A Review on Diagnostic Procedures for the Cardiovascular System

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Abstract: ***Cardiovascular disease (CVD) is the leading cause of mortality worldwide and an important cause of disability, diagnostic procedures, ranging from non-invasive to invasive testing, are valuable diagnostic tools for the cardiovascular system. The purpose of this review study was to summarize the cardiovascular disease (CVD) and tools used for diagnosis and assessment of CVD. We searched electronic databases of the cardiovascular disease (CVD) and tools used for diagnosis and assessment of CVD .This study describes some of the more common pathologic entities in the cardiovascular system , provides a description of diagnostic procedures in evaluation of cardiac disease such as Blood tests and Diagnostic imaging modalities (Plain film, cardiac catheterization, nuclear medicine, echocardiography , computed tomography (CT), magnetic resonance imaging (MRI) and Radiation Risks. This review provides a description of the various diagnostic imaging techniques for cardiovascular system, although clinical experience remains limited, careful evaluation of safety as well as validation of diagnostic and prognostic value of these techniques in clinical trials is still needed.***

Keywords: Cardiovascular disease (CVD), computed tomography (CT), magnetic resonance imaging (MRI), Plain film

1. Introduction

Cardiovascular diseases (CVD) will be the main cause of morbidity and mortality in 2015 according to a WHO report. The main problem is related to the long-time delay between the start of the development of atherosclerosis in young adults and the manifestation many decades later.(1,2) Despite a recent decline in a CVD mortality in men and women, the main problem is related to the acute manifestation as the acute coronary syndrome (ACS), which leads 30 – 50% of subjects to sudden and fatal outcomes. [3, 4] In addition, about 20% of first and recurrent acute myocardial infarctions (MI) are silent. [5,6] The lifetime risk of coronary artery disease (CAD) after the age of 40 years is 49% for men and 32% for women.[7] These data are confirmed for Europe despite a strong decline in hospital deaths. [8,9] Another problem is related to the fact that the number of sudden cardiac death amounts to 300 000 in the general US population. It is about 10 times higher than in those patients who are defined as prone to sudden death due to low ejection fraction, ventricular arrhythmias, and acute MI. 10 For cardiologists, this gains specific interest, because even well-known cardiologists experienced early (≤65 years) sudden cardiac deaths [11 – 14].

1.1The normal heart

The heart is a muscular organ about the size of a fist. With every heartbeat, the heart pumps blood that carries oxygen and nutrients to all parts of the body. The heart beats about 70 times per minute in a person at rest. The heart rate increases when a person is active or experiences strong emotions. Heart muscle receives its own blood supply from a system of coronary arteries. A good blood supply is vital for the normal function of the heart [15].

1.2 cardiovascular Diseases

CVDs due to atherosclerosis: Ischemic heart disease or coronary artery disease (e.g. heart attack), cerebrovascular disease (e.g. stroke), diseases of the aorta and arteries, including hypertension and peripheral vascular disease, (Other CVDs: congenital heart disease, rheumatic heart disease, cardiomyopathies, and cardiac arrhythmias.) The disability-adjusted life year (DALY) is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death (premature death). CVDs and their risk factors are major contributors to global morbidity and mortality [15– 19].Tobacco smoking, physical inactivity, unhealthy diets and the harmful use of alcohol are the main behavioral risk

factors of CVDs. These risk factors are shared by other major NCDs such as cancer, diabetes and chronic respiratory disease.

1.2.1 Pattern of heart disease in Sudan

In 1937, an analysis was made of 100 consecutive cases of heart disease admitted to Khartoum Hospital: 80 had cardiovascular syphilis, followed by rheumatic heart disease. In 1961 the same author, Dr Halim, analysed 958 consecutive cardiac cases admitted to Khartoum Hospital. Hypertension and rheumatic heart disease (RHD) were the commonest two diagnoses at 44.4 and 25.4% of the sample, respectively. Ischemic heart disease (IHD) was 12.6 % and syphilitic heart disease regressed to 6.0%.[20] Two other similar studies investigating the pattern of heart disease were conducted in the 1980s and 1990s. The first study conducted by Khalil et al. was in a community hospital in Khartoum North Hospital and included 539 patients from 1980 to 1983. [21]The other was performed in 1992 in Al Shaab Hospital, which is a tertiary referral hospital, by Kurdufani et al. and included 1 000 patients. They show that the tetrad of hypertensive heart disease, rheumatic heart disease, ischaemic heart disease and cardiomyopathy are the main cardiovascular causes for hospital admission. These results are comparable to the recent Heart of Soweto study, [22] which also showed that these four disease categories, together with pericardial disease, are the main cardiac causes for hospital presentation in Soweto, South Africa.

