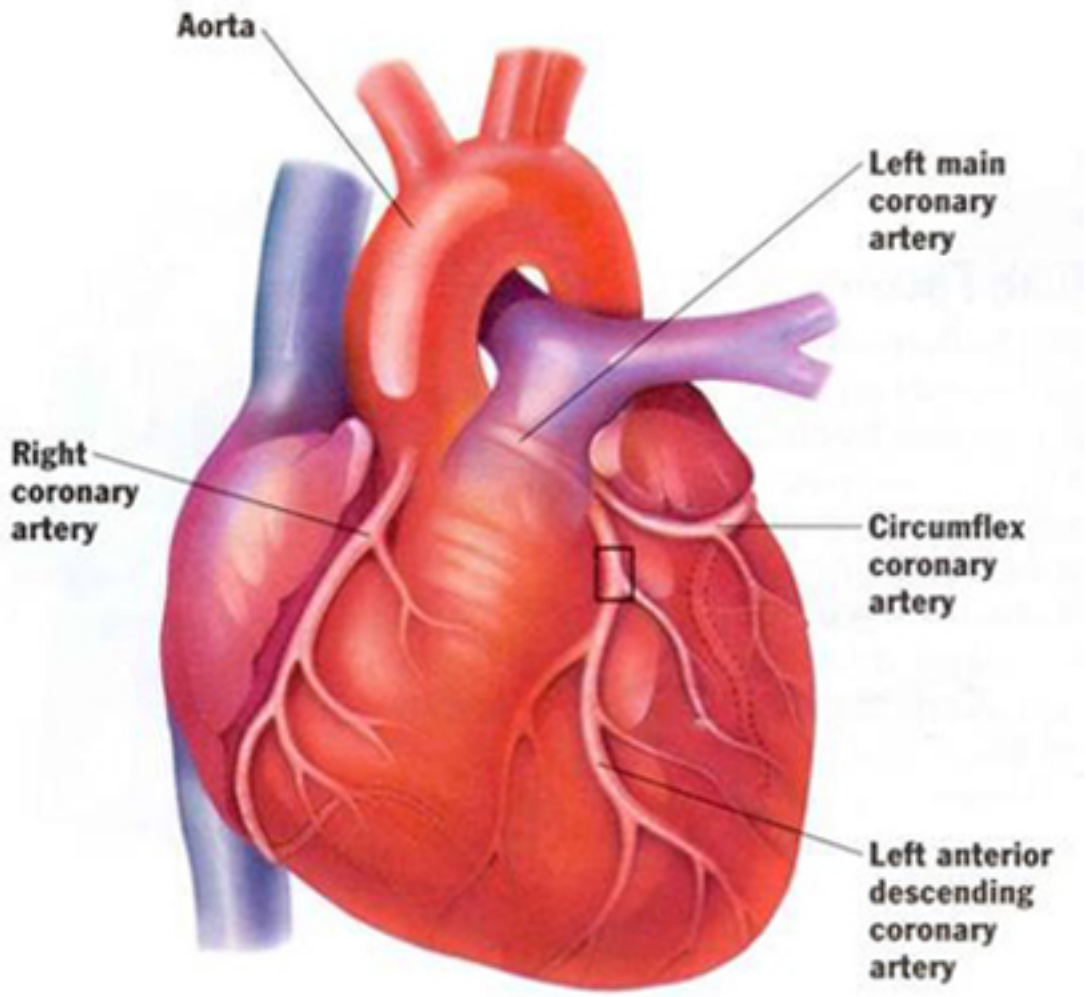
Heart Diseases and Cardiac Procedures



Alanis Washington

Ryder Wilkerson

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Chapter 1

Myocardial Infarction (Heart Attack)

Myocardial infarction

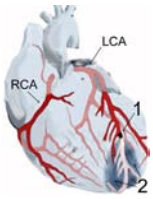


Diagram of a **myocardial infarction** (2) of the tip of the anterior wall of the heart (an *apical infarct*) after occlusion (1) of a branch of the left coronary artery (LCA, right coronary artery = RCA).

ICD-10	I21.-I22.
ICD-9	410
DiseasesDB	8664
MedlinePlus	000195
eMedicine	med/1567 emerg/327 ped/2520
MeSH	D009203

Myocardial infarction (**MI**) or **acute myocardial infarction** (**AMI**), commonly known as a **heart attack**, is the interruption of blood supply to a part of the heart, causing heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids (fatty acids) and white blood cells (especially macrophages) in the wall of an artery. The resulting ischemia (restriction in blood supply) and oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death (*infarction*) of heart muscle tissue (*myocardium*).

Classical symptoms of acute myocardial infarction include sudden chest pain (typically radiating to the left arm or left side of the neck), shortness of breath, nausea, vomiting,

palpitations, sweating, and anxiety (often described as a sense of impending doom). Women may experience fewer typical symptoms than men, most commonly shortness of breath, weakness, a feeling of indigestion, and fatigue. Approximately one quarter of all myocardial infarctions are "silent", without chest pain or other symptoms.

Among the diagnostic tests available to detect heart muscle damage are an electrocardiogram (ECG), echocardiography, and various blood tests. The most often used markers are the creatine kinase-MB (CK-MB) fraction and the troponin levels. Immediate treatment for suspected acute myocardial infarction includes oxygen, aspirin, and sublingual nitroglycerin.

Most cases of STEMI (ST elevation MI) are treated with thrombolysis or percutaneous coronary intervention (PCI). NSTEMI (non-ST elevation MI) should be managed with medication, although PCI is often performed during hospital admission. In people who have multiple blockages and who are relatively stable, or in a few emergency cases, bypass surgery may be an option.

Heart attacks are the leading cause of death for both men and women worldwide. Important risk factors are previous cardiovascular disease, older age, tobacco smoking, high blood levels of certain lipids (triglycerides, low-density lipoprotein) and low levels of high density lipoprotein (HDL), diabetes, high blood pressure, obesity, chronic kidney disease, heart failure, excessive alcohol consumption, the abuse of certain drugs (such as cocaine and methamphetamine), and chronic high stress levels.

Classification

There are two basic types of acute myocardial infarction:

- **Transmural**: associated with atherosclerosis involving major coronary artery. It can be subclassified into anterior, posterior, or inferior. Transmural infarcts extend through the whole thickness of the heart muscle and are usually a result of complete occlusion of the area's blood supply.
- **Subendocardial**: involving a small area in the subendocardial wall of the left ventricle, ventricular septum, or papillary muscles. Subendocardial infarcts are thought to be a result of locally decreased blood supply, possibly from a narrowing of the coronary arteries. The subendocardial area is farthest from the heart's blood supply and is more susceptible to this type of pathology.

Clinically, a myocardial infarction can be further subclassified into a ST elevation MI (STEMI) versus a non-ST elevation MI (non-STEMI) based on ECG changes.

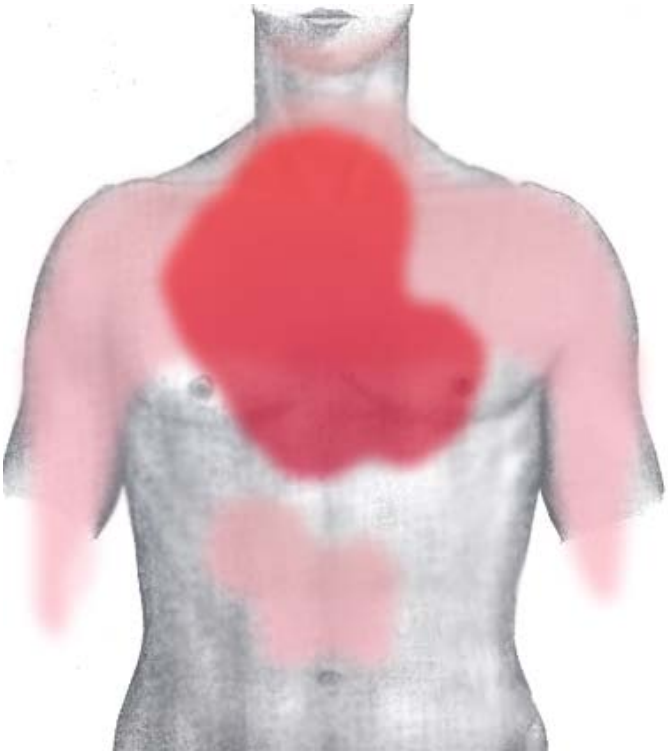
The phrase "heart attack" is sometimes used incorrectly to describe sudden cardiac death, which may or may not be the result of acute myocardial infarction. A heart attack is different from, but can be the cause of cardiac arrest, which is the stopping of the heartbeat, and cardiac arrhythmia, an abnormal heartbeat. It is also distinct from heart

failure, in which the pumping action of the heart is impaired; severe myocardial infarction may lead to heart failure, but not necessarily.

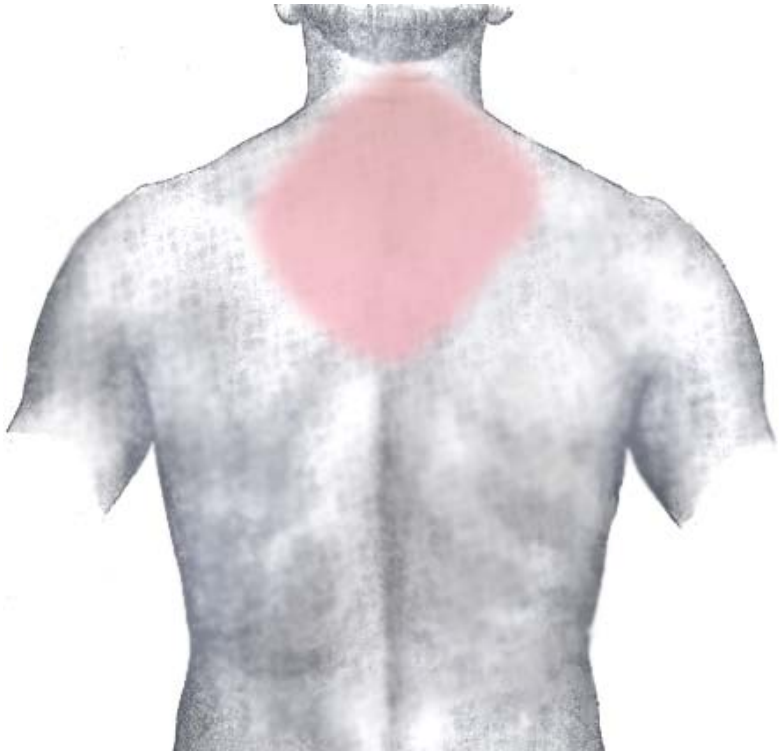
A 2007 consensus document classifies myocardial infarction into five main types:

- Type 1 – Spontaneous myocardial infarction related to ischaemia due to a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection
- Type 2 – Myocardial infarction secondary to ischaemia due to either increased oxygen demand or decreased supply, e.g. coronary artery spasm, coronary embolism, anaemia, arrhythmias, hypertension, or hypotension
- Type 3 – Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischaemia, accompanied by presumably new ST elevation, or new LBBB, or evidence of fresh thrombus in a coronary artery by angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood
- Type 4 – Associated with coronary angioplasty or stents:
  - Type 4a – Myocardial infarction associated with PCI
  - Type 4b – Myocardial infarction associated with stent thrombosis as documented by angiography or at autopsy
- Type 5 – Myocardial infarction associated with CABG

Signs and symptoms



Rough diagram of pain zones in myocardial infarction (dark red = most typical area, light red = other possible areas, view of the chest).



