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Intitulé

VALUE OF GLOBAL LONGITUDINAL STRAIN BY TWO DIMENSIONAL SPECKLE-TRACKING ECHOCARDIOGRAPHY IN PREDICTING CORONARY ARTERY DISEASES

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Je tiens à remercier infiniment ***Monsieur le Professeur Cherti*** *,*
d'avoir accepté d'encadrer ce travail.. Vous nous avez accueillis avec beaucoup de gentillesse et d'égard. Veuillez croire, cher maître à notre estime et notre respectueuse considération.

On remercie également tous nos professeurs de Cardiologie
pour le très beau parcours que nous avons passé ces quatre années ,
pour nous avoir appris le sens de la rigueur du sérieux
et de la persévérance.

Vous nous avez assister avec patience pendant toutes
ces années d'études, avec le souci de bien nous apprendre
le savoir-faire de notre métier.

Liste des abréviations

ABBREVIATIONS

ACS : Acute coronary syndrome

AF : Atrial fibrillation

APVD : Atroventricular plane displacement

AVC : Aortic valve closure

BSA : Body surface area

CA : Coronary angiography

CABG : Coronary artery bypass grafting

CAD : Coronary artery disease

CCTA : Coronary computed tomography angiography

CMR : Cardiac magnetic resonance

CRP : C-reactive protein

CVD : Cardiovascular disease

DM : Diabetes Mellitus

ECG : Electrocardiogram

EDD : End diastolic diameter

EF : Ejection fraction

ESD : End systolic diameter

EST : Exercice stress testing

FFR : Fractional flow reserve

GCS : global circumferential strain

GFR : Glomerular filtration rate

GLS : Global longitudinal strain

GRS : Global radial strain

HF : Heart failure

HTN : Arterial hypertension

IVS : Intra ventricular septum

LAD : Left anterior descending artery

LBBB : Left bundle branch block

LCx : Left circumflex artery

LPSS : Segmental longitudinal peak strain

LV : Left ventricular

MAPSE : Mitral annular plane systolic excursion

MI : Myocardial infarction

MVG : Left ventricular mass

OMT : Optimal medical therapy

PAD : Peripheral artery disease

PCI : Percutaneous coronary intervention

PW : Pulsed wave

RCA : Right coronary artery

RLS : Regional longitudinal peak systolic strain

RLSLAD : Regional longitudinal strain in LAD territory

RV : Right ventricle

RWMAs : Regional wall motion abnormalities

SCD : Sudden cardiac death

STE : Speckle trackingechocardiography

SV **:** Stroke volume

TDI : Tissue Doppler imaging

TTE : Transthoracic echocardiography

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Introduction

I. INTRODUCTION

Accurate detection of CAD remains paramount in the practice of cardiology. Traditionally, the characterization of ‘significant’ CAD has relied upon visual evaluation of coronary artery stenosis during invasive coronary angiography (CA).

Early detection and intervention is paramount in patients with significant CAD to prevent adverse cardiac events, including myocardial infarction leading to left ventricular (LV) dysfunction.

The performance of non-invasive techniques is generally reported in terms of sensitivity and specificity.

Certain techniques are broadly available because of their relative low technical and personnel demands [such as stress electrocardiogram (ECG)] or good availability [stress echocardiography, coronary computed tomography angiography (CCTA), and single-photon emission computed tomography (SPECT)], while others, like positron emission tomography (PET) and stress cardiac magnetic resonance (CMR), although powerful, are much less available and their applicability is still limited by infrastructural and capacity requirements (1).

During the early stages of the disease process, global LV functional parameters of volume and ejection fraction (EF) are usually preserved. Unless there has been a previous infarction or stunning of the myocardium, regional wall motion abnormalities (RWMAs) are not evident at rest, and noninvasive detection of ischemia by transthoracic echocardiography (TTE) requires stress provocation. Stress echocardiography remains a widely accepted imaging

modality for the assessment of CAD, but it is limited by operator dependence, subjectivity, and qualitative interpretation of RWMAs as well as a failure to reach a diagnostic target heart rate[1](3).

Thus we are in need of a simple, non-invasive method to improve the selection of patients who are referred for coronary angiography.

Myocardial deformation imaging using two-dimensional (2D) speckle-tracking echocardiography (STE) is a valuable tool, providing comprehensive quantitative assessment of myocardial function beyond EF and qualitative assessment of RWMAs (2).

In fact, the longitudinally arranged subendocardial fibers are more vulnerable due to their direct exposure to the intraventricular blood pressure and the anatomy of the coronary circulation. As a result, longitudinal function is impaired first in CAD. Measurements of longitudinal motion and deformation are therefore, the most sensitive markers of coronary artery disease especially in patients with severe coronary stenosis, where intermittent ischemia may result in subtle forms of stunning that may be detectable with strain measurements (1).

The aim of the present study was to evaluate the diagnostic performance of 2D STE in the detection of significant CAD .The aim was also to determine the utility of 2D strain to predict the severity and the localization of the CAD.

Patients and méthodes

II. PATIENTS AND METHODS

The aim of this study was to evaluate the diagnostic accuracy of 2D global longitudinal strain (GLS) obtained by 2D-STE speckle tracking echocardiography in prediction of CAD in patients without wall-motion abnormalities in standard echocardiography.The aim was also to determine the utility of 2D strain to predict the severity and the localization of the CAD.

1. Patients

A prospective study was done in cardiology department in the two military hospitals of Morocco and Tunisia during a period of three years from March 2018 to April 2021. It included one hundred twenty one patients with suspected CAD (stable angina pectoris, STEMI and NSTEMI).

Inclusion criteria included patients between 18 and 80 years of age and indication for coronary angiography (CA) according to current guidelines.

Exclusion criteria included previously known CAD, previous percutaneous coronary intervention (PCI), open heart surgery or severe WMA , heart failure and LV systolic dysfunction , severe valvular disease and concomitant disease as connective tissue disease or drug therapy which affect cardiac function as cytotoxic drugs.

All patients received medical treatment according to current guidelines. Patients benefited from transthoracic echocardiography (TTE), 2-D speckle tracking echocardiography (2D-STE) and coronary angiography.

2. Methods

a) Conventional Transthoracic echocardiography (TTE):

Examination was done by using General Electric VIVID 9 with M4S transducer, with a frequency of 1.5–4.3 MHz and high frame rate (60–90 frame/s).

b) Strain analyses:

Regional longitudinal peak systolic strain (RLS) was measured in all views between aortic valve opening and closing for the 6 basal, 6 midventricular, and 4 apical segments. (**Figure 1**) .

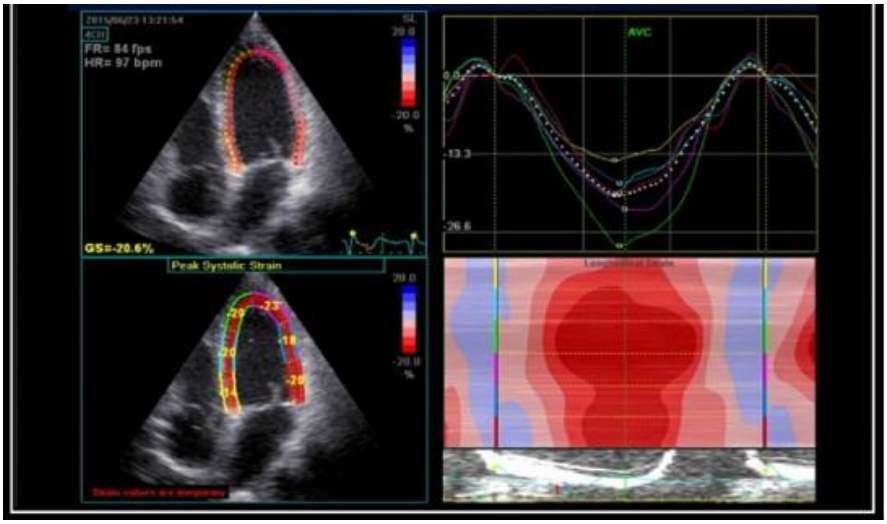

Figure 1: Apical four-chamber view and Corresponding strain curves

c) Coronary Angiography (CA) :

We performed coronary angiography (CA) by the percutaneous radial approach. Coronary angiograms were obtained for each coronary vessel in >2

projections. We considered significant all and stenosis with >70% reduction in the arterial lumen area (3).

3. Statistical analysis

We used the ‘‘SPSS for Windows” software package for all analysis.

A p value of less than 0.05 was considered significant.

Résultats

III. RESULTS

With regard to age, it was 60.89 ± 10.4 in group 1 versus 58.12 ± 7.45 in group 2 (control group) p =0.82. The majority of patients were male (68.59%). Regarding risk factors of the studied patients; 38 patients (31.4%) had DM, 49 patients (40.5%) had HTN, 40 patients (33%) were dyslipidemic ,79 patients (65.3%) were smoker, as shown in **Table 1**.

We classified patients into two groups: the contral groupe (normal coronary angiography) which included 50 patients (41.66%) and patients with CAD which included 71 patients (58.33%)

	Significant obstruction Group (1) N = (71)	Control Group (2) N = (50)	P
Age	60.89 ± 10.4	58.12 ± 7.45	0.82
Gender F **M**	9 (12.7%) 62 (87.3%)	9(30%) 21(70%)	0.99
Smoking	38(53.5%)	18(60%)	0.15
Diabetes mellitus	30(42.3%)	8(26%)	0.36
Hypertension	35(49.3%)	14(46.7%)	0.72
Dyslipidemia	31(43.7%)	9(30%)	0.10
Resting ECG **Positive** **Normal**	 29(40.8%) 36(50.7%)	 - -	
PCI	53(74.6%)	-	
CABG	7(9.9%)	-	

Table 1: Comparison of the clinical and demographic characteristic of the study population

- 36 patients (50.7%) with normal resting ECG had coronary artery diseases.