The contribution of HIV/AIDS to heart disease in Sudan, particularly cardiomyopathy and pericardial disease is unclear. However, this is expected to be less than what is seen in many parts of sub-Saharan Africa, as Sudan has one of the lowest HIV prevalence rates in this region. HIV prevalence rate for adults aged 15 to 49 in Sudan is 1.4% (1–2%) [23] compared to 5.2% for sub-Saharan Africa in 2008 [24].

1-2-2 Epidemiology Cardiovascular Diseases in Africa

Several medical conditions that affect the cardiovascular system are restricted to or affect predominantly Africans. They can be considered neglected diseases because, despite affecting considerable numbers of people, they have not been the subject of systematic research or structured control programs and did not benefit from translation of knowledge obtained in other areas of human knowledge. Their epidemiology and natural history are often incompletely described, and the etiology and pathogenesis are unclear, leading to little or no improvement in medical care for patients, and absence of effective preventive measures for their control.

The epidemiology of cardiovascular diseases in Africa, reported mainly on hospitalized patients, may not represent the true pattern of heart disease in the continent but suggests a high burden of neglected conditions such as rheumatic valve disease, cardiomyopathies, and tuberculous pericarditis [24–29].

1.2.3 Cardiovascular diseases in Sub-Saharan Africa

The pattern of cardiovascular diseases in Sub-Saharan Africa is unique, including uncorrected congenital heart defects, persistence of conditions associated with poverty and infections which have not yet been controlled (rheumatic heart disease, endomyocardial fibrosis, cor pulmonale due to schistosomiasis), emergence of diseases related to changes in living habits (hypertension and stroke, ischaemic heart disease) and diseases associated to the HIV infection (tuberculous pericarditis, pulmonary hypertension, cardiomyopathy). Data on the economic implications of cardiovascular disease and heart failure in sub-Saharan Africa are scarce, but, there is clear evidence that the cost of managing cardiovascular emergencies such as stroke, heart failure and hypertensive emergencies cannot be afforded by the majority of the population [30]. Recent data on the high economic and social costs of cardiovascular diseases to the national health services and the communities comes also from Tanzania, where respondents from all income strata reported decrease in self-rated health, worsening of the ability to participate in moderate and vigorous activities, and emotional problems following cardiovascular-related hospitalization [31].

1.2.4 The epidemic of cardiovascular disease in the developing world:

The epidemic of cardiovascular disease (CVD) is a global phenomenon, and in the current environment, the magnitude of this increase in incidence and prevalence in the developing world and newly industrialized nations has potentially major complications for those high income nations that characterize much of the developed world. The early half of the 20th century witnessed a rapidly growing epidemic of CVD as a result of industrialization, urbanization, increased prosperity, and social upheaval in the higher income countries, followed by an impressive decline in mortality from CVD during the latter half of the 20th century. A recent study of five countries emphasizes that a much higher proportion of deaths occur in the working age population in Brazil, India, and South Africa in contrast to the USA and Portugal. [32] Despite limitations in regard to the quality of data collection, the potential consequences of the burden of CVD falling upon the ‘breadwinners’ of the community are sobering; LIMIC are faced with a dual burden of communicable and degenerative diseases which require tertiary care and a consequent diversion of limited resources. In conjunction with the loss of productive years of life, the consequences lead to economic constraints with an impact on both the private and the public sectors. Moreover, the demographic tide is inexorably shifting, and it is estimated that by 2010, 70% of the world’s elderly will live in LIMIC and the trend towards urbanization will accelerate. [33] Other studies project that the increase in mortality due to coronary heart disease and stroke will be approximately three-fold higher in developing countries in comparison to the developed nations. These trends are illustrated by changes in the distribution of the causes of death in China between 1973 and 2005 with a marked fall in rates due to