Back view

The onset of symptoms in myocardial infarction (MI) is usually gradual, over several minutes, and rarely instantaneous. Chest pain is the most common symptom of acute myocardial infarction and is often described as a sensation of tightness, pressure, or squeezing. Chest pain due to ischemia (a lack of blood and hence oxygen supply) of the heart muscle is termed angina pectoris. Pain radiates most often to the left arm, but may also radiate to the lower jaw, neck, right arm, back, and epigastrium, where it may mimic heartburn. Levine's sign, in which the patient localizes the chest pain by clenching their fist over the sternum, has classically been thought to be predictive of cardiac chest pain, although a prospective observational study showed that it had a poor positive predictive value.

Shortness of breath (dyspnea) occurs when the damage to the heart limits the output of the left ventricle, causing left ventricular failure and consequent pulmonary edema. Other symptoms include diaphoresis (an excessive form of sweating), weakness, light-headedness, nausea, vomiting, and palpitations. These symptoms are likely induced by a massive surge of catecholamines from the sympathetic nervous system which occurs in response to pain and the hemodynamic abnormalities that result from cardiac dysfunction. Loss of consciousness (due to inadequate cerebral perfusion and cardiogenic shock) and sudden death (frequently due to the development of ventricular fibrillation) can occur in myocardial infarctions.

Women and older patients report atypical symptoms more frequently than their male and younger counterparts. Women also report more numerous symptoms compared with men

(2.6 on average vs 1.8 symptoms in men). The most common symptoms of MI in women include dyspnea (shortness of breath), weakness, and fatigue. Fatigue, sleep disturbances, and dyspnea have been reported as frequently occurring symptoms which may manifest as long as one month before the actual clinically manifested ischemic event. In women, chest pain may be less predictive of coronary ischemia than in men.

Approximately one fourth of all myocardial infarctions are silent, without chest pain or other symptoms. These cases can be discovered later on electrocardiograms, using blood enzyme tests or at autopsy without a prior history of related complaints. A silent course is more common in the elderly, in patients with diabetes mellitus and after heart transplantation, probably because the donor heart is not fully innervated by the nervous system of the recipient. In diabetics, differences in pain threshold, autonomic neuropathy, and psychological factors have been cited as possible explanations for the lack of symptoms.

Any group of symptoms compatible with a sudden interruption of the blood flow to the heart are called an acute coronary syndrome.

The differential diagnosis includes other catastrophic causes of chest pain, such as pulmonary embolism, aortic dissection, pericardial effusion causing cardiac tamponade, tension pneumothorax, and esophageal rupture. Other non-catastrophic differentials include gastroesophageal reflux and Tietze's syndrome.

Causes

Heart attack rates are higher in association with intense exertion, be it psychological stress or physical exertion, especially if the exertion is more intense than the individual usually performs. Quantitatively, the period of intense exercise and subsequent recovery is associated with about a 6-fold higher myocardial infarction rate (compared with other more relaxed time frames) for people who are physically very fit. For those in poor physical condition, the rate differential is over 35-fold higher. One observed mechanism for this phenomenon is the increased arterial pulse pressure stretching and relaxation of arteries with each heart beat which, as has been observed with intravascular ultrasound, increases mechanical "shear stress" on atheromas and the likelihood of plaque rupture.

Acute severe infection, such as pneumonia, can trigger myocardial infarction. A more controversial link is that between *Chlamydophila pneumoniae* infection and atherosclerosis. While this intracellular organism has been demonstrated in atherosclerotic plaques, evidence is inconclusive as to whether it can be considered a causative factor. Treatment with antibiotics in patients with proven atherosclerosis has not demonstrated a decreased risk of heart attacks or other coronary vascular diseases.

There is an association of an increased incidence of a heart attack in the morning hours, more specifically around 9 a.m. Some investigators have noticed that the ability of platelets to aggregate varies according to a circadian rhythm, although they have not proven causation.

Risk factors

Risk factors for atherosclerosis are generally risk factors for myocardial infarction:

- Diabetes (with or without insulin resistance) – the single most important risk factor for ischaemic heart disease (IHD)
- Tobacco smoking
- Hypercholesterolemia (more accurately hyperlipoproteinemia, especially high low density lipoprotein and low high density lipoprotein)
- Low HDL
- High Triglycerides
- High blood pressure
- Family history of ischaemic heart disease (IHD)
- Obesity (defined by a body mass index of more than 30 kg/m², or alternatively by waist circumference or waist-hip ratio).
- Age: Men acquire an independent risk factor at age 45, Women acquire an independent risk factor at age 55; in addition individuals acquire another independent risk factor if they have a first-degree male relative (brother, father) who suffered a coronary vascular event at or before age 55. Another independent risk factor is acquired if one has a first-degree female relative (mother, sister) who suffered a coronary vascular event at age 65 or younger.
- Hyperhomocysteinemia (high homocysteine, a toxic blood amino acid that is elevated when intakes of vitamins B_2, B_6, B_{12} and folic acid are insufficient)
- Stress (occupations with high stress index are known to have susceptibility for atherosclerosis)
- Alcohol Studies show that prolonged exposure to high quantities of alcohol can increase the risk of heart attack
- Males are more at risk than females.

Many of these risk factors are modifiable, so many heart attacks can be prevented by maintaining a healthier lifestyle. Physical activity, for example, is associated with a lower risk profile. Non-modifiable risk factors include age, sex, and family history of an early heart attack (before the age of 60), which is thought of as reflecting a genetic predisposition.

Socioeconomic factors such as a shorter education and lower income (particularly in women), and unmarried cohabitation may also contribute to the risk of MI. To understand epidemiological study results, it's important to note that many factors associated with MI mediate their risk via other factors. For example, the effect of education is partially based on its effect on income and marital status.

Women who use combined oral contraceptive pills have a modestly increased risk of myocardial infarction, especially in the presence of other risk factors, such as smoking.

Inflammation is known to be an important step in the process of atherosclerotic plaque formation. C-reactive protein (CRP) is a sensitive but non-specific marker for

inflammation. Elevated CRP blood levels, especially measured with high sensitivity assays, can predict the risk of MI, as well as stroke and development of diabetes. Moreover, some drugs for MI might also reduce CRP levels. The use of high sensitivity CRP assays as a means of screening the general population is advised against, but it may be used optionally at the physician's discretion, in patients who already present with other risk factors or known coronary artery disease. Whether CRP plays a direct role in atherosclerosis remains uncertain.

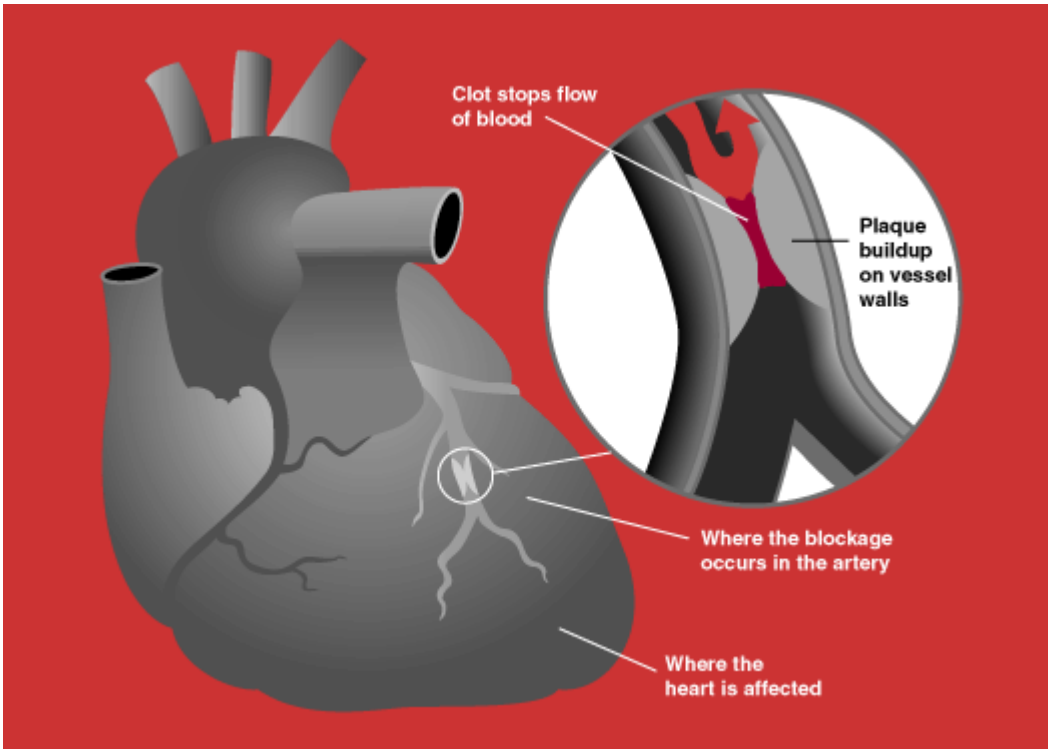
Inflammation in periodontal disease may be linked to coronary heart disease, and since periodontitis is very common, this could have great consequences for public health. Serological studies measuring antibody levels against typical periodontitis-causing bacteria found that such antibodies were more present in subjects with coronary heart disease. Periodontitis tends to increase blood levels of CRP, fibrinogen and cytokines; thus, periodontitis may mediate its effect on MI risk via other risk factors. Preclinical research suggests that periodontal bacteria can promote aggregation of platelets and promote the formation of foam cells. A role for specific periodontal bacteria has been suggested but remains to be established. There is some evidence that influenza may trigger a acute myocardial infarction.

Baldness, hair greying, a diagonal earlobe crease (Frank's sign) and possibly other skin features have been suggested as independent risk factors for MI. Their role remains controversial; a common denominator of these signs and the risk of MI is supposed, possibly genetic.

Calcium deposition is another part of atherosclerotic plaque formation. Calcium deposits in the coronary arteries can be detected with CT scans. Several studies have shown that coronary calcium can provide predictive information beyond that of classical risk factors.

The European Society of Cardiology and the European Association for Cardiovascular Prevention and Rehabilitation have developed an interactive tool for prediction and managing the risk of heart attack and stroke in Europe. HeartScore is aimed at supporting clinicians in optimising individual cardiovascular risk reduction. The Heartscore Programme is available in 12 languages and offers web based or PC version.

Pathophysiology



A myocardial infarction occurs when an atherosclerotic plaque slowly builds up in the inner lining of a coronary artery and then suddenly ruptures, causing catastrophic thrombus formation, totally occluding the artery and preventing blood flow downstream.

Acute myocardial infarction refers to two subtypes of acute coronary syndrome, namely **non-ST-elevated myocardial infarction** and **ST-elevated myocardial infarction**, which are most frequently (but not always) a manifestation of coronary artery disease. The most common triggering event is the disruption of an atherosclerotic plaque in an epicardial coronary artery, which leads to a clotting cascade, sometimes resulting in total occlusion of the artery. Atherosclerosis is the gradual buildup of cholesterol and fibrous tissue in plaques in the wall of arteries (in this case, the coronary arteries), typically over decades. Blood stream column irregularities visible on angiography reflect artery lumen narrowing as a result of decades of advancing atherosclerosis. Plaques can become unstable, rupture, and additionally promote a thrombus (blood clot) that occludes the artery; this can occur in minutes. When a severe enough plaque rupture occurs in the coronary vasculature, it leads to myocardial infarction (necrosis of downstream myocardium).

