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VERIFYING SIGNS OF COVID-19 STROKE THROUGH IMAGING

By: Robert L. Bard, MD and Dr. Pierre Kory, MD | September 2, 2020

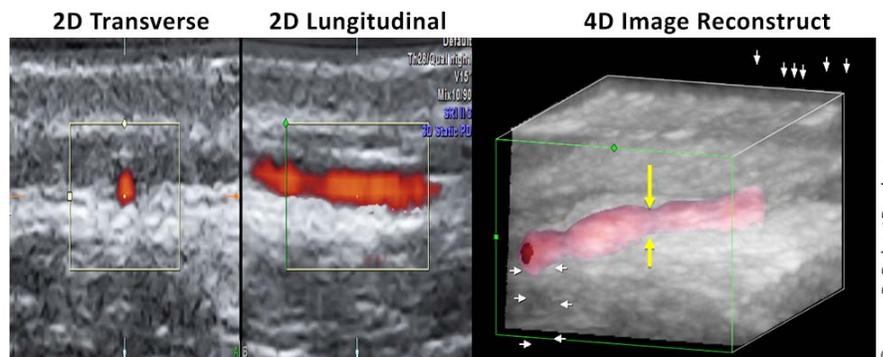
ABSTRACT

Early detection and prevention of arterial and venous disease is key to minimizing the effects of arterial obstruction & hemorrhage, brain aneurysms, and strokes from venous thrombosis. The association of trauma to PTSD is now followed by advanced Doppler ultrasound and functional MRI. This abnormal physiology may also manifest as arterial dissection, collagen disease, inflammatory arthritis, dermatitis, ocular disorders, GI disturbances, limb pain, aneurysms of the brain and aorta. Devastating strokes in the Covid-19 era occur in the younger age group and the Latin population is at higher risk.

INTRODUCTION

Interest in arteritis was elevated with the study of Takayasu's disease in the 1970s when advances in contrast arteriography diagnosed diffuse vascular involvement causing strokes and aneurysms in multiple sites. While this arterial inflammation is more common in Asians, in the US, blacks are nearly three times more likely to have a stroke at age 45 than whites. The pediatric population seems to be at higher risk for this arteritis as evidenced by their unusual rate of Covid-19 affliction affecting the vasculature and called "MULTIPLE ACUTE INFLAMMATORY SYNDROME". Birth control pills is a distinct cause of such disease in younger women while cancer, alcoholism and obesity raise the incidence at all ages.

TEMPORAL ARTERITIS



Arterial narrowing in patient with headache / visual changes

We have learned over the last century that blockages of coronary arteries to the heart and carotid arteries to the brain are precipitated by inflammation of the inner walls of the vessel, called the "intima"

While thickening of the interior wall of vessels gradually occurs over time and is aggravated by diet, stress and hypertension (high blood pressure), the acutely disabling event is when there is an abrupt tear of the overlying plaque which ruptures debris which then forms a blood clot which blocks blood flow or the clot travels deeper into the brain and blocks blood flow. Similarly, abnormal heart rhythms such as "atrial fibrillation", causes the pooling of blood in the heart which predisposes to clot formation and the clots can then travel into the brain causing a stroke. In Covid-19, the virus causing severe inflammation in the blood which then promotes clot formation which can travel through the vascular system and affect almost every organ system in the human body, with the brain and lungs being the most

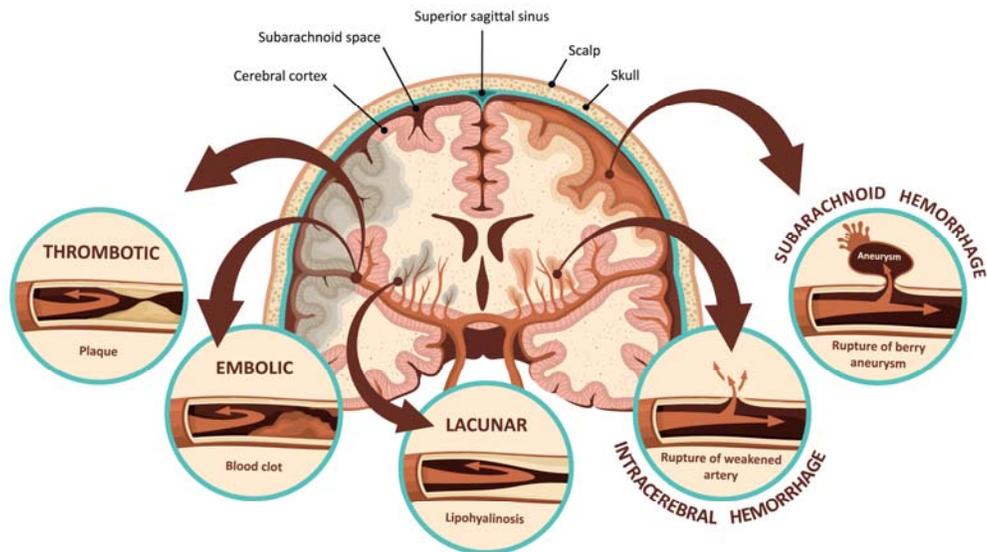
affected.. An article in September NEUROLOGY reported by Medscape documented the incidence of large artery stroke as the presenting symptom of COVID-19 was highest in men under the age of 50 years.

