast material (i.e., iodine)	1.0 - 5 mSv** [42, 43, 44, 45]
Cardiac ultrasound / echocardiogram	Noninvasive. If unable to physically exercise, then dobutamine may be injected to mimic exercise. May include contrast (i.e., agitated saline or commercial ultrasound contrast agents). [46]	0.00 mSv (no radiation)
Nuclear myocardial perfusion imaging (MPI)		
• SPECT perfusion imaging	Intravenous administration of nuclear contrast with imaging at rest, followed by walking on a treadmill with another injection afterwards of nuclear contrast. If unable to physically exercise, then an A2A adenosine receptor agonists (i.e., regadenoson coronary vasodilator for cardiolite stress test) can be injected to mimic exercise	10 -15 mSv with technetium-99 [48] 25 – 30 mSv with thallium-201 [48] (seldom used in current clinical practice)
• PET perfusion imaging	Requires injection of radiotracer (e.g., 50 mCi of ^{82}rubidium or 20 mCi of ^{13}ammonia for rest and stress perfusion). [47] If unable to physically exercise, then pharmacologic stress testing can be achieved via the vasodilators regadenoson, adenosine, dipyridamole, or inotropic/chronotropic agents such as dobutamine with or without atropine	4 mSv with ^{82}rubidium or ^{13}ammonia [49] (older reports suggest higher radiation exposure) [48, 47]
• MUGA ventricular imaging (seldom use in current clinical practice)	Requires injection of radiotracer	5 – 10 mSv with technetium-99m-pertechnetate [50]
CMR	Most cardiac protocols involve injection of contrast (i.e., gadolinium)	0.00 mSv (no radiation)
Cardiac catheterization	Cardiac catheterization involves insertion of a catheter tube into the artery or vein in the groin, neck, or arm, which is then threaded into the heart.	2 – 7 mSv for diagnostic cardiac catheterization [51] 10 mSv or higher for interventional catheterization [52, 52]
DXA total body composition scan	Noninvasive	≤ 0.001mSv for typical body composition (minimal radiation; technicians not required to wear garments to protect from radiation)
Hepatic imaging		
• Ultrasound of liver	Noninvasive	0.00 mSv (no radiation)
• VCTE/fibroscan	Noninvasive	0.00 mSv (no radiation)
• CT	May involve injection of contrast (e.g., iohexol)	3.0 mSv
• MRI-PDFF	May involve injection of contrast (i.e., gadolinium)	0.00 mSv (no radiation)
• MRS	May involve injection of contrast (i.e., gadolinium)	0.00 mSv (no radiation)
Carotid ultrasound, peripheral doppler imaging, ultrasound flow-mediated dilation, and pulse amplitude tonometry Fingertip infrared light transmission photoplethysmograpy for endothelial function	Noninvasive	0.00 mSv (no radiation)

Daily background radiation	0.007 mSv
Yearly background radiation	3.0 mSv
Roundtrip Transatlantic Flight	0.100 mSv
Chest X-ray	0.02 – 0.1 mSv
Mammogram	0.40 mSv
DXA AP spine scan	0.001 – 0.004 mSv
Older body PET / CT scans	15 - 25.0 mSv
Older whole body CT scans	10 - 20 mSv

* The standard measure of radiation is Sievert (Sv) or millisievert (mSv) or microsievert (uSv) units where 1 Sv = 1000 mSv = 1,000,000 uSv. Humans have natural daily radiation exposure of about 0.007 mSv from soil, rocks, radon, and outer space.

** Quality CCTA images with ~ 1 mSv radiation exposure can sometimes be obtained in younger patients without overweight/obesity, or when utilizing low-dose CCTA protocols. [42, 43, 53]

CMR = Cardiac magnetic resonance, CT = computerized tomography, DXA = Dual x-ray absorptiometry, FFR = Fractional flow reserve, IVUS = Intravascular ultrasound, MRI = Magnetic resonance imaging, MRI-PDFF = MRI proton density fat fraction, MRS = Magnetic resonance spectroscopy, MUGA = Multiple-gated acquisition scan, OCT = Optical coherence tomography, PET = Positron emission tomography, SPECT = Single-photon emission computerized tomography, VCTE = Vibration-controlled transient elastography.

4. Cardiac exercise stress testing

Preventive cardiology incorporates both primary and secondary CVD prevention. Understanding the extent of CVD disease in both asymptomatic and symptomatic patients helps the clinician better recommend therapeutic interventions towards the goal of preventing future CVD events. Non-invasive cardiac imaging studies in patients with stable coronary obstructive symptoms (stable ischemic heart disease or “chronic coronary syndrome”) can help diagnose ischemic heart disease and are often performed prior to cardiac catherization. [29] In most

Reference Chart 2
Sensitivity and Specificity of Cardiac Imaging Studies [29, 54, 55].

Imaging Test	Sensitivity	Specificity
Anatomically significant coronary artery disease*		
Coronary Calcium Imaging/Score	98%	40%
Exercise electrocardiogram	58%	62%
Stress echocardiogram (Echo)	85%	82%
Coronary computed tomography angiography (CCTA)	96%	82%
Single-photon emission computed tomography (SPECT)	87%	70%
Positron emission tomography (PET)	90%	85%
Stress cardiac magnetic resonance (CMR)	90%	80%
Functionally significant coronary artery disease**		
Coronary computed tomography angiography (CCTA)	93%	53%
CCTA with fractional flow reserve (FFR)	85%	78%
Single-photon emission computed tomography (SPECT)	73%	83%
Positron emission tomography (PET)	89%	85%
Stress cardiac magnetic resonance (CMR)	89%	87%

* Anatomically significant CAD is sometimes defined as > 50% stenosis of the left main coronary artery, 70% stenosis of any major coronary vessel, or 30 – 70% stenosis with fractional flow reserve of ≤ 0.8. [56]

** Heart function imaging involves assessing blood flow within coronary arteries. The significance of a coronary artery obstruction can be assessed by measuring (directly or virtually) the pressure differential before and after a coronary artery stenosis (fractional flow reserve). The cut-off point for functionally significant CAD is often reported as ≤ 0.8, with other flow coronary blood flow metrics being dependent on the individual imaging technique. [56, 57, 42].

cases, the use of imaging studies to diagnose ischemia is performed with exercise testing, such as through use of a treadmill or bicycle. Imaging with exercise testing can enhance accuracy of the stress testing, especially in patients with non-interpretable electrocardiograms. The purpose of physical exercise coupled with imaging studies is to evoke coronary (macro and micro) blood flow, and promote other functional cardiovascular responses, during times of greater oxygen and nutrient demands of the heart (i.e., during times of "stress" such as via exercise).

Thus, stable patients suspected of myocardial ischemia who are able to exercise, and who have interpretable ECG/s, are best "stressed" via physical exercise (i.e., treadmill or bicycle). Incorporating exercise in a cardiac "stress test" allows for non-imaging assessment of hemodynamic response (i.e., heart rate, blood pressure), ST- segment analysis, and onset of dysrhythmias. Stress electrocardiography alone is reported to have sensitivity and specificity of 50 – 80%, depending on the source and patient population studied. [30,29] (Reference Chart 2) In patients with ECG abnormalities (e.g., left bundle branch block, changes consistent with left ventricular hypertrophy, ST-T wave changes), the addition of heart imaging (e.g., echocardiography or MPI such as SPECT or PET) to exercise cardiac stress testing may help identify and quantify cardiac dysfunction and/or ischemia.

A patient at low to intermediate CVD risk with a negative cardiac stress test [i.e., demonstrating no chest pain and no electrocardiographic evidence of ischemia after undergoing standard exercise protocols and achieving ten metabolic equivalents (METS)] is at low risk for future CVD events and or CVD mortality. [31] However, among patients with exercise treadmil stress tests suggesting possible ischemia, then depending on CVD risk, only 39% may subsequently have positive imaging/angiogram evidence of atherosclerosis. [32] Thus, among patients presenting with intermediate likelihood of CVD, exercise cardiac stress testing (i.e., treadmill or bicycle) plus cardiac imaging (e.g., echocardiogram, MPI, or PET) is more specific than an exercise stress test alone. Furthermore, in patients with uninterpretable ECG's, or in patients unable to exercise, and/or who undergo pharmacologic cardiac stress testing, concomitant heart imaging studies are often required.