EF (%) Mean ± SD	**59.72 ± 4.77**	**64.73 ± 3.47**	**<0.05**
EDD	48.16±4.85	46.72±4.14	0.92
ESD	30.05±5.03	29.46±2.89	0.41
IVS	10.62±2.11	8.48±2.1	0.12
PW	9.30±1.99	8.66±1.31	0.14
MVG	96.00±6.39	81.98±18.23	0.08
VOLLA	35.26±11.47	26.5±7.17	0.02
E/A	1.20±1.64	1.34±0.43	0.06
E/Ea	6.77±2.54	6.73±3.18	0.26
PAPS	29.20±5.95	27.09±8.74	0.08
SRV	12.54±1.85	13.34±1.21	0.16

Table 2: Conventional echocardiographic parameters

GLS (%) Mean ± SD	**-17.68 ± 3.07**	**-22.35 ± 3.07%**
LAD	**-17.55± 3.17**	-
LCx	**-18.50± 2.02**	-
RCA	**-17.56± 2.80**	-

Table 3**:** Global/Territorial longitudinal strain parameters

- GLS in the CAD group had a significant decrease compared to contral group (-17.68 ± 3.07% vs -22.35 ± 3.07% p=0.02).
- LVEF had also a significant decrease compared to contral group(60.72 ± 4.77% vs 64.73 ± 3.47%) .

Angiographic findings	N(%)
Control group	30(29%)
CAD group	71(70.3%)
•**Single vessel disease**	19(26.8%)
•**Double vessel disease**	26(36.6%)
•**Three vessel disease**	19(26.8%)
•**LAD**	55(77.5%)
•**LCX**	38(53.5%)
•**RCA**	28(39.4%)

Table 4: Angiographic findings of the study population.

- The optimal cutoff value of GLS in predicting significant CAD was -16.08 (AUC was 0.72 and p value 0.04). The sensitivity and specificity were 80% and 97% respectively .
- GLS was not decreasing by increasing number of stenotic coronary arteries (GLS -22.35 ± 3.07; -15.67 ± 3.47, -17.58 ± 2.95 and -17.41 ± 3.01) for patients with control group , single vessel disease, double vessel disease and triple vessel disease respectively.

	Control group	SVD	DVD	TVD
GLS(%)	-22.35 ± 3.07	-15.67 ± 3.47	-17.58 ± 2.95	-17.41 ± 3.01

Table 5: Relationship GLS and severity

	GLS(%)	
EF(%)	**R**	**P**
	0.45	**0.027**

Table 6: Correlation between GLS and EF

- We found a significant positive correlation between GLS and EF (r 0.45; p = 0.027).

Discussion

IV. DISCUSSION

In the present study, GLS was significantly lower among patients with significant CAD than those with non significant CAD with mean values of GLS (-17.68 ± 3.07 vs -22.35 ± 3.07%).We also found that GLS less than -16.08% may predict significant obstructive CAD (stenosis >70%) in 90% of patients with sensitivity and specificity (80%, 97%) respectively. So we found that GLS measurements had high diagnostic accuracy in predicting CAD.

1. Epidemiology of coronary arteries disease

Despite falling rates of age-adjusted mortality, CAD remains the leading cause of death worldwide (3). Advanced diffuse CAD is becoming an important entity of modern cardiology as the population ages and patients with historical coronary procedures are no longer suitable for further revascularisation. Advances in the treatment of diffuse obstructive CAD are hampered by a poor understanding of the factors implicated in its development. Patients with diffuse CAD are at risk of developing refractory angina – resistant to conventional revascularisation techniques such as PCI or CABG and not adequately controlled by OMT. Studies have shown that up to 12% of symptomatic patients undergoing coronary angiography are ineligible for revascularisation (4). Patients with this condition often have restricted physical capacity and severely impaired quality of life. Although alternative strategies have been investigated, no satisfactory treatment currently exists. Although the likelihood of developing clinically significant CAD is closely linked to the presence of traditional risk factors, the morphology of CAD among individuals is highly variable – some people develop diffuse flow-limiting CAD, whereas others, with similar risk factor profiles, have much more limited disease. The difference in distribution

and geometry of CAD is challenging to explain in mechanistic terms since the endothelium is equally exposed to injury stimulants.

a) Definition and prevalence of diffuse (obstructive) CAD

There is no single definition of diffuse CAD. Moreover, a number of phrases are used interchangeably to represent an expanding group of patients unsuitable for conventional revascularisation, or patients in whom therapeutic options have been exhausted (5). A flow limiting lesion can be considered diffuse in the presence of a significant (usually 70%) stenosis longer than 20 mm or multiple significant stenoses in the same artery or significant narrowing involving the whole length of the coronary artery . In some studies, diffuse CAD has been defined when ‘more than two-thirds of the left or right coronary artery is affected by irregularities or stenoses (5). The American college of cardiology/American heart association classification system uses 11 variables to stratify lesions into one of four categories (A [simplest], B1, B2 and C [most complex]) predictive of interventional success (4). Type A lesions are discrete by definition (20 mm). Type B lesions display various complexities in between types A and C. Various surveys show that approximately 15% of patients are ineligible for revascularisation (6). In the Mediators of Social Support (MOSS) study, 41% of patients with three vessel CAD were unsuitable for revascularisation . A more recent analysis of 16,215 patients undergoing coronary angiography revealed that 5.9% of people with advanced (three vessel) CAD (1.3% overall) had anatomy that precluded standard revascularisation techniques (7).

b) Development of coronary atherosclerosis

- **Genetic factors**

Genome-wide association studies have shown that more than 55 loci are related to coronary atherosclerosis. Each individual inherits genetic variants (i.e., minor alleles, polymorphisms, mutations), but only individuals who inherit a combination of multiple variants are at the greatest risk for the development of the disease (7) It should be mentioned that most of these genetic variants related to coronary atherosclerosis are located at DNA sequences that do not code proteins. Only 15 of the genetic variants are related to known risk factors [7 to low density lipoprotein cholesterol (LDL-C), 4 to arterial hypertension (HTN), 2 to triglycerides, 1 to high density lipoprotein cholesterol (HDL-C) and 1 to thrombosis]. The first described genetic variant found to be associated with coronary atherosclerosis is located on the short arm of chromosome 9 (chromosome 9p21) with yet unknown function; it appears that this genetic variant increases the risk of a first coronary heart disease event, but not subsequent events. Of interest, this variant is associated with periodontitis and gout, both conditions that are associated with increase inflammation, but not with C-reactive protein (CRP) (7).For years it has been known that the incidence of myocardial infarction (MI) is related to the ABO blood type; having alleles for blood type A or B is associated with a greater risk for MI compared to blood type O. Group A or B are also associated with higher levels of von Willebrand factor complex(10,11). Evidence that LDL-C plays an important role in the development and progression of coronary atherosclerosis has been known for decades. One of the major observations that demonstrated the genetic link between LDL-C and coronary atherosclerosis was by Brown and Goldstein discovering a mutation in the LDL-C receptor in patients with familial hypercholesterolemia, premature coronary atherosclerosis and early death (7). This observation was crucial for the development of statins, a pharmacologic

agent that has been widely used in primary and secondary prevention of atherosclerosis, resulting in a significant decrease in cardiovascular disease (CVD) events and CVD death. Another significant discovery with a genetic link is the enzyme PCSK9 and its effects on LDL-C and coronary atherosclerosis. The enzyme PCSK9 (chromosome 1p32.3) increases the degradation of LDL-C receptors. Mutations that increase the function of PCSK9 are associated with high levels of LDL-C and increase incidence of coronary atherosclerosis. In contrast, mutations that result in loss of function of PCSK9 are associated with low levels of LDL-C and decrease incidence of coronary atherosclerosis. These observations resulted in the development of monoclonal antibodies that inhibit the function of the PCSK9 enzyme (7) Administration of these agents to patients with hypercholesterolemia who were treated with a statin produced a dramatic decrease in LDL-C (this decrease was in addition to that obtained with statins) and to a significant decrease in CVD events. More recently, a mutation in ANGPL4 has been identified. ANGPL4 is known to inhibit lipoprotein lipase increasing triglyceride levels; carriers with a loss of function mutation were shown to have lower blood levels of triglycerides and lower incidence of coronary atherosclerosis compared to non-carriers. The data suggest that lipoprotein lipase pathway plays an important role in the development of coronary atherosclerosis; it follows that new drugs modulating these pathways can be developed in the near future potentially decreasing the incidence of coronary atherosclerosis (7). Although low levels of HDL-C are associated with coronary atherosclerosis, therapeutic interventions that increase HDL-C currently have not demonstrated any effect on survival or reduction in CVD events.

- Environmental factors

In addition to cholesterol, other risk factors for coronary atherosclerosis are shown in **Figure 2**. HTN and diabetes mellitus (DM) are major risk factors contributing to the development of coronary atherosclerosis. Even isolated systolic HTN in young and middle age adults has been shown to be associated with a higher incidence of coronary atherosclerosis. It follows that optimal medical management of HTN and DM, as recent data have shown, is of great clinical significance. A sedentary lifestyle may predispose to obesity and DM, which are associated with hyperlipidemia and an inflammatory process. Thus, moderate exercise and a balance diet, particularly a Mediterranean diet, are recommended. It is important at this point to emphasize the major risk of second and third-hand smoking that is associated with inflammation and continues to be a serious problem in several countries including "developed" countries (7).

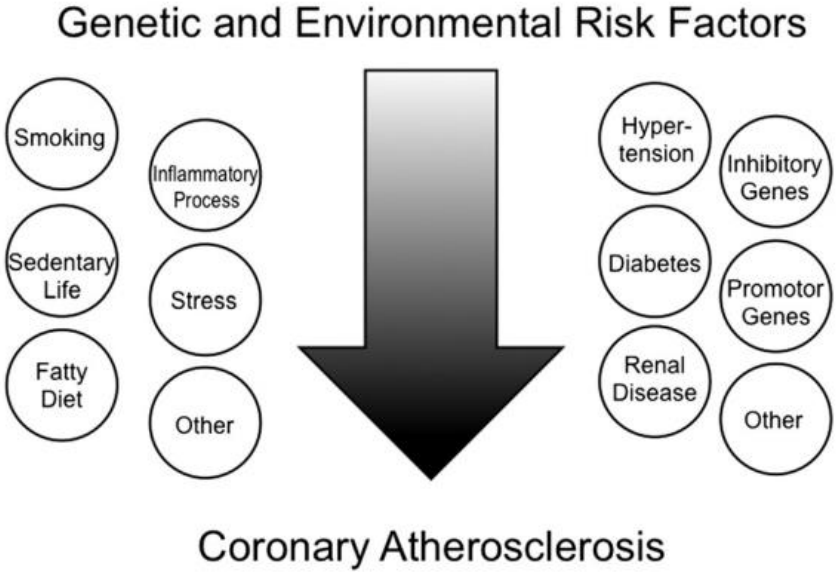

Figure 2: Genetic and environmental risk factors that promote the development and progression of coronary atherosclerosis