communicable diseases and an increase in the proportion due to cerebro-CVD and cancer.[34] India provides a striking example of a country with contrasting burdens of disease. Despite the surge in the Indian economy over the last two decades, in 1999 to 2001, the Federal Agricultural Organization reported that approximately 213.7 million people were considered undernourished. 35 This contrasts with a report on the prevalence of obesity in affluent girls' schools in Delhi, in which 22% of children to 17 years were overweight and 6% obese. [36] In addition, although India is a young country, the ≥60 years age group, the majority of who are poor, is large and comprises 5% of the total population and is projected to rise to 113 million people by 2016. Similarly, South Africa is faced with a collision of four excessive health burdens; communicable diseases (HIV, Aids); non-communicable diseases among a population in whom the proportion of the elderly is predicted to triple between 1985 and 2025; maternal, neonatal, and child mortality, and the consequences of injury and violence. [37]

1.3 Diagnostic tests in evaluation of cardiac disease

1.3.1 Blood tests

The cardiac enzymes (creatine kinase and lactase dehydrogenase) have largely been superseded by troponin (T or I) as the serum cardiac marker of choice (troponin is a peptide). The almost absolute specificity of troponin to cardiac muscle has led to the recent re-definition of myocardial infarction using elevated serum troponin as the primary diagnostic criterion. Troponin is detected in the serum approximately 4–10 hours after the onset of myocardial infarction, peaks at 12–48 hours and remains elevated for 4–10 days.1 CK-MB (myocardium-bound fraction of creatine kinase) is a suitable alternative when troponin assay is not available. CK-MB is elevated 4–8 hours after myocardial infarction, peaks at approximately 12 hours and returns to normal after 2–3 days. CK-MB remains elevated for a much shorter time than troponin, is a useful indicator for early re-infarction and provides an estimate of the size of the infarct [38].

1.3.2 Diagnostic imaging

An ideal modality used for noninvasive imaging of CHD should be able to delineate all aspects of the anatomy, including abnormalities of cardiac structure as well as those involving extracardiac vessels, evaluate physiological consequences of CHD such as measurement of blood flow and pressure gradients across stenotic valves or blood vessels, be cost-effective and portable, not cause excessive discomfort and morbidity, and not expose patients to harmful effects of ionizing radiation. No single modality satisfies all these requirements because noninvasive imaging of CHD poses several unique challenges. Patients range in size from a 200-g fetus to an adult weighing more than 120 kg. Each extreme poses technical difficulties specific to the imaging modality used [39].

1.3.2.1 Conventional Radiographs

The most common imaging test for evaluating the heart and great vessels is the chest radiograph, which consists of an upright posterior-to-anterior (PA) and left lateral (LAT) projections. The terms PA and left lateral refer to the direction the x-ray beam takes through the body before it reaches the radiographic cassette. Chest radiographs are usually obtained with high kilovoltage and milliamperage to minimize exposure time and cardiac motion. When possible, the distance between the x-ray tube source and the film is at least 6 feet to minimize magnification and distortion. The examination is ideally performed with the patient at maximal inspiration. A good rule of thumb for estimating adequate inspiration is to be able to count 9 to 10 posterior ribs or 5 to 6 anterior ribs from the lung apices to the hemidiaphragms through the aerated lungs (Figure 1) [40].