Patients unable to undergo adequate exercise stress testing (e.g., relative immobility due to deconditioning, frailty, obesity, stroke, orthopedic impairments, neuropathy, lung disease) may require pharmacologic stress testing. Examples of pharmacologic stress agents include regadenoson (A2a receptor agonist), adenosine (nonselective adenosine receptor agonist), dipyridamole (nonselective vasodilator and antiplatelet agent that raises adenosine levels), and dobutamine (sympathomimetic). Regadenoson is the most common pharmacologic vasodilator used for pharmacological SPECT stress testing. [33,34]

5. Imaging studies

Safety considerations of imaging studies include the degree of their invasiveness and amount of radiation exposure (Reference Chart 1). [35] Invasiveness is defined here as access to the body via inserting a diagnostic device or injecting imaging media through incision or percutaneous puncture. Potential radiation exposure may be especially important in cardio-oncology. [36]

The most invasive CVD imaging study is cardiac catheterization. (Reference Chart 1) Cardiac catheterization remains the initial imaging procedure of choice for patients whose history, signs, symptoms and/or CVD imaging test results suggest high risk for myocardial dysfunction (e.g., high CVD risk features on a cardiac exercise stress test). This is especially true if it is anticipated the cardiac catheterization may be accompanied by a therapeutic intervention (i.e., PCI, thrombectomy, atherectomy). Complications of cardiac catheterization include bruising/bleeding at the catheter insertion site, myocardial infarction, stroke and other thrombotic complications, vascular injury, cardiac dysrhythmias, infection, contrast induced nephropathy, or allergic reaction to the contrast dye (i.e., iodine).

The invasiveness, radiation exposure, and cost associated with cardiac catheterization have prompted development of alternative noninvasive imaging procedures, many having limited radiation exposure. Radiation exposure is important because ionizing radiation contributes to cell death, cellular injury, or cell mutation potentially leading to cancer. (Non-ionizing radiation includes electric and magnetic fields, radio waves, microwaves, infrared, ultraviolet, and visible radiation, which have insufficient energy to ionize atoms or molecules.) The degree of radiation exposure is dependent on the dose of tracer infused, length of the imaging procedure, and the number of times the procedure is performed. Examples of CVD imaging studies with limited invasiveness include CAC, CCTA, & MPI. CVD imaging studies with limited invasiveness and no or minimal radiation exposure include CMR and ultrasound. (See Reference Chart 1)

5.1. Computerized tomography (CT) coronary artery calcium (CAC) [58]

A coronary artery calcium (CAC) score utilizes CT to assess the amount of calcium found in coronary arteries. Arterial calcium reflects

Table 1
Ten things to know about computerized tomography coronary artery calcium (CAC) measurements.

(1) For most patients, the higher the CAC score, the higher the atherosclerotic burden and the higher the risk of a subsequent CVD event.
(2) The Multi-Ethnic Study of Atherosclerosis Risk Score (https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx) assesses CHD risk based upon sex, age, race/ethnicity (e.g., Caucasian, Chinese, African American, and Hispanic), diabetes, smoking, family history of myocardial infarction, total cholesterol, high density lipoprotein cholesterol, systolic blood pressure, lipid lowering medications, hypertension medications *and CAC scoring*. [3, 61, 41] The Astronaut Cardiovascular Health and Risk Modification (Astro-CHARM) Coronary Calcium Atherosclerotic Cardiovascular Risk Calculator (http://astrocharm.org/) is an ASCVD risk calculator that incorporates multiple ASCVD risk factors, including age, sex, systolic blood pressure, hypertension treatment, total and high density lipoprotein cholesterol, smoking, diabetes mellitus, family history of myocardial infarction, high sensitivity C-reactive protein *and CAC scores*. [62]
(3) Patients most likely to benefit from CAC testing include asymptomatic individuals not known to have CVD, but who are 40 years and older without diabetes mellitus, individuals in whom primary CVD prevention therapeutics are being considered (e.g., statins), and/or individuals having borderline to intermediate 10-year ASCVD risk estimate of 5 – 20% (i.e., borderline risk = 5 – 7.5% and intermediate risk = 7.5 – 20%). [41, 63, 64]
(4) CAC scoring is generally not recommended for patients at low, < 5% 10-year ASCVD risk or patients with known CVD or patients at high, greater than 20% 10-year ASCVD risk.
(5) Generally, a CAC score of > 0 – 400 AU identifies individuals at minimal to mild to moderate CVD risk. An individual with a CAC score of 1 – 99 may have a risk of CVD death, myocardial infarction, or unstable angina of 2 % in ~ 2 years. An individual with a CAC score of 100 – 400 may have a risk of CVD death, myocardial infarction, or unstable angina of 4% in ~ 2 years. [65] In appropriate individuals, statin therapy is strongly indicated when the CAC score is > 100 AU, [63] or ≥ 75th percentile. [64]
(6) A CAC score of zero AU suggests a low risk of subsequent CVD event (i.e., acute myocardial infarction, coronary death, stroke, revascularization) over at least the next 8 years. [66] Individuals with an initial CAC score of zero may consider a second scan 3-7 or more years later. [67] Unless the patient has intervening onset or worsening of CVD risk factors or diminished adherence to healthful nutrition and physical activities, individuals with double-zero CAC may not need an additional scan in the near future afterwards, because their risk of a CVD is ≤ 2% within 8-years after the repeat CAC score. [66]
(7) A CAC score of ≥ 1000 AU represent a unique very high-risk phenotype of extreme coronary atherosclerosis with mortality outcomes commensurate with high-risk secondary prevention patients. [68] Such patients are at very high risk for a CVD event. [66] Similarly, patients with high baseline CAC scores of ≥ 400 AU are also at high CHD/ASCVD risk* (10 – 15% ten-year ASCVD risk); repeat CAC scoring is not appropriate for patients with CAC scores ≥ 400 AU, especially if treated with statins. [69] Patients with baseline CAC scores of 100 – 399 AU may have a > 5% 10-year ASCVD risk and be candidates for statin therapy. If statin therapy is implemented, then repeat CAC scoring may provide little additional benefit. [69] Patients with CAC scores of 1 – 100 AU who elect to defer statin therapy or other preventive measures may benefit from repeat CAC in 5 years. [69] Especially if statin therapy is implemented, once a CAC score is found to be ≥ 100, then it is unclear that repeat CAC scores provide additional, clinically meaningful information.
(8) Individuals with a positive CAC score of potential unclear clinical significance include patients with extensive calcification due to older age, patients with kidney disease (vascular medial sclerosis), patients treated with statins (i.e., reports suggest statins may increase CAC in some patients), and some patients with high levels of physical activity. [58, 70, 71, 72] Given that CAC scores are unlikely to regress, CAC scores do not track response to cardiovascular preventive therapy (i.e., response to statins). While alcohol drinkers in general may have increased frequency of atherosclerotic plaque in the coronary arteries despite reduced or zero CAC scores, [73, 74] heavy consumption of hard liquor may sometimes increase CAC scores. [75, 76]
(9) Individuals with a negative CAC score of potential unclear clinical significance include younger individuals who may have non-calcified atherosclerosis, patients with microvascular dysfunction, such as some women (and men) with non-obstructive ischemic heart disease (as may be assessed by PET). [77]
(10) A low CAC score should not negate CVD risk factor management. For example, a low CAC score in a patient otherwise at high CVD risk should not give a false sense of security, and interpreted as negating the need for aggressive lipid management (e.g., stopping statin therapy in patients with Familial Hypercholesterolemia, who while young, may still have "soft" uncalcified plaque).