HISTORY

A medical research team at Metropolitan Hospital in New York first noticed unusual neurologic symptoms in young and middle aged patients in the late 1960s. As a division of the NY Medical College system, they were fortunate to have an active interventional radiology

department specializing in neuroimaging and arteriography. The observation of distortion and occlusion of arteries supplying the brain, kidneys, GI tract and lower limbs to various degrees from single to multiple locations was closely linked to the Japanese disorder known as Takayasu's arteritis at the time and recently renamed "arteritis." A clinical finding of this arterial inflammation in the abdominal aorta was pain in the upper abdomen by the great vessels by palpation. Astute physicians were successfully treating this with commonly available "aspirin."

However, the chronic and diffuse nature of arteritis often weakened the vessel wall producing aneurysmal dilation and rupture. Today we find sophisticated non-invasive or minimally invasive modalities to be the first line of interrogation of vasculitis.



ISCHEMIC vs HEMORRHAGIC STROKE

COVID AND STROKE

COVID-19 was rapidly understood as a disease caused by severe and widespread inflammation and "hypercoagulability" (a tendency to spontaneously form clots in the blood vessels. Autopsies have revealed extensive small vessel strokes, with such strokes often occurring despite aggressive blood thinner treatment and regardless of the timing of the disease course, suggesting that it plays a role very early in the disease process. In one autopsy series, there was a widespread presence of small clots with acute stroke observed in over 25%. In a recent review of the incidence of stroke in COVID-19, almost 2% of all hospital patients suffered a stroke, which is 8x higher than in patients with influenza. More worrisome is that this is almost definitely a gross underestimate given the many likely missed strokes in patients who died on ventilators who were too ill to obtain imaging, the general restrictions on and lack of autopsies, and the well-recognized decrease in the number of patients with acute stroke symptoms seeking medical attention in the COVID-19 era. Another worrisome finding from a recent study of COVID-19 cases found that 45.5% of patients reported neurologic symptoms [4]. This under-recognized epidemic of neurological symptoms and strokes in COVID-19 highlights the need for more intensive imaging and investigation to achieve not only earlier



Dr. Pierre Kory, pulmonary and critical care specialist has treated countless Covid-19 cases and targets the many confirmed short and long term effects on the body including blood clots and stroke.

recognition and improved treatment of patients but in furthering understanding of COVID-19 effects on brain function.

DIAGNOSIS BY IMAGING

Blood flow abnormalities in the arterial system are best study by Doppler imaging like the weather Doppler showing tornadoes. Multiple options exist for blood flow analysis including:

- CAROTID SONOGRAM
- TRANSORBITAL DOPPLER
- 3D/4D VESSEL DENSITY HISTOGRAM
- SOFT TISSUE OCT
- 7 TESLA MRI
- CAROTID DOPPLER
- CONTRAST ENHANCED ULTRASOUND
- ENDOARTERIAL 3D DOPPLER
- REFLECTANCE CONF. MICROSCOPY
- HYBRID IMAGING
- EYE SONOGRAPHY
- TRANSCRANIAL DOPPLER
- RETINAL OCT
- SMALL COIL MRI

CAROTID SONOGRAM: While cerebrovascular disease is often diagnosed ex post facto after a catastrophic episode with MRI and CT, the non invasive Doppler analysis of the vascularity is generally checked with ultrasound for plaque and obstruction. A useful measure of the risk of coronary and cerebrovascular disorder is the carotid intimal thickness (CIMT). Standard depth of the inner wall thickness is a measure best obtained by high resolution sonograms since a reading over 0.9mm indicates increased risk. The newer sonogram units have depth resolution of 0.02mm making this a preferred non invasive option.



CAROTID DOPPLER: Flow abnormalities of turbulence and absence are commonly evaluated with this modality. Plaque forms more readily in aberrant flow patterns and high velocity regions accompanying narrowing.