c) Progression of coronary atherosclerosis

When an atherosclerotic plaque develops in the wall of a coronary artery, the artery undergoes remodeling in which the luminal area of the vessel is enlarged (7). Thus, although an atherosclerotic plaque is present, the luminal area of the artery may not be diminished. The degree of luminal stenosis, therefore, may not be directly related to the size of the atherosclerotic plaque and for this reason a large atherosclerotic plaque may produce a small degree of stenosis (**Figure 3A**). Atherosclerotic plaques could be stable or unstable. An unstable atherosclerotic plaque is characterized by a large lipid pool, high concentrations of macrophages that suggest an inflammatory process, small amount of collagen, and a thin cap that covers the plaque. In contrast, a stable atherosclerotic plaque is characterized by a small lipid pool, large amount of collagen, low density of macrophages suggesting a minimal or no inflammatory process, and a thick cap that covers the plaque. A stable atherosclerotic plaque at any time may become unstable, while an unstable plaque may be stabilized. An unstable plaque may rupture, however, plaque rupture more often results in disease progression and less often to intravascular thrombosis and vascular occlusion (**Figure 3B**) (8).A ruptured plaque in which thrombus formation does not produce complete occlusion of the artery may result in unstable angina or a non-ST elevation MI. An acute complete occlusion of the artery results in a ST elevation MI (STEMI). Acute MI and myocardial necrosis results in left ventricular (LV) dysfunction, LV remodeling, and ischemic cardiomyopathy with or without symptoms of HF. Often a varying degree of mitral regurgitation is present. One clinical picture of the disease may lead to another. Occasionally during superficial plaque rupture (erosion), chest pain lasting more that 20 min may occur without myocardial necrosis; this episode essentially is an acute ischemic syndrome, however, since the pain usually is not related to exertion and often disappears for an extended period of time it may be characterized as “atypical” chest pain. It should be emphasized that several unstable plaques may

be present at the same time in the same patient with varying degrees of instability and progression. At present, diagnostic invasive or non-invasive techniques are of limited value to define plaques that are likely to progress and cause an ACS. Overall prognosis is not just related to one atherosclerotic lesion, but to the total atherosclerotic burden, LV function and co-existence of mitral regurgitation (8).

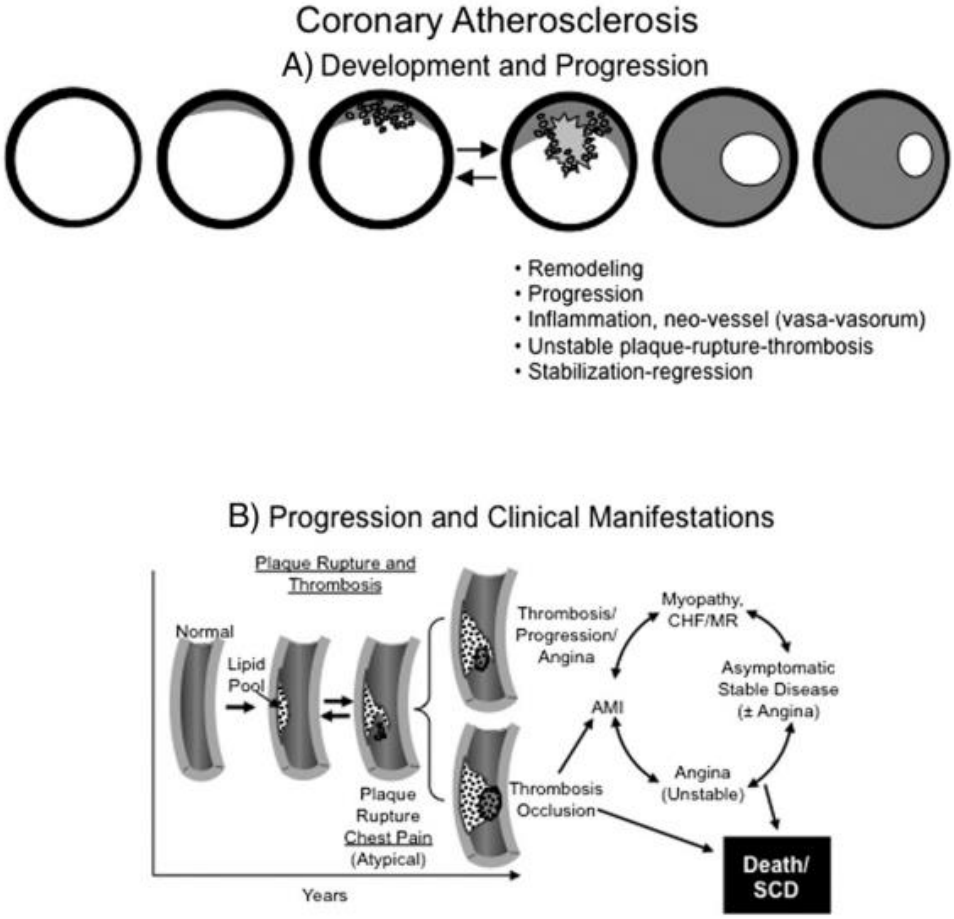

Figure 3**A**: Coronary atherosclerosis is a dynamic disease process. When an atherosclerotic plaque develops in the wall of a coronary artery, the artery undergoes remodeling in which the luminal area of the artery and the plaque area are not linearly related. Inflammatory process and neo-vessel (vasa-vasorum) may be present in the plaque. After rupture of an atherosclerotic plaque, thrombosis may occur that leads to progression of the disease (more often) and/or to an acute coronary syndrome. A stable plaque may become

unstable and an unstable plaque may be stabilized (bi-directional arrows). **B**: Progression of coronary atherosclerosis and clinical manifestations are shown. An atherosclerotic plaque (lipid pool) may become unstable. An unstable plaque may rupture leading to intravascular thrombosis resulting in an acute coronary syndrome, sudden cardiac death (SCD) or progression of the disease (most often). One clinical picture of coronary atherosclerosis may lead to another. An unstable plaque may be stabilized.

2. Anatomy of the Coronary Arteries

The anatomic arrangement of the coronary arteries in the normal heart is well described. Experience of those treating patients with atherosclerosis, ischemic heart disease, and congenital cardiac malformations have demonstrated the value of this knowledge in ensuring optimal treatments.

a) Nomenclature

The coronary arteries are the first branches of the aorta, arising usually from two of the three aortic sinuses of Valsalva (**Figure 4**). They have previously been named in numerous ways according to the orientation of the heart (James, 1961). It is unfortunately for those working in the clinical arena that the most popular names are based on the Valentine orientation of the heart, with the chambers described as if the heart sits on its apex, which is inherently incorrect (James, 1961, 1965; Cook and Anderson, 2002). These deficiencies in nomenclature become obvious when the heart is considered in its appropriate anatomical position within the chest cavity (Cook and Anderson, 2002). It is a basic rule of human anatomy that features should be described relative to the bodily coordinates. There is no reason why this convention should be ignored when describing the heart. Thus, note should be taken of the fact that, in the normal situation, the long axis of the heart points inferiorly and to the left in an

oblique fashion. This is the more important for angiographers and radiologists, as proper anatomical descriptions are critical in making correlations with the electrocardiogram, which is based on electrodes placed with the subject considered as occupying the anatomic position. It was the electrophysiological community that first emphasized the importance of attitudinally correct nomenclature for those working in the clinical setting. It is equally important when describing the coronary arteries. For example, using current terminology, inferior myocardial infarction is allegedly produced by blockage of the so-called posterior descending coronary. When the heart is considered in its location within the body, however, it is readily apparent that this artery is located inferiorly, and occupies the interventricular groove (**Figure 5**). It makes more sense, therefore, to describe it as the inferior interventricular artery.

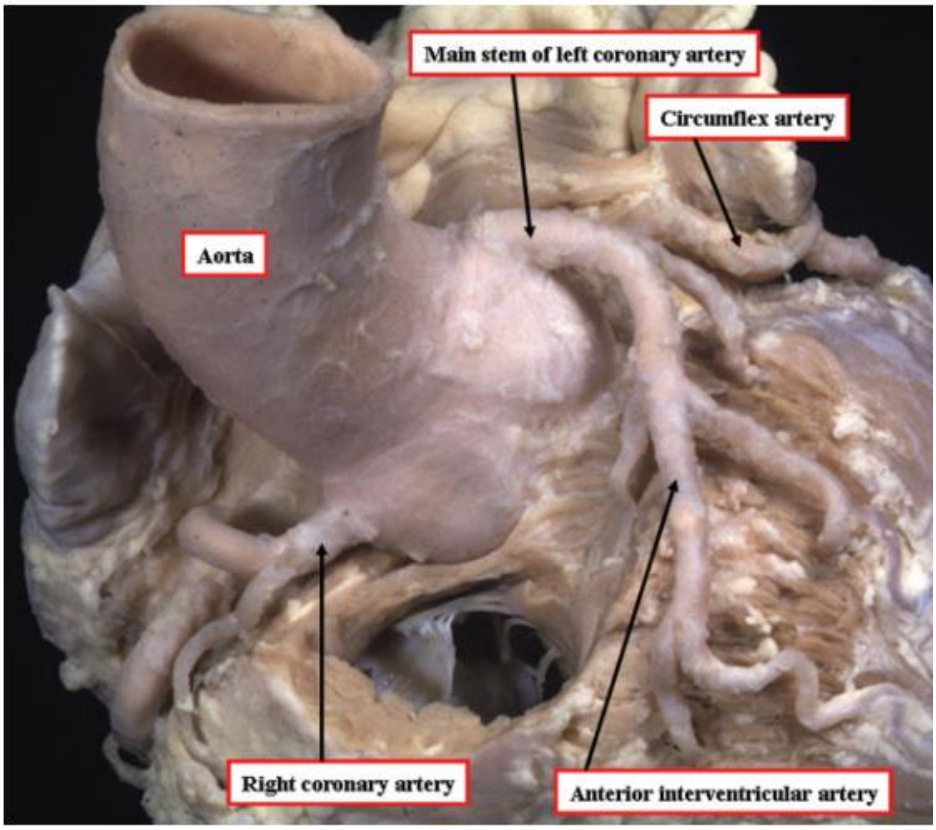

Figure 4: Origin of coronary arteries

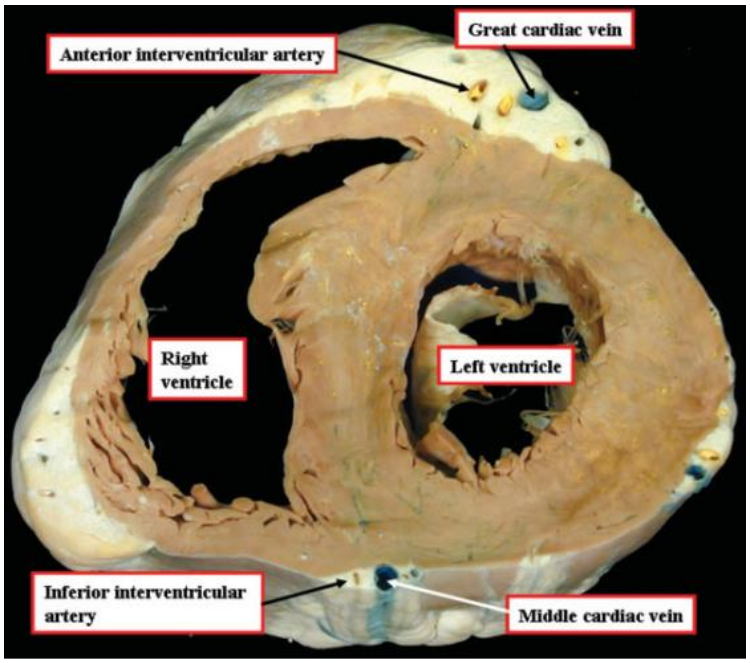

Figure 5: This is a cross section of a human heart specimen.
When the heart is examined in attitudinally correct orientation, it is readily apparent that the artery occupying the socalled ‘‘posterior interventricular groove’’ is located inferiorly, and thus should be called the inferior interventricular artery

b) Normal anatomy of the coronary arteries[2] (22)