Sentinel Guidelines and References
2021 National Lipid Association Scientific Statement on Coronary Artery Calcium Scoring [60]
2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol [64]
2018 Coronary Calcium Score and Cardiovascular Risk [41]
2020 Coronary Calcium StatPearls [58]
2018 Coronary Artery Calcium: If Measuring Once Is Good, Is Twice Better? [69]

*CHD = coronary heart disease (e.g., myocardial infarction or death from coronary heart disease)
*ASCVD = Atherosclerotic cardiovascular disease is often defined as acute coronary syndrome, myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, peripheral artery disease, and aortic aneurysm – all of atherosclerotic origin [64].

vascular injury, inflammation, and repair. Coronary calcium is a marker of plaque burden. It is not a measure of plaque vulnerability to rupture or degree of coronary stenosis. Due to vessel remodeling early in atherosclerosis, enlargement of coronary arteries may occur, mitigating signs or symptoms of stenosis, despite substantial plaque burden. This pathogenic clinical scenario is often clarified by CAC. Other cardiac imaging (i.e., with exercise stress testing) are more appropriate for patients with angina and/or obstructive CAD. However, CAC is a non-invasive cardiac procedure that can assess plaque burden, that is best used in asymptomatic patients to help guide the need for further cardiac evaluation or help determine the timing and degree of aggressiveness in managing existing CVD risk factors. [29]

CAC scores may be increased with older age, men versus women for same age, metabolic syndrome, high blood glucose, high blood pressure, increased atherogenic lipoprotein cholesterol burden, cigarette smoking, chronic kidney disease, and elevated C-reactive protein levels. [58] Assessment of coronary artery calcium is most often performed by multidetector computed tomography (MDCT); CAC does not require contrast. [41] The Agatston score reflects the total area of calcium deposits in coronary arteries, and the density of the calcium.

CAC Agatston Unit (AU) scores and coronary plaque burden can be categorized as: [59]

- 0: No identifiable calcified coronary atherosclerosis
- 1–100: Calcification suggestive of mild coronary atherosclerosis
- 100 to 400: Calcification suggestive of moderate coronary atherosclerosis
- 400 or above: Calcification suggestive of severe coronary atherosclerosis
- 1000 or above: Calcification suggestive of extreme coronary atherosclerosis

In a Scientific Statement from the National Lipid Association, CAC scoring: [60]

- Informs ASCVD risk discrimination and reclassification
- Aids in ASCVD risk prediction, regardless of race, gender, or ethnicity

Table 2
Ten things to know about coronary computed tomography angiography (CCTA) [29].

(1) CCTA has a high negative predictive value, such that if negative, then clinically meaningful CVD risk. CCTA may be especially valuable in assessing patients with chest pain or related symptoms, but without known CHD and who are at low to intermediate CVD risk. CCTA guided changes in management can improve clinical outcomes. [82]
(2) CCTA is a potential non-invasive imaging test of choice in patients with symptoms of chest pain where obstructive CAD cannot be reasonably established by history and physical exam alone.
(3) CCTA may also be helpful to rule out left main CAD. The absence of coronary artery stenosis with CCTA imaging is associated with a favorable prognosis.
(4) Evaluation of the severity of coronary stenosis can be derived from estimating pressure differences via "virtual" fractional flow reserve derived from CCTA (FFR_{CT}). [83]
(5) CCTA can assess non-obstructive coronary artery plaque, which can inform CVD preventive management. Management decisions guided by CCTA in patients with stable chest pain may reduce CHD and MI mortality at 5 years, without prompting a higher rate of coronary angiography or coronary revascularization. [84]
(6) Poor image quality and severe calcification can overestimate CCTA coronary artery stenosis.
(7) CCTA is not recommended in patients with extensive coronary calcification (which may occur with older age and kidney failure), cardiac dysrhythmias (including tachycardia), significant obesity, and in patients unable to hold their breath – all which may adversely affect image quality.
(8) CCTA image quality may be impaired in patients with prior cardiac revascularization.
(9) The contrast with CCTA is contraindicated in patients with contrast dye allergies.
(10) Contrast (i.e., iodine) induced acute kidney injury occurs due to contrast-mediated hypoperfusion, direct tubular toxicity, and vasoconstriction. CCTA contrast should be used with caution in patients with kidney insufficiency and warrants adequate fluid intake in those receiving contrast. [85] Additional risk factors for CCTA contrast induced nephropathy beyond renal insufficiency (i.e., estimated glomerular filtration rate <45 ml min / 1.73m^2) include severe heart disease, dehydration, diabetes mellitus, multiple iodinated doses in a short time interval (<24 h) and use of nephrotoxic medications, such as non-steroidal anti-inflammatory drugs and diuretics. [86]

Sentinel Guidelines and References
2021 Epicardial fat and coronary artery disease: Role of cardiac imaging [81]
2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: Recommendations for cardiovascular imaging [29]
2018 Coronary CT Angiography and 5-Year Risk of Myocardial Infarction [84]
2015 Outcomes of anatomical versus functional testing for coronary artery disease [87]
2015 Cardiac CT vs. Stress Testing in Patients with Suspected Coronary Artery Disease: Review and Expert Recommendations [88]

- Aids the clinician to allocate statin therapy based on ASCVD risk
- May inform decision-making about add-on therapies to statins, especially if CAC scores are very high
- Aids decision-making about aspirin and anti-hypertensive therapy

Reference Chart 1 describes the relative radiation exposure with CAC. Table 1 lists ten things to know about computerized tomography coronary artery calcium (CAC) measurements.

5.2. Coronary computed tomography angiography (CCTA)

Atherosclerotic progression begins with early reversible subendothelial lipid accumulation, early inflammation, and minimal fibrosis. Further atherosclerotic progression may lead to lipid plaque, chronic inflammation, fibrosis, and perivascular adipose tissue remodeling – which if untreated, may ultimately become irreversible. [78] CCTA can measure lipid rich plaque, [79] as well as perivascular fat and inflammation. [80,81]

Clinically, CCTA is a cardiac imaging study utilizing CT that is often used to quantify coronary atherosclerotic burden. When combined with FFR, CCTA can help determine the functional significance of stenotic lesions. With use of an iodine intravenous contrast agent, CCTA can visualize the coronary artery lumen. CCTA is sensitive for anatomically significant CAD (e.g., obstructive CAD and nonobstructive calcified plaques) and reasonably sensitive for functionally significant CAD. However, CCTA is not specific for functionally significant CHD. (Reference Chart 2) [29] Reference Chart 1 describes the relative radiation exposure with CCTA. Table 2 lists ten things to know about coronary computed tomography angiography (CCTA).

5.3. Cardiac ultrasound (echocardiography)

Echocardiography utilizes ultrasound waves (sound wave range beyond that audible by humans) to provide hemodynamic information about heart function. When accompanied by stress testing, echocardiography is often used to assess myocardial ischemia (i.e., coronary artery atherosclerosis), left ventricular function (i.e. heart failure, cardiomyopathy) and structural heart disease (i.e., valvulopathy, congenital heart disease, aneurysm, cardiac tumor, pericarditis, endocarditis, aortic dissection, heart chamber thrombosis). [89] Approaches to echocardiography include transthoracic chest wall approach or transesophageal approach. Types of echocardiography include: [90,89]

- **M-mode:** "Motion mode" generates tracing images rather than picture images.
- **Doppler (previously known as B or "Brightness-mode"):** Assesses blood flow and can be characterized as continuous-wave, pulsed-wave or color-flow. Continuous and pulse wave doppler echocardiography images allow for calculated flow velocity, as well as estimates for volume and pressure gradients across heart valves.
- **2-D (two-dimensional) echocardiography:** Provides cross-sectional real-time motion images of the heart
- **3-D (three-dimensional) echocardiography:** Able to view real-time motion of the heart via 3-D images

Stress echocardiography is reasonably sensitive and specific for diagnosing coronary artery disease in symptomatic patients. (Reference Chart 2). However, despite its noninvasive safety, "routine" echocardiograms should not be performed in asymptomatic patients ("inappropriate use"), as this may lead to false positive or equivocal findings, resulting in unnecessary downstream consultations and procedures. [91] Reference Chart 1 describes how cardiac ultrasound results in no radiation exposure. Table 3 lists ten things to know about echocardiography.