If impaired blood flow to the heart lasts long enough, it triggers a process called the ischemic cascade; the heart cells in the territory of the occluded coronary artery die (chiefly through necrosis) and do not grow back. A collagen scar forms in its place. Recent studies indicate that another form of cell death called apoptosis also plays a role in the process of tissue damage subsequent to myocardial infarction. As a result, the patient's heart will be permanently damaged. This Myocardial scarring also puts the

patient at risk for potentially life threatening arrhythmias, and may result in the formation of a ventricular aneurysm that can rupture with catastrophic consequences.

Injured heart tissue conducts electrical impulses more slowly than normal heart tissue. The difference in conduction velocity between injured and uninjured tissue can trigger re-entry or a feedback loop that is believed to be the cause of many lethal arrhythmias. The most serious of these arrhythmias is ventricular fibrillation (*V-Fib*/VF), an extremely fast and chaotic heart rhythm that is the leading cause of sudden cardiac death. Another life threatening arrhythmia is ventricular tachycardia (*V-Tach*/VT), which may or may not cause sudden cardiac death. However, ventricular tachycardia usually results in rapid heart rates that prevent the heart from pumping blood effectively. Cardiac output and blood pressure may fall to dangerous levels, which can lead to further coronary ischemia and extension of the infarct.

The cardiac defibrillator is a device that was specifically designed to terminate these potentially fatal arrhythmias. The device works by delivering an electrical shock to the patient in order to depolarize a critical mass of the heart muscle, in effect "rebooting" the heart. This therapy is time dependent, and the odds of successful defibrillation decline rapidly after the onset of cardiopulmonary arrest.

Diagnosis

The diagnosis of myocardial infarction can be made after assessing patient's complaints and physical status. ECG changes, coronary angiogram and levels of cardiac markers help to confirm the diagnosis. ECG gives valuable clues to identify the site of myocardial damage while coronary angiogram allows visualization of narrowing or obstructions in the heart vessels. At autopsy, a pathologist can diagnose a myocardial infarction based on anatomopathological findings.

A chest radiograph and routine blood tests may indicate complications or precipitating causes and are often performed upon arrival to an emergency department. New regional wall motion abnormalities on an echocardiogram are also suggestive of a myocardial infarction. Echo may be performed in equivocal cases by the on-call cardiologist. In stable patients whose symptoms have resolved by the time of evaluation, Technetium (99mTc) sestamibi (i.e. a "MIBI scan") or thallium-201 chloride can be used in nuclear medicine to visualize areas of reduced blood flow in conjunction with physiologic or pharmocologic stress. Thallium may also be used to determine viability of tissue, distinguishing whether non-functional myocardium is actually dead or merely in a state of hibernation or of being stunned.

WHO criteria formulated in 1979 have classically been used to diagnose MI; a patient is diagnosed with myocardial infarction if two (probable) or three (definite) of the following criteria are satisfied:

1. Clinical history of ischaemic type chest pain lasting for more than 20 minutes
2. Changes in serial ECG tracings

3. Rise and fall of serum cardiac biomarkers such as creatine kinase-MB fraction and troponin

The WHO criteria were refined in 2000 to give more prominence to cardiac biomarkers. According to the new guidelines, a cardiac troponin rise accompanied by either typical symptoms, pathological Q waves, ST elevation or depression or coronary intervention are diagnostic of MI.

Prevention

The risk of a recurrent myocardial infarction decreases with strict blood pressure management and lifestyle changes, chiefly smoking cessation, regular exercise, a sensible diet for patients with heart disease, and limitation of alcohol intake.

Patients are usually commenced on several long-term medications post-MI, with the aim of preventing secondary cardiovascular events such as further myocardial infarctions, congestive heart failure or cerebrovascular accident (CVA). Unless contraindicated, such medications may include:

- Evidence supports the consumption of polyunsaturated fats instead of saturated fats as a measure of decreasing coronary heart disease.
- Antiplatelet drug therapy such as aspirin and/or clopidogrel should be continued to reduce the risk of plaque rupture and recurrent myocardial infarction. Aspirin is first-line, owing to its low cost and comparable efficacy, with clopidogrel reserved for patients intolerant of aspirin. The combination of clopidogrel and aspirin may further reduce risk of cardiovascular events, however the risk of hemorrhage is increased.
- Beta blocker therapy such as metoprolol or carvedilol should be commenced. These have been particularly beneficial in high-risk patients such as those with left ventricular dysfunction and/or continuing cardiac ischaemia. β-Blockers decrease mortality and morbidity. They also improve symptoms of cardiac ischemia in NSTEMI.

- ACE inhibitor therapy should be commenced 24–48 hours post-MI in hemodynamically-stable patients, particularly in patients with a history of MI, diabetes mellitus, hypertension, anterior location of infarct (as assessed by ECG), and/or evidence of left ventricular dysfunction. ACE inhibitors reduce mortality, the development of heart failure, and decrease ventricular remodelling post-MI.

- Statin therapy has been shown to reduce mortality and morbidity post-MI. The effects of statins may be more than their LDL lowering effects. The general consensus is that statins have plaque stabilization and multiple other ("pleiotropic") effects that may prevent myocardial infarction in addition to their effects on blood lipids.

- The aldosterone antagonist agent eplerenone has been shown to further reduce risk of cardiovascular death post-MI in patients with heart failure and left ventricular dysfunction, when used in conjunction with standard therapies above. Spironolactone is another option that is sometimes preferable to eplerenone due to cost.

- Omega-3 fatty acids, commonly found in fish, have been shown to reduce mortality post-MI. While the mechanism by which these fatty acids decrease mortality is unknown, it has been postulated that the survival benefit is due to electrical stabilization and the prevention of ventricular fibrillation. However, further studies in a high-risk subset have not shown a clear-cut decrease in potentially fatal arrhythmias due to omega-3 fatty acids.

Blood donation may reduce the risk of heart disease for men, but the link has not been firmly established.

A Cochrane review found that giving heparin to people who have heart conditions like unstable angina and some forms of heart attack reduces the risk of having another heart attack. However, heparin also increases the chance of suffering from minor bleeding.

Management

An MI is a medical emergency which requires immediate medical attention. Treatment attempts to salvage as much myocardium as possible and to prevent further complications, thus the phrase "time is muscle". Oxygen, aspirin, and nitroglycerin may be administered. Morphine was classically used if nitroglycerin was not effective; however, it may increase mortality in the setting of NSTEMI. A 2009 and 2010 review of high flow oxygen in myocardial infarction found increased mortality and infarct size, calling into question the recommendation about its routine use. Percutaneous coronary intervention (PCI) or fibrinolysis are recommended in those with an STEMI.

Complications

Complications may occur immediately following the heart attack (in the acute phase), or may need time to develop (a chronic problem). Acute complications may include heart failure if the damaged heart is no longer able to adequately pump blood around the body; aneurysm or rupture of the myocardium; mitral regurgitation, particularly if the infarction causes dysfunction of the papillary muscle; and arrhythmias, such as ventricular fibrillation, ventricular tachycardia, atrial fibrillation and heart block. Longer-term complications include heart failure, atrial fibrillation, and the increased risk of a second myocardial infarction.

Prognosis

The prognosis post myocardial infarction varies greatly, depending on a person's health, the extent of the heart damage and the treatment given. For the period 2005 – 2008 in the

United States the median mortality at 30 days was 16.6% with a range from 10.9% to 24.9% depending on the hospital. Using variables available in the emergency room, people with a higher risk of adverse outcome can be identified. One study found that 0.4% of patients with a low risk profile died after 90 days, whereas in high risk people it was 21.1%.

Some of the more reproduced risk stratifying factors include: age, hemodynamic parameters (such as heart failure, cardiac arrest on admission, systolic blood pressure, or Killip class of two or greater), ST-segment deviation, diabetes, serum creatinine, peripheral vascular disease and elevation of cardiac markers. Assessment of left ventricular ejection fraction may increase the predictive power. The prognostic importance of Q-waves is debated. Prognosis is significantly worsened if a mechanical complication such as papillary muscle or myocardial free wall rupture occur. Morbidity and mortality from myocardial infarction has improved over the years due to better treatment.

Epidemiology

Myocardial infarction is a common presentation of ischemic heart disease. The WHO estimated in 2002, that 12.6 percent of worldwide deaths were from ischemic heart disease with it the leading cause of death in developed countries, and third to AIDS and lower respiratory infections in developing countries. Worldwide more than 3 million people have STEMIs and 4 million have NSTEMIs a year.

Coronary heart disease is responsible for 1 in 5 deaths in the United States. It is becoming more common in the developing world such that in India, cardiovascular disease (CVD) is the leading cause of death. The deaths due to CVD in India were 32% of all deaths in 2007 and are expected to rise from 1.17 million in 1990 and 1.59 million in 2000 to 2.03 million in 2010. Although a relatively new epidemic in India, it has quickly become a major health issue with deaths due to CVD expected to double during 1985–2015. Mortality estimates due to CVD vary widely by state, ranging from 10% in Meghalaya to 49% in Punjab (percentage of all deaths). Punjab (49%), Goa (42%), Tamil Nadu (36%) and Andhra Pradesh (31%) have the highest CVD related mortality estimates. State-wise differences are correlated with prevalence of specific dietary risk factors in the states. Moderate physical exercise is associated with reduced incidence of CVD in India (those who exercise have less than half the risk of those who don't).

Legal implications

At common law, a myocardial infarction is generally a disease, but may sometimes be an injury. This has implications for no-fault insurance schemes such as workers' compensation. A heart attack is generally not covered; however, it may be a work-related injury if it results, for example, from unusual emotional stress or unusual exertion. Additionally, in some jurisdictions, heart attacks suffered by persons in particular occupations such as police officers may be classified as line-of-duty injuries by statute or policy. In some countries or states, a person who has suffered from a myocardial

infarction may be prevented from participating in activity that puts other people's lives at risk, for example driving a car or flying an airplane.

Research

Patients who receive stem cell treatment by coronary artery injections of stem cells derived from their own bone marrow after a myocardial infarction (MI) show improvements in left ventricular ejection fraction and end-diastolic volume not seen with placebo. The larger the initial infarct size, the greater the effect of the infusion. Clinical trials of progenitor cell infusion as a treatment approach to ST elevation MI are proceeding.

There are currently 3 biomaterial and tissue engineering approaches for the treatment of MI, but these are in an even earlier stage of medical research, so many questions and issues need to be addressed before they can be applied to patients. The first involves polymeric left ventricular restraints in the prevention of heart failure. The second utilizes *in vitro* engineered cardiac tissue, which is subsequently implanted *in vivo*. The final approach entails injecting cells and/or a scaffold into the myocardium to create *in situ* engineered cardiac tissue.

Chapter 2

Alcoholic Cardiomyopathy and Hypertensive Heart Disease

Alcoholic cardiomyopathy

Alcoholic cardiomyopathy	
ICD-10	I42.6
ICD-9	425.5
MedlinePlus	000174
eMedicine	med/286
MeSH	D002310

Alcoholic cardiomyopathy is a disease in which the chronic long-term abuse of alcohol leads to heart failure. Alcoholic cardiomyopathy is a type of dilated cardiomyopathy. Due to the direct toxic effects of alcohol on heart muscle, the heart is unable to pump blood efficiently, leading to heart failure. It can affect other parts of the body if the heart failure is severe. It is most common in males between the ages of 35-50.

