

NEUROLOGIC COMPLICATIONS OF CARDIAC AND AORTIC DISEASE

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Stroke is the most common and recognized complication of cardiac and aortic disease. However, there are other neurologic complications that can result from cardiovascular dysfunction such as encephalopathy, meningitis, myelopathy, radiculopathy, neuropathy, and possibly even migraine. Prompt recognition and diagnosis may allow us to better treat and perhaps even prevent many neurologic complications of cardiac and aortic disease.

Heart

1. Cardioembolic stroke

- a. Stroke is the most common neurologic complication of cardiac disease—20-30% of ischemic strokes are cardioembolic.¹
- b. Emboli arise from: valvular disease, stasis of blood flow, or a venous source that reaches the brain via abnormal connection between the right and left sides of the heart.
- c. Nonvalvular atrial fibrillation/flutter (AF) is the main risk factor for cardioembolic stroke
 - i. Both the incidence and prevalence of AF are expected to rise
 - ii. AF is often paroxysmal, so it can be difficult to detect. Detection requires cardiac monitoring—either conventional or prolonged.
 1. Conventional: EKG, Holter monitor, etc.
 2. Prolonged monitoring: ambulatory or implantable devices
 - i. Prolonged monitoring detects AF in ~10-15% of patients with cryptogenic stroke^{2,3}
 - ii. Likelihood of detection increases with: age, prior cortical or cerebellar infarct, prolonged PR interval, frequent premature atrial contractions, and higher CHADS₂ score⁴
 - iii. Increasing incidence and detection of AF has consequently led to an increase in the number of patients being treated with anticoagulants. However, some patients are precluded from taking anticoagulants due to bleeding risk. For these patients, left atrial appendage (LAA) closure may be an alternative option for stroke prevention, as closure prevents thromboembolism formation without the need for anticoagulation.
 1. Various surgical procedures and devices can be used to close the LAA
 - a. The WATCHMAN implant was approved by the FDA in 2015⁵

2. Patent Foramen Ovale

- a. *In utero*, the foramen ovale allows maternally-oxygenated blood to pass from the right to left atria of the heart, bypassing the fetal lungs. Pressure changes at birth close the foramen. However, for 25% of individuals, closure fails or is incomplete, resulting in a patent foramen ovale (PFO). A PFO is usually not harmful, but, epidemiologically, PFO prevalence is higher than expected in patients with cryptogenic stroke and migraine (especially migraine with aura).
 - i. Cryptogenic stroke
 1. Possible mechanism is paradoxical embolism (venous source) from right-to-left shunt through the PFO.
 2. Difficult to determine if PFO is incidental or not. A complete evaluation to exclude other causes of stroke is necessary.
 - a. ROPE score⁶ is a tool that can aid clinicians in determining if the PFO is incidental or not.

3. PFO closure
 - a. Utilization of off-label atrial septal occlude devices is increasing
 - i. Randomized-controlled trials have not shown a benefit over medical therapy⁹⁻¹¹
 - ii. AAN guideline published in 2016 recommends against PFO closure outside of a research setting¹²
 4. Antiplatelet therapy is recommended for secondary stroke prevention, unless there is an indication for anticoagulation, such as an acute deep vein thrombosis.¹²
- ii. Migraine
 1. Theorized mechanism for PFO-related migraines is abnormal shunting of microemboli or neuroactive substances (e.g. serotonin) to the brain that would normally be removed by the lungs.
 - a. Observation studies have reported reduced migraine frequency following PFO closure
 - b. Randomized-controlled trials have not shown a decrease in frequency or severity following PFO closure^{7,8}

