TEE for Detection of Myocardial Ischemia

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Objectives
1. Define myocardial ischemia
2. Explore the role of non-invasive testing in CAD
3. Understand the role of echocardiography to diagnose myocardial ischemia, specifically the use of stress echo, contrast, perfusion and strain

Definition of Myocardial Ischemia

Cardiac ischemia defines a decrease in blood flow and oxygen to heart muscle that results from to two broad categories: (1) reduced supply or (2) increased demand. Ischemia can occur in the presence of normal or abnormal coronary arteries. Patients may be asymptomatic with abnormal coronaries.

Ischemic Cascade	Tests
Anatomic lesion	CCTA
Endothelial/microvascular	CFR
Malperfusion	MPI
Myocardial dysfunction	SE
ECG	ECG
Symptoms	

Myocardial ischemia is often described in terms of the **Ischemic Cascade** a series of biochemical reactions initiated within seconds after ischemia from inadequate blood supply. This is perhaps better thought of in terms of **Ischemic Constellation**, a collection of observations that may occur in a variety of sequences following ischemia.

Diagnosis of Myocardial Ischemia

Diagnosis of an acute myocardial infarction (AMI) depends on the presence of two out of three characteristics:
1. symptoms of acute ischemia (chest pain); which may be absent in up to 33% of patients
2. ECG changes: ST segment change occurs in 60% of patients, but is inconclusive in 40%
3. Enzyme elevation (total CK, CK-MB, AST and LDH), cardiac troponin leak from damaged myocytes early after myocardial injury. Elevation of cardiac troponins can occur without ischemic heart disease.

Acute coronary syndrome (ACS) describes situations of a sudden blockage of blood flow to myocardium that may result in STEMI, non-STEMI and unstable angina. Enzyme elevation diagnoses ACS in the absence of symptoms and ECG changes. Currently available data demonstrate no threshold below which elevations of troponin are harmless and without negative implications for prognosis.

Non-Invasive Testing

Coronary angiography remains the reference standard for diagnosing ischemic heart disease, but does not provide information about the severity and extent of ischemia. Thus, there is an expanded role for non-invasive cardiac imaging procedures to identify and treat CAD that causes ischemia rather then just the presence and degree of stenosis. These tests assess inducible ischemia in the form of new regional wall motion abnormality (RWMA) or perfusion defect. Functional testing is more useful than noninvasive anatomic evaluation and exercise testing is more informative than pharmacologic testing.

Non-Invasive Cardiac Tests	Tests
Functional	
Exercise ECG	EECG
Stress Echocardiography	SE
Nuclear (SPECT, PET)	MPI
Cardiac MRI	CMRI
Coronary Flow Reserve	CFR
Anatomic	
CT Angiography	CCTA
Coronary Artery Calcium Score	CACS

Non-Invasive Tests	Sens (%)	Spec (%)
Exercise ECG	45-50	85-90
Exercise stress ECHO	**80-85**	**80-88**
Exercise stress SPECT	73-92	63-87
Dobutamine stress ECHO	**79-83**	**82-86**
Dobutamine stress MRI	79-88	81-91
Vasodilator stress ECHO	**72-79**	**92-95**
Vasodilator stress SPECT	90-91	75-84
Vasodilator stress MRI	67-94	61-85
Coronary CTA	95-99	64-83
Vasodilator stress PET	81-97	74-91

During stress testing the patient's HR and BP increase, raising myocardial oxygen demand. If this is unmet with an adequate blood supply from severe coronary stenosis, subendocardial ischemia typically occurs. The stress test terminates when the patient develops symptoms, diagnostic ST changes, or when the HR reaches 85–90% of a maximum predetermined rate based on the patient's age. Perform stress echocardiography in patients with known or suspected CAD only when exercise ECG stress test is either non-diagnostic or non-interpretable (LBBB or pacemaker).

Exercise stress test has relatively lower sensitivity and specificity for diagnosing ischemia. Analyses for other imaging modalities have different sensitivities and specificities. The coronary arteriographic cut off for luminal

diameter stenosis at which wall thickening abnormalities occur is 54% for exercise, 58% for dobutamine, and 60% for dipyridamole. The sensitivities/specificities for stress tests in the detection of CAD are exercise (85/77%), dobutamine (80/86%), and dipyridamole (78/91%).