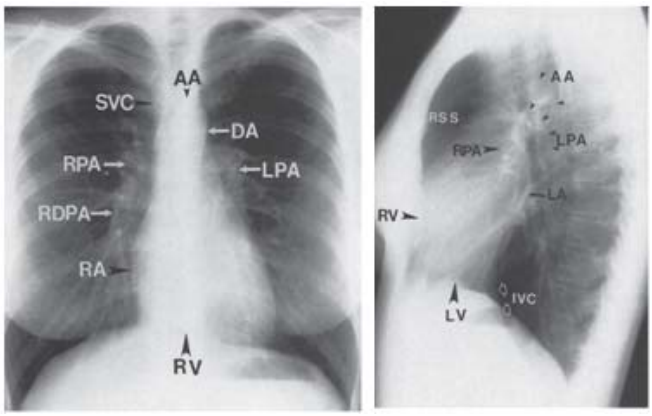

Figure 1: Normal PA and lateral radiographs. (A) PA view of normal chest. RA, right atrium; RDPA, right descending pulmonary artery; RPA, right main pulmonary artery; SVC, superior vena cava; AA, aortic arch; DA, proximal descending thoracic aorta; LPA, left pulmonary artery; RV, right ventricle. (B) Lateral view of normal chest. RV, right ventricle; RSS, retrosternal clear space; AA, ascending aorta; LPA, left pulmonary artery; RPA, right pulmonary artery en face; IVC, inferior vena cava; LA, left atrium; LV, left ventricle.

1.3.2.2 Echocardiography

Since the 1980s, echocardiography has been the noninvasive imaging modality of choice for diagnosis and follow-up of children and adults with CHD and has been shown to be reliable in the diagnosis of most forms of CHD, with major diagnostic errors occurring in only 0.2% to 2% infants.[41,42] New echocardiographic techniques developed in recent years, including real-time 3D echocardiography, strain/strain rate imaging, and speckle tracking, have greatly expanded the capabilities of cardiac ultrasound to evaluate anatomy and physiology of CHD.

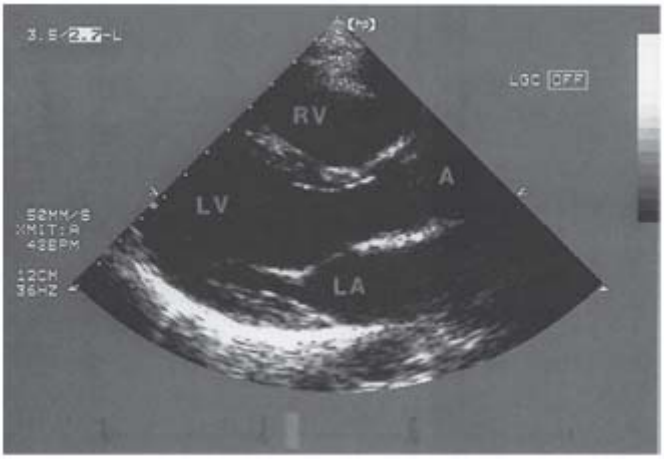

Figure 2: Normal transthoracic echocardiogram from a healthy subject. Views are taken from the left midparasternal region through an intercostal space. The structure closest to the apex of the screen is the chest wall. The mitral valve, separating the left atrium and left ventricle, is partially open in this image from early systole. A, aorta; LA, left atrium; LV, left ventricle; RV, right ventricle

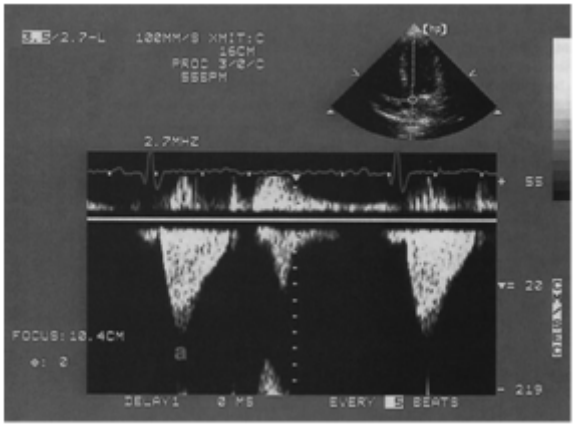

Figure 3: Transthoracic spectral Doppler tracing taken from an intercostals space over the cardiac apex. The Doppler sample is placed in line with the left ventricular outflow and aorta (shown in miniature echocardiogram image at top right). Velocity of flow is denoted along left edge of tracing in cm/s. The Doppler tracing shows that aortic peak velocity (a) is normal (140 cm/s). This technique can reliably assess the presence of and quantitate the severity of aortic stenosis.

