Pattern and prevalence of Carotid and lower extremeties arterial disease in different degrees of severity of multivessel cronary artery disease Egyptian patients assesed by syntax score

Thesis

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Abstract

Background: Atherosclerosis is a diffuse process that may affect different vascular beds with considerable overlap between coronary, cerebrovascular and peripheral arterial disease. These conditions are related to similar predisposing risk factors and genetic predisposition. Presence of atherosclerosis at one arterial site should prompt the clinician to assess for an involvement, symptomatic or asymptomatic, at other arterial distributions. Currently, No data is known about the relationship between the the numerical value of syntax score as an estimate of severity of coronary artery disease and other vascular beds affection in form of carotid and lower limbs arterial atherosclerotic disease. We aimed to assess the strength of these relationships.

Methods: This study included 100 consecutive patients who had coronary artery disease diagnosed by coronary angiography. They were distributed according to syntax score into: low(56 patients), moderate (25 patients) or high syntax score(19 patients).In the all patients, carotid duplex U/S was done for the assessement of the carotid IMT and the summation value of the carotid plaques dimensions(mm^2). Also bilateral lower limbs arterial duplex was done for assessment of CFA IMT and ABI . We studied the correlation between the numerical valvue of syntax score with the numerical value of both carotid IMT and the summation value of carotid plaques dimensions.We also studied the correlation between the numerical value of the syntax score and the numerical value of both CFA IMT &ABI.

Conclusion : In our study, We concluded that in patients with carotid disease, there was a significant positive correlation between the numerical value of carotid IMT and syntax score with (P) value:0.002. There were also a significant positive correlation between the summation value of carotid plaques dimensions and the numerical value of syntax score with (P) value :0.001. In PAD, there were a significant negative correlation between the numerical value of ABI and the numerical value of syntax score with (P) value:0.001 . There were no siginificant correlation between the numerical value of CFA IMT and the syntax score with (P) value:0.769.

Key words: Coronary artery disease, carotid disease, PAD, syntax score.

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List of abbreviations

2D-US	Two-Dimensional Ultra-Sound
ATA	Anterior Tibial Artery
ACAS	Asymptomatic Carotid Artery Stenosis
AP	Antro-posterior
Apo	Apolipoprotein
BP	Blood Pressure
C. Pneumoniae	Chlamedia Pneumoniae
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CAS	Carotid Artery Stenting
CCA	Common Carotid Artery
CEA	Carotid Endarterectomy
CHD	Coronary Heart Disease
CIMT	Carotid Intima-Media Thickness
CMV	Cytomegalovirus
CRAO	Central Retinal Artery Occlusion
CREST	Carotid Revascularization Endarterectomy vs. Stent Trial
CRP	C - Reactive Protein
CS	Cross Section
CT	Computed Tomography
CVS	Cerebrovascular stroke
DBP	Diastolic Blood Pressure
DSA	Digital Subtraction Angiography
DM	Diabetes mellitus
ECA	External Carotid Artery
ECG	Electrocardiogram
ECM	Extracellular Membrane
ECs	Endothelial Cells
ECST	European Carotid Surgery Trial
EDV	End-Diastolic Velocity
eNOS	Endothelial Nitric Oxide Synthase
FDA	Food and Drug Administration
FH	Family History
Fig	Figure
HDC	Histidine Decarboxylase
HDL	High Density Lipoprotein
HSP	Heat Shock Protein
HTN	Hypertension
IAD	Intra-cranial Atherosclerotic Disease
IC/CC	Internal Carotid/Common Carotid
ICA	Internal Carotid Artery