Echocardiography to Diagnose Myocardial Ischemia

Echocardiography has an important first line imaging role as a complement to history, physical, ECG and cardiac biomarkers in ACS. In chronic stable CAD, stress echocardiography adds diagnostic and prognostic value. Poor acoustic windows, contraindications to pharmacological stress, and the need for expertise limits the use of echocardiography in this setting. Tissue Doppler Imaging (TDI), strain and contrast extend the possibilities and supply additional functional or geometrical information.

Stress Echocardiography (SE)

SE is one of the most important tools at the bedside for assessing myocardial ischemia and viable myocardium. Studies demonstrate the prognostic advantage of exercise echocardiography in patients with known and unknown CAD and LBBB, and the diagnosis of restenosis after non-surgical revascularization.

Indications Stress Echocardiography
• CAD diagnosis
• Assess adequacy pre/post revascularization
• Risk stratification in known CAD
• Identifying the location of ischemia
• Preoperative risk assessment
• Evaluate cardiac cause of exertional dyspnea
• To assess valve disease
• LBBB

Developments in hardware, digital software and improvements in ultrasound techniques yield excellent results from SE. SE relies on the assessment of regional wall motion abnormalities (RWMA). Wall motion (and perfusion) changes are more accurate than ECG changes to detect CAD. Wall motion is more specific; perfusion changes are more sensitive. Reporting of SE results often relies on the qualitative assessment of RWMA. Quantitative assessment using the LV wall motion score index (WMSI) averages the wall motion score of 17 myocardial segments. The diagnostic accuracy of SE depends on the type of stress procedure, the digital processing technique and the echocardiographer's experience.

SE can involve physical exercise (bicycles and treadmills), atrial pacing, and various drugs (dobutamine, dipyridamole and adenosine). Dipyridamole or adenosine induces ischemia by creating flow mismatch in myocardial territories. The sensitivity of dobutamine SE (DSE) is lower than peak exercise echocardiography, but one can perform DSE in patients who are unable to exercise. Despite the high accuracy of exercise SE in the diagnosis of CAD, multiple factors such as suboptimal image quality and poor endocardial border detection reduces accuracy. Contrast echocardiography improves endocardial border visualization and is indicated when suboptimal imaging is present.

Dobutamine

Low-dose DSE can detect viable myocardium and has prognostic value over clinical and functional variables for myocardial viability in chronic ischemic LV dysfunction. In the ischemic response, segmental function worsens during stress to cause hypokinesis, akinesis and dyskinesis. A resting akinesia that becomes dyskinetic during stress reflects the purely passive phenomenon of increased intraventricular pressure from normally contracting walls and is not true active ischemia. To assess viability, a segment with resting dysfunction may show either sustained improvement during stress indicating a non-jeopardized myocardium (stunned) or improve during early stress with subsequent deterioration at peak (biphasic response). The biphasic response is suggestive of viability and ischemia, with jeopardized myocardium fed by a critically coronary stenosis.

DSE	Normal	Ischemia	Stunned or hibernate	Infarction (Necrotic)
Baseline	Normal	Normal	Hypo/a/-kinetic	Hypo/a/-kinetic
Low dose	Normal	Normal	Improved	Hypo/a/-kinetic
High dose	Hyperkinetic	Hypo/a/-kinetic	Hypo/a/-kinetic	Hypo/a/-kinetic
	Normokinetic at rest and normal or hyperkinetic during stress	Function worsens during stress to hypo/a/-kinesis	Resting dysfunction improves with low dose but worsens with high	Segment remains fixed during stress
Hypokinesia: decrease of endocardial movement and systolic thickening Akinesia: absence of endocardial movement and systolic thickening Dyskinesia: paradoxical outward movement and possible systolic thinning				

Myocardial Contrast Echocardiography (MCE) or Myocardial Perfusion Echocardiography (MCPE)