Symptoms

Symptoms presented by the occurrence of alcoholic cardiomyopathy are the result of the heart failing and usually occur after the disease has progressed to an advanced stage. Therefore the symptoms have a lot in common with other forms of cardiomyopathy. These symptoms can include:

- Ankle, feet, and leg swelling
- Overall swelling
- Loss of appetite
- Shortness of breath, especially with activity
- Breathing difficulty while lying down

- Fatigue, weakness, faintness
- Decreased alertness or concentration
- Cough containing mucus, or pink, frothy material
- Decreased urine output (oliguria)
- Need to urinate at night (nocturia)
- Palpitations
- Irregular or rapid pulse

Diagnosis

Abnormal heart sounds, murmurs, ECG abnormalities, and enlarged heart on chest x-ray may lead to the diagnosis. Echocardiogram abnormalities and cardiac catheterization or angiogram to rule out coronary artery blockages, along with a history of alcohol abuse can confirm the diagnosis.

Treatment

Treatment for alcoholic cardiomyopathy involves lifestyle changes, including complete abstinence from alcohol use, a low sodium diet, and fluid restriction, as well as medications. Medications may include ACE inhibitors, beta blockers, and diuretics which are commonly used with other forms of cardiomyopathy to reduce the strain on the heart. Persons with congestive heart failure may be considered for surgical insertion of an ICD or a pacemaker which can improve heart function. In cases where the heart failure is irreversible and worsening, heart transplant may be considered.

Treatment will possibly prevent the heart from further deterioration, and the cardiomyopathy is largely reversible if complete abstinence from alcohol is maintained.

Hypertensive heart disease

Hypertensive heart disease	
ICD-10	I11., I13.
ICD-9	402
MedlinePlus	000163
eMedicine	article/162449

Hypertensive heart disease is any of a number of complications of arterial hypertension that affects the heart.

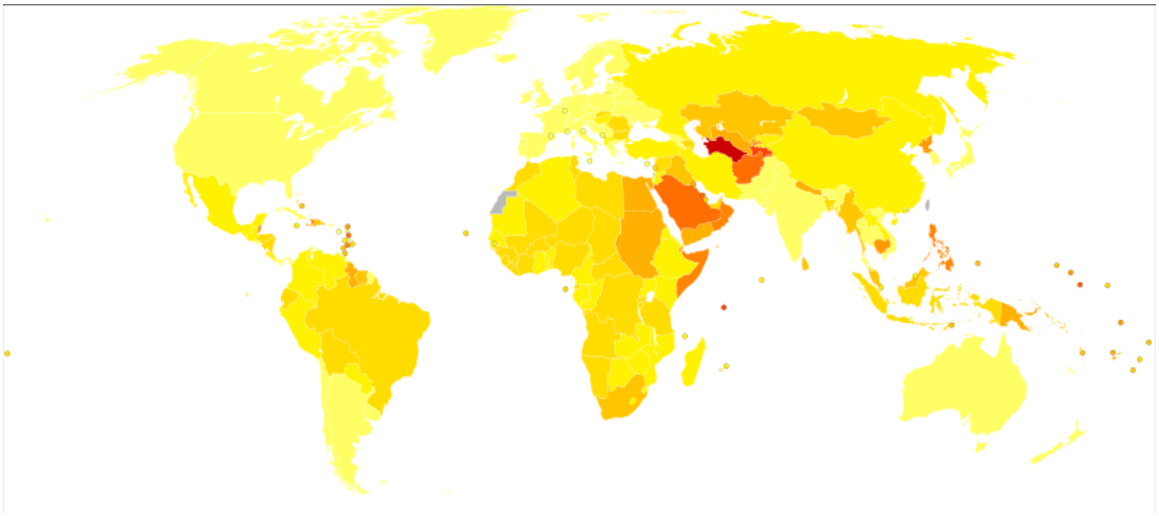
Symptoms

- Fatigue
- Cardiomegaly
- Irregular pulse
- Swelling of feet
- Weight gain
- Nausea
- Shortness of breath
- Difficulty sleeping flat in bed
- Bloating
- Greater need to urinate at night

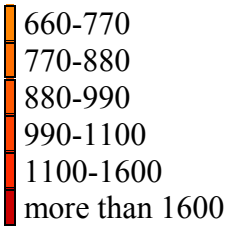
Conditions (potential complications)

- Left ventricular hypertrophy
- Coronary heart disease
- Congestive heart failure
- Hypertensive cardiomyopathy
- Cardiac arrhythmias

Epidemiology



Disability-adjusted life year for hypertensive heart disease per 100,000 inhabitants in 2004.
no data
less than 110
110-220
220-330
330-440
440-550
550-660


660-770
770-880
880-990
990-1100
1100-1600
more than 1600

Chapter 3

Cardiovascular Disease

Cardiovascular disease	
ICD-10	I51.6
ICD-9	429.2
DiseasesDB	28808
MeSH	D002318

Heart disease or **cardiovascular diseases** is the class of diseases that involve the heart or blood vessels (arteries and veins). While the term technically refers to any disease that affects the cardiovascular system (as used in MeSH C14), it is usually used to refer to those related to atherosclerosis (arterial disease). These conditions usually have similar causes, mechanisms, and treatments.

In practice, cardiovascular disease is treated by cardiologists, thoracic surgeons, vascular surgeons, neurologists, and interventional radiologists, depending on the organ system that is being treated. There is considerable overlap in the specialties, and it is common for certain procedures to be performed by different types of specialists in the same hospital.

Most countries face high and increasing rates of cardiovascular disease. Each year, heart disease kills more Americans than cancer. In recent years, cardiovascular risk in women has been increasing and has killed more women than breast cancer. A large histological study (PDAY) showed vascular injury accumulates from adolescence, making primary prevention efforts necessary from childhood.

By the time that heart problems are detected, the underlying cause (atherosclerosis) is usually quite advanced, having progressed for decades. There is therefore increased emphasis on preventing atherosclerosis by modifying risk factors, such as healthy eating, exercise and avoidance of smoking.

Pathophysiology

Population based studies in the youth show that the precursors of heart disease start in adolescence. The process of atherosclerosis evolves over decades, and begins as early as childhood. The Pathobiological Determinants of Atherosclerosis in Youth Study demonstrated that intimal lesions appear in all the aortas and more than half of the right coronary arteries of youths aged 7–9 years. However, most adolescents are more concerned about other risks such as HIV, accidents, and cancer than cardiovascular disease.

This is extremely important considering that 1 in 3 people will die from complications attributable to atherosclerosis. In order to stem the tide of cardiovascular disease, primary prevention is needed. Primary prevention starts with education and awareness that cardiovascular disease poses the greatest threat and measures to prevent or reverse this disease must be taken.

Obesity and diabetes mellitus are often linked to cardiovascular disease In fact, cardiovascular disease is the most life threatening of the diabetic complications and diabetics are two- to four-fold more likely to die of cardiovascular-related causes than nondiabetics.

Diagnosis

Associated diagnostic markers

- Low-density lipoprotein
- Lipoprotein(a)
- Apolipoprotein A1
- Apolipoprotein Bho

Screening

Some biomarkers are thought to offer a more detailed risk of cardiovascular disease. However, the clinical value of these biomarkers is questionable. Currently, biomarkers which may reflect a higher risk of cardiovascular disease include:

- Higher fibrinogen and PAI-1 blood concentrations
- Elevated homocysteine, or even upper half of normal
- Elevated blood levels of asymmetric dimethylarginine
- Inflammation as measured by C-reactive protein
- Elevated blood levels of brain natriuretic peptide (also known as B-type) (BNP)
- Elevated levels of NT-proBNP

Prevention

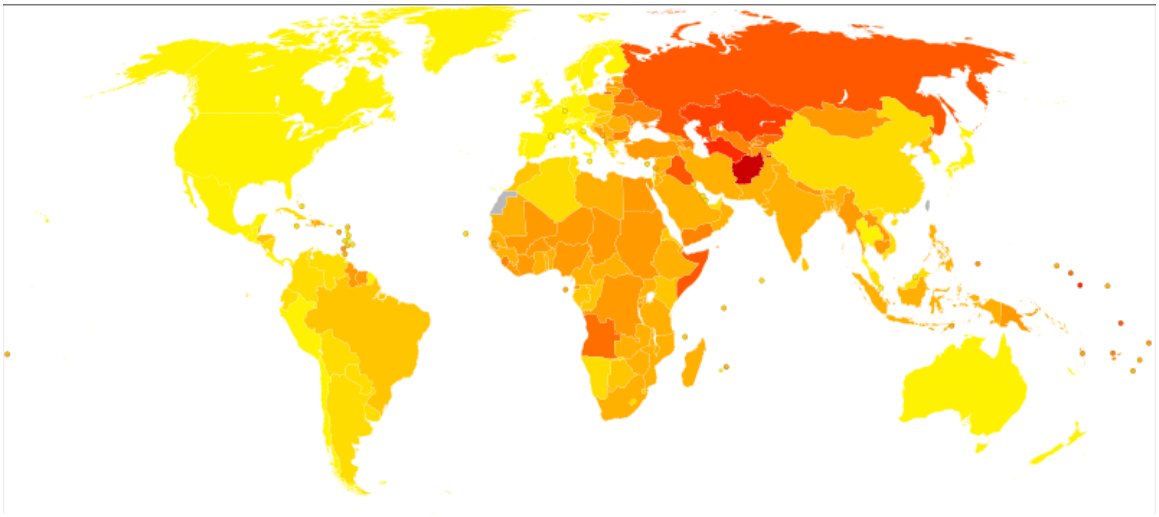
Evidence shows that the Mediterranean diet improves cardiovascular outcomes. As of 2010 however vitamins have not been found to be effective at preventing cardiovascular disease.

Modifiable risk factors to improve or prevent atherosclerosis include: diet high in fibers from vegetables while low in saturated fat and cholesterol; tobacco cessation and avoidance of second-hand smoke; decreased alcohol consumption; lower blood pressures if elevated through the use of antihypertensive medications; strict diabetes management; decrease BMI if overweight or obese; increase daily activity to 30 minutes of moderate to vigorous exercise; and decrease emotional stress in day to day life.

Management

Cardiovascular disease is treatable with initial treatment primarily focused on diet and lifestyle interventions. Medication may also be useful for prevention.

Epidemiology



Disability-adjusted life year for cardiovascular diseases per 100,000 inhabitants in 2004.

- no data
- less than 900
- 900-1650
- 1650-2300
- 2300-3000
- 3000-3700
- 3700-4400
- 4400-5100
- 5100-5800
- 5800-6500
- 6500-7200

Research

The first studies on cardiovascular health were performed in 1949 by Jerry Morris using occupational health data and were published in 1958. The causes, prevention, and/or treatment of all forms of cardiovascular disease remain active fields of biomedical research, with hundreds of scientific studies being published on a weekly basis. A trend has emerged, particularly in the early 2000s, in which numerous studies have revealed a link between fast food and an increase in heart disease. These studies include those conducted by the Ryan Mackey Memorial Research Institute, Harvard University and the Sydney Center for Cardiovascular Health. Many major fast food chains, particularly McDonald's, have protested the methods used in these studies and have responded with healthier menu options.