5.4. Nuclear myocardial perfusion imaging (MPI) [29]

Nuclear myocardial perfusion imaging through Single Photon Emission Computed Tomography (SPECT) utilizes small amounts of nuclear

Table 3
Ten things to know about cardiac ultrasound (echocardiography) [29, 89]

(1) Transthoracic echocardiography is the most common approach, with transesophageal echocardiography preferred in patients with conditions that compromise transthoracic imaging quality (e.g., obesity, certain lung conditions). Contrast options include agitated saline or commercial ultrasound contrast agents (Reference Chart #1). [46] Contrast echocardiography may improve diagnostic performance regarding left ventricular opacification or microvascular perfusion imaging. [92]
(2) Transesophageal echocardiography may provide better resolution images of the left heart, evidence of potential endocarditis, mitral and aortic valves, and aorta (i.e., aortic dissection).
(3) Doppler echocardiography can assess stroke volume, heart chamber pressure gradients, valvular regurgitations, and intracardiac shunts.
(4) In patients with angina-like chest pain, echocardiography can help diagnose alternative cardiac etiologies of chest pain, identify regional wall-motion abnormalities, determine left ventricular ejection fraction, and evaluate diastolic dysfunction for stratification purposes (i.e., surgical risk based upon cardiac status).
(5) As with stress SPECT, stress PET, and stress CMR, stress echocardiography provides cardiac functional assessment.
(6) Echocardiography is commonly used to assess left ventricular ejection fraction, which is "normally" ~ 50 - 70%. Heart failure with reduced ejection fraction (HFrEF) is defined as heart failure with ejection fraction < 50%.
(7) While heart failure can occur with reduced ejection fraction, symptomatic heart failure can also occur with preserved ejection fraction (HFpEF) (i.e., ejection fraction ≥ 50%). [93]
(8) Echocardiography may provide helpful information regarding microcirculatory dysfunction that may contribute to angina without obstructive lesions in major coronary arteries. Angina and ischemia-like electrocardiographic changes without wall motion abnormalities on echocardiography may suggest microvascular dysfunction. [94, 95]
(9) In many patients, echocardiogram assessment of heart function and anatomy can provide peri-operative risk stratification.
(10) Echocardiogram assessment can provide cross-sectional and longitudinal cardiac assessment in patients undergoing chemotherapy, helping to monitor for potential adverse effects of chemotherapy on cardiac structure and function. Evidence of echocardiographic left ventricular global longitudinal strain may be reflective of subclinical ventricular dysfunction and provide prognostic information in patients receiving cardiotoxic chemotherapy. [96]

Sentinel Guidelines and References
2021 Novelties in 3D Transthoracic Echocardiography [97]
2021 Usefulness of Stress Echocardiography in the Management of Patients Treated with Anticancer Drugs [98]
2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: Recommendations for cardiovascular imaging [29]
2020 Echocardiography update for primary care physicians: a review [89]
2004 Understanding the echocardiogram [90]

tracer (i.e., the isotope technetium-99 or thallium-201) injected into the blood to assess myocardial segments that do not take up the tracer (i.e., damaged myocardium) or areas with delayed uptake of the tracer (i.e., ischemic myocardium). SPECT can also help assess the patency of grafted blood vessels after coronary bypass. Techetium-99 is a radiotracer often attached to a small protein (sestamibi). Thallium-201 is typically supplied as thallous chloride. Technetium-99 has lower radiation exposure and is preferred; Thallium-201 is rarely used in current clinical practice. (Reference Chart 1) The radiotracers are generally injected into the blood with imaging occurring at rest, or with exercise (e.g., "*nuclear stress test*," "*exercise thallium scan*," "*exercise technetium-99 sestamibe scan*"), or both. For patients unable to physically exercise, then an A2A adenosine receptor agonist (i.e., regadenoson coronary vasodilator for cardiolite stress test) can be injected as an alternative to exercise.

A positron emission tomography (PET) scan of the heart utilizes a radiotracer (i.e., often ^{82}rubidium or ^{13}ammonia for rest and stress perfusion). [47] Uptake of the radiotracer by the myocardium is proportional to myocardial blood flow. Thus, coronary flow reserve can be added to PET to improve CVD risk assessment. Strengths of PET MPI include high diagnostic accuracy, safety with low radiation exposure (lower than SPECT), efficient with 5-min image acquisition times (may take only 30 minutes to perform), ability to accommodate ill or higher-risk patients, ability to assess patients with large body habitus, and ability to assess non-obstructive coronary microvascular dysfunction. [99] PET is often used as a noninvasive imaging test to assess coronary flow reserve (Table 5), that may assist with diagnosis, prognosis, and management of patients with a range of ASCVD, including both multivessel obstructive CAD and diffuse coronary microvascular dysfunction. Cardiac microvascular dysfunction may be especially clinically relevant in women, patients with heart failure with preserved ejection fraction, metabolic syndrome, diabetes mellitus, cardio-oncologic complications, and inflammatory-related disease. [100,101] Patients with stable ischemic heart disease (SIHD) vary in their cardiac anatomy and function. In addition to obstructive coronary lesions, it is estimated that 3 – 4 million men and women in the US have symptoms of myocardial ischemia with no evidence of obstructive CAD. [102] Along with heart failure with preserved ejection fraction, other cardiac conditions that may occur more often in women include Takotsubo cardiomyopathy, cerebral small-vessel disease, preeclampsia, pulmonary arterial hypertension, endothelial dysfunction in diabetes, diabetes cardiomyopathy, rheumatoid arthritis, systemic lupus erythematosus and systemic sclerosis, and small vessel cardiac disease – which suggests a common etiologic linkage of these cardiac conditions. [103] An illustrative strategy that may help balance safety and diagnostic yield would be to employ ultra-low dose radiation protocols involving stress-only imaging, with SPECT or PET used when possible for patients undergoing MPI. [104]

A multiple-gated acquisition (MUGA) scan involves utilizes a radiotracer (e.g., technetium-99m-pertechnetate) attached to red blood cells to evaluate the size of the chamber of the heart. MUGA was historically among the most common cardiac imaging studies for measuring left ventricular ejection fraction (LVEF) MUGA scans are currently seldom used in favor of other imaging studies such as echocardiography and CMR.

Reference Charts 1 & 2 describe the radiation exposure using MPI techniques, as well as their sensitivity and selectivity. Table 4 lists ten things to know about nuclear myocardial perfusion imaging.

5.5. Cardiac magnetic resonance (CMR)

CMR is an imaging study that utilizes magnetic, radio frequency waves (not ionizing radiation) to create cross sectional/2-dimentional, 3-dimentional, and even 4-dimentional images. CMR can help assess valvular heart disease, ischemic heart disease, cardiomyopathies, congenital heart disease, cardiac tumors, and pericardial disease (pericarditis). [115,116,117] CMR can also measure subendocardial and subepicardial perfusion to assess for potential coronary microvascular dysfunction in patients with nonobstructive coronary artery disease. [118] Determination of the value of CMR for imaging of cardiac anatomy such as MINOCA is evolving. [119] Among examples where stress CMR may be cost effective include patients with stable ischemic heart disease and non-diagnostic coronary CT angiography. [120] Utilization of CMR for

Table 4
Ten things to know about nuclear myocardial perfusion imaging (MPI).

(1) SPECT is a perfusion imaging study that typically uses technetium-99 (^{99m}Tc). ^{99m}Tc produces less radiation than thallium-201 (^{201}Tl), ~6 mSV versus ~17 mSV respectively. This helps explain why ^{201}Tl is often only used during shortages of ^{99m}Tc.
(2) MPI may utilize different tracers, depending upon the imaging device, and purpose of the imaging (e.g., perfusion imaging, atherosclerosis imaging, metabolic imaging, inflammation imaging, and/or innervation/sympathetic imaging) [105]
(3) The degree MPI accurately predicts CVD risk depends on "Appropriate Use." (see prior "Appropriate Use" section). Appropriate use of MPI can help stratify CVD risk; inappropriate use of MPI may not help stratify CVD risk. [106]
(4) MPI may help augment CAC CVD risk stratification. [26]
(5) MPI imaging may help identify obstructive coronary artery disease as the etiology of chest pain. [107]
(6) MPI can be used in patients with immobility, cardiac rhythm disorders, impaired kidney function, or presence of cardiac devices.
(7) Over 50% of patients may be unable to adequately exercise during MPI, with an inability to achieve 85% of maximum predicted heart rate and 5 metabolic equivalents (METS). This often prompts the alternative of pharmacologic stress testing (regadenoson, adenosine, dipyridamole, dobutamine) [108]
(8) If stress MPI is normal, resting MPI may be redundant and not necessary. [109, 110] Employing stress MPI results alone may reduce radiation and cost.
(9) PET has a high sensitivity and specificity to detect anatomic and functional atherosclerotic lesions useful for CVD risk stratification (Reference Chart 2).
(10) As with CMR, PET may help identify functional abnormalities suggestive of microvascular CAD. [12]

Sentinel Guidelines and References
2021 Nuclear cardiology: state of the art [111]
2021 Nuclear Medicine SPECT Scan Cardiovascular Assessment, Protocols, and Assessment [112]
2020 Review of cardiovascular imaging in the Journal of Nuclear Cardiology 2019: Positron emission tomography, computed tomography, and magnetic resonance [113]
2020 Noninvasive Imaging of Ischemic Heart Disease and Coronary Microvascular Dysfunction in Women. [114]
2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: Recommendations for cardiovascular imaging [29]

Table 5
Ten things to know about cardiac magnetic resonance (CMR).