3. Endocarditis

- a. Defined as inflammation of the endocardium—the inner layer of the heart and surface of the valves. It is categorized as either infective or non-infective.
- b. Infective
 - i. Caused by a bacterial or, less frequently, fungal infection¹³
 1. 80% of cases are caused by streptococcal or staphylococcal infections
 - a. *Staphylococcus aureus* infection high risk for neurologic complications
 2. Infection with *Candida* or *Aspergillus* less common, but neurologic complications common (~60% of patients)
 - ii. Risk factors include rheumatic heart disease, prosthetic valves, intracardiac devices, congenital heart defects, HIV/AIDS, and intravenous drug use¹⁴.
 - iii. Complications from endocarditis are protean—15-47% of patients will develop neurologic complications.
 1. Stroke is the most common neurologic complication, and, for 15-20% of patients, stroke is the initial presenting symptom of infective endocarditis.
 - a. Most strokes are ischemic, but subarachnoid and intracerebral hemorrhages also occur.
 - i. Hemorrhages can be secondary to: septic endarteritis, transformation of an ischemic infarct, or rupture of a mycotic aneurysm (uncommon, accounts for only ~3% of endocarditis-related hemorrhages)¹³
 2. Septic emboli can seed the nervous system, resulting in meningoencephalitis, cerebritis, or abscess formation.
 - iv. Initiation of antiplatelet or anticoagulant medications is not recommended in cases of infective endocarditis.
 1. For patients with a mechanical valve and ischemic stroke or hemorrhage, anticoagulation should be held for at least two weeks¹⁵.
- c. Non-infective
 - i. Characterized by sterile vegetations composed of platelets and fibrin aggregates. Referred to as nonbacterial thrombotic endocarditis, or, historically, as either marantic or Libman-Sacks endocarditis.

1. Marantic endocarditis occurs in “wasting states”—classically in patients with cancer.
 2. Libman-Sacks endocarditis occurs in rheumatologic disease—classically in patients with systemic lupus erythematosus.
- ii. Ischemic stroke is the main complication of non-infective endocarditis. Unlike infective endocarditis, anticoagulation is recommended in patients with non-infective endocarditis¹³.

4. Cardiac Tumors

- a. Primary cardiac tumors are rare, and the majority are classified as “benign”. However, even benign tumors can cause:
- i. Cardiac dysfunction (obstruction, arrhythmia)
 - ii. Constitutional symptoms (fever, weight loss, myalgias/arthralgias)
 - iii. Ischemia (embolization of tumor fragments or thrombi from the tumor surface)
- b. Myxomas and papillary fibroelastomas are the most common primary cardiac tumors in adults, and the tumor types most frequently associated with neurologic complications¹⁶.
- i. Myxoma¹⁷
 1. Account for ~50% of all primary cardiac tumors in adults, 75% are located in the left atrium
 2. 12-45% will develop neurologic complications:
 - a. Cerebral, spinal cord, or retinal infarcts
 - b. Intracranial aneurysm formation¹⁸
 - i. Rare complication, usually fusiform aneurysms (as opposed to saccular)
 - ii. Results from tumor cells directly invading the vessel walls
 - ii. Papillary fibroelastoma¹⁹
 1. Can arise from any endothelial surface, but are mostly found on the surface of the valves (most commonly the aortic, followed by the mitral)
 2. Neurologic complications are more common than cardiac
 - a. Stroke/TIA is the main neurologic complication, and is the presenting symptom for ~30% of patients

5. Cognitive Impairment/Dementia

- a. Heart disease is a risk factor for cognitive impairment/dementia²⁰
- i. Risk is mostly attributable to stroke and vascular disease—patients with coronary disease are also likely to have cerebrovascular disease
 - ii. AF and heart failure may increase the risk of cognitive impairment independent of cerebrovascular disease or stroke²¹.
 1. Potential explanation is that decreased cardiac output (irregular or fast heart rate, reduced ejection fraction) causes cerebral hypoperfusion and neuronal injury.
 - a. Studies have demonstrated improved cognition with improvement in cardiac output/cerebral blood flow, such as after heart transplantation²⁰.
 - iii. Cardiac surgery is a risk factor for cognitive impairment/dementia—either from the procedure itself or from a complication, such as stroke.
 1. Potential mechanism for cognitive impairment from the procedure itself: microemboli, intraoperative hypotension or oxygen desaturation, use of general anesthesia, triggering a systemic inflammatory response.
 2. CABG procedures using extracorporeal cardiopulmonary bypass (“on-pump”) were felt to increase the risk of cognitive impairment, with rates as high as 41%²².