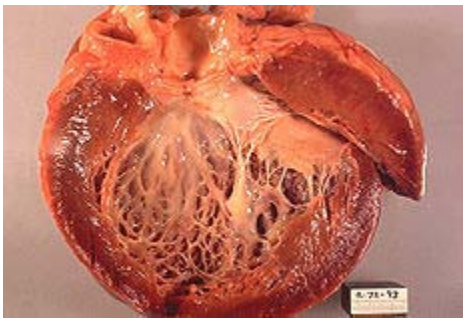
A fairly recent emphasis is on the link between low-grade inflammation that hallmarks atherosclerosis and its possible interventions. C-reactive protein (CRP) is an common inflammatory marker that has been found to be present in increased levels in patients at risk for cardiovascular disease. Also osteoprotegerin which involved with regulation of a key inflammatory transcription factor called NF-κB has been found to be a risk factor of cardiovascular disease and mortality.

Some areas currently being researched include possible links between infection with *Chlamydophila pneumoniae* and coronary artery disease. The *Chlamydia* link has become less plausible with the absence of improvement after antibiotic use.

Chapter 4

Dilated Cardiomyopathy

Dilated cardiomyopathy



Gross pathology of idiopathic cardiomyopathy. Opened left ventricle of heart shows a thickened, dilated left ventricle with subendocardial fibrosis manifested as increased whiteness of endocardium. Autopsy.

ICD-10	I42.0
ICD-9	425.4
OMIM	212110
DiseasesDB	3066
MedlinePlus	000168
eMedicine	med/289 emerg/80 ped/2502
MeSH	D002311

Dilated cardiomyopathy or **DCM** is a condition in which the heart becomes weakened and enlarged and cannot pump blood efficiently. The decreased heart function can affect the lungs, liver, and other body systems.

DCM is one of the cardiomyopathies, a group of diseases that primarily affect the myocardium (the muscle of the heart). Different cardiomyopathies have different causes

and affect the heart in different ways. In DCM a portion of the myocardium is dilated, often without any obvious cause. Left or right ventricular systolic pump function of the heart is impaired, leading to progressive cardiac enlargement and hypertrophy, a process called *remodeling*.

Dilated cardiomyopathy is the most common form of non-ischemic cardiomyopathy. It occurs more frequently in men than in women, and is most common between the ages of 20 and 60 years. About one in three cases of congestive heart failure (CHF) is due to dilated cardiomyopathy. Dilated cardiomyopathy also occurs in children.

Causes

Although in many cases no cause (etiology) is apparent, dilated cardiomyopathy is probably the result of damage to the myocardium produced by a variety of toxic, metabolic, or infectious agents. It may be due to fibrous change of the myocardium from a previous myocardial infarction. Or, it may be the late sequel of acute viral myocarditis, such as with coxsackievirus B and other enteroviruses, possibly mediated through an immunologic mechanism. Autoimmune mechanisms are also suggested as a cause for dilated cardiomyopathy.

Dilated cardiomyopathy can also be caused by alcohol abuse (Alcoholic cardiomyopathy), or other toxic exposure, although the cause-and-effect relationship with alcohol alone is debated. Nonalcoholic toxic insults include administration of certain chemotherapeutic agents, particularly doxorubicin(Adriamycin), and cobalt.

Other potential causes include thyroid disease, stimulant use, and chronic uncontrolled tachycardia. Many cases of dilated cardiomyopathy are described as *idiopathic* - meaning that the cause is unknown.

Recent studies have shown that those subjects who have an extremely high occurrence (several thousands a day) of premature ventricular contractions (extrasystole) can develop dilated cardiomyopathy. In these cases, if the extrasystole are reduced or removed (for example, via ablation therapy) the cardiomyopathy usually regresses.

Dilated cardiomyopathy also occurs more frequently in pregnancy than in the normal population. It occurs late in gestation or several weeks to months postpartum as a peripartum cardiomyopathy. It is reversible in half of cases.

Genetics

About 25-35% of patients have familial forms of the disease, with most mutations affecting genes encoding cytoskeletal proteins, while some affect other proteins involved in contraction. The disease is genetically heterogeneous, but the most common form of its transmission is an autosomal dominant pattern. Autosomal recessive (as found, for example, in Alström syndrome or Duchenne muscular dystrophy), X-linked, and mitochondrial inheritance of the disease is also found. Some relatives of patients with

dilated cardiomyopathy have preclinical, asymptomatic heart-muscle changes. Other cytoskeletal proteins involved in DCM include α-cardiac actin, desmin, and the nuclear lamins A and C. Mitochondrial deletions and mutations presumably cause DCM by altering myocardial ATP generation.

Although the disease is more common in African-Americans than in Caucasians, it may occur in any patient population.

Associations include:

Type	OMIM	Gene	Locus
CMD1A	115200	LMNA	1q21
CMD1B	600884	unknown (TMOD1 candidate)	9q13
CMD1C	601493	LDB3	10q22-q23
CMD1D	601494	TNNT2	1q32
CMD1E	601154	SCN5A	3p
CMD1F	602067		6q23
CMD1G	604145	TTN	2q31
CMD1H	604288		2q14-q22
CMD1I	604765	DES	2q35
CMD1J	605362	EYA4	6q23-q24
CMD1K	605582		6q12-q16
CMD1L	606685	SGCD	5q33
CMD1M	607482	CSRP3	11p15.1
CMD1N	607487	TCAP	17q12
CMD1O	608569	ABCC9	12p12.1
CMD1P	609909	PLN	6q22.1
CMD1Q	609915		7q22.3-q31.1
CMD1R		ACTC	15q14
CMD1S		MYH7	14q12
CMD1T		TMPO	12q22
CMD1U		PSEN1	14q24.3
CMD1V		PSEN2	1q31-q42
CMD1W	611407	VCL	10q22-q23
CMD1X		FCMD	9q31
CMD1Y	611878	TPM1	15q22.1
CMD1Z	611879	TNNC1	3p21.3-p14.3
CMD1AA	612158	ACTN2	1q42-q43
CMD2A	611880	TNNI3	19q13.4
CMD3A	300069	TAZ	Xq28

Associated symptoms

For many affected individuals, dilated cardiomyopathy is a condition which will not limit the quality of life. A minority, however, experience significant symptoms and there is sometimes a risk of sudden death. Evaluation by a cardiologist is recommended to confirm the diagnosis and to assess the outlook and particularly the risk of complications. In some patients, symptoms of left- and right-sided congestive heart failure develop gradually. Left ventricular dilatation may be present for months or even years before the patient becomes symptomatic.

Vague chest pain may be present, but typical angina pectoris is unusual and suggests the presence of ischemic heart disease as well. Syncope due to arrhythmias and systemic embolism may occur.

Physical examination

The patient may present variable degrees of cardiac enlargement, and findings of congestive heart failure. In advanced stages of the disease, the pulse pressure is narrowed and the jugular venous pressure is elevated. Third and fourth heart sounds are common. Mitral or tricuspid regurgitation may occur, presented by systolic murmurs upon auscultation.

Laboratory examinations

Generalized enlargement of the heart is seen upon normal chest X-ray. Pleural effusion may also be noticed, which is due to pulmonary venous hypertension.

The electrocardiogram often shows sinus tachycardia or atrial fibrillation, ventricular arrhythmias, left atrial abnormality, and sometimes intraventricular conduction defects and low voltage. Echocardiogram shows left ventricular dilatation with normal or thinned walls and reduced ejection fraction. Cardiac catheterization and coronary angiography are often performed to exclude ischemic heart disease.

Treatment

Years ago the statistic was that the majority of patients, particularly those over 13 (if passed on genetically and has taken place earlier in life) and over 55 years of age, died within 3 years of the onset of symptoms (stage 5 of CHF) – and such figures can still be found in many textbooks. The situation has improved dramatically in recent years with drug therapy that can slow down progression and in some cases even improve the heart condition. Death is due to either congestive heart failure or ventricular tachy- or bradyarrhythmias.

Patients are given the standard therapy for heart failure, typically including salt restriction, angiotensin-converting enzyme (ACE) inhibitors, diuretics, and digitalis. Anticoagulants may also be used. Alcohol should be avoided. Artificial pacemakers may be used in patients with intraventricular conduction delay, and implantable cardioverter-defibrillators in those at risk of arrhythmia. These forms of treatment have been shown to improve symptoms and reduce hospitalization.

In patients with advanced disease who are refractory to medical therapy, cardiac transplantation may be considered.

Reverse remodeling

The progression of heart failure is associated with left ventricular remodeling, which manifests as gradual increases in left ventricular end-diastolic and end-systolic volumes, wall thinning, and a change in chamber geometry to a more spherical, less elongated shape. This process is usually associated with a continuous decline in ejection fraction. The concept of cardiac remodeling was initially developed to describe changes which occur in the days and months following myocardial infarction. It has been extended to cardiomyopathies of non-ischemic origin, such as idiopathic dilated cardiomyopathy or chronic myocarditis, suggesting common mechanisms for the progression of cardiac dysfunction. Literally, reverse remodeling is the process of reversing the remodeling, or in other words,it is a process of a temporary or a permanent correction of the heart. A 2004 article gives a description of the current therapies that support reverse remodeling and suggests a new approach to the prognosis of cardiomyopathies.

Alternative treatment

Alternative treatments are promoted by some, including food supplements Coenzyme Q10, L-Carnitine, Taurine and D-Ribose, and there is some evidence for the benefits of Coenzyme Q10 in treating heart failure.

Dilated cardiomyopathy in dogs, cats and other pets

Dilated cardiomyopathy is a heritable disease in some dog breeds, including the Boxer, Dobermann, Great Dane, Irish Wolfhound and St Bernard. Treatment is based on medication, including ACE inhibitors, loop diuretics and phosphodiesterase inhibitors.

Dilated cardiomyopathy is also a disease affecting some cat breeds, including the Oriental Shorthair, Burmese, Persian, and Abyssinian. As opposed to these hereditary forms, non-hereditary DCM used to be common in the overall cat population before the addition of taurine to commercial cat food.

There is also a high incidence of heritable dilated cardiomyopathy in captive Golden Hamsters (mesocricetus auratus), thanks in no small part to their being highly inbred. The incidence is high enough that several strains of Golden Hamster have been developed to serve as animal models in clinical testing for human forms of the disease.

Chapter 5

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy	
ICD-10	I42.1–I42.2
ICD-9	425.4
OMIM	192600
DiseasesDB	6373
MedlinePlus	000192
eMedicine	med/290 ped/1102 radio/129
MeSH	D002312

Hypertrophic cardiomyopathy is a disease of the myocardium (the muscle of the heart) in which a portion of the myocardium is hypertrophied (thickened) without any obvious cause. It is perhaps most well-known as a leading cause of sudden cardiac death in young athletes. The occurrence of hypertrophic cardiomyopathy is a significant cause of sudden unexpected cardiac death in any age group and as a cause of disabling cardiac symptoms. Younger people are likely to have a more severe form of hypertrophic cardiomyopathy

HCM is frequently asymptomatic until sudden cardiac death, and for this reason some suggest routinely screening certain populations for this disease.