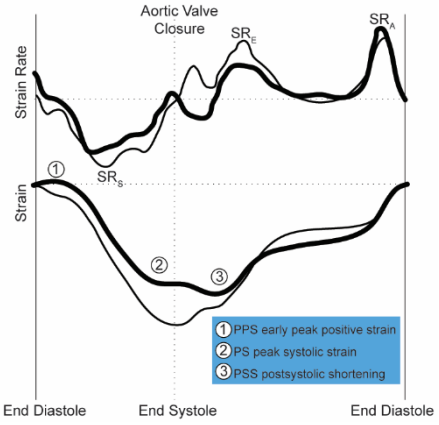
MCE is an ultrasound-based technique for assessing myocardial perfusion and can help detect CAD and has prognostic value over regional wall motion analysis. It may triage patients who have normal perfusion but abnormal troponins, ECG or RWMA. In AMI, MCPE delineates the area at risk for necrosis, the extent of collateral blood flow and aids the evaluation of the microvasculature for "noreflow" areas.

MCPE requires specific software and imaging techniques using contrast and a low mechanical index. Contrast microbubbles behave like RBCs in the myocardium so that any change in signal intensity or brightness represents a change in myocardial blood flow in a region of interest (ROI). With normal myocardial blood flow, 90% of the coronary circulation resides within the myocardial capillaries, RBCs travel at 1 mm/s at rest, and signal intensity returns to normal after 5-7 cardiac cycles. During stress or exercise with vasodilation and increased capillary blood flow, the rate of return of signal intensity is faster at 2–3 cardiac cycles.

Assessment of the rate of microbubble replenishment is qualitative or quantitative using specialized software. The quantitative approach takes the difference between maximum and basal blood flow to give the coronary flow reserve. A semi-qualitative MCPE involves assigning a numerical contrast score to each segment (0 = minimal or absent contrast opacification, 1 = reduced or heterogeneous opacification, 2 = homogenous opacification). Calculation of the perfusion score index (PSI) is a sum of the scores divided by the number of segments analyzed. The PSI at rest subtracted from the PSI at stress gives the ischemic burden of myocardium.

Strain

Tissus Doppler Imaging (TDI) provides a new insight into the analysis of myocardial mechanics in patients with CAD. Strain and strain rate measurements can potentially evaluate acute systolic and diastolic ischemic changes. Strain imaging can differentiate active from passive motion, which is difficult on visual examination. Longitudinal fibers present in the subendocardium are sensitive to ischemia and can show regional and global changes. Myocardial ischemia leads to a reduction in regional myocardial function. This is assessed from individual strain curves which show key findings:



1. Systolic lengthening (dyskinesis) in early systole may occur in transmural ischemia
2. Reduced peak systolic strain (hypokinesis)
3. Post systolic shortening (PSS) which is segmental shortening after the end of LV ejection. This finding is sensitive but not specific as it can occur in the presence of ischemia, scar or other conditions

In acute infarction, strain better defines the transitional zone between intact and dysfunctional myocardium and is superior to velocity imaging for defining anatomical extension of dysfunctional myocardium. Although abnormalities of PSS-related parameters alone persisted after recovery from 2-min occlusion, abnormalities of other deformation parameters, such as strain rate during early diastole, did not. These data suggest that assessment of PSS by speckle tracking echocardiography is useful for detecting myocardial ischemic memory.

Myocardial ischemia affects both global and regional LV systolic function. Global longitudinal strain (GLS) measured by 2D STE has a good correlation with the ischemic segments quantified by CMR for patients with first-time MI and can serve as a clinical diagnostic factor for assessing the MI area. 2D-STE-derived cut-off values for GLS (–21%) and global longitudinal SR (–0.9 s-1) are highly specific and sensitive for the detection of post-MI LV systolic dysfunction. LV strain on 2D echocardiography is well studied in patients with ACS. For patients with STEMI, LV GLS is an important predictor of post-discharge adverse outcomes. Following non-NSTEMI, LV GLS can also help discriminate which patients will successfully recover LV function from those who will develop adverse LV remodeling. Moreover, decreased GLS within 24 hours of revascularization for acute MI can reliably predict which patients are more likely to achieve a composite end-point of any of the following: all-cause mortality, hospitalization with re-infarction, HF, or stroke at six-month follow up.