IDL	Intermediate Density Lipoprotein
IFN-γ	Interferon γ
IHD	Ischemic Heart Disease
IJV	Internal Jagular Vein
IMT	Intima-Media Thickness
IVUS	Intra-Vascular Ultrasound
JNC	Joint National Committee
LDL	Low Density Lipoproteins
LDLR	Low Density Lipoprotein Receptors
LM	Left main
LV	Left Ventricle
MCA	Middle Cerebral Artery
MCP-1	Monocyte Chemoattractant Protein-1
MI	Myocardial Infarction
MMP	Matrix Metalloproteinase
MRA	Magnetic Resonance Angiography
MRI	Magnetic Resonance Imaging
mRNA	Messenger Riboneuclier Acid
MT-MMPs	Membrane-Type Matrix Metalloproteinases
NASCET	North American Symptomatic Carotid Endarterectomy Trial
NSTEMI	Non ST Elevation Myocardial Infarction
NO	Nitric Oxide
NS	Not Significant
PCA	Posterior cerebral artery
PLA_2	Phospholipase A_2
P.com	Posterior Communicating
PS	Plaque Score
PSV	Peak Systolic Velocity
PTA	Percutaneous transluminal angioplasty
PVD	Peripheral vascular disease
RI	Resistivity Index
ROS	Reactive Oxygen Species
SBP	Systolic Blood Pressure
SMCs	Smooth Muscle Cells
TCD	Trans-Cranial Doppler
THA	Transient Hemispherical Attack
TIAs	Transient Ischeamic Attacks
TIMPs	Tissue Inhibitor of Metalloproteinases
TMB	Transient Monocular Blindness
TNFα	Tumor Necrosis Factor α
USDA	United States Departement of Agricultre
VCAM-1	Vascular Connection Adhesion Molecule-1
VLDL	Very Low Density Lipoprotein

VSMCs Vs WHO	Vascular Smooth Muscle Cells versus World Health Organization

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Introduction

Peripheral arterial disease is a common manifestation of atherosclerotic disease process, affecting from 12 to 14% of the general population and as many as 20% of individuals over the age of 75 (1).

Patients with peripheral arterial disease often have coexisiting cerebrovascular disease and/or coronary artery disease and therefore have poor prognosis and reduced expectancy (2).
Coronary heart disease accounts for half of the total mortality , whereas vascular disease in general accounts for almost two thirds of the total mortality (3).

Diabetes mellitus, hypertension, hyperlipidemia, smoking and age are important risk factors for peripheral arterial disease. PAD is also an important risk factor for lower extremity amputation in patients with chronic foot ulcers(4).

Carotid and peripheral arterial diseases may be asymptomatic or symptomatic by TIAs, cerebrovascular strokes or even sudden death**(**in carotid atherosclerotic disease due to thrombosis or atheroembolism**)**, or intermittent claudication, critical limb ischemia, rest pain and gangerene or even amputation**(**in lower extremities atherosclerotic disease**)** (5).
The non invasive laboratory diagnosis of peripheral and carotid arterial diseaes provides a higher estimate of the disease since these tests have a high sensitivity and as well as specificity for detecting angiographically defined arterial occlusive disease.

Color coded dupplex ultrasound is considered a valuable, cheap, easy and non invasive diagnostic tool for carotid and peripheral arterial diseases.Using color Doppler , B-mode and pulsed wave Doppler can give us an accurate diagnostic tool for estimation of pattern and severity of carotid and peripheral arterial disease as well as estimation of intimal medial thickness, presence of plaques and its characterization, kinking, aneurysmal dilation or wall dissection, while in peripheral arterial disease it can estimate aortoiliac disease, stenotic or occlussive lesions, estimation of severity and nessecity for medical or interventional treatment using Ankle/Brachial index.

The syntax score (synergy between PCI with TAXUS™ and cardiac surgery) which is postulated by Syntax trial to prospectively characterize the anatomy of coronary vasculature with respect to the number of lesions and their functional impact, location , and complexity.(6).

It is calculated by a computer program consisting of sequential and interactive self giuded 12 main questions .

The 1st 3 questions determine :dominence, total number of the lesions and vessel segments involved per lesion. The last 9 questions refer to adverse lesion charecteristics and repeated for each lesion:total occlusion, trifurication, bifurication, aorto-ostial lesions, severe tortousity, lenghth more than 20mm, heavy calcification, thrombus, diffuse disease/small vessel..

Aim Of the work

The aim of this work is to asses the pattern and prevelence of carotid and lower extremeties arterial atherosclerotic disease in coronary artery disease Egyptian patients assesed by syntax score which is considered as an estimate for the severity and complexity of coronary atherosclerotic disease to assess the relationship between their coincidence.