A cardiomyopathy is a primary disease that affects the muscle of the heart. With hypertrophic cardiomyopathy (HCM), the sarcomeres (contractile elements) in the heart replicate causing heart muscle cells to increase in size, which results in the thickening of the heart muscle. In addition, the normal alignment of muscle cells is disrupted, a phenomenon known as *myocardial disarray*. HCM also causes disruptions of the electrical functions of the heart. HCM is most commonly due to a mutation in one of 9 sarcomeric genes that results in a mutated protein in the sarcomere, the primary component of the myocyte (the muscle cell of the heart).

While most literature so far focuses on European, American, and Japanese populations, HCM appears in all racial groups. The incidence of HCM is about 0.2% to 0.5% of the general population.

Myosin heavy chain mutations are associated with development of familial hypertrophic cardiomyopathy.

Obstructive and non-obstructive

Depending on whether the distortion of normal heart anatomy causes an obstruction of the outflow of blood from the left ventricle of the heart, HCM can be defined as obstructive or non-obstructive.

- The obstructive variant of HCM, **Hypertrophic obstructive cardiomyopathy** (**HOCM**) has also historically been known as **idiopathic hypertrophic subaortic stenosis** (**IHSS**) and **asymmetric septal hypertrophy** (**ASH**).

- Another, non-obstructive variant of HCM is **apical hypertrophic cardiomyopathy**, also called Yamaguchi Syndrome or Yamaguchi Hypertrophy, first described in individuals of Japanese descent.

Genetics

Hypertrophic cardiomyopathy is inherited as an autosomal dominant trait and is attributed to mutations in one of a number of genes that encode for one of the sarcomere proteins including:

Gene	Locus	Type
MYH7	14q12	CMH1
TNNT2	1q32	CMH2
TPM1	15q22.1	CMH3 (115196)
MYBPC3	11p11.2	CMH4 (115197)
?	?	CMH5
PRKAG2	7q36	CMH6 (600858)
TNNI3	19q13.4	CMH7
MYL3	3p	CMH8 (608751)
TTN	2q24.3	CMH9
MYL2	12q23-q24	CMH10
ACTC1	15q14	CMH11 (612098)
CSRP3	11p15.1	CMH12 (612124)

About 50-60% of patients with a high index of clinical suspicion for HCM will have a mutation identified in at least 1 of 9 sarcomeric genes. Approximately 45% of these

mutations occur in the β myosin heavy chain gene on chromosome 14 q11.2-3, while approximately 35% involve the cardiac myosin binding protein C gene. Since HCM is typically an autosomal dominant trait, children of an HCM parent have 50% chance of inheriting the disease-causing mutation. Whenever a mutation is identified through genetic testing, family-specific genetic testing can be used to identify relatives at-risk for the disease (HCM Genetic Testing Overview). In individuals without a family history of HCM, the most common cause of the disease is a de novo mutation of the gene that produces the β-myosin heavy chain.

An insertion/deletion polymorphism in the gene encoding for angiotensin converting enzyme (ACE) alters the clinical phenotype of the disease. The D/D (deletion/deletion) genotype of ACE is associated with more marked hypertrophy of the left ventricle and may be associated with higher risk of adverse outcomes.

Children and Cardiomyopathy

While much has been written about adults with HCM, information regarding children and cardiomyopathy is limited. At this point, it is estimated 30,000 children are affected by cardiomyopathy of all types (dilated, hypertrophic, restricted, etc.) are considered. It is important for families of affected children to seek the care of a pediatric cardiologist. Cardiologists trained in adult medicine (via an internal medicine training program) are not familiar with the treatment of children with cardiomyopathy. This can lead to an improper prognosis, lack of proper medication or wrong diagnosis.

Once HCM has been identified in a family, it is advisable to have all immediate family members tested as soon as possible. Children often do not show signs of HCM and the first sign many children display is that of sudden cardiac arrest. Both invasive and non-invasive techniques exist to detect thickening of the left ventricle and other abnormalities associated with HCM. The most common non-invasive diagnostic test for detecting HCM is electrocardiography, though the most sensitive test for diagnosing HCM is genetic testing.

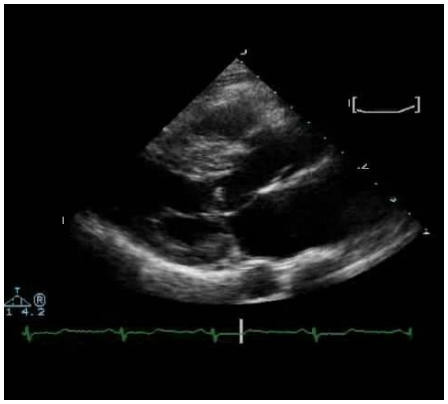
Beta blockers are often prescribed as the first medical treatment for HCM in children. Many options exist, so it is important to remember to inform one's doctor if undesirable side-effects occur so a switch can be made. Stopping a beta blocker treatment without the consent of your doctor is never advised.

Anatomic characteristics

Individuals with HCM have some degree of left ventricular hypertrophy. Usually this is an asymmetric hypertrophy, involving the inter-ventricular septum, and is known as asymmetric septal hypertrophy (ASH). This is in contrast to the concentric hypertrophy seen in aortic stenosis or hypertension. About two-thirds of individuals with HCM have asymmetric septal hypertrophy.

About 25% of individuals with HCM demonstrate an obstruction to the outflow of blood from the left ventricle during rest. In other individuals obstruction only occurs under certain conditions. This is known as dynamic outflow obstruction, because the degree of obstruction is variable and is dependent on the amount of blood in the ventricle immediately before ventricle systole (contraction).

Dynamic outflow obstruction



Echocardiogram demonstrating systolic anterior motion of the anterior leaflet of the mitral valve

Dynamic outflow obstruction (when present in HCM) is usually due to systolic anterior motion (SAM) of the anterior leaflet of the mitral valve. Systolic anterior motion of the mitral valve (SAM) was initially thought to be due to the septal subaortic bulge, narrowing the outflow tract, causing high velocity flow and a Venturi effect—a local underpressure in the outflow tract. Low pressure was thought to suck the mitral valve anteriorly into the septum. But SAM onset is observed to be a low velocity phenomenon: SAM begins at velocities no different from those measured in normals . Hence, the magnitude and importance of Venturi forces in the outflow tract are much less than previously thought, and Venturi forces cannot be the main force that initiates SAM.

Recent echocardiographic evidence indicates that drag, the pushing force of flow is the dominant hydrodynamic force on the mitral leaflets . In obstructive HCM the mitral leaflets are often large and are anteriorly positioned in the LV cavity due to anteriorly positioned papillary muscles that at surgery are often "agglutinated" onto the LV anterior wall by abnormal attachments .

The mid-septal bulge aggravates the malposition of the valve and redirects outflow so that it comes from a lateral and posterior direction. The abnormally directed outflow may be visualized behind and lateral to the enlarged mitral valve, where it catches it, and pushes it into the septum . There is a crucial overlap between the inflow and outflow portions of the left ventricle . As SAM progresses in early systole the angle between outflow and the protruding mitral leaflet increases. A greater surface area of the leaflets is now exposed to drag which amplifies the force on the leaflets – drag increases with increasing angle relative to flow. An analogy is an open door in a drafty corridor: the

door starts by moving slowly and then accelerates as it presents a greater surface area to the wind and finally it slams shut. The necessary conditions that predispose to SAM are: anterior position of the mitral valve in the LV, altered LV geometry that allows flow to strike the mitral valve from behind, and chordal slack . SAM may considered anteriorly directed mitral prolapse . In both conditions the mitral valve is enlarged and is displaced in systole by the pushing force of flow resulting in mitral regurgitation.

Because the mitral valve leaflet doesn't get pulled into the left ventricular outflow tract (LVOT) until after the aortic valve opens, the initial upstroke of the arterial pulse will be normal. When the mitral valve leaflet gets pushed into the LVOT, the arterial pulse will momentarily collapse and be followed by a second rise, as the left ventricular pressure overcomes the increased obstruction that SAM of the mitral valve causes. This can be seen on the physical examination as a double tap upon palpation of the apical impulse and as a double pulsation upon palpation of the carotid pulse, known as *pulsus bisferiens*.

Associated symptoms

The clinical course of HCM is variable. Many patients are asymptomatic or mildly symptomatic. The symptoms of HCM include dyspnea (shortness of breath), chest pain (sometimes known as *angina*), uncomfortable awareness of the heart beat (palpitations), lightheadedness, fatigue, fainting (called syncope) and sudden cardiac death. Dyspnea is largely due to increased stiffness of the left ventricle, which impairs filling of the ventricles and leads to elevated pressure in the left ventricle and left atrium. Symptoms are not closely related to the presence or severity of an outflow tract gradient. Often, symptoms mimic those of congestive heart failure (esp. activity intolerance & dyspnea), but treatment is very different. To treat with diuretics (a mainstay of CHF treatment) will exacerbate symptoms in hypertrophic cardiomyopathy by decreasing ventricular volume and increasing outflow resistance.

Risk factors for sudden death in individuals with HCM include a young age at first diagnosis (age < 30 years), an episode of aborted sudden death, a family history of HCM with sudden death of relatives, specific mutations in the genes encoding for troponin T and myosin, sustained supraventricular or ventricular tachycardia, ventricular septal wall thickness over 3 cm, hypotensive response to exercise, recurrent syncope (especially in children), and bradyarrhythmias (slow rhythms of the heart).

Physical examination

Differentiating hypertrophic cardiomyopathy and valvular aortic stenosis

	Aortic stenosis	Hypertrophic cardiomyopathy
Echocardiography		
Aortic valve calcification	Common	No
Dilated ascending aorta	Common	Rare
Ventricular hypertrophy	Concentric LVH	Asymmetric, often involving

		the septum
Physical examination		
Murmur of AI	Common	No
Pulse pressure after PVC	Increased	Decreased
Valsalva maneuver	Decreased intensity of murmur	Increased intensity of murmur
Carotid pulsation	Normal or tardus et parvus	Brisk, jerky, or bisferiens pulse (a collapse of the pulse followed by a secondary rise)

The physical findings of HCM are associated with the dynamic outflow obstruction that is often present with this disease.

Upon auscultation, the cardiac murmur will sound similar to the murmur of aortic stenosis. However, a murmur due to HCM will increase in intensity with any maneuver that decreases the volume of blood in the left ventricle (such as standing or the strain phase of a Valsalva maneuver). Classically, the murmur is also loudest at the left parasternal edge, 4th intercostal space, rather than in the aortic area.

If dynamic outflow obstruction exists, physical examination findings that can be elicited include the pulsus bisferiens and the double apical impulse with each ventricular contraction. These findings, when present, can help differentiate HCM from aortic stenosis. In addition, if the individual has premature ventricular contractions (PVCs), the change in the carotid pulse intensity in the beat after the PVC can help differentiate HCM from aortic stenosis. In individuals with HCM, the pulse pressure will decrease in the beat after the PVC, while in aortic stenosis, the pulse pressure will increase. However, the murmur intensity increases with both Aortic Stenosis and HCM post-PVC.

Screening

HCM is frequently asymptomatic until sudden cardiac death, and is the leading cause of sudden cardiac death in young athletes. HCM can be detected with an echocardiogram with 80%+ accuracy, which can be preceded by screening with an electrocardiogram (ECG) to test for heart abnormalities. History and physical examination alone are ineffective, giving warning of heart abnormalities in only 3% of patients before sudden cardiac death. One study found that the incidence of sudden cardiovascular death in young competitive athletes declined in the Veneto region of Italy by 89% since introduction of routine Hypertrophic Cardiomyopathy Screening of athletes.