- **The Aortic Origins of the Coronary Arteries**

Sinuse of Valsalva occupied the initial portion of the aortic root, which house the leaflets of the aortic valve, being confined distally by the sinutubular junction (Vlodaver et al., 1975). In the normal heart, the two sinuses adjacent to

[2] Loukas, M., Groat, C., Khangura, R., Owens, D. G., & Anderson, R. H. (2009). *The normal and abnormal anatomy of the coronary arteries. Clinical Anatomy, 22(1), 114–128.* doi:10.1002/ca.20761

the pulmonary trunk give rise to the major coronary arteries, namely the right coronary artery and the main stem of the left coronary artery . The origins of these arteries can vary significantly in relation to the sinutubular junction, and also in their proximity to the zones of apposition between the valvar leaflets, the so-called commissures (Muriago et al., 1997). In this respect, deviations of take-off that are within 1 cm of the sinutubular junction in the adult heart are considered variations of normal, whereas origins deviating by greater than 1 cm relative to the junction constitute ectopic origin, or high take-off (Vlodaver et al., 1975). It is exceedingly unusual for a major coronary artery to take origin from the aortic sinus distant from the pulmonary trunk. Based on these origins, therefore, the aortic sinuses of Valsalva can be named as the right coronary, left coronary and non-coronary sinuses, respectively .

- **Right Coronary Artery**

The right coronary artery, which in nine-tenths of individuals supplies most of the diaphragmatic surface of the ventricular mass, emerges from the right coronary aortic sinus in the upper part of the right anterior surface of the aortic root. In many instances, two arterial orifices are found in this sinus, with the second orifice most often giving rise to the infundibular, or conal, artery, but sometimes giving rise to the artery of the sinus node (Schlesinger et al., 1949; James, 1961). Having emerged from its aortic sinus, the right coronary artery occupies the right atrioventricular groove . Its first part extends to the right, or acute, margin of the ventricular mass, where it gives rise to the acute marginal artery, with several atrial branches taking origin from its cranial surface. It also gives rise in this part of its course to the infundibular artery, if this vessel has not

taken origin directly from the aorta, and in just over half the population, to the artery supplying the sinus node. The right artery itself then continues to encircle the vestibule of the tricuspid valve, extending to the cardiac crux. Throughout this course, the artery gives rise to the right inferior ventricular branches, which supply the diaphragmatic wall of the right ventricle (Vlodaver et al., 1975; Williams et al., 1989). In nine-tenths of the population, having reached the crux, the right coronary artery gives rise to the inferior interventricular artery and the artery to the atrioventricular node, then continuing to supply a variable portion of the diaphragmatic wall of the left ventricle. This arrangement is called right ventricular coronary arterial dominance (James, 1961; Ludinghausen, 2003). Of the named branches of the right coronary artery, the infundibular or conal branch is present in approximately half the population. Patients with well-developed infundibular arteries have more extensive distribution to the anterior wall of the right ventricle through the preventricular and ventricular branches of this artery. In some individuals, the artery anastomoses with an infundibular branch of the anterior interventricular artery, forming the so-called arterial circle of Vieussens (Loukas et al., 2007). The acute marginal artery is a consistent vessel that extends along the acute margin of the ventricular mass, reaching to the apex of the heart (Ludinghausen, 2003). Anastomoses are found at the apex between this artery and the anterior interventricular artery (James, 1961). When the right coronary artery is dominant, it gives rise to the artery supplying the atrioventricular node, typically from a U-loop that extends in the tissue plane forming the floor of the triangle of Koch. This, artery in conjunction with the septal perforating branches of the anterior interventricular artery, supplies the

proximal right and left branches of the atrioventricular conduction axis in nine-tenths of individuals, with sole supply by the nodal artery reported in one-tenth of cases (James, 1961). The inferior interventricular artery arises from the right coronary artery in all of those nine-tenths of individuals with right coronary arterial dominance, and from the circumflex artery in the remaining one-tenth, the latter feature allegedly being more common in males (James, 1961). Branches of this artery can meet parallel branches of the right marginal artery, and perpendicular branches of the anterior interventricular artery, in the inferior atrioventricular groove and at the apex (James, 1961). Perforating branches from the artery supply the myocardium of the inferior part of the muscular ventricular septum, the adjacent ventricular walls, and the infero-septal papillary muscle of the mitral valve in those individuals with right coronary arterial dominance (Estes et al., 1966a,b). In rare cases, the anterior interventricular artery can extend into the inferior interventricular groove, taking over the territory usually supplied by the inferior interventricular artery (Levin and Baltaxe, 1972).

- The Main Stem of the Left Coronary Artery

Left coronary artery arises from the left coronary aortic sinus slightly below the sinutubular ridge, although like the right coronary artery, it can also have a high take-off. As it exits from the aortic sinus, it enters the leftward margin of the transverse sinus, being positioned between the left atrial appendage and the pulmonary trunk . Its course is rarely longer than 1 or 2 cm in the adult, after which it divides into the circumflex and anterior interventricular branches. It is these two arteries, together with the right coronary artery, that make up the three arteries of so-called ‘‘3 vessel coronary arterial disease.’’ The

trunk of the main stem, at between 5 and 10 mm in diameter, is typically much larger than the right coronary artery. Its branches usually supply a larger volume of myocardium, including most of the left ventricle, the muscular ventricular septum, and the supero-lateral papillary muscle of the mitral valve, as well as giving branches to the left atrium, and in just under half the population also supplying the artery to the sinus node (Estes et al., 1966b). In around one-quarter of the population, the main stem also gives rise to an intermediate branch and in rare cases to two intermediate arteries (Ludinghausen, 2003).

✓ **The Anterior Interventricular Artery**

This artery, also known as the left anterior descending artery, is one of the main branches of the main stem of the left coronary artery. It emerges on the antero-superior, sternocostal, surface of the heart, curving around the base of the pulmonary trunk to enter the anterior interventricular groove (James, 1961). It then proceeds towards the apex, in some cases continuing round the apex and extending for variable distances within the inferior interventricular groove, and rarely, as discussed above, replacing the inferior interventricular artery (James, 1961; Gregg and Fisher, 1963). The artery supplies branches to the apical portions of the walls of both right and left ventricles (James, 1961). During its descent, the anterior interventricular artery may give off as many as three diagonal branches, which arise at acute angles towards the left margin of the heart to supply the sternocostal surface, and a variable number of septal perforating branches. The first, and sometimes the second or third, of these perforating branches are important, because they nourish the branches of the atrioventricular conduction axis. These perforating branches are at risk when the surgeon performed the Ross procedure (Muresian, 2006). The anterior

interventricular artery can also give rise to an infundibular branch, which as discussed can produce an anastomotic circle around the subpulmonary infundibulum (Vlodaver et al., 1975).

✓ **The Circumflex Artery**

This artery is the other branch of the main stem of the left coronary artery. It is typically comparable in size to the anterior interventricular artery. It passes posteriorly from the main stem, running in the left atrioventricular groove. In most individuals, it courses for a relatively short distance within the left atrioventricular groove before terminating as the obtuse marginal artery or arteries (James, 1961; Vlodaver et al., 1975). In one-tenth of individuals, nonetheless, the circumflex artery reaches the crux of the heart, where it gives rise to the artery supplying the atrioventricular node , and can extend beyond the crux to supply the diaphragmatic surface of the right ventricle. This is so-called left coronary arterial dominance (Williams et al., 1989). Throughout its course, the circumflex artery gives rise to ventricular branches, which supply the lateral and posterior walls of the left ventricle and the superolateral papillary muscle of the mitral valve (Estes et al., 1966b). In some instances, these branches include the intermediate artery seen when the left main stem branches into three rather than two arteries. Further smaller and unnamed branches also arise from the circumflex artery to nourish the root of the aorta, along with the atrial and ventricular myocardium adjacent to the atrioventricular groove (Bary and Patton, 1953). In some hearts, a large branch, known as the left atrial circumflex artery, leaves the circumflex artery close to its origin. This branch can, on occasion, be even larger than the circumflex artery itself (James, 1961).

c) Coronary Arterial Dominance

Right coronary artery that supplies the inferior wall of the right ventricle and the inferior diaphragmatic portion of the muscular ventricular septum (**Figure 4**), whereas the branches of the left coronary artery supply the majority

of the sternocostal walls of the heart and the obtuse margin of the left ventricle (Schlesinger et al., 1949). In up to half the population, the dominant right coronary artery, in addition to supplying the inferior interventricular artery, also supplies a significant part of the diaphragmatic wall of the left ventricle (Williams et al., 1989). In these individuals, it is the branches of the right coronary artery that typically supply the infero-septal papillary muscle of the mitral valve, and sometimes the supero-lateral muscle (Estes et al., 1966b). An accessory inferior interventricular artery is found on occasion, arising from the left infero-lateral branch and running over the diaphragmatic surface of the left ventricle (Vlodaver et al., 1975). In case of an extremely dominant right coronary artery, with hypoplasia of the circumflex artery, the branches of the right coronary artery can supply all the inferior wall of the left ventricle (Hadziselimovic, 1982). A dominant circumflex artery was reported in one-fifth of the series examined by Ludinghausen (2003), although this reflects the definition used for arterial dominance, because it is usually accepted that only one-tenth of the population has left coronary arterial dominance. Indeed, in only one-tenth of the series of Ludinghausen did the circumflex artery gives rise to the inferior interventricular artery . In the other one-tenth, it was the anterior interventricular artery, giving rise to many anterior septal branches and many inferior interventricular septal branches, which was considered to be the dominant vessel.