1.3.2.3 CMR

Technical advances during the last decade have brought CMR into the mainstream of noninvasive cardiac imaging. Well established clinical applications of CMR in patients with CVD include anatomic assessment of cardiovascular anomalies before and after surgery, quantification of biventricular function, magnetic resonance angiography (MRA), measurement of systemic and pulmonary blood flow, quantification of valve regurgitation, identification of myocardial ischemia and fibrosis, and tissue characterization.

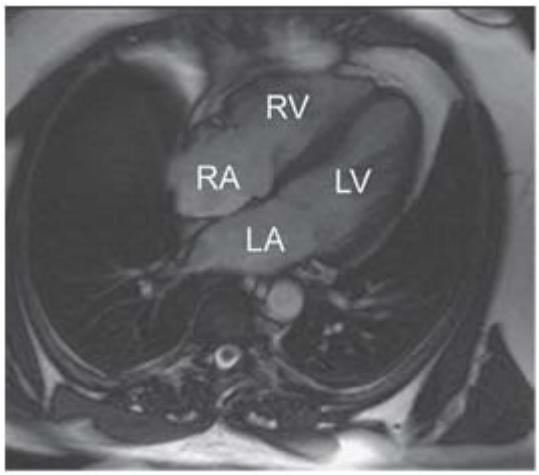

Figure 4: Axial, short-axis MR images with normal anatomy. LV, left ventricle; RA, right atrium; RV, right ventricle

1.3.2.4 CCT

The role of CCT in evaluating the thoracic vasculature and the trachea bronchial tree is now well established [43,44] Recent advances in multi detector technology have led to improved spatial and temporal resolutions allowing coronary artery imaging and gated cine imaging to evaluate ventricular function.

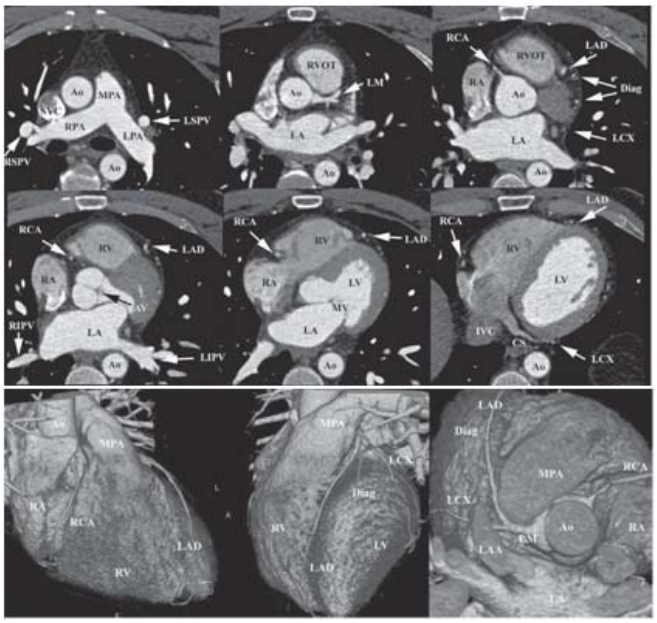

Figure 5: Normal anatomy at cardiac CT angiography. (A) Axial composite image and (B) 3D volume rendered images in right anterior oblique, left anterior oblique and cephalad projections (from left to right). Ao, aorta; AV, aortic valve; CS, coronary sinus; Diag, diagonal branch; IVC, inferior vena cava; LA, left atrium; LAA, left atrial appendage; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main coronary artery; LIPV, left inferior pulmonary vein; LPA, left pulmonary artery; LSPV, left superior pulmonary vein; LV, left ventricle; MV, mitral valve; MPA, main pulmonary artery; RA, right atrium; RCA, right coronary artery; RIPV, right inferior pulmonary vein; RPA, right

pulmonary artery; RSPV, right superior pulmonary vein; RV, right ventricle; RVOT, right ventricular outflow tract; SVC, superior vena cava.