United States

There are several potential challenges associated with routine screening for HCM in the United States. First, the U.S. athlete population of 15 million is almost twice as large as Italy's estimated athlete population. Second, these events are extremely rare in the U.S.,

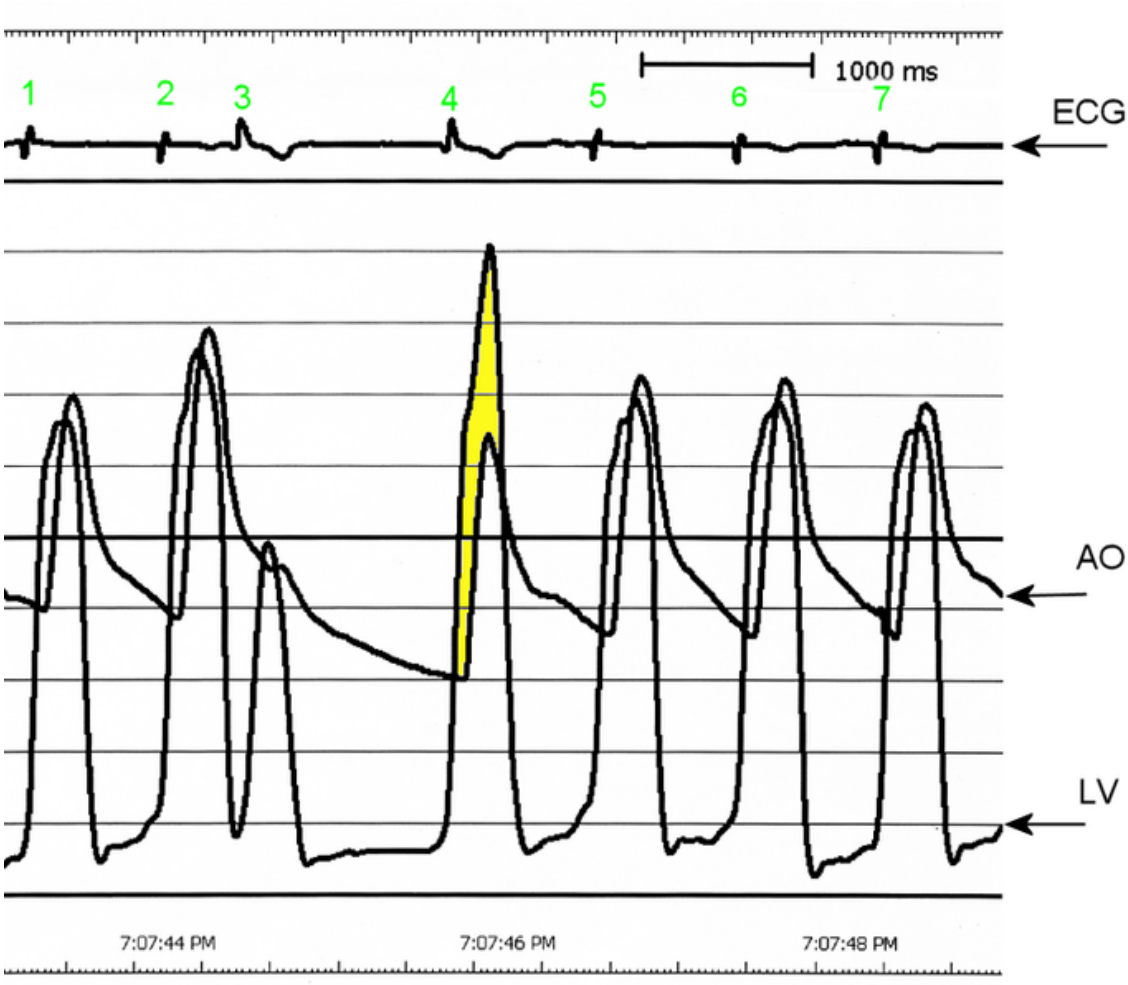
with less than 100 deaths due to HCM in competitive athletes per year, or about 1 death per 220,000 athletes.

In the United States such screening is not routine and the American Heart Association has "consistently opposed" routine screening.

Diagnostic testing

A diagnosis of hypertrophic cardiomyopathy is based upon a number of features of the disease process. While there is use of echocardiography, cardiac catheterization, or cardiac MRI in the diagnosis of the disease, other important factors include ECG and genetic test findings and if there is any family history of HCM or unexplained sudden death in otherwise healthy individuals.

Cardiac catheterization



Pressure tracings demonstrating the Brockenbrough–Braunwald–Morrow sign
AO = Descending aorta; LV = Left ventricle; ECG = Electrocardiogram.
After the third QRS complex, the ventricle has more time to fill. Since there is more time

to fill, the left ventricle will have more volume at the end of diastole (increased preload). Due to the Frank–Starling law of the heart, the contraction of the left ventricle (and pressure generated by the left ventricle) will be greater on the subsequent beat (beat #4 in this picture). Because of the dynamic nature of the outflow obstruction in HCM, the obstruction increases *more* than the left ventricular pressure increase. This causes a fall in the aortic pressure as the left ventricular pressure rises (seen as the yellow shaded area in the picture).

Upon cardiac catheterization, catheters can be placed in the left ventricle and the ascending aorta, to measure the pressure difference between these structures. In normal individuals, during ventricular systole, the pressure in the ascending aorta and the left ventricle will equalize, and the aortic valve is open. In individuals with aortic stenosis or with HCM with an outflow tract gradient, there will be a pressure gradient (difference) between the left ventricle and the aorta, with the left ventricular pressure higher than the aortic pressure. This gradient represents the degree of obstruction that has to be overcome in order to eject blood from the left ventricle.

The **Brockenbrough–Braunwald–Morrow sign** is observed in individuals with HCM with outflow tract gradient. This sign can be used to differentiate HCM from aortic stenosis. In individuals with aortic stenosis, after a premature ventricular contraction (PVC), the following ventricular contraction will be more forceful, and the pressure generated in the left ventricle will be higher. Because of the fixed obstruction that the stenotic aortic valve represents, the post-PVC ascending aortic pressure will increase as well. In individuals with HCM, however, the degree of obstruction will increase more than the force of contraction will increase in the post-PVC beat. The result of this is that the left ventricular pressure increases and the ascending aortic pressure *decreases*, with an increase in the LVOT gradient.

While the Brockenbrough–Braunwald–Morrow sign is most dramatically demonstrated using simultaneous intra-cardiac and intra-aortic catheters, it can be seen on routine physical examination as a decrease in the pulse pressure in the post-PVC beat in individuals with HCM.

Treatment

In all patients with hypertrophic cardiomyopathy risk stratification is essential to attempt to ascertain which patients are at risk for sudden cardiac death. In those patients deemed to be at high risk the benefits and infrequent complications of defibrillator therapy are discussed; devices have been implanted in as many as 15% of patients at HCM centers. Treatment of symptoms of obstructive HCM is directed towards decreasing the left ventricular outflow tract gradient and symptoms of dyspnea, chest pain and syncope. Medical therapy is successful in the majority of patients. The first medication that is routinely used is a beta-blocker (metoprolol, atenolol, bisoprolol, propranolol). If symptoms and gradient persist, disopyramide may be added to the beta-blocker. Alternately a calcium channel blocker such as verapamil may be substituted for a beta blocker. It should be stressed that most patients' symptoms may be managed medically

without needing to resort to interventions such as surgical septal myectomy, alcohol septal ablation or pacing. Severe symptoms in non-obstructive HCM may actually be more difficult to treat because there is no obvious target (obstruction) to treat. Medical therapy with verapamil and beta-blockade may improve symptoms. Diuretics should be avoided, as they reduce the intravascular volume of blood, decreasing the amount of blood available to distend the left ventricular outflow tract, leading to an increase in the obstruction to the outflow of blood in the left ventricle.

Surgical myectomy

Surgical septal myectomy is an open heart operation done to relieve symptoms in patients who remain severely symptomatic despite medical therapy. It has been performed successfully for more than 25 years. Surgical septal myectomy uniformly decreases left ventricular outflow tract obstruction and improves symptoms, and in experienced centers has a surgical mortality of less than 1%. It involves a median sternotomy (general anesthesia, opening the chest, and cardiopulmonary bypass) and removing a portion of the interventricular septum. Surgical myectomy resection focused just on the subaortic septum, to increase the size of the outflow tract to reduce Venturi forces may be inadequate to abolish systolic anterior motion (SAM) of the anterior leaflet of the mitral valve. With this limited sort of resection the residual mid-septal bulge still redirects flow posteriorly: SAM persists because flow still gets behind the mitral valve. It is only when the deeper portion of the septal bulge is resected that flow is redirected anteriorly away from the mitral valve, abolishing SAM. With this in mind, a modification of the Morrow myectomy termed extended myectomy, mobilization and partial excision of the papillary muscles has become the excision of choice. In selected patients with particularly large redundant mitral valves, anterior leaflet plication may be added to complete separation of the mitral valve and outflow.

Alcohol septal ablation

Alcohol septal ablation, introduced by Ulrich Sigwart in 1994, is a percutaneous technique that involves injection of alcohol into one or more septal branches of the left anterior descending artery. This is a technique with results similar to the surgical septal myectomy procedure but is less invasive, since it does not involve general anaesthesia and opening of the chest wall and pericardium (which are done in a septal myomectomy). In a select population with symptoms secondary to a high outflow tract gradient, alcohol septal ablation can reduce the symptoms of HCM. In addition, older individuals and those with other medical problems, for whom surgical myectomy would pose increased procedural risk, would likely benefit from the lesser invasive septal ablation procedure.

When performed properly, an alcohol septal ablation induces a controlled heart attack, in which the portion of the interventricular septum that involves the left ventricular outflow tract is infarcted and will contract into a scar. Which patients are best served by surgical myectomy, alcohol septal ablation, or medical therapy is an important topic and one which is intensely debated in medical scientific circles.