3. Normal left ventricular deformation during the cardiac cycle

a) Normal left ventricular structure

A knowledge of the orientation of its muscle fibers is vital in understanding its complex function. Some authors do not agree with this concept of a single helical muscle band. Several studies (autopsy and tagged MRI) (9) have proved that the LV comprises two helical fiber geometries that are continuous, i.e. a right-handed helix in the subendocardium that gradually changes to a left-handed helix in the subepicardium. Mathematical models have proved that the counterdirectional helix is energetically efficient and equalizes redistribution of stress and strain during the cardiac cycle (9). The base and upper septum have more circumferential fibers and from mid-wall to apex, the fibers run obliquely. This double helix is embryologic in origin .The first region of differentiation of myoblasts into striated fibers is in the epicardium. They have an obliquely horizontal orientation. The LV empties laterally into the right ventricle through the interventricular canal. The fibers are parallel to the path of ejection. Weiss (9) demonstrated that cell lines are laid parallel to the direction of mechanical tension applied. The inner fibers are laid when the LV has developed considerably as it becomes larger, the interventricular canal becomes smaller and the aorta becomes the main pathway of ejection. The endocardial helix is therefore in a different direction from the epicardial helix.

b) Normal left ventricular deformation during the cardiac cycle

Nuclear magnetic resonance tagging with 3D MRI enables non-invasive tracking throughout the LV myocardium during the cardiac cycle (9).

- ✓ **Radial displacement**

This is directed inward throughout the LV. The magnitude is greatest in the apical inferior and lateral walls and least in the septum and apicoanterior wall, reflecting contraction and bulk rotation about a septolateral axis with anterior motion at the apex. Shortening strains are maximal at the apex, moving axially from apex to base, causing descent of the mitral annulus.

✓ **Longitudinal deformation**

Shortening along the long axis occurs by descent of the base toward the apex. The displacement magnitudes are greatest at the base, decreasing linearly toward the apex.

✓ **Circumferential deformation**

When viewed from the base, it is clockwise initially, and anticlockwise up to end-systole. More apically, the initial rotation is more prominent (9). The magnitude of circumferential deformation is maximal at the base of the ventricle.

4. Basing testing

a) Biochemical tests

Laboratory investigations are using to identify possible causes of ischaemia, to establish cardiovascular risk factors and associated conditions, and to determine prognosis : Haemoglobin; thyroid hormone; glycated haemoglobin (HbA1c) in every patient with suspected CAD.

We also should evaluate the lipid profil (Total cholesterol, high density lipoprotein cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglyceride) to establish the patient's risk profile and ascertain the need for treatment. The presence of PAD is increasing the likelihood of CAD and renal dysfunction and have a negative impact on prognosis .We should also evaluate

renal function with estimation of the glomerular filtration rate (GFR). It may also be reasonable to measure the uric acid level, as hyperuricaemia is a frequent comorbid condition and may also affect renal function.

b) Resting electrocardiogram

The resting 12 lead ECG is an indispensable component of the initial evaluation of a patient with chest pain without an obviously non-cardiac cause. Even in the absence of repolarization abnormalities, an ECG can demonstrate indirect signs of CAD (pathological Q waves ,left bundle branch block (LBBB) and impairment of atrioventricular conduction..].

c) Chest X-ray

Chest X-ray is part of the initial assessment of patients with chest pain. The test may occasionally be helpful in assessing patients with suspected HF and remains useful to detect patients with pulmonary problems and to rule-out another cause of chest pain.

d) Cardiac magnetic resonance (CMR)

CMR is useful to provide information on cardiac anatomy and systolic cardiac function. It help to assess global and regional function. Late gadolinium enhancement CMR can reveal a typical pattern of scarred myocardium in patients who have already experienced an MI .

e) Conventional Echocardiography

Echocardiographic is a good tool to provide important information about cardiac function and anatomy.We can demonstrate a decreased LV function and/or regional wall motion abnormalities. Decreased diastolic LV function seems to be an early sign of ischaemic myocardial dysfunction . Echocardiography help to exclude alternative causes of chest pain. In the other hand,concurrent cardiac diseases can be diagnostic by echocardiography such as valvular heart diseases, HF, and most cardiomyopathies, but these diseases can coexist with obstructive CAD(10).

The most common echocardiographic abnormality seen in coronary artery disease is abnormal motion of left ventricular wall segments .It is detected on hospital admission in 84 per cent of the patients with acute transmural myocardial infarction, and its location corresponds closely to the electrocardiographic site of infarction (10). The left septal and/or anterior left ventricular wall echoes are abnormal with anterior infarction , and the posterior left ventricular endocardial echoes are abnormal with inferior myocardial infarction . The abnormal motion may be less than normal, absent or paradoxical (10), and the motion pattern alone does not distinguish between acute infarction and chronic coronary artery disease. Abnormal motion also occurs with subendocardial infarction, but it is generally less in degree and more often returns to normal during hospitalization . Wall motion seldom returns to normal following transmural anterior infarction, but sometimes it does after transmural inferior infarction.

5. Selecting appropriate testing

Patient with symptoms unresponsive to medical therapy or typical angina at a low level of exercise, and an initial clinical evaluation(which include echocardiogram and, in selected patients, exercise ECG) that indicates a high event risk, have to proceed directly to invasive coronary angiography . Guidelines recommend the use of either noninvasive functional imaging of ischaemia or anatomical imaging using coronary CT angiography (CTA) as the initial test for diagnosing CAD.

a) Functional non-invasive tests

We can detect myocardial ischaemia through ECG changes, stress CMR or stress echocardiography can demonstrate wall motion abnormalities , SPECT, PET, myocardial contrast echocardiography or contrast CMR can detect perfusion changes .Ischemia can be provoked by exercise or pharmacological stressors, either by increased myocardial work and oxygen demand, or by heterogeneity in myocardial perfusion by vasodilatation.

b) Anatomical non-invasive evaluation

Coronary CTA remains a good test for the detection of obstructive coronary stenoses defined by invasive CA. However, there are stenoses estimated by visual inspection which are not necessarily functionally significant .So,the presence or absence of non-obstructive coronary atherosclerosis on coronary CTA provides prognostic information and can be used to guide preventive therapy .

c) Role of the exercise electrocardiogram

Exercise ECG has an inferior diagnostic performance compared with diagnostic imaging tests .It has limited power to rule-in or rule-out obstructive CAD. We also have to keep in mind the risk of false-negative and false-positive test results. An exercise ECG is of no diagnostic value in patients with ECG abnormalities (for examples:LBBB, paced rhythm, Wolff-Parkinson-White syndrome…)

d) Role of stress echocardiography

Stress echocardiography is the combination of 2D echocardiography with a physical, pharmacological, or electrical stress (11). The diagnostic endpoint for the detection of myocardial ischaemia is the induction of a transient change in regional function during stress. A transient regional imbalance between oxygen demand and supply usually results in myocardial ischaemia, the signs and symptoms of which can be used as a diagnostic tool. As a rule, the less informative the exercise ECG test is, the stricter the indication for stress echocardiography will be. Out of five patients, one is unable to exercise, one exercises submaximally, and one exercises maximally but the ECG is uninterpretable (11).

Stress echocardiography is an established technique for the assessment of known or suspected CAD. It is recommended in all major cardiology guidelines in several clinical settings. However, its status of established technology, should prompt its clinical use as the preferred non-invasive imaging technique due to its low cost, wide availability and lack of radiation exposure. Though these unique features, an utilization gap remains with nuclear techniques percevied as more objective in the face of a comparable diagnostic and prognostic accuracy. The flexible use of stressors (exercise, inotropic and vasodilating) maximazes the

feasibility, avoids specific contra-indications and allows tailoring the exam on each individual patient .

e) Role of CCTA

CCTA is a well-tolerated and reliable non-invasive imaging technique . The high negative predictive value of CCTA, to exclude the presence of CAD renders CT as a suitable first-line diagnostic test in symptomatic patients with low to intermediate pretest likelihood of CAD, and may be considered an alternative to bicycle stress testing, SPECT myocardial perfusion imaging or stress echo.

6. Impact of clinical likelihood on the selection of a diagnostic test

The selection of a non-invasive test depends on patient characteristics, local expertise, and the availability of tests. Some diagnostic tests performs better than others. For example we can combine Stress echocardiography or SPECT perfusion imaging with dynamic exercise testing . IT may be preferred if additional information available from the exercise test, such as exercise tolerance or heart rate response to exercise, is considered important. We cannot use exercise ECG for diagnostic purposes in the presence of ECG abnormalities that prevent the evaluation of ischaemia. We need to weigh risks related to different diagnostic tests against the benefits to the individual. Also we need to take into account contraindications to pharmacological stressors and contrast agents (iodine-based contrast agents and gadolinium-based chelates) (11).

7. Limitation of non invasive diagnostic tests

Noninvasive diagnostic techniques have large application as screening tests in patients with chest pain. The features of the ideal test should be limited cost, wide availability, and accuracy. Exercice stress testing (EST) is inexpensive and physiologic, but it has low diagnostic accuracy, and its application in a population with generally low to intermediate pretest probability of disease is problematic. The diagnostic accuracy of stress echocardiography and stress scintigraphy is higher, but only the former approach has the cost and availability features required for a first-line examination. Unfortunately, independent of the pharmacologic agent adopted, echocardiography achieves a rather modest sensitivity, although its specificity is high. Therefore wide use of pharmacologic stress echocardiography as first-line examination in patients without a history of CAD but with suspect chest pain could be hazardous. Conversely, perfusion imaging is confirmed as highly effective for making the diagnosis of CAD and even for obtaining a reliable evaluation of disease extent. However, availability and economic problems remain major obstacles to its general use.