- a. This has been called into question recently, with studies noting no significant difference between CABG procedures using or not using cardiopulmonary bypass. Furthermore, the cognitive decline may be secondary to pre-existing cerebrovascular disease and not the procedure itself²³.

Aorta

6. Aortic aneurysm

- a. Defined as an enlargement of the aorta >50% of the expected diameter
 - i. Approximately 4.5 cm for the thoracic aorta (ascending aorta, aortic arch, and descending aorta)
 - ii. Approximately 3 cm for the abdominal section of the aorta
- b. Risk factors for development: older age, male gender, hypertension, atherosclerosis, tobacco use, and family history of aortic aneurysm.
- c. Compared to abdominal aortic aneurysms, thoracic aortic aneurysms are more often associated with genetic disorders (Marfan or Turner syndromes), bicuspid aortic valve, or inflammatory conditions—either infectious (Syphilis) or non-infectious (giant cell/temporal arteritis)²⁴.
- d. Rarely aortic aneurysms can cause neurologic complications from direct compression
 - i. Thoracic: Hoarseness via compression of the left recurrent laryngeal nerve
 - ii. Abdominal: lumbosacral plexopathy, radiculopathy, mononeuropathy, or even cauda equina syndrome have all been reported²⁵.

7. Aortic dissection

- a. Aortic aneurysms increase the risk of aortic dissection. Dissections are classified as:
 - i. Type A—dissections that involve the ascending aorta
 - ii. Type B—all other dissections
- b. Most patients with an aortic dissection present with chest and/or back pain, but ~25% of patients develop a neurologic complication²⁶. Dissections can be painless, and for these patients the presenting symptom may be neurologic.
 - i. Ischemic stroke—most common neurologic complication (most often with Type A dissections)—results from:
 1. Involvement of the great vessels
 2. Thromboembolism
 3. Severe hypotension resulting in cerebral hypoperfusion
 - ii. Spinal cord infarction from interrupted flow from the radicular arteries
 - iii. Horner's syndrome from the dissection extending into a carotid artery
- c. Roughly 2-14% of patients develop neurologic complications after surgical or endovascular repair of aortic dissections or aneurysms²⁷:
 - i. Ischemic stroke or spinal cord infarction are the most common
 - ii. A rare complication is development of a syndrome resembling progressive supranuclear palsy²⁸.

8. Thoracic aortic plaques

- a. Atherosclerosis of the ascending aorta and aortic arch is an under-recognized risk factor for ischemic stroke
 - i. Aortic plaques are a source for emboli—embolism can be spontaneous or iatrogenic
 - ii. Plaque characteristics that increase the risk of embolism and stroke: mobile, >4mm, non-calcified, lipid-rich core, and/or ulcerated²⁹.

- b. Treatment
 - i. Current guidelines recommend statin and antiplatelet therapy for secondary stroke prevention³⁰
 - 1. ARCH trial is the only prospective randomized-controlled trial comparing antiplatelet (clopidogrel + aspirin) versus anticoagulation (warfarin) for prevention of stroke in patients with complex aortic arch plaques. The trial was stopped early due to poor recruitment and lack of funding—the results are inconclusive³¹.

9. Coarctation of the Aorta

- a. A congenital narrowing of the aorta—can occur at any level, but occurs most frequently in the arch.
- b. Symptoms depend on the location of the narrowing and degree of stenosis—classically patients will have arterial hypertension in the arms and hypotension/weak pulses in the legs.
 - i. Neurologically, the increased arterial pressure can cause headaches, dizziness, and increases the risk of intracerebral hemorrhage.
- c. Patients with aortic coarctation should be screened for intracranial aneurysm—10% will harbor an unruptured aneurysm³².
 - i. Bicuspid aortic valve and thoracic aortic aneurysm are also associated with intracranial aneurysms.

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