EYE SONOGRAPHY: Sonofluoroscopy of the orbital soft tissues and eyes is performed in multiple scan planes with varying transducer configurations and frequencies. Power and color Doppler use angle 0 and PRF at 0.9 at optic nerve head. 3D imaging of optic nerve and carotid, central retinal arteries and superficial posterior ciliary arteries performed in erect position before and after verbal communication. Retinal arterial flow is measured. Optic nerve head bulging is checked as increased intracranial pressure may be demonstrable.

TRANSORBITAL DOPPLER: R/L ciliary arteries have normal Doppler flows of 10cm/s which is symmetric.

CONTRAST ENHANCED ULTRASOUND: Widely used European nonionic contrast injection allows imaging capillary size vessels and perfusion characteristics

TRANSCRANIAL DOPPLER: This measures the flow in the anterior, middle and posterior cerebral arteries as well as Circle of Willis.

3D/4D VESSEL DENSITY HISTOGRAM: Multiple image restoration and reconstruction shows retinal vessel density of 25% at the optic nerve head and adjacent region with quantitative accuracy.

ENDOARTERIAL 3D DOPPLER: Microcatheters inserted into the arterial or venous system provide measurement of wall thickness and presence of inflammatory vessels inside the intima.

RETINAL OCT: Subtraction techniques done with OCT optical coherence tomography may show changes in the caliber of the retinal vessels with verbal ideation.

SOFT TISSUE OCT: The depth of penetration may be extended to 2-3mm allowing for analysis of vascular changes in erythematous or erythropoor dermal areas. Thrombosis may be observed.

REFLECTANCE CONFOCAL MICROSCOPY: This microscopic analysis of the cells also quantifies microvascular pathology and is a potential modality for studying vasculitis.

SMALL COIL MRI: High resolution systems used for animal study and superficial organs can image the intra-arterial anatomy

including dynamic contrast imaging on standard 1.5T and 3T units.

7 TESLA MRI: High field systems analyse signal abnormalities rapidly with high resolutions.

HYBRID IMAGING: Hybrid imaging refers to combining diagnostic modalities to assess disease and monitor therapy.

TREATMENT OPTIONS

CEUS and nanoparticle delivery of dexamethasone may be used to reduce plaque inflammation and stroke occurrence. Intraarterial unstable plaque, most commonly found in the carotid artery, readily ruptures (acutely blocking flow) or dislodges causing distal embolism and arterial occlusion often in the brain, extremities and GI tract. While the composition of this plaque is mostly fibrin and lipid, it is the ulceration, bleeding and active inflammation that produces catastrophic outcomes. Neovascularization plays a central role in plaque initiation, progression and rupture. Quantifying these inflammatory microvessels is a surrogate marker of plaque instability and stroke risk. Histopathologic evidence shows plaque with high vessel density is more likely to rupture. [5]

SUMMARY

Covid-19 affliction of the arterial and venous systems with clot formation and vessel inflammation affect every organ system in the body. Arteritis of the small vessels involves the lungs, heart, brain, kidneys and liver predominantly which increases stroke risk in the absence of other contributing factors. Advanced ultrasound imaging offers early detection alerts and image guided therapeutics are now available. Anti inflammatory treatments, such as the MATH+ protocol used to treat Covid-19 pulmonary disease, might be useful in reducing intra-arterial inflammation and preventing plaque rupture.

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Dr. Bard received the 2020 nationally acclaimed Ellis Island Award for his lifetime achievement in advanced cancer diagnostic imaging. He co-founded the 9/11 CancerScan program to bring additional diagnostic support to all first responders from Ground Zero. His main practice in midtown, NYC (Bard Diagnostic Imaging- www.CancerScan.com) uses the latest in digital imaging technology and has been also used to help guide biopsies and in many cases, even replicate much of the same reports of a clinical invasive biopsy. Imaging solutions such as high-powered sonograms, Power Doppler Histogram, sonofluoroscopy, 3D/4D image reconstruction and the Power Doppler Histogram are safe, noninvasive, and do not use ionizing radiation.



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Dr. Kory is Board Certified in Internal Medicine, Critical Care, and Pulmonary Medicine. He served as the Medical Director of the Trauma and Life Support Center at the University of Wisconsin where he was an Associate Professor and the Chief of the Critical Care Service. He is considered a pioneer and national/international expert in the field of Critical Care Ultrasound and is the senior editor of the widely read textbook "Point-of-Care Ultrasound" (winner of the President's Choice Award for Medical Textbooks from the British Medical Association in 2015). Most recently, Dr. Kory joined the emergency volunteer team during the early COVID-19 pandemic in NYC at Mount Sinai Beth Israel Medical Center. He is also a founding member of the Front Line COVID-19 Critical

Working Group (flccc.net) composed of 5 critical care experts that devised the COVID-19 treatment protocol called MATH+ (www.covid19criticalcare.com/)

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