Chapter (1):Atherosclerosis

Atherosclerosis : (also known as **arteriosclerotic vascular disease** or **ASVD**) is a condition in which an artery wall thickens as a result of the accumulation of fatty materials such as cholesterol. It is a syndrome affecting arterial blood vessels, a chronic inflammatory response in the walls of arteries, caused largely by the accumulation of macrophage white blood cells and promoted by low-density lipoproteins (plasma proteins that carry cholesterol and triglycerides) without adequate removal of fats and cholesterol from the macrophages by functional high density lipoproteins (HDL). It is commonly referred to as a hardening or furring of the arteries. It is caused by the formation of multiple plaques within the arteries. Atherosclerosis affects the entire arterial tree, but mostly larger, high-pressure vessels such as the coronary, renal, femoral, cerebral, and carotid arteries. [7]

Causes

The main cause of atherosclerosis is yet unknown, but is hypothesized to fundamentally be initiated by inflammatory processes in the vessel wall in response to retained low-density lipoprotein (LDL) molecules. Once inside the vessel wall, LDL molecules become susceptible to oxidation by free radicals, and become toxic to the cells. The damage caused by the oxidized LDL molecules triggers a cascade of immune responses which over time can produce an atheroma. The LDL molecule is globular shaped with a hollow core to carry cholesterol throughout the body. [8] [9]

The body's immune system responds to the damage to the artery wall caused by oxidized LDL by sending specialized white blood cells (macrophages and T-lymphocytes) to absorb the oxidized-LDL forming

specialized foam cells. These white blood cells are not able to process the oxidized-LDL, and ultimately grow then rupture, depositing a greater amount of oxidized cholesterol into the artery wall. This triggers more white blood cells, continuing the cycle.

Eventually, the artery becomes inflamed. The cholesterol plaque causes the muscle cells to enlarge and form a hard cover over the affected area. This hard cover is what causes a narrowing of the artery, reduces the blood flow and increases blood pressure.

Some researchers believe that atherosclerosis may be caused by an infection of the vascular smooth muscle cells; chickens, for example, develop atherosclerosis when infected with the Marek's disease herpesvirus. Herpesvirus infection of arterial smooth muscle cells has been shown to cause cholesteryl ester (CE) accumulation. Cholesteryl ester accumulation is associated with atherosclerosis.Also, cytomegalovirus (CMV) infection is associated with cardiovascular diseases[10], [11],[12]

Risk factors

Various anatomic, physiological and behavioral risk factors for atherosclerosis are known. These can be divided into various categories: congenital vrsus acquired, modifiable or not, classical or non-classical. Risks multiply, with two factors increasing the risk of atherosclerosis fourfold. Hyperlipidemia, hypertension and cigarette smoking together increases the risk seven times. [13], [14]

1)-Modifiable

- Diabetes or Impaired glucose tolerance (IGT)

- Dyslipoproteinemia:
    - High serum concentration of low-density lipoprotein (LDL) and / or very low density lipoprotein (VLDL) particles.
    - Low serum concentration of high density lipoprotein (HDL is the protective particles)
    - An LDL:HDL ratio greater than 3:1
- Tobacco smoking, impaired endothelium-dependent flow mediated dilatation has been found in long-term smokers, also cigarette smoking increases risk for atherosclerosis by 3-4 folds or more.
- Hypertension , on its own increasing risk by 60%
- Elevated serum C-reactive protein concentrations
- Vitamin B_6 deficiency. [15],[16],[17],[18]

2)-Nonmodifiable

- Advanced age , Male sex , positive family history of any or some of the complication of atherosclerosis (e.g. coronary heart disease or stroke), Genetic abnormalities, e.g. familial hypercholesterolemia

3)-Lesser or uncertain

The following factors are of relatively lesser importance, are uncertain or unquantified:

- Obesity (in particular central obesity, also referred to as *abdominal* or *male-type* obesity), a sedentary lifestyle, Hypercoagulability.[19][20][21] .
- Postmenopausal estrogen deficiency, High intake of saturated fat (may raise total and LDL cholesterol) , Intake of trans fat