8. Limitation of conventional echocardiography

a) Left ventricular ejection fraction

LV ejection fraction (EF) is widely used in diagnosis, management, and prognosis of many pathological conditions, especially in heart failure, ischemic, and valvular diseases (12).LVEF can easily be calculated through endocardial border delineation, or alternatively, it can be ‘‘eyeball’’ estimated, but it’s a subjective evaluation. The most commonly used and recommended echocardiographic 2-D measurement for volume measurements is the modified Simpson’s rule with biplane planimetry , although a three-dimensional evaluation is today possible using new-generation echo scanners. The LVEF is a dimensionless parameter, and it is expressed as a percentage (%). It is the ratio of the difference between the end-systolic and the end-diastolic volumes and the end-diastolic volume (EDV) itself .LVEF could be a well away from this but it has many limitations.

✓ Limitations of ejection fraction measurement

In some patients, we it is difficult to obtain true two- and four-chamber apical views and find sub-optimal images. In the latter case, contrast should be used to enhance endocardial when it cannot be evaluated sufficiently. Three-dimensional echocardiography remains a highly reproducible method that allows improvements in accuracy and feasibility (12) of LV volumes and EF estimations.It can eliminate the need for geometric modelling, which is inaccurate in case of ventricular aneurysms, asymmetrical ventricles, wall motion abnormalities, and the error caused by foreshortened views, also in symmetrical ventricles .however, this approach requires expertise and could be time consuming. LVEF depends on several parameters such as myocardial

contractility, heart rate, loading conditions, and dyssynchrony of contraction. Moreover,interpretation of the LVEF values can be misleading when the EDV is too big or too small: in fact, patients with the same EF may have different SVs and, vice versa, patients with identical SV may have different EFs. In the other hand we can find many patients with severe coronary artery obstruction and normal left ventricular function at rest..

b) Left ventricular longitudinal function

It entails the movement of the mitral annulus toward the cardiac apex and depends on the shortening of the LV longitudinal myocardial fibers . In healthy subjects and in patients with advanced dilated cardiomyopathy, longitudinal function accounts for up to the 60 % of the SV (12). We can assess the LV longitudinal function in different ways.

✓ M-mode echocardiography

The mitral annular plane systolic excursion (MAPSE) can be measured by this technique. It is a simple method, quickly performed, and feasible. A depression of MAPSE can evidence subtle systolic impairment in nearly one quarter of patients with HF and preserved EF (12) and in other conditions often characterized by normal EF, such as arterial hypertension and aortic stenosis.MAPSE is moreover an independent predictor of adverse outcome in many pathological conditions, as chronic HF, stable CAD and chronic AF.

✓ Limitations of M-mode echocardiography

MAPSE has many limitations. First of all, it is an angle-dependent measure, so it could be erroneous if the ultrasound beam is not properly aligned to the mitral annulus. Also, MAPSE is limited to the mitral annulus so it can be reduced in case of regional motion impairment even with no significant reduction of global LV function. MAPSE is affected by left atrial contraction via the Frank–Starling mechanism (12).That may explain the presence of reduced MAPSE in patients with atrial fibrillation (AF). In several cases it is difficult to measure AVPD for example when we have mitral annulus calcification, mitral and aortic valve prostheses, mitral valve surgery, prominent hypertrophic interventricular basal septum, and septal papillary muscle .

✓ Tissue Doppler Imaging

We generally take this measure in the apical four-chamber view: We can evaluate the annular velocity at the septal and the lateral annulus and the values can be averaged . TDI is used in clinical practice because of measurement simplicity, good reproducibility, and feasibility in almost all patients regardless

of echocardiographic image quality. Many studies have demonstrated the utility of this parameter for detecting acute ischemia , adding improved accuracy compared to conventional visual wall motion reading.

✓ Limitations of tissue Doppler Imaging

However, there are many limits of TDI. The most important one is related to its angle dependence, as any other Doppler method. Also, TDI velocities are affected by translational motions of the whole heart and by tethering effects, that is, passive motion of LV hypokinetic/akinetic myocardial segments. Finally, TDI does not track mitral annulus motion.

9. Speckle tracking echocardiography

Speckle tracking echocardiography (STE) is a novel echocardiographic tool to assess myocardial function (13). It represents the result of random interferences between tissue scatterers.

Two-dimensional STE technique has a high temporal and spatial resolution and, being a semiautomatic software.It has a good inter- and intra-observer reproducibility. Compared to Doppler strain, this technique had the advantage to be angle independent.Also it is not affected by translational motions of the heart and we can assess simultaneously the entire LV myocardium (13). Therefore, STE can allow a reliable assessment of myocardial deformation along the tridimensional geometrical axes (longitudinal, circumferential, and radial strain; **Figures 6, 7, 8**) throughout the cardiac cycle. Longitudinal strain, in particular, has a high sensitivity and reliability, and this allowed the American FDA to approve longitudinal speckle tracking analysis directly on newer echoscanners, while other STE analyses can be performed offline.

a) Global longitudinal strain

In general, the maximal extent of longitudinal systolic myocardial deformation (peak systolic strain) and its peak rate (peak systolic strain rate) have been used, both regionally and globally, in the literature. GLS has gained increasing interest: It is generally calculated from the mean of the 17 cardiac segments (**figure 9**) obtained from the three standard apical four-chamber, two-chamber and long-axis views.

GLS has proven to be useful both as a prognostic and a diagnostic indicator in addition or as an alternative to the LVEF. As a prognostic indicator, GLS showed to be superior to LVEF and other longitudinal markers in identifying heart failure patients with poor outcome (13). As a diagnostic indicator, GLS has been successfully applied to predict cardio-toxicity due to oncologic treatments, allowing earlier recognition of cardiac impairment compared to conventional evaluation of LV systolic function. In the field of cardio-toxicity, GLS has the potential to become a new standard for recognition of LV systolic dysfunction.

The STE technique has been also extensively applied in the field of cardiac resynchronization therapy to quantify LV dyssynchrony. Other current clinical applications of strain imaging are diagnosis of cardiac amyloidosis, myocarditis with normal LVEF, and evaluation of cardiomyopathies, like hypertrophic and dilated cardiomyopathies (13).

