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Ultrasonography of CIMT and plaques as a surrogate as a surrogate atherosclerosis used for prediction of future stroke and peripheral cardiovascular diseases.

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ABSTRACT

The presented study proposed the sonographic evaluation of carotid intima media thickness (CIMT) and plaques correlated with age, gender and risk factors of hypertension and diabetes mellitus. The evaluation importance of CIMT and plaques are surrogate biomarkers for future cardiac disease, stroke and peripheral arteries disease. Patients and method: studied 84 patients (45 males and 39 females) which were referred to our hospital had vague complaint, hypertension, diabetes mellitus or referred patients had two risk factors of hypertension and diabetes mellitus. Ultrasound with high frequency transducer was used for carotid intima media thickness (CIMT) and plaques measurements for assessment of the atherosclerosis. Results: values of CIMT and plaques were increased gradually by increasing age as well as were higher in men than women and increased also in patients with risk factors, which are associated with cardiovascular disease or stroke. Conclusion: the asymptomatic and symptomatic patients were referred to the hospital for carotid ultrasound. CIMT and plaques predict future cardiovascular disease, stroke and peripheral artery disease (PAD). Ultrasound underwent for presented patients to determination and delineation of carotid arteries intima media thickness and plaques. CIMT and plaques were increased by age and higher in patients with risk factors, as well as higher in men than women.

Key words: US, CIMT, Plaques, Surrogate markers, Age, Gender, Risk factors.

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Introduction

Carotid artery ultrasound is indicated in patients having clinical symptom and signs suggestive of hemiplegia, pule weakness, arterial bruit. It is indicated also in the patients who have atherosclerotic risk factors (diabetes mellitus, hypertension, hyperlipidemia and smoking). Doppler ultrasound measurements of carotid arteries wall thickness is the most widely used imaging tool. CIMT and plaques Doppler ultrasound measurements is a popular imaging technique and the method of choice for prediction of risks and future vascular disease. It is very useful for quantification of subclinical arterial atherosclerosis; also it assesses the diagnosis and the extent of carotid artery stenosis. The advantage of this technique is easy to performed, non-invasive, inexpensive, does not involve radiation, hasn't adverse biological changes, can be repeated many times and clearly standardized method to predict risk of atherosclerosis (1,2,3,4,5,6). Observation of the common carotid artery (CCA), bulbous or bifurcation (Bulb or Bif) and internal carotid artery (ICA) is indispensable in assessment of the carotid intima media thickness (CIMT) and plaques. The CIMT in the bulb was higher than in CCA and ICA, whereas CIMT was higher in proximal ICA and in distal CCA (Figure 2). CIMT is a reference value for assessment of subclinical atherosclerotic changes in young adults (3,7). CIMT and plaques generally are defined as vascular damage. Atherosclerosis is a chronic vascular inflammatory disease silent for few decades before symptoms occur. Evaluation of CIMT for asymptomatic vascular damage is a marker of subclinical or preclinical atherosclerosis and search for target organ damage. Normal CIMT is 0.4–0.5 mm in children and 0.6–0.9 mm in adult ages. CIMT increased with increasing age and higher in men than in women but in other studies, both genders were equal. In the previous studies the CIMT more than 0.9 mm or plaque is considered as a vascular damage, whereas in the other studies up to 0.1 mm is accepted (4,8,9,10,11,12). Plaque is defined as localized elevation of lesion with thickness of more than

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1.0 mm on the surface of intima media complex. The parameters of plaque are size, morphology, surface (smooth, irregular or ulcerative surface), echogenicity (soft tissue hypoechoic, mixed heterogeneous echogenic or calcified hyperechoic plaques) and mobility (mobile plaque or non-mobile), (4,11). CIMT and plaque are a surrogate pathobiological processes and significant marker of atherosclerosis used for prediction of future stroke, PAD and cardiovascular disease. In routinely screening of cardiovascular risk the American heart association considered IMT as a marker of early atherosclerosis as well as the only recommended sonographic parameters used (11,13,14,15).

Patients and methods

From January 2017 to November 2017, underwent ultrasound for 84 consecutive Libyan patients, ranging 10 to 85 years of age were 45 (54%), males and 39 (46%) females. The referred patients to our Hospital in Zliten were with history of hypertension (HPT), diabetes mellitus (DM) or vague complaint (no clear symptoms and no risk factors) to undergo carotid Doppler ultrasound. Patients' position was laying supine with relaxed neck, mild lateral rotation of the head and used the right hand for both carotid arteries. (ClearVue 350) Philips ultrasound medical system machine with two dimensional gray-scale images, high frequency (7.5 MHz) linear array transducer used for superficial structural examination. Carotid ultrasound longitudinal and axial sections images (figure 1A,B) were obtained mainly for bifurcation, common and internal carotid arteries. Manual measurement of the carotid arteries intima media complex thickness was on the far wall of the right and left carotid arteries for evaluation of atherosclerotic CIMT and plaques in patients with asymptomatic and with risk factors for prediction of stroke, cardiovascular and peripheral arterial diseases. This is the usual international way of measurement of CIMT and plaques (16,17).