Current guidelines do not recommend quantitative assessment of the magnitude of regional deformation because of lack of reference values, suboptimal reproducibility, and considerable inter-vendor

measurement variability. Indeed, inter-vendor differences for segmental strain values may be even higher than that reported for global values, which partly relates to vendor specific differences local tracking of speckles as part of noise reduction algorithms. Strain may diagnose myocardial ischemia, but the insufficient standardization of technology does not recommend it as a general tool for this purpose. However, in unclear clinical cases, consider regional strain as a supplementary method.

LV strain imaging can assess myocardial viability by stress echocardiography. Stunned myocardium is characterized by (a) decreased systolic deformation and PSS at rest and (b) almost normal systolic deformation and disappearance of PSD with dobutamine. In chronic infarction, dobutamine is associated with low or no deformation increase, depending on the fibrosis extension. Significant coronary stenosis was defined as a >1% reduction in longitudinal strain with an increase in PSS of at least two contiguous segments in the specific coronary artery territory at peak stress compared with baseline.

Table 1 Summary of longitudinal deformation characteristics at rest and during dobutamine stress for each ischaemic substrate

	Rest			Dobutamine stress					
				Low dose			Peak dose		
	PSSR	SS	PSS	PSSR	SS	PSS	PSSR	SS	PSS
Control	N	N	0*	↗	↗	0	↗↗	/↘	0
Acute ischaemia	↓	↓	↑	↘	↘	↗	↘↘	↘↘	↗↗
Stunning	↓	↓	↑	↗	↗	↘	↗↗	/↘	0
Chronic ischaemia/hibernation	↓	↓	↑	↗	↗	↗	↘	↘	↗↗
Non-transmural infarction	↓↓	↓↓	↑	↘	↘	↗	↘↘	↘↘	↗↗
Transmural infarction	0	0	0	→	→	→	→	→	→

Adapted from Bijnens *et al.*[7]
*May be present in up to two-fifths of the normal population at rest but if present is of low magnitude.
0 Absent; ↓ Reduced; ↑ Increased; ↗ Increased vs rest; ↘ Decreased vs rest;/↘ Initial increase followed by decrease; ↗↗ Further increasing; ↘↘ Further decreasing.
PSS, post-systolic shortening; PSSR, peak systolic strain rate, SS, systolic strain.

In healthy adults, both peak tissue velocities and SR increase linearly with increasing HR. Strain has a biphasic pattern, initially increasing at low stress, but remaining constant or even decreasing slightly as HR increases. This suggests that SR rather than strain itself may be a more sensitive marker of changes in myocardial function during stress. PSS is highly sensitive to ischemia, occurring in 100% of ischemic segments, and the magnitude of post-systolic strain increases both with resting ischemia or demand ischemia. To maximize the specificity of the stress test it is important to be able to distinguish between pathological and non-pathological PSS, by using the ratio of PSS to peak strain to improve specificity.

Readings

1. Stillman A, et al. Imaging the myocardial ischemic cascade. Int J Cardiovasc Imaging 2018; 34: 1249. https://doi.org/10.1007/s10554-018-1330-4
2. Maznyczka A, et al The ischaemic constellation: an alternative to the ischaemic cascade—implications for the validation of new ischaemic tests Open Heart 2015;2:e000178. https://doi: 10.1136/openhrt-2014-000178.
3. Pellikka PA, et al. ASE recommendations for performance, interpretation, and application of stress echocardiography. J Am Soc Echocardiogr 2007;20(9):1021–1041.
4. Porter TR, Xie F. Myocardial perfusion imaging with contrast ultrasound. JACC Cardiovasc Imaging 2010;3(2):176–187.
5. Opdahl A, et al. Strain, Strain Rate, Torsion, and Twist: Echocardiographic Evaluation. Curr Cardiol Rep 2015;17: 15.
6. Yang, Li-Tan et al. Strain Imaging with a Bull's-Eye Map for Detecting Significant Coronary Stenosis during Dobutamine Stress Echocardiography. J Am Soc Echocardiogr 2017;30(2):159-167.
7. Bijnens B, *et al*. Investigating cardiac function using motion and deformation analysis in the setting of coronary artery disease. Circulation 2007;116:2453–64.
8. Joyce E, Delgado V, Bax JJ, *et al* Advanced techniques in dobutamine stress echocardiography: focus on myocardial deformation analysis. *Heart* 2015;101:72-81.