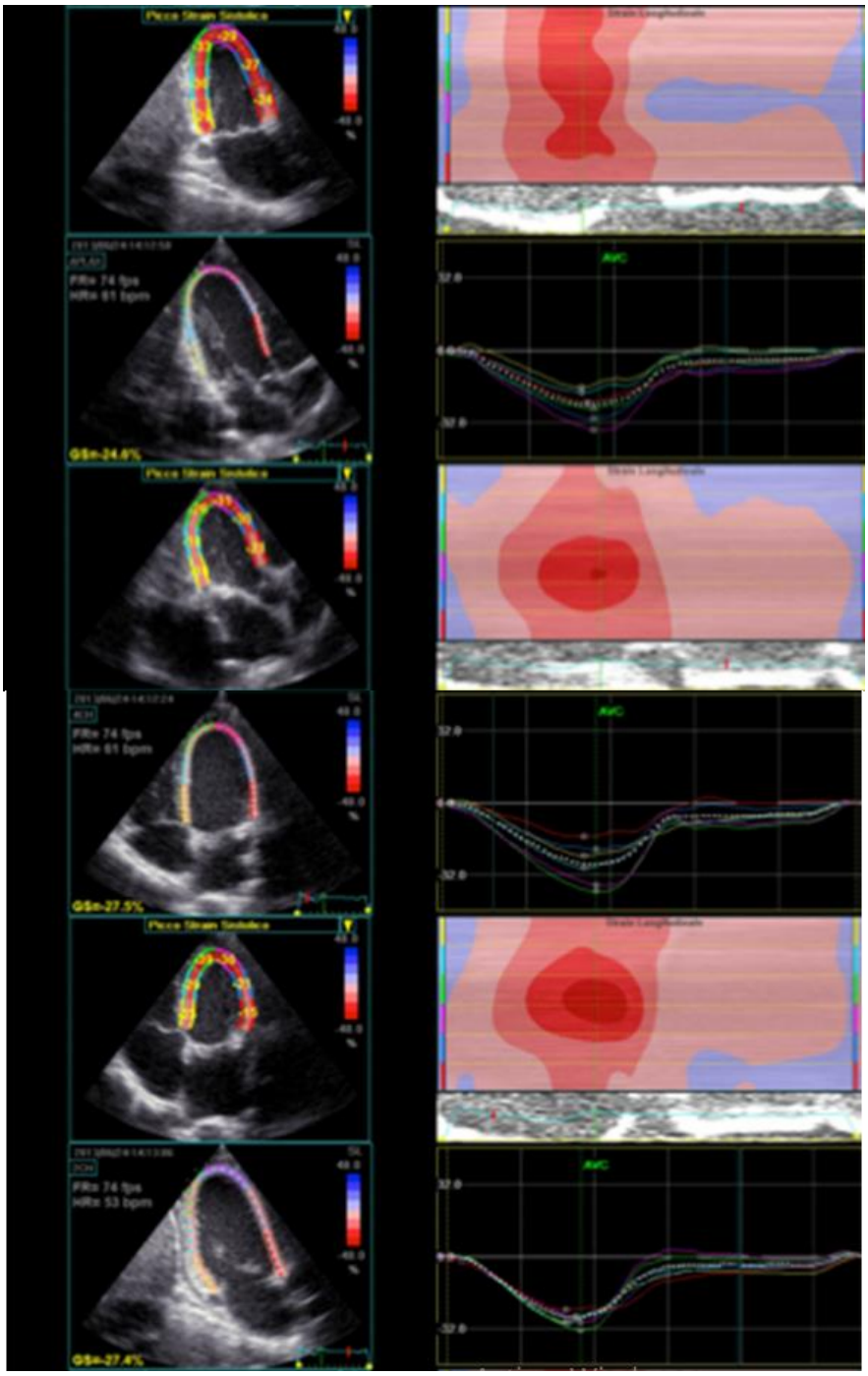

Figure 6: Londitudinal strain measured in 4-, 2- and 3-chamber views

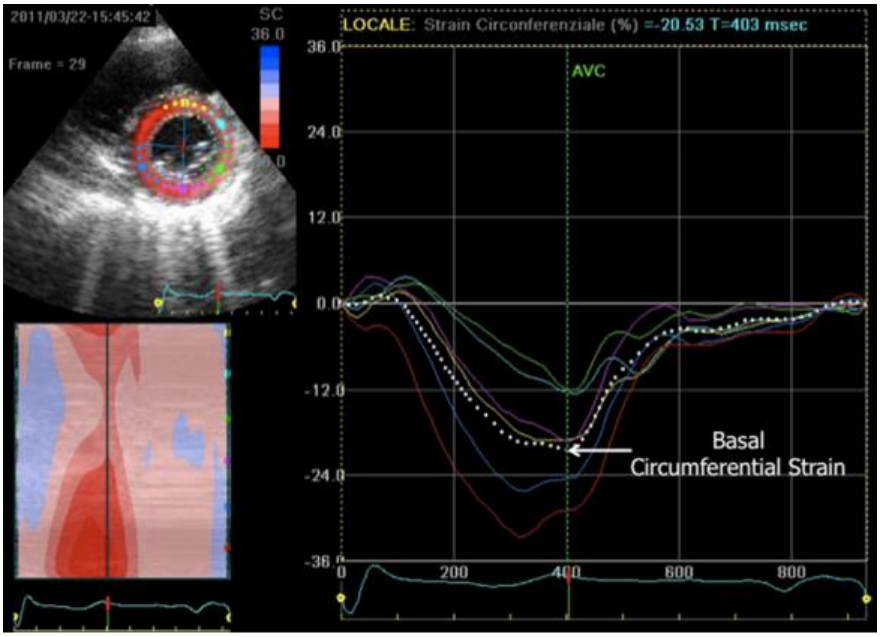

Figure 7: Measurement of basal circumferential strain

Figure 8: Measurement of basal radial strain

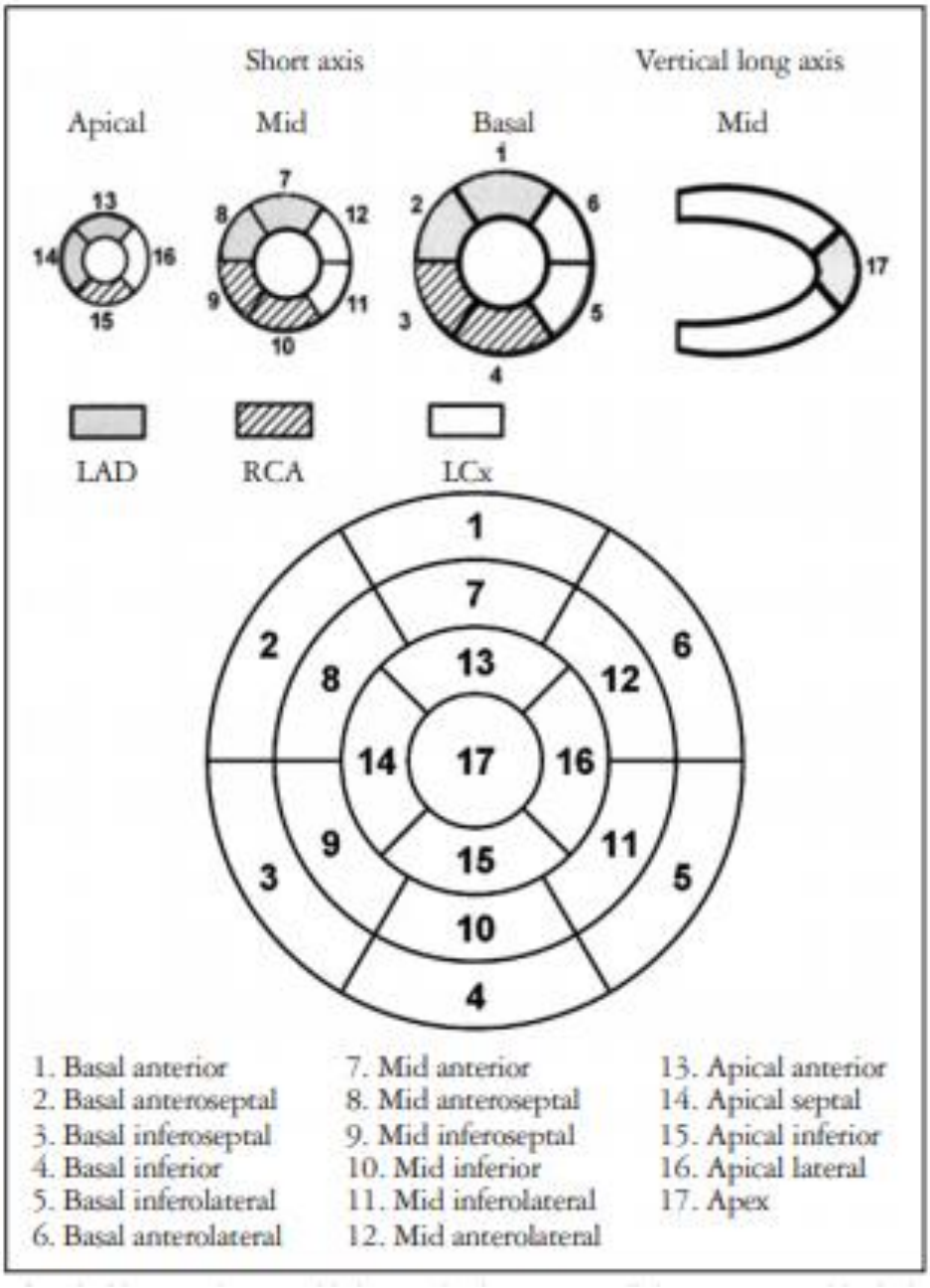

Figure 9: Nomenclature of left ventricular myocardial segments with their distribution according to coronary artery territories.

b) Radial and circumferential strain

STE allows the assessment of the percentage of radial thickening (**Figure 8**) and of circumferential shortening (**Figure 7**) of the myocardial wall. Radial strain draws positive curves, while circumferential strain negative ones. These methods are not well studied are still reserved for research purposes and fewer clinical trial applied these to evaluate the systolic function.

Radial and circumferential strain have are many limitations. Measurements in the radial plane were shown to correlate less well with the reference tool of ultrasonomicrometry with respect to longitudinal strain. An important limitation that should not be ignored is the plane motion. During systole, the base of the ventricle moves toward the apex. This will mean that the speckle pattern present in one frame might be different from that in the next frame. While these changes are small, they may have an important effect on the data derived (13).

10. Utility of strain-echocardiography in coronary heart diseases

a) Normal strain values

The routine application of myocardial strain parameters in clinical practice requires the definition of a normal range and understanding of its reliability. Yingchoncharoen et al. performed a meta-analysis of 24 eligible articles including 28 valid datasets published between 2009 and 2011, and found that the reported normal GLS (n = 2,597) was -19.7 % [95 % confidence interval (CI) -20.4 to -18.9 %], normal GCS (n = 599) was -23.3 % (95 % CI -24.6 to -22.1 %) and normal GRS (n = 568) was 47.3 % (95 % CI 43.6–51.0 %), indicating narrower normal variations in GLS and GCS than in GRS. One of the most important potential limitations to widespread clinical application of this technique is intervendor differences in normal strain values, as highlighted by several investigators. Takigiku et al. determined the normal range of 2D-STE-derived LV strain and their vendor-specific differences in a multicenter prospective study in 817 Japanese healthy subjects (age range 0–88 years) using an ultrasound system from one of the three different vendors (13). They showed that the normal values of GLS (Vendor 1: -21.3 ± 2.1 %, Vendor 2: -18.9 ± 2.5 % and Vendor 3: -19.9 ± 2.4 %), GCS (Vendor 1: -22.8 ± 2.9 %, Vendor 2: -22.2 ± 3.2 % and Vendor 3: -30.5 ± 3.8 %) and GRS (Vendor 1: 54.6 ± 12.6 %, Vendor 2: 36.3 ± 8.2 % and Vendor 3: 51.4 ± 8.0 %) were significantly different between the three vendors with the smallest differences in GLS measurements. They also demonstrated that the feasibility for strain measurements was also different among the three vendors (Vendor 1: 83 %, Vendor 2: 70 % and Vendor

3: 88 %, p\0.01). Very recently, Farsalinos et al. demonstrated that the absolute differences in 62 volunteers between nine different vendors for average GLS value were up to 3.7 and 3.5 % strain units from the average of two or three apical views (GLSAV) and from the four chamber view (GLS4CH), respectively (13). They also found that intra- and inter-observer relative mean errors were lower than those for LVEF and most other conventional echocardiographic parameters.

In view of these recent findings, 2D-STE-derived strain, especially GLS, can be safely used in routine clinical practice, but the system and software from the same vendor should be used for longitudinal follow-up in the same patients. As the left ventricle is composed of 3 myocardial layers (inner layer, mid-wall layer and outer layer), the degree of transmural gradient of systolic strain and the layer-to-layer interactions can be different among the three orthogonal directions, which may contribute to the direction-specific differences in the extent of inter-vendor variation.

b) Age and gender differences

Age- and gender-differences in cardiac structure and LV diastolic function are well recognized in healthy subjects. Sun et al. reported that GLS became less negative with aging, while the GCS became more negative and the GRS remained unchanged (13). Zghal et al. reported that GLS was less negative in elderly subjects (75–95 years) than in young subjects (17–45 years) but there was no significant change in GCS and GRS. It is assumed that GLS can be much more sensitive to aging-associated changes in LV systolic function than GCS and GRS. Recently, Cheng et al. performed 2D-STE examinations in 793 healthy adults (64 % women) between 45 and 84 years of age, and found that women had 1.7 % greater GLS ($p<0.0001$), 3.2 % greater GCS ($p<0.0001$) and 2.9 % greater GRS ($p = 0.024$) compared with men in multivariate analyses. Interestingly, the result from the HUNT-study showed that myocardial deformation was consistently higher in women, except in the group of participants aged >60 years. It is well recognized that parameters of early LV diastolic relaxation assessed by mitral inflow and mitral annular velocities decline with age, and women have greater LV relaxation than men until the menopause. As LV relaxation occurs in a series of energy-consuming steps and is physiologically coupled to contraction, the age and gender-related differences in indices of LV myocardial systolic strain values shown in these studies make good sense from a pathophysiological perspective (13).

c) Utility of strain to determine the diagnosis of CAD:

- Utility of global longitudinal strain

Echocardiography is the leading cardiac imaging technique in patients with suspected cardiac disease. However, conventional echocardiography at rest

provides little information regarding the presence and extent of CAD. The using of the visual interpretation of WMA (based on the assessment of myocardial thickening and endocardial excursion) with the conventional 2DE is subjective, operator dependent, demands complete visualization of the endocardium and is subject to the vicissitudes of cardiac loading and heart rate.

In the present study, GLS was significantly lower among patients with significant CAD than those with control groups with mean values of GLS (-17.68 ± 3.07% vs -20.02 ± 8.31).