RESULT:

The evaluation of carotid intima media thickness (CIMT) and plaques was in patients without risk factors and in patients with risk factors (hypertension, diabetes mellitus or combined both of these risk factors). The CIMT was correlated with age, gender and risk factors. The patients with no risk factors were ultrasonography examined and divided into age groups. In each age group assessed the average of CIMT as shown in (table 1).

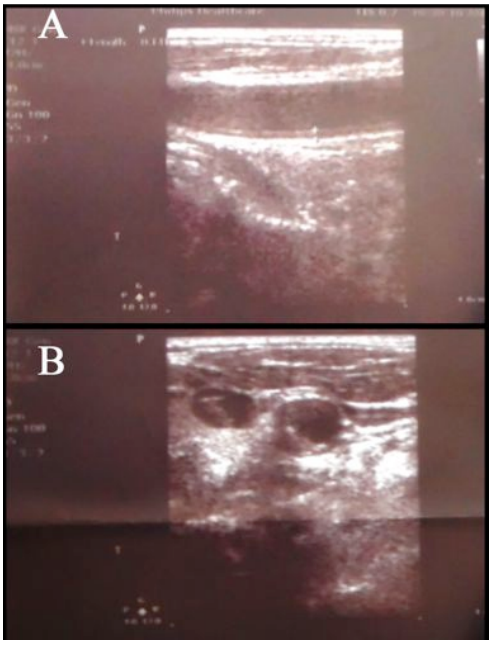

Figure 1: (A) longitudinal section; IMT measurement in the carotid artery between blood intima and media-adventitia, (B) axial section; partially calcified plaques in the carotid artery wall

Table 1; average of CIMT in male and female asymptomatic patients of various age groups

Age groups	CIMT in males	CIMT in females
< 20	0.5	0.5
21 – 30	0.6	0.5
31 – 40	0.7	0.6
41 – 50	0.8	0.7
51 – 60	1.0	0.9
61 – 70	1.1	1.0
➢ 70	1.1	1.1

Table 2: number of patients with normal and with increasing in CIMT and plaques

Patients with CIMT	< 40 ys	< 40 ys	Total
Increased CIMT	52	20	72
Normal CIMT	4	8	12
Total	56	28	84

In patients with no risk factors, the average of CIMT was 0.5 mm in age group of less than 21 years and gradually increased with increased age up to 1.1 mm in age group exceeds 70 years (table 1, figure 2).

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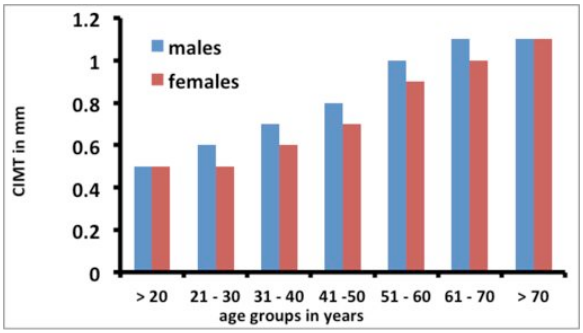

Figure 2: Average CIMT in millimeters of asymptomatic patients among age groups of males and females.

Division of total examined patients (84 patients) into two groups; one group with age below 40 years and the other group with age 40 years old or above. 56 patients were more than 40 years (52 patients with increased CIMT and only 4 patients with normal CIMT). 28 patients were less than 40 years (20 patients with increased CIMT and 8 patients with normal CIMT). Statistically (X^2 = 7.0, P < 0.01) was significant increasing of CIMT and plaques in middle and old aged patients (table 2).

In middle and advanced age groups CIMT and plaques was associated with partial calcification (figure 3 a and b). Increasing in CIMT and plaques in ultrasound imaging shown with various sizes, calcified or non-calcified (soft tissue), irregular and ulcerated surface (figures 4a,b).

Table 3: CIMT in millimeters in patients with risk factors.