(1) CMR may provide additional imaging information for patients when an echocardiogram is inconclusive, such as in patients with obesity. [121]
(2) As with stress MPI via SPECT or PET, or stress echocardiography, stress CMR is an example of a non-invasive functional imaging test that can assess myocardial ischemia. [29]
(3) As with PET, CMR may be useful as a noninvasive imaging study for patients with suspected coronary microvascular angina, which may be especially important for women. [122]
(4) CMR assesses ventricular mass, volume, and systolic function, and can be used to assess valvular heart disease and cardiac remodeling. [123]
(5) CMR can visualize cardiomyopathies, such as restrictive, hypertrophic, and dilated cardiomyopathies. [124, 125]
(6) CMR can assess pericardial disease (i.e., pericarditis). [126]
(7) CMR can visualize congenital heart disorders and cardiac tumors. [126]
(8) Some patients with claustrophobia may be unable/unwilling to undergo CMR; mild sedation may help (i.e., diazepam). [127]
(9) Due to its magnetic field, CMR should not be performed on patients with devices or implants that are not certified as CMR safe (pacemakers, implantable cardioverter defibrillators, inner ear implants, neuromuscular stimulators, drug infusion pumps, intrauterine devices, metal fragments and uncertified brain aneurysm clips and dental implants). [128] CMR can be performed in patients with many orthopedic protheses (e.g., titanium), with some exceptions (e.g., certain screws). [129]
(10) CMR contrast dye (i.e., gadolinium) should be use with caution in patients with severe kidney insufficiency, as this may increase the risk of nephrogenic systemic fibrosis. [130] CMR nephrogenic systemic fibrosis can occur months after exposure and may be manifest by erythematous and edematous skin plaques mainly to the extremities, joint contractures, and respiratory failure. Beyond renal dysfunction, other risk factors for gadolinium-based contrast nephrogenic systemic fibrosis include proinflammatory state (e.g., major surgery, infection, malignancy), thrombotic events, and high-dose erythropoietin dose. [131]

Sentinel Guidelines and References
2021 Cardiovascular Imaging in Obesity [121]
2020 Standardized cardiovascular magnetic resonance imaging (CMR) protocols: 2020 update [132]
2020 Society for Cardiovascular Magnetic Resonance (SCMR) Position Paper on clinical indications for cardiovascular magnetic resonance [133]
2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: Recommendations for cardiovascular imaging [29]

cardiac anatomic disease may be more limited in the US relative to other countries.

Reference Chart 1 describes how CMR results in no radiation exposure. Stress CMR has a high sensitivity for detecting anatomically and functionally significant CAD (e.g., obstructive CAD) (Reference Chart 2), but is less specific for anatomically significant CHD (Reference Chart 2). In general, CMR is commonly used to evauate cardiomyopathy, and occasionally as an alternative myocardial perfusion tool in the setting of a stress test.

Table 5 lists ten things to know about CMR.

5.6. Cardiac catheterization [with or without intravascular ultrasound (IVUS) or coronary optical coherence tomography (OCT)]

Cardiac catheterization is an invasive procedure that involves inserting a catheter into an artery or vein in the groin, neck, or arm, which is then threaded into the heart. Contrast (e.g., iodine or gadolinium) dye is injected into the heart and vessels to assess narrowing or blockages of coronary arteries and assess cardiac structure (e.g., heart valves, left ventricular function). In addition to the imaging part of the procedure, catheterization may also allow for therapeutic PCI, repairing of septal defects, balloon valvuloplasty, or heart biopsy. Reference Chart 1 describes the invasiveness and relative radiation exposure of cardiac catheterization.

Fractional flow reserve (FFR) is often obtained via cardiac catheterization and represents the pressure differential before and after a coronary artery stenosis. As noted in Reference Chart 2, the cut-off point for functionally significant CAD is often reported as < 0.8. [30] Thus, anatomically significant CAD is sometimes defined as > 50% stenosis of the left main coronary artery, 70% stenosis of any major coronary vessel, or 30–70% stenosis with fractional flow reserve of < 0.8. [30]

Table 6
Ten things to know about cardiac catheterization.

(1) Cardiac catheterization, potentially followed by stent placement or revascularization, is a diagnostic procedure of choice in patients with acute coronary syndrome (e.g., myocardial infarction or unstable angina).
(2) Several million cardiac catheterizations are performed per year, with the rate of major complications (e.g., death, myocardial infarction, stroke, unplanned coronary bypass grafting, and pericardial effusion) occurring < 1 per 1000 left heart catheterizations.
(3) Iodine containing contrast material > 240 mg/kg utilized during cardiac catheterization within 7 days of cardiac surgery may increase the risk of acute kidney injury. [144] Acute renal failure represents 17% of complications of cardiac catheterization. Among the more common factors that may increase the risk for contrast induced nephropathy includes older age, presence of chronic diseases (e.g., hypertension and diabetes mellitus), high volume of contrast, heart failure, and previous kidney disease. Other associated factors for contrast induced nephropathy include hypotension, longer procedure time, and atrial fibrillation. [145]
(4) In patients with intermediate lesions (30 – 70%), FFR should be performed to assess for functional (hemodynamic) significance.
(5) In stable patients with moderate or severe ischemia and without clinically significant angina or left main CAD (e.g., via CCTA), an initial invasive strategy of coronary catheterization with or without revascularization may not reduce the risk of ischemic CVD or death from any cause compared to medical therapy, suggesting that cardiac catheterization might reasonably be reserved for optimal medical therapy failure. [146]
(6) IVUS characterizes (i.e., intramural and/or extramural) and quantifies (i.e., area, volume) atherosclerotic plaque.
(7) Compared to cardiac angiography alone, IVUS provides incrementally additional information regarding the arterial vessel wall, vessel dimensions, and plaque characteristics that may help optimize stent placement and mitigate stent complications. [147]
(8) IVUS can help evaluate stent failure (i.e., stent thrombosis or stent restenosis).
(9) OCT is a catheter-based imaging technology that can characterize coronary artery plaque, identify vulnerable coronary artery plaque, characterize and identify intracoronary thrombosis (red and white thrombi), and assess neointima formation after stent placement.
(10) OCT can provide guidance for coronary interventions, such as determine the lesion length and vessel lumen diameter, which may assist with PCI procedures.

Sentinel Guidelines and References
2020 Initial Invasive or Conservative Strategy for Stable Coronary Disease [146]
2020 Intravascular Ultrasound StatPearls. [134]
2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: Recommendations for cardiovascular imaging [29]
2019 Safety and Risk of Major Complications with Diagnostic Cardiac Catheterization [148]
2018 Coronary Optical Coherence Tomography [135]

Intravascular ultrasound (IVUS) is an imaging technique that may be conducted during cardiac catheterization that utilizes sound waves to assess both intramural (impinging on the coronary lumen) and extramural (ectatic) atherosclerotic plaque. It is performed using a dedicated catheter with ultrasound-based technology to provide a cross sectional image with a 360° view of the vessel. [134] Coronary optical coherence tomography (OCT) is an intracoronary artery diagnostic imaging study that can be performed during cardiac catheterization. Coronary OCT can help visualize the microstructure of normal and diseased arteries and can identify calcified plaque and neointima formation after stent placement. [135]

While OCT may provide better image resolution of the coronary arteries, IVUS has greater imaging penetration than OCT, where large lipid-rich plaques may impair the ability to image the vessel border with OCT. [136] OCT requires contrast (often iodine-based), [137]which increases the risk of contrast induced nephropathy. Alternative OCT contrasts such as dextran may help avoid acute kidney injury. [138] Contrast induced nephropathy [136] is a poor prognostic factor that often delays hospital discharge and increases costs. [139] In short, OCT may be superior to IVUS in assessing the cause of stent failure, calcific coronary disease, and MINOCA. Conversely, [139] IVUS may be superior in patients with left main coronary artery disease, renal dysfunction, aorto-coronary ostial lesions, and chronic total occlusion. [139]

Another example of an intra-coronary imaging study includes near infrared spectroscopy (NIRS). [140] Other functional intra-coronary measures that can be obtained during cardiac catheterization intracoronary include instantaneous wave-free ratio (iFR), [141] index of microvascular resistance (IMR), [142] and minimal luminal area (MLA). [143]

Table 6 lists ten things to know about cardiac catheterization [with or without intravascular ultrasound (IVUS) or coronary optical coherence tomography (OCT)].