Previous studies evaluated patients with suspected CAD, to assess rest GLS to predict obstructive CAD following invasive angiography.They found significant decrease in GLS in patients with significant CAD compared to non-significant CAD. This finding was similar to our results.

The study of Ng et al. (14) enrolled 177 patients evaluated for stable CAD, and found that mean value of resting (GLS) was -16.3 ± 2.4 in patients with CAD+ and -19.1 ± 2.9 in patients with CAD- ($p = 0.001$).

In the Montgomery study (15) ,GLS was significantly lower among patients with significant CAD than those with non-significant CAD with mean values of GLS(-16.8 ± 3.2 vs -19.1 ± 3.4, $p < 0.000$). They showed that GLS =<17.8 may predict significant obstruction (>50%) of CAD, with sensitivity 66% and specificity 76%.

Our results are in agreement with Biering-Soerensen et al. (16) study.296 consecutive patients were included.They have clinically suspected stable angina pectoris without previous cardiac disease, and normal left ventricular ejection fraction.They found that GLS was significantly lower in patients with CAD

compared with patients without CAD (-17.1 2.5% versus -18.8 2.6%; P < 0.001).They showed that GLS <18.4% may predict significant obstruction (>70%) of CAD, with sensitivity 74% and specificity 58%.

In the present study, we found that GLS less than -16.08 may predict significant obstructive CAD (stenosis >70%) with sensitivity 80% and specificity 97%. (**Table 3**) So we found that GLS measurements at rest had high diagnostic accuracy in predicting coronary artery disease.

The optimal GLS diagnostic cutoff value varies significantly among previous studies could be explained by GLS may depend on the clinical characteristics of patients, the effect of diastolic function and their hemodynamic parameters (blood pressure) during image acquisition, by using different equipment, different design, vendor-dependent 2D-STE software and operator skills.

To provide some guidance, a peak GLS in the range of -20% can be expected in a healthy person according to the recommandations of the American society of echocardiography and the European association of Cardiovascular Imaging (17) and in the present study we used this cutoff value.

- Utility of circumferential strain

In the present study , radial, transverse, circumferential strain and synchrony analysis were not performed.

In the Bansal et al study (18) ,30 patients with known or suspected ischemic heart disease were evaluated by means of different two-dimensional speckle-based strain techniques, which use tagged harmonic phase magnetic resonance imaging as a reference standard. They measured peak systolic

longitudinal, radial, and circumferential strain with all three techniques. They found that the discriminative power for the detection of regional myocardial abnormality was highest for circumferential strain with automated function imaging.

In another study, Parker et al.(19) performed a dobutamine stress echocardiography study for the detection of critical stenosis and compared the efficacy of 3D fractional shortening measured by 3D echocardiography with strain and strain rate obtained from sonomicrometry. Similar sensitivity, specificity, and area under the curve values were found for 3D fractional shortening, area strain, and circumferential strain and strain rate, but those for longitudinal strain and strain rate were found to be less specific.

These two studies show the greater importance of circumferential deformation parameters in ischemic heart disease.

d) Utility of strain to determine the severity of CAD:

Many studies showed that GLS declined incrementally with increasing severity of CAD defined by increasing number of stenotic coronary vessels.

In our study ,GLS doesn't decreasing by increasing number of stenotic coronary vessels.We found that (GLS -15.67 ± 3.47 versus -17.58 ± 2.95 versus -17.41 ± 3.01); for patients with 1-vessel disease, 2- vessel disease and 3-vessel disease respectively. This could be explained by the inequality of the number of patients with single, double and three vessel disease. For example we had 10 patients with DVD and in the other hand only 4 patients with single vessel disease.

Accumulating evidence shows that significant coronary stenosis can impair strains and 2D STE is useful to detect CAD.However,the power of the GLS in detecting the severity of CAD is uncertain.

e) GLS and EF

In the present study ,patients with significant CAD had significant decrease in the ejection fraction (EF) [59.72 ± 4.77 vs 64.7 ± 3.47, $p < 0.05$] compared with the control group . This finding is in agreement with Sharma and al. (20) .

In the present study,we found that GLS had highly significant positive correlation with EF. This result is in concordant with results of Biering-Soerensen et al.(16).

Conclusion

The present study suggests that myocardial longitudinal strain imaging by 2D speckle-tracking might be of help in the diagnostic work-up of CAD in patients with apparent normal global and regional systolic function. It is a promising, easy to perform and quick imaging method to predict CAD.

GLS has high sensitivity and specificity 80% and 97% respectively for early detection of significant CAD. 2D-STE improve the value of conventional echocardiography in the detection of the CAD, identifying high-risk patients by determining the severity of the CAD

As a non-invasive method, it may provide more valuable information for clinical physician by early detection of LV dysfunction related to significant CAD.

This new technique should be incorporated into the diagnostic algorithm when there is suspicion of CAD. It may act as an early adjunctive marker of cardiac ischemia.

In addition, TLS may be helpful in identifying which coronary artery is affected.

Further studies are needed to validate these results and before it is clinically accepted.

Résumés

ABSTRACT

Title: The **value of global longitudinal strain by two dimensional speckle tracking echocardiography in predicting coronary artery disease**

Key words : coronary artery disease ,echocardiography ,global longitudinal strain

Introduction: Two-dimensional (2D) speckle-tracking echocardiographic (STE) imaging is frequently performed in the assessment of cardiovascular diseases.

Purpose: We aim to investigate the role of the global longitudinal strain (GLS) value assessed via 2D STE imaging to detect significant coronary artery disease (CAD) in patients normal echocardiography (LVEF >50% without wall-motion abnormalities).

Methods: This study enrolled one hundred twenty one patients with suspected CAD.Inclusion criteria included patients between 18 and 80 years of age and indication for coronary angiography (CA) according to current guidelines.Exclusion criteria included previously known CAD, WMA and LV systolic dysfunction (patients with depressed left ventricular function (EF <50% at rest).All patients received medical treatment according to current guidelines.Patients underwent transthoracic echocardiography(TTE),2-Dspeckle tracking echocardiography(2D-STE) and coronary angiography.

Results : Patients were classified into those with normal coronary angiography, which included 50 patients (41.66%) and patients with CAD which included 71 patients (58.33%).CAD group had a significant decrease in both GLS (-17.68 ± 3.07% vs -22.35 ± 3.07% p=0.02) and LVEF (60.72 ± 4.77% vs 64.73 ± 3.47%) compared to contral group.We found that the optimal cutoff value of GLS in predicting significant CAD was -16.08 (AUC was 0.72 and p value 0.04) with sensitivity and specificity were 80% and 97% respectively. GLS has highly significant positive correlation with EF (r 0.45;p=0.027).

Conclusions: Global longitudinal strain (GLS) assessed with 2D STE is a promising, easy to perform and quick imaging method to predict CAD .

Titre: Role du 2D strain pour prédire la maladie coronaire

MOTS clés: 2D strain , maladie coronaire ,echographie normale

Introduction:

La détection de la maladie coronaire par échocardiographie reste un défi, avec la nécessité d'effectuer une imagerie de stress pour détecter l'ischémie. Le but de cette étude était de déterminer si le 2D strain peut prédire une coronaropathie significative chez les patients sans troubles de la cinétique segmentaire et une FEVG conservée.

MÉTHODES :

L'étude a inclu cent vingt et un patients adressés pour suspicion de maladie coronaire. Ils avaient une échographie normale (FE >50 %;absence de troubles de la cinétique segmentaire) . ils ont bénéficié d'une échocardiographique Doppler conventionnelle ,d'une une imagerie Doppler tissulaire et d'une imagerie par strain .

RÉSULTATS:

Le groupe CAD présentait une diminution significative à la fois du GLS (-17,68 ± 3,07 % vs -22,35 ± 3,07 % p = 0,02) et de la FEVG (60,72 ± 4,77 % vs 64,73 ± 3,47 %) par rapport au groupe témoin. La valeur seuil optimale de GLS pour prédire une CAD significative était de -16,08 (AUC était de 0,72 et valeur p de 0,04). La sensibilité et la spécificité étaient respectivement de 80 % et 97 %. GLS a une corrélation positive hautement significative avec EF (r 0,45; p = 0,027).

CONCLUSION :

Le GLS est un indice sensible permettant de détecter une coronaropathie significative chez les patients sans troubles de la cinétique segmentaire et avec une FE normale. Il s'agit probablement d'un outil précieux pour le diagnostic précoce de la coronaropathie.

العنوان: دور السلالة ثنائية الأبعاد في التنبؤ بمرض الشريان التاجي

الكلمات الرئيسية: السلالة ثنائية الأبعاد ، مرض الشريان التاجي ، الموجات فوق الصوتية العادية

مقدمة:

لا يزال اكتشاف مرض الشريان التاجي عن طريق تخطيط صدى القلب يمثل تحديًا ، إلى جانب الحاجة إلى إجراء تصوير الإجهاد للكشف عن نقص التروية. كان الهدف من هذه الدراسة هو تحديد ما إذا كانت السلالة ثنائية الأبعاد يمكن أن تتنبأ بمرض الشريان التاجي المهم في المرضى الذين لا يعانون من اضطرابات حركية قطعية و LVEF المحتبس.

أساليب :

اشتملت الدراسة على 121 مريضاً تمت إحالتهم للاشتباه في إصابتهم بمرض الشريان التاجي. كان لديهم الموجات فوق الصوتية العادية (EF> 50 ٪ ؛ عدم وجود اضطرابات في حركية القطعية). تلقوا تخطيط صدى القلب التقليدي بالدوبلر وتصوير الأنسجة دوبلر وتصوير الإجهاد.

النتائج:

شهدت مجموعة CAD انخفاضًا كبيرًا في كل من GLS (-17.68 ± 3.07٪ مقابل -22.35 ± 3.07٪ p = 0.02) و LVEF (60.72 ± 4.77٪ مقابل 64.73 ± 3.47٪) مقارنة بمجموعة التحكم. كانت القيمة الفاصلة المثلى لـ GLS للتنبؤ بـ CAD كبيرة هي -16.08 (كانت AUC 0.72 وكانت القيمة p 0.04). كانت الحساسية والنوعية 80٪ و 97٪ على التوالي. GLS له علاقة إيجابية ذات دلالة إحصائية مع EF (r 0.45 ؛ p = 0.027).

استنتاج:

GLS هو مؤشر حساس للكشف عن أمراض الشرايين التاجية الهامة في المرضى الذين لا يعانون من اضطرابات حركية قطاعية ومع EF طبيعية. ربما تكون أداة قيمة للتشخيص المبكر لمرض الشريان التاجي.

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