Mean CIMT	HPT	DM	HPT , DM	Total
Increased	2.1	3.0	3.4	8.5
Normal	0.9	0.7	0.6	2.2
Total	3.0	3.7	4.0	10.7

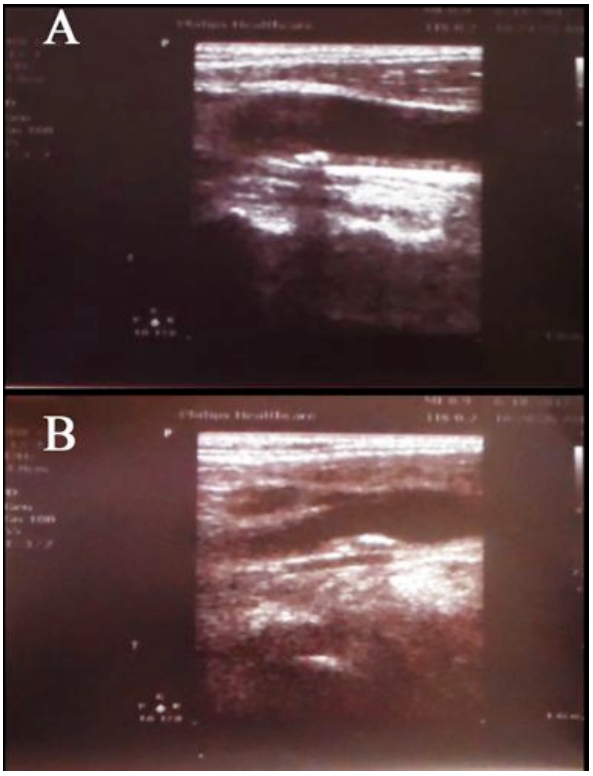

Figure 3: (a) Calcified plaque with hyper-atrophy of IMT of distal common carotid artery, (b) Calcified plaque at bifurcation and proximal internal carotid artery

Table 4: Observation of CIMT in asymptomatic and risky male & female patients

Average CIMT in pt.	males	females	total
Patients with no risk factor	0.7	0.6	1.3
Hypertensive patients	2.1	1.8	3.9
Diabetic patients	3.0	2.5	5.5
Diabetic & hypertensive pt.	3.4	3.1	6.5
Total	9.2	8.0	17.2

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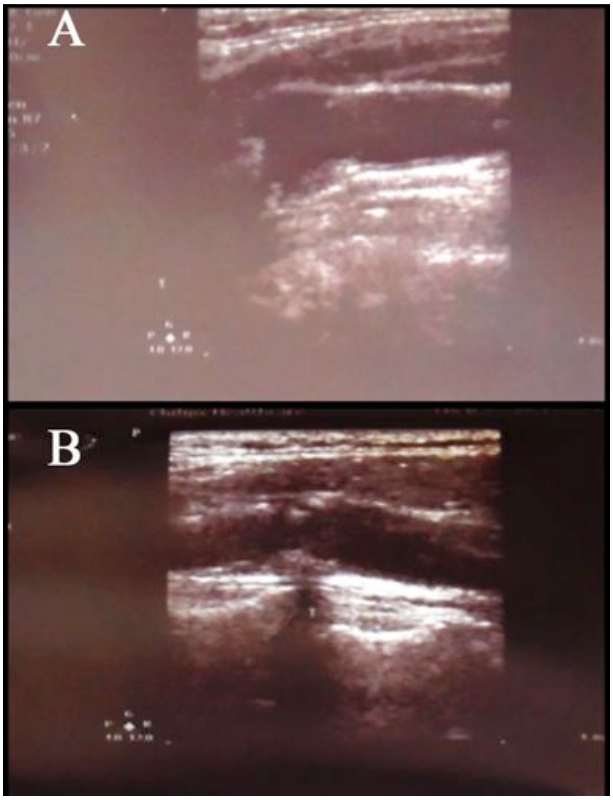

Figure 4; (a) plaques with irregular and ulcerated surface causes narrowing in the proximal internal carotid artery, (b) the image showed soft tissue plaque with low echogenicity in bulb of the carotid artery.

Mean value of CIMT in the examined patients with no risk factors from both genders were usually young, were from 0.6 to 0.9 mm. In patients with risk factors, the mean values of CIMT and plaques were from 2.1 to 3.4 mm (table 3). In this subset cases the value of CIMT and plaques was highly significant association with risk factors (X2 = 8.5092, P < 0.005).