1.3.2.5 Nuclear Scintigraphy

These techniques use radioisotope-labeled compounds to quantify ventricular function, blood flow, myocardial perfusion, and metabolism. [45] Ventricular volumes, ejection fraction, cardiac output, and regurgitant fraction can be calculated using multiple gated acquisitions obtained after equilibration of 99mTc-labeled red blood cells or albumin. Reversible myocardial ischemia can be identified by assessing myocardial perfusion under stress based on uptake of 99mTc or 201Tl measured using single-photon emission computed tomography. Positron emission tomography can be used to evaluate myocardial viability and metabolism. Although tomographic imaging has rendered planar imaging obsolete for general myocardial perfusion imaging (MPI) [46], planar imaging is still important in certain circumstances particularly, for example, radionuclide ventriculography. Planar imaging is usually performed by angling the gamma camera to the desired position; for example, in radionuclide ventriculography the gamma camera is usually positioned in the 45 degree left anterior oblique (LAO) projection with 15–30 degrees of caudal tilt. The LAO angle is then adjusted to obtain clear separation of the ventricles (known as the "best septal view") and the caudal tilt can also be adjusted to obtain separation of the atria from the ventricles [47]. For MPI it has conclusively been shown to be superior to planar imaging. Attenuation can be a particular problem in MPI. Although methods of correcting for attenuation are available they all suffer from a variety of problems and hence their clinical value is uncertain [48]. Breast binding, using a broad strap, around the chest can be useful in both sexes as it prevents movement and may help to reduce breast attenuation artifact. However, it is essential that consistency in application is achieved, especially in myocardial perfusion imaging.

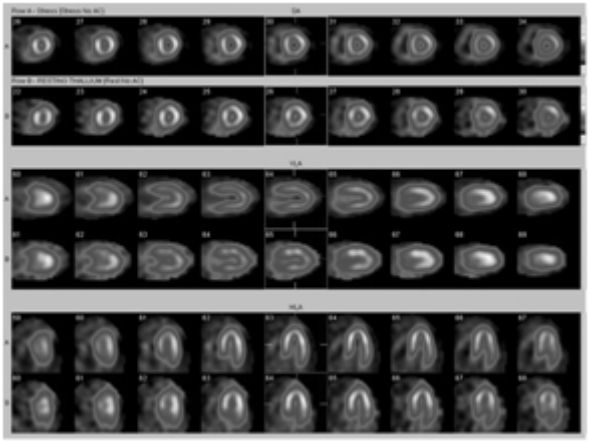

Figure 6: Normal myocardial stress/rest study. Stress imaging performed with technetium-99m tetrofosmin following treadmill exercise achieving target heart rate. Resting images performed using thallium-201. Homogeneous perfusion of the left ventricular cavity is seen with both stress images (top of image pairs) and rest images.

1.3.2.6 ECG

The electrocardiogram (ECG) is widely used for monitoring. ECG changes appear early in the course of diabetes, and usually include alterations such as sinus tachycardia, QTc prolongation, QT dispersion, changes in heart rate variability, ST–T changes, and left ventricular hypertrophy. These changes and others, detected with the use of a resting ECG, often together with an exercise ECG, are used to detect silent ischaemia, assess prognosis and predict future risk. Because the ECG is a non-invasive and relatively easy test to perform, it is used in the series of investigations conducted as part of the annual clinical evaluation of people with diabetes around the world.[49] The use of this modality however varies substantially, guided essentially by the availability of ECG machines and the cost of such investigations. As a result, the regional office of the International Diabetes Federation (IDF) for Africa recommends ECG monitoring in diabetes only at the secondary or tertiary level of the healthcare system where facilities for performing an ECG are more readily available.50 Therefore in sub-Saharan Africa, the majority of patients with diabetes who receive care in primary healthcare facilities do not have routine ECG screening. Failure to perform regular ECGs means that opportunities to improve cardiovascular health in this population are being missed. Furthermore, our knowledge of the major ECG abnormalities and their determinants in this environment remains very limited.