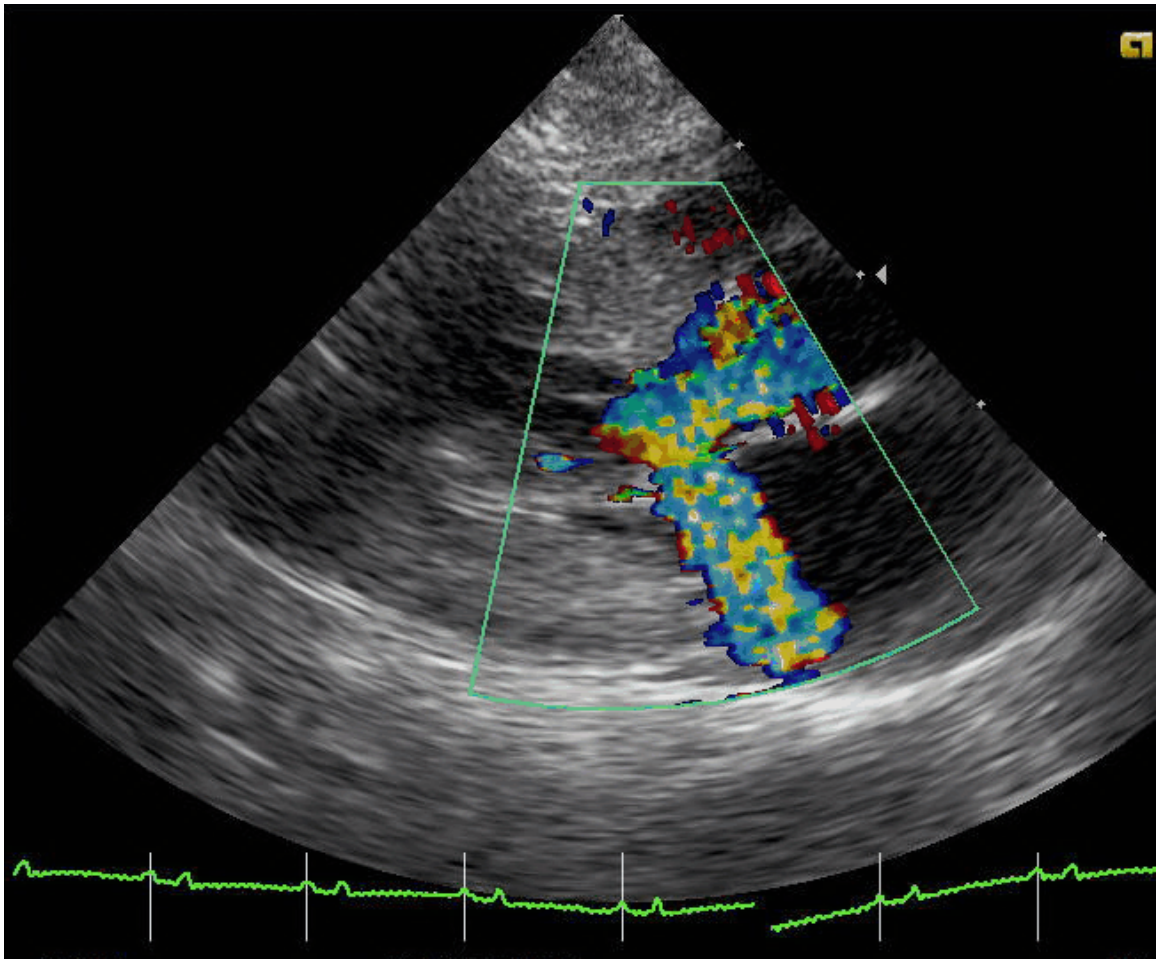
Ventricular pacing

The use of a pacemaker has been advocated in a subset of individuals, in order to cause asynchronous contraction of the left ventricle. Since the pacemaker activates the interventricular septum before the left ventricular free wall, the gradient across the left ventricular outflow tract may decrease. This form of treatment has been shown to provide less relief of symptoms and less of a reduction in the left ventricular outflow tract gradient when compared to surgical myectomy.

Cardiac transplantation

In cases that are refractory to all other forms of treatment, cardiac transplantation is an option.

Related disorders



Echocardiography of Hypertrophic-obstructive cardiomyopathy (HOCM) in a cat

Feline hypertrophic cardiomyopathy (HCM) is the most common heart disease in cats; the disease process and genetics are believed to be similar to the disease in humans. In

Maine Coon and American Shorthair cat breeds, HCM has been confirmed as an autosomal dominant inherited trait. The first genetic mutation (in cardiac myosin binding protein C) responsible for feline hypertrophic cardiomyopathy was discovered in 2005 in Maine Coon cats. A test for this mutation is available. About one third of Maine Coon cats tested for the mutation have been shown to be either heterozygous or homozygous for the mutation, although many of these cats have no clinical signs of the disease. Some Maine Coon cats with clinical evidence of hypertrophic cardiomyopathy test negative for this mutation, strongly suggesting that a second mutation exists in the breed. The cardiac myosin binding protein C mutation identified in Maine Coon cats has not been found in any other breed of cat with HCM but more recently another myosin binding protein C mutation has been identified in Ragdoll cats with HCM.

Turkish Angoras also may be susceptible to HCM because of this gene. The CatScan study performed at the Royal Veterinary College, London, is looking at the prevalence of the disease within a normal population of apparently healthy domestic cats (non-pedigree). This study has just begun (October 2009) and the results of should be available in early 2012.

While there is no cure for HCM, early detection and regular echocardiograms are key to trying to ward off life-threatening problems. Early signs may include a murmur or even heart failure. Unfortunately, death may occur without any other signs present, making the disease a difficult and often deadly one. While medication is commonly given to cats with HCM that have no clinical signs, no medication has been shown to be helpful at this stage and it has been shown that an ACE inhibitor is not beneficial until heart failure is present (at which time a diuretic is most beneficial). Diltiazem generally produces no demonstrable benefit. Atenolol is commonly administered when systolic anterior motion of the mitral valve is present.

Thromboembolic disease (TED) is relatively common sequelae of Feline HCM. The aetiology remains a little uncertain, but it is thought that ischemic damage to the hypertrophied left ventricular myocardium facilitates thrombus formation and subsequent embolism. Classically the embolus lodges at the iliac bifurcation of the aorta, occluding either one or both of the common iliac arteries. Clinically this presents as a cat with complete loss of function in one or both hindlimbs. The hindlimbs are cold, and the cat is in considerable pain. This pain derives from the exaggerated inflammatory response to the embolus at the point of impact, and the inflammatory mediators released generally have a vasoconstrictor effect further exacerbating the problem. Emboli may, rarely, lodge in other locations, typically the renal or ovarian/testicular arteries as they exit the abdominal aorta.

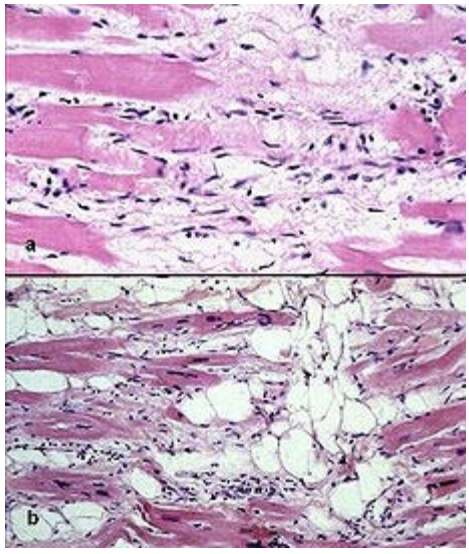
Treatment of TED is variable - typically very low doses of aspirin may be prescribed (aspirin however is extremely toxic to cats and should only be prescribed and administered by a veterinary surgeon). Plavix is also another widely used drug that may or may not prevent clot formation in HCM cats. The FATCAT study at Purdue University is addressing the efficacy of aspirin vs. Plavix for the prevention of a second clot in cats that have already experienced a clot. Thrombolytic agents (e.g., tissue

plasminogen activators) have been used successfully, but their cost is usually prohibitively high in veterinary medicine. Despite the relative efficacy of treatment, the prognosis for cats with TED is poor as they are likely to have significant HCM already, and a recurrent bout of TED is very likely. For this reason euthanasia is often considered in TED cats.

Chapter 6

Arrhythmogenic Right Ventricular Dysplasia

Arrhythmogenic right ventricular dysplasia



Photomicrograph of an ARVC heart.

ICD-10	I42.8
OMIM	107970
DiseasesDB	29750
MeSH	D019571

Arrhythmogenic right ventricular dysplasia (AVRD), also called **arrhythmogenic right ventricular cardiomyopathy** (ARVC) or **arrhythmogenic right ventricular dysplasia/cardiomyopathy** (ARVD/C), is an inherited heart disease.

AVRD is caused by genetic defects of the parts of heart muscle (also called *myocardium* or *cardiac muscle*) known as desmosomes, areas on the surface of heart muscle cells

which link the cells together. The desmosomes are composed of several proteins, and many of those proteins can have harmful mutations.

The disease is a type of nonischemic cardiomyopathy that involves primarily the right ventricle. It is characterized by hypokinetic areas involving the free wall of the right ventricle, with fibrofatty replacement of the right ventricular myocardium, with associated arrhythmias originating in the right ventricle.

AVRD is often found in association with diffuse palmoplantar keratoderma, and woolly hair, because their genes are nearby and often inherited together.

ARVC/D is an important cause of ventricular arrhythmias in children and young adults. It is seen predominantly in males, and 30-50% of cases have a familial distribution.

Genetics

It is usually inherited in an autosomal dominant pattern, with variable expression. Novel studies showed that mutations (point mutations) in genes encoding for desmosomal proteins are the main causatives for the development of this disease. Recently it could be shown, that mutations in the desmin-gene could cause ARVC. Desmin is a intermediate filament protein, which is linked to the desmosomes. The penetrance is 20-35% in general, but significantly higher in Italy. Seven gene loci have been implicated in ARVD. However, about 50% of families that express ARVD that undergo genetic screening do not show linkage with any of the known chromosomal loci. It is unclear whether the pathogenesis varies with the different loci involved. Standard genetic screening test are currently tested and evaluated in different state of the art cardiovascular research centres and hospitals.

Types include:

Type	OMIM	Gene	Locus
ARVD1	107970	*TGFB3*	14q23-q24
ARVD2	600996	*RYR2*	1q42-q43
ARVD3	602086	?	14q12-q22
ARVD4	602087	?	2q32.1-q32.3
ARVD5	604400	*TMEM43*	3p23
ARVD6	604401	?	10p14-p12
ARVD7	609160	?	10q22.3
ARVD8	607450	*DSP*	6p24
ARVD9	609040	*PKP2*	12p11
ARVD10	610193	*DSG2*	18q12.1-q12
ARVD11	610476	*DSC2*	18q12.1
ARVD12	611528	*JUP*	17q21

Incidence

The incidence of ARVD is about 1/10,000 in the general population in the United States, although some studies have suggested that it may be as common as 1/1,000. It accounts for up to 17% of all sudden cardiac deaths in the young. In Italy, the incidence is 40/10,000, making it the most common cause of sudden cardiac death in the young population.

Presentation

Up to 80% of individuals with ARVD present with syncope or sudden cardiac death. The remainder frequently present with palpitations or other symptoms due to right ventricular outflow tract (RVOT) tachycardia (a type of monomorphic ventricular tachycardia).

Symptoms are usually exercise-related. In populations where hypertrophic cardiomyopathy is screened out prior to involvement in competitive athletics, it is a common cause of sudden cardiac death.

The first clinical signs of ARVD are usually during adolescence. However, signs of ARVD have been demonstrated in infants.

Pathogenesis

The pathogenesis of ARVD is largely unknown. Apoptosis (programmed cell death) appears to play a large role. It is unclear why only the right ventricle is involved. The disease process starts in the subepicardial region and works its way towards the endocardial surface, leading to transmural involvement (possibly accounting for the aneurysmal dilatation of the RV). Residual myocardium is confined to the subendocardial region and the trabeculae of the RV. These trabeculae may become hypertrophied.

Aneurysmal dilatation is seen in 50% of cases at autopsy. It usually occurs in the diaphragmatic, apical, and infundibular regions (known as the triangle of dysplasia). The left ventricle is involved in 50-67% of individuals. If the left ventricle is involved, it is usually late in the course of disease, and confers a poor prognosis.

There are two pathological patterns seen in ARVD, Fatty infiltration and fibro-fatty infiltration.