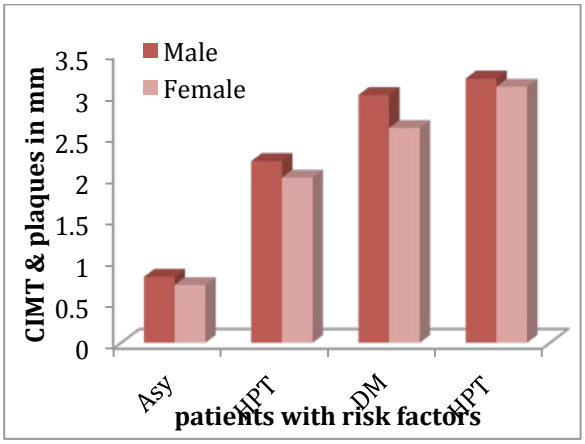

Figure 5: Values of CIMT and plaques in millimeters of patients with risk factors between both genders

The average of CIMT in patients with no risk factors was within normal limits in both genders, whereas average of CIMT and plaques was higher in men than in women, but this difference was non-significant between males and females (P < 0.975), this result was shown in (table 4, figure 5).

Discussion:

Atherosclerosis develops gradually, slowly and starting from childhood in varying velocity. The first detected changing of atherosclerosis is an increase in IMT. Ultrasound measurements used for carotid arteries intima media thickness. B-mode gray scale ultrasound is the method of choice for imaging CIMT and plaques. This non-invasive imaging technique of CIMT and plaques measurements where used for assessment the extent of the carotid artery atherosclerotic changes which are surrogate biomarker for the future risk factors of the vascular disease (1,9,10,11). Carotid arteries intima media thickness (CIMT) and plaques measurements for asymptomatic and for patient with risk factors are markers of preclinical atherosclerosis which associated with cardiac diseases, stroke and peripheral arterial disease.

IMT correlated with age and gender. Normal mean value of CIMT at age 10 years was between 0.4 to 0.5 mm, while from the fifth decade of life or older, the values of CIMT were from 0.7 to 0.8 mm. The values of CIMT are increased with advancing ages resulting to biomechanical parameters e.g. blood flow and tension on the vascular wall (8). Generally, CIMT is an abnormal when exceeds 0.9 mm as well as correlated with subclinical atherosclerosis of the arteries. Determination and delineation of carotid artery thickness with revealing atherosclerosis is a marker for preclinical evaluation of risk factors of the myocardial infarction, stroke and peripheral vascular disease (PAD) (4). CIMT measurements using ultrasonography and changes rate is used as a surrogate endpoint to assess early effect of drug therapy and the early demonstration of the biomarker atherosclerosis of the asymptomatic cardiovascular disease which represents the target of early treatment and prevention (8,9,12,18).

In our study the CIMT strongly dependent on age, risk factors and correlated with gender;

In this study, the value of CIMT in children and adult patients with no risk factors was 0.5 mm in age group of less than 21 years and gradually mild increased by increasing age up to 1.1 mm in age group exceeds 70 years (table 1, figure 2). Mild changes in CIMT in those non-risky older age groups from younger to older age groups might be due to decreased carotid elasticity by increasing age(19).

Risk factors usually develop in adult patients and aggravated by age increasing. In patients with risk

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factors compared CIMT and plaques between patients with ages below 40 years and patients above 40 years. There was significant difference in CIMT and plaques in patents above 40 years old (table 2). This difference might be due to risk factors, affecting on the increasing in thickness and decreasing in elasticity of carotid artery wall in middle and older ages as in the other literatures.

In this study, the CIMT and plaques in patients who had risk factor of HPT or DM (separately or combined both of DM and HPT) was monitored ultrasonographically. Significantly increasing in CIMT and plaque in patients with risk factors (DM or HPT) and more prominent in patients with multiple risk factors (DM and HPT together) compared to patients who had not risk factors. So, the value of CIMT and plaques in patients with risk factors was significantly increased by increasing of risk factors similar to the other several studies. This increasing in CIMT and plaques predicted risk of cardiovascular events, stroke and PAD (table 3, figure 5).

There was mild difference in the values of CIMT and plaques between males and females patients how had risk factors. Increasing of CIMT and plaques in males with risk factors was higher than in females (table 4, figure 5), but statistically the difference in this study was non-significant similar to the findings in previous some studies, whereas the in other studies values of CIMT and plaques were significantly different.

Conclusion:

In our study, the values of carotid intima media thickness (CIMT) and plaques were significantly increased in middle and old ages of both genders and increased by increasing age groups as well as significantly increased in patients with risk factors. The difference in the values of CIMT and plaques in males and females was non-significant changes similar to some previous studies. This depicted atherosclerosis in the patients assesses the future risk of stroke, cardiovascular and peripheral artery disease.

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