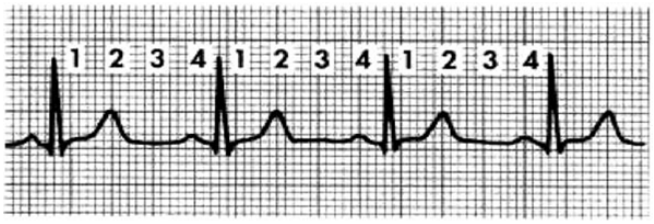

Figure 7: The normal ECG tracing

1.3.2.7 Angiogram

Conventional catheter angiography was the main modality available for the radiological evaluation of the peripheral vessels in the past [51].Conventional catheter angiography with digital subtraction (DSA) is the gold standard for arterial imaging. DSA uses images subtraction so that bones don't obscure vascular details. Contrast resolution improved through use of image enhancement soft ware, lower volume of contrast media can be used, image acquisitions is rapid, angiography provide better anatomic details and high resolution , hemodynamic information regarding pressure gradient across stenosis can be obtain simultaneously, most importantly percutaneous interventions (Angioplasty – Stenting) are Possible at the same time .It is an invasive procedure requiring intra-arterial catheter with resultant complication rate of approximately (1%). The use of iodinated contrast media is associated with contrast Reaction and nephrotoxicity especially in patient with

renal complomise [52].

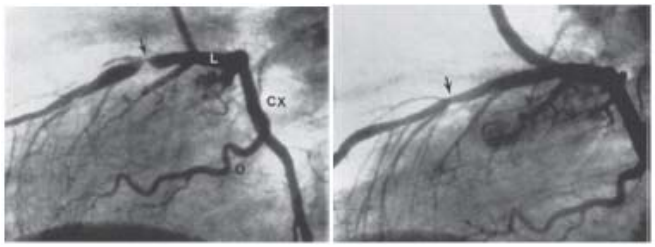

Figure 8: (A) Coronary arteriogram. Images were obtained from the left lateral projection with contrast injection into the left main coronary artery. The left anterior descending (L), left circumflex (CX), and first obtuse marginal (O) branches are visualized. Severe stenosis is seen in the midportion of the left anterior descending artery (arrow) in this patient, who had unstable angina pectoris. (B) Coronary arteriogram, same projection and patient as in (A), obtained 1 day later. The stenosis in the left anterior descending coronary artery (arrow) has been reduced after percutaneous balloon angioplasty.

1.4 Radiation Risks

Among noninvasive modalities for cardiac imaging, CCT and nuclear scintigraphy involve exposure to ionizing radiation. A growing body of literature has shown that exposure to even low doses of ionizing radiation increases the lifetime risk of developing cancer.[53] Importantly, children are at much greater risk than adults from a given dose of radiation both because they are inherently more radiosensitive and because they have more remaining years of life during which a radiation induced cancer could develop. For example, compared with a 40-year-old adult receiving a similar dose of radiation to the chest, an infant has a 4- to 5-fold higher lifetime risk of developing lung cancer.[54] In addition, organs receive higher radiation doses when scanned in a child compared with an adult. Radiation dose associated with gated 16-slice CCT (_15 mSv) is almost 3-fold larger than that associated with conventional coronary angiography (_5 mSv). Several new techniques to reduce radiation dose of CCT are being developed, but their implementation in clinical practice remains limited at the present time. Ionizing radiation, even at very low doses, is potentially capable of causing serious and lasting biological damage. If this were not so, the stringent measures that have to be taken to limit the amount of radioactivity administered to the patient, and thereby the radiation dose, would be unnecessary. Indeed they would be undesirable since the key factor limiting radionuclide image quality is the very low count density that results from the strict protocols of dose limitation.

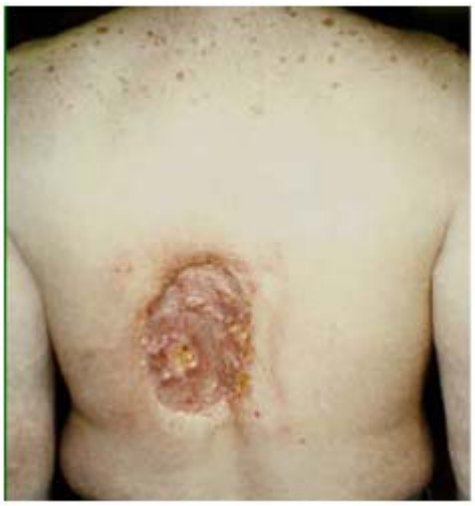

Figure 9: Appearance of radiation-induced skin injury approximately 18 to 21 months following multiple coronary angiography and angioplasty procedures – evidence of progressive tissue necrosis.

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