5.7. Dual x-ray absorptiometry (DXA) body composition

DXA is commonly used to assess bone mineral density (BMD) in patients at risk for osteoporosis. In women, trabecular volumetric BMD may be independently and inversely related to CAC scores, [149] while cortical volumetric BMD may be independently and directly related to CAC scores. [150] While not often done clinically, emerging research suggests that DXA can assess abdominal aortic calcification, which is a risk factor for ASCVD. [151] Increased abdominal aortic calcification is associated with increased risk for osteoporosis [152].

DXA is also a “gold standard” to assess body composition. Many DXA scanners can assess percent body fat, android fat, visceral fat, lean body mass, and bone mass. DXA scans also provide the clinician and patient colorful images with detailed descriptions of personalized information regarding body composition. Reference Chart 1 describes the invasiveness and relative radiation exposure of DXA. The risk of radiation exposure is often about 5% of a standard chest X-ray, about the same as an intercontinental flight; technicians do not have to wear radiation protective garments.

Patients with increased android fat (i.e., abdominal and visceral adiposity) are at increased CVD risk. DXA assessment of body composition can be obtained for a cross-sectional assessment at a point in time, and for longitudinal assessment after implementation of healthful nutrition, physical activity, anti-obesity pharmacotherapy, or bariatric surgery. These longitudinal DXA assessments in patients at higher CVD risk are not influenced by treatments such as statins. Table 7 lists ten things to know about dual x-ray absorptiometry (DXA) body composition.

5.8. Hepatic imaging for NAFLD

As with obesity, nonalcoholic fatty liver disease (NAFLD) is a factor associated with increased CVD risk. [158] (1) NAFLD encompasses the spectrum of fatty liver not related to alcohol consumption (e.g., fatty liver and hepatosteatitis). While NAFLD can be cause by genetics, infectious diseases, and various medications, NAFLD is most often associated with, or caused by CVD risk factors such as obesity/adiposopathy, type 2 diabetes mellitus, dyslipidemia, and sleep disorders. While insulin resistance may be a contributing mechanism to each of these CVD risk factors, it is not the only mechanism. In one example, while obstructive sleep apnea (OSA) is often associated with insulin resistance, OSA can also contribute to NAFLD due to hypoxia, inflammation, endotoxemia, and gut barrier dysfunction. [159]

Table 7
Ten things to know about dual x-ray absorptiometry (DXA) body composition.

(1) DXA scans for body composition can measure percent body fat, android fat, visceral fat, lean body mass, and bone mineral density.
(2) Lean body mass is defined as total body mass less nonessential or storage adipose tissue (i.e., water, protein, bone, essential body fat) and has wide variance among individuals, depending on an individual's mass of muscle, organs, and bone, which in turn is largely dependent on height, gender, genetics, nutrition, physical activity and overall health.
(3) An increase in body mass (lean body mass or adipose tissue mass) increases resting energy expenditure.
(4) The Obesity Medicine Association has established cutoff points for percent body fat (% BF) for women: pre-obesity = 30 – 34% BF and obesity ≥ 35 BF%; for men pre-obesity = 25 – 29% BF and obesity ≥ 30 BF%. The American Council on Exercise Classification has no categorization for pre-obesity or overweight, and defines obesity as ≥ 32% BF for women and ≥ 25% BF for men.
(5) Android and visceral adiposity correlate with increased CVD risk. Epicardial fat has direct adiposopathic potential to adversely affect the heart. Epicardial and visceral adipose tissue share the same mesodermal embryonic origin, directly correlate with one another; both are associated with increased coronary artery calcification. Adipocyte hypertrophy and adipose tissue expansion may result in adiposopathic endocrinopathies and immunopathies (e.g., hormonal and pro-inflammatory responses from adipocyte hypertrophy and adipose tissue accumulation) [153, 154] that can directly contribute to CVD (i.e., epicardial proinflammatory signaling) and indirectly contribute to CVD (i.e., promotion of insulin resistance, high blood sugar, high blood pressure, and high blood lipids – all CVD risk factors).
(6) Percent body fat by DXA measures may not always correlate well with other percent body fat assessment devices – sometimes having % BF values 10% higher or more.
(7) For most DXA measures, the android region is defined as the area between the ribs and the pelvis; visceral fat is the intraabdominal fat surrounding body organs.
(8) While generally accurate for populations, body mass index (kilogram weight per meter squared height or kg/m^2) may not be accurate in assessing body fat in individuals, especially those with increased muscle mass or sarcopenia. While percent body fat more accurately reflects body composition, the greatest support in correlating body fat to CVD is central adiposity (measures of waist circumference), as well as android and visceral fat. According to the Obesity Medicine Association, "optimal" android fat is < 3 pounds (~1400 grams) and optimal visceral fat is < 1 pound (~500 grams). Within individuals (particularly women) total percent body fat may not reflect android or visceral fat measures. Some women with increased overall percent body fat may have no detectable visceral fat via DXA; the average rate of onset of CVD in women is ~ 10 years later than men. [1, 2]
(9) Not all DXA facilities perform body composition (i.e., many DXA scans are performed exclusively for bone mineral density). Not all DXA can distinguish between visceral and subcutaneous fat, nor accomodate patients with higher body mass index (i.e., ≥ 350 pounds).
(10) The addition of a waist circumference to other non-DXA measures of percent body fat (e.g., air displacement plethysmography, bioelectrical impedance, underwater weighing densitometry) may provide complementary prognostic information regarding CVD risk.

Sentinel Guidelines and References
2021 Obesity Medicine Association Obesity Algorithm [101]
2017 Visceral fat reference values derived from healthy European men and women. [155]
2015 Does Visceral Fat Estimated by DXA Independently Predict Cardiometabolic Risk in Adults? [156]
2014 Imaging Body Fat: Techniques and Cardiometabolic Implications [157]

Nonalcoholic fatty liver is commonly defined as ≥ 5% liver fat (hepatosteatosis) without hepatocellular injury. Nonalcoholic steatohepatitis (NASH) is the presence of ≥ 5% hepatosteotosis, lobular inflammation, plus hepatocellular injury (hepatocyte ballooning with or without fibrosis). Hepatosteatosis alone rarely progresses to cirrhosis and liver failure. Conversely, patients with NASH are at increased risk of cirrhosis and liver failure. Diagnosis of NAFLD may include use or measurement of aspartate transaminase / alanine transaminase (AST/ALT) ratio index, various serum biomarkers, NAFLD Fibrosis score, Fibrosis 4 calculator, enhanced liver fibrosis score, fibrometer, fibrotest, and hepatascore. Hepatic imaging may include liver ultrasound, vibration-controlled transient elastography (VCTE or Fibroscan), CT of the liver, MRI proton density fat fraction, and magnetic resonance spectroscopy. Table 8 lists ten things to know about hepatic imaging for NAFLD.

5.9. Carotid ultrasound, peripheral Doppler imaging, ultrasound flow-mediated dilation, other tests of endothelial function, and peripheral vascular imaging

Carotid plaques are atherosclerotic lesions located in the carotid arteries that increase the risk of stroke. Imaging studies to evaluate carotid artery atherosclerotic lesions include CT and MRI. [166] Another imaging technique includes carotid ultrasound, which utilizes sound waves to evaluate the anatomy of carotid arteries. Carotid ultrasound is a procedure that also usually includes doppler assessment of carotid blood flow. [167] Decades ago, it was commonplace in lipid-altering drug development that B-mode ultrasound carotid intima medial-media thickness (CIMT) imaging studies would be conducted in the interim between shorter-term lipid efficacy clinical trials (e.g., often 12 week trials) and CVD outcomes studies (e.g., 2–5 years). The rationale was to demonstrate potential lack of atherosclerosis disease progression in the carotid arteries, or perhaps regression with lipid-altering therapy. Such imaging results could be reported after lipid efficacy publications and before CVD outcome result publications. Largely because of the lack of acceptance of CIMT studies by regulatory agencies in the drug development process, minimal improvement in predicting CVD risk beyond established CVD risk scores, and because of misinterpretation and/or mischaracterization of CIMT results, [168] CIMT studies are less commonly performed now in CVD prevention pharmacotherapy development programs (i.e., lipid-altering drugs). [169] However, international guidelines do support the presence of plaque on CIMT as identifying patients at higher CVD risk. [158]

The correlation of peripheral vascular disease with CAD is a justification why an ankle brachial index (ABI) of < 0.9 is considered an atherosclerotic CHD risk-enhancing factor. [64] ABI is measured via doppler-aided blood pressure differential assessments, but typically does not involve imaging. Plethysmography is the measured changes in volume of an organ or body, as in air displacement plethysmography (BOD POD). [101] Plethysmography to assess venous flow (e.g., evaluation of possible deep vein thrombosis) can be performed via impedance, ultrasonography or air plethsmography. [170] Peripheral doppler imaging (e.g., B-mode doppler ultrasound and duplex ultrasound) can assess both peripheral venous and arterial disease. [170] Emerging doppler techniques include pulse wave velocity, vascular optical tomographic (i.e., cross-sectional) imaging, and polymer-based sensors (i.e., hemodynamic monitor or HeMo). [170]

Endothelial dysfunction may be consequence and predictor of atherosclerosis. An ultrasound flow-mediated dilation imaging study of the brachial artery is a noninvasive tool utilized to assess endothelial function and can be used to predict future CVD events. [171] While flow mediated dilation may improve on risk scores (i.e., Framingham risk score) in predicting CHD, when adjusted for confounders, the as-

Table 8
Ten things to know about hepatic imaging for NAFLD.

(1) Non-specific hepatic ultrasound may miss NAFLD with liver fat content < 20%.
(2) Vibration-controlled transient elastography (VCTE or Fibroscan) is a non-invasive ultrasound technique that can measure controlled attenuation parameter (CAP), which is a measure of hepatic steatosis. VCTE can also measure hepatic "stiffness," which reflects congestion, inflammation, and hepatic fibrosis.
(3) Hepatic computed tomography (CT) has limited use in clinical practice due to radiation exposure that exceeds other liver fat imaging studies.
(4) Magnetic resonance imaging is commonly used to measure liver fat, via proton density fat fraction (MRI-PDFF) which can assess the entire liver and that can be used with multiple MRI platforms.
(5) Magnetic resonance spectroscopy (MRS) can measure fat in small regions of interest; but not all MRI platforms have the capability to perform MRS.
(6) Nutritional medical therapy directed towards reducing imaging presence of hepatic fat (NAFLD) are similar to a heart healthy diet, such as evidenced-based meal plans limiting saturated fats and limiting ultra -processed/refined carbohydrates (e.g., Mediterranean diet). [1]
(7) Longitudinal hepatic imaging in patients with NAFD may help track progress of therapy, [160] such as after implementation of appropriate nutrition, as well as dynamic and resistance training that increases peripheral insulin sensitivity, reduce circulating free fatty acids and glucose, reduce lipotoxicity, increase hepatic fatty-acid oxidation, decrease fatty acid synthesis, and that may help prevent mitochondrial and hepatocellular damage. [161]
(8) Among patients with overweight or obesity, weight loss of 3 – 5% may reduce hepatic imaging consistent with steatosis, with weight loss of 7 – 10% usually needed to improve histopathological features of NASH (e.g., fibrosis).
(9) No pharmacotherapy has an approved indication to treat NAFLD and reduce imaging findings of liver fat. However, vitamin E 800 IU may provide biochemical and histological improvement in fatty liver in some adult patients with NASH without diabetes mellitus.
(10) Some drugs may reduce imaging findings of hepatic fat such as peroxisome proliferator activated receptor gamma agonists and glucagon like protein – 1 receptor agonists.

Sentinel Guidelines and References
2018 Current guidelines for the management of non-alcoholic fatty liver disease: A systematic review with comparative analysis [162]
2018 The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. [163]
2017 Imaging evaluation of non-alcoholic fatty liver disease: focused on quantification. [164]
2016 A comparison of liver fat content as determined by magnetic resonance imaging-proton density fat fraction and MRS versus liver histology in non-alcoholic fatty liver disease. Acta Radiol. [165]
2021 Obesity Medicine Association Obesity Algorithm [101]

Table 9
Ten things to know about carotid ultrasound, peripheral doppler imaging, ultrasound flow-mediated dilation, other tests of endothelial function, and peripheral vascular imaging.

(1) Peripheral artery disease as assessed by ABI < 0.9. While not an imaging study, an ABI < 0.9 is considered an atherosclerotic CHD risk-enhancing factor. [64]
(2) Peripheral artery disease can also be assessed by imaging studies such as peripheral doppler imaging.
(3) Guidelines support the presence of plaque on CIMT as identifying patients at high CVD risk. [158]
(4) Plethysmography is the measure of changes in volume, and is a technique most often used to assess venous flow (i.e., evaluation of possible deep vein thrombosis).
(5) Plethysmography for peripheral venous and arterial can be performed via impedance and ultrasound.
(6) Imaging studies can assess endothelial dysfunction, which may be consequence and predictor of atherosclerosis.
(7) An ultrasound flow-mediated dilation imaging study of the brachial artery is a noninvasive tool utilized to assess endothelial function and can be used to predict future CVD events.
(8) Duplex ultrasound, CTA, or MRA of the lower extremities is useful to diagnose anatomic location and severity of stenosis for patient with peripheral artery disease when revascularization is being considered.[179]
(9) Invasive peripheral artery angiography is useful for patients with critical limb ischemia or patients with lifestyle limiting claudication having an inadequate response to guideline directed management and therapy in whom revascularization is being considered. [179]
(10) Invasive and noninvasive angiography (e.g., CTA MRA) should not be performed for the anatomic assessment of patients with asymptomatic peripheral artery disease unless the delineation of anatomy would change treatment. [179]

Sentinel Guidelines and References
2019 Global perspective on carotid intima-media thickness and plaque: should the current measurement guidelines be revisited? [169]
2018 Peripheral vascular disease assessment in the lower limb: a review of current and emerging non-invasive diagnostic methods. [170]
2018 Endothelial Function: A Short Guide for the Interventional Cardiologist [178]
2017 Flow Mediated Dilation as a Biomarker in Vascular Surgery Research [180]
2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. [179]

sociation of brachial flow mediated dilation with CHD may no longer be significant, and may not improve discrimination and classification of CVD risk within intermediate risk individuals. [172]

Other imaging studies that can assess endothelial function include invasive atomic force microscopy, myographs, and before and after images of invasive intra-arterial administration of vasoactive substances. Non-invasive imaging studies of endothelial function include enclosed zone flow mediated dilation, digital (finger) pulse amplitude tonometry, digital photoplethsmography, arterial pulse wave analysis, and others. [173,174,175,176] From a cardiac standpoint, among the more common historic techniques to assess endothelial function include coronary epicardial vasoreactivity via quantitative coronary angiography, coronary microvascular function via Doppler, flow mediated dilation, venous occlusive plethysmography and finger plethysmography. [177] While the non-research, clinical utility of endothelial function assessment remains unclear, monitoring of endothelial function has the theoretical potential to provide information on vascular health, predictor of future adverse cardiovascular events, and assessment of the effectiveness of stent placement and medications such as statins, beta-blockers, and angiotensin converting enzyme inhibitors. [178]

Table 10
Ten things to know about imaging of other body organs applicable to preventive cardiology (brain, kidney, and ovary).

(1) In individuals without symptomatic cardiovascular, cerebrovascular, or peripheral vascular disease, CVD risk factors such as diabetes mellitus, obesity, hyperlipidemia, and cigarette smoking are independently associated with brain imaging changes ***before*** the manifestation of clinical cardiovascular or cerebrovascular disease. [181]
(2) Brain imaging findings associated with CVD risk factors include: (a) structural brain changes such as reduction in whole-brain volume, (b) white matter changes such as white matter hyperintensities and microbleeds, and (c) functional brain changes such as reduced cerebral blood flow. [181, 190, 191]
(3) Brain image findings of structural, white matter, and functional brain changes associated with CVD risk factors may contribute to cognitive decline. [190, 192]
(4) CVD risk factors that contribute to reduced whole brain volume on brain imaging include hypertension, obesity, dyslipidemia, and cigarette smoking. [181, 193]
(5) Even light physical activity can help maintain brain volume over time. [181, 193]
(6) Fibromuscular dysplasia is an arteriopathy that predominantly occurs in younger women that may result in aneurysm, dissection, or occlusion of the renal, carotid, vertebral arteries, and coronary arteries. Clinically, fibromuscular dysplasia may contribute to hypertension, neurological signs and symptoms, and dissection of an epicardial artery resulting in unstable angina, myocardial infarction, left ventricular dysfunction, or possibly sudden cardiac death. [194] Noninvasive imaging of the kidneys include duplex ultrasound, CT angiography, and magnetic resonance angiography. [195] Definitive diagnosis of fibromuscular dysplasia and imaging-directed potential treatment usually requires catheter-based angiography of the renal arteries, and possible percutaneous angioplasty. [196] Cardiac angiographic features of fibromuscular dysplasia include spontaneous coronary artery dissection, smooth narrowing of coronary arteries, intramural hematoma, coronary artery spasm, and tortuosity (historically described as "string of beads"). [194]
(7) Also, while not specifically applicable to kidney imaging, the presence of kidney disease can affect decisions regarding cardiac imaging:
  - The decision to perform cardiac imaging study in patients with CKD should be directed towards individuals at higher CVD risk (e.g., with symptomatic CVD) and those most likely to benefit from revascularization. [183]
  - Stress echocardiography, MPI SPECT, and MPI PET are safe in patients with kidney insufficiency.
  - Coronary CT angiography utilizes iodinated contrast which increases the risk of contrast-induced nephropathy; CMR utilizes gadolinium-based contrast agents that increase the risk of nephrogenic systemic fibrosis. [183]
  - Many patients with CKD have extensive coronary artery calcification, limiting the diagnostic value of CCTA. [183]
(8) The findings of "cysts" on imaging women with PCOS represent antral follicles arrested in development that accumulate follicular fluid giving the appearance of cysts. [197] Due to improved ultrasound imaging techniques, some believe the threshold for polycystic ovary morphology should be 19 – 25 follicles per ovary, instead of the more established criteria of 12 or more follicles per ovary. [198]
(9) The diagnosis of polycystic ovaries is usually made via ultrasound, which should not be performed for this purpose in girls < 8 years of age. [199]
(10) The presence of polycystic ovary morphology is not required for the diagnosis of PCOS. The Rotterdam Consensus for PCOS includes two or more of the following: [200]
  - Hyperandrogenism (clinical or biochemical)
  - Ovulatory dysfunction (menstrual irregularities)
  - Polycystic ovary morphology by ultrasound

Sentinel Guidelines and References
2020 Cardiac imaging for Coronary Heart Disease Risk Stratification in Chronic Kidney Disease [183]
2019 Chronic Kidney Disease and Coronary Heart Disease [185]
2018 Recent advances in renal imaging. [186]
2018 International evidence-based guideline for the assessment and management of polycystic ovary syndrome. [199]
2014 Brain imaging changes associated with risk factors for cardiovascular and cerebrovascular disease in asymptomatic patients [181]

Peripheral vascular imaging is often considered for patients with suspected limb ischemia having noncompressible arteries (ABI > 1.4) or objectively measured obstruction (ABI ≤ 0.9). Even if ABI is within the normal or borderline range, a nonhealing wound or gangrene of the extremities might suggest the need for additional diagnostic procedures. Perfusion assessments include toe-brachial index, transcutaneous oxygen pressure, and skin perfusion pressure. If the totality of this diagnostic evidence supports limb ischemia, then imaging studies to consider include duplex ultrasound, computed tomography angiography (CTA), magnetic resonance angiography (MRA), or invasive angiography. [179] Table 9 lists ten things to know about carotid ultrasound, peripheral doppler imaging, ultrasound flow-mediated dilation, other tests of endothelial function, and peripheral vascular imaging.

5.10. Imaging other body organs applicable to preventive cardiology (brain, kidney, and ovary)

In addition to heart and peripheral vasculature, body composition, and evaluation of hepatic fat, assessment of other organs may have applicability to preventive cardiology, such as the brain, kidney, and ovaries.

Imaging of the brain can be achieved by multiple different techniques, such as PET, MRI, MRS, and others. In persons without symptomatic cardiovascular, cerebrovascular, or peripheral vascular disease, CVD risk factors such as diabetes mellitus, obesity, hyperlipidemia, and cigarette smoking are independently associated with brain imaging changes before the clinical manifestation of cardiovascular or cerebrovascular disease. Types of structural brain changes associated with one or more of these CVD risk factors include reduction in whole-brain volume, white matter changes, and functional brain changes such as reduced cerebral blood flow. Identification of brain changes due to CVD risk factors represents an opportunity to intervene before irreversible deleterious brain damage occurs. [181]

Patients with chronic kidney disease (CKD) are at increased risk for CAD, with the risk for CVD increasing with worsening kidney function. [1] Most cases of adult-onset CKD are due to the major CVD risk factors of diabetes mellitus and hypertension, with obesity, cigarette smoking, and older age also risk factors for both CKD and CVD. [182] Patients with CKD are at increased risk for complications related to revascularization, and long-term results are less favorable compared to individuals with normal kidney function. [183] Examples of the adverse CVD consequences of CKD progression include non-atherosclerotic CVD, left ventricular hypertrophy, cardiac dysthymias, sudden cardiac death, diffuse arterial calcification, mitral annular and aortic valve calcification, [184] hemorrhagic stroke, and increased risk for mortality after a CVD event. [185] Currently, kidney imaging techniques (e.g., ultrasound, CT, and MRI) assess kidney size and density, nephrolithiasis, and crude markers of parenchymal damage (e.g., gross anatomic defects such as systemic disease, malignancies, and obstructive nephropathy). Newer imaging methods may enhance non-invasive detection of structural, functional, and molecular kidney changes, such as dynamic contrast-

enhanced magnetic resonance imaging (DCE-MRI) and blood oxygen level-dependent (BOLD) MRI, and the use of novel contrast agents, such as microbubbles and nanoparticles. [186] Regarding cardiac imaging in patients with CKD, the choice of cardiac imaging should be based on the clinical presentation, matching the desired information to the most appropriate imaging test, and the imaging procedure that avoids use of potentially nephrotoxic agents.

Polycystic ovary syndrome is among the most common endocrine disorder in women of reproductive age and occurs due to an imbalance of reproductive hormones in pre-menopausal women (with some metabolic abnormalities potentially extending into perimenopause). [187] The presence of polycystic ovaries alone may not be associated with increased CVD risk. [188] However, PCOS is often associated with CVD risk factors such as insulin resistance, glucose intolerance, diabetes mellitus, hypertension, dyslipidemia (increased triglycerides and decreased high density lipoprotein cholesterol), metabolic syndrome, increased C-reactive protein, increased CAC scores, increased carotid intima-medial thickness, endothelial dysfunction, and sleep apnea. [1,2,101,189] Table 10 lists ten things to know about imaging of other body organs applicable to preventive cardiology (brain, kidney, and ovary).

6. Conclusion

The “ASPC Top Ten Imaging 2021” is intended to be complementary to the “ASPC Top Ten CVD Risk Factors,” and summarizes ten things to know about ten imaging studies related to CVD prevention. The “ASPC Top Ten Imaging 2021” represents a starting point for those interested in CVD evaluation and CVD risk assessment. Knowledge of CVD cardiac and non-cardiac imaging can help guide preventive cardiology management and treatment. Just as the practice of preventive cardiology is a whole-body discipline, so should clinicians engaged in preventive cardiology understand multi-organ imaging modalities that might assist in assessing CVD risk. Such imaging methods naturally include evaluation of the heart. But imaging relative to cardiovascular disease prevention also includes dual x-ray absorptiometry (DXA) body composition, hepatic imaging, peripheral artery / endothelial function imaging, and images of other body organs applicable to preventive cardiology (brain, kidney, ovary). Many cardiologists engaged in preventive cardiology routinely perform heart-centered imaging. Many non-cardiologists engaged in preventive cardiology routinely perform non-heart centered imaging applicable to preventive cardiology. Cardiologists and non-cardiologists alike may benefit from a basic working knowledge of imaging studies applicable to preventive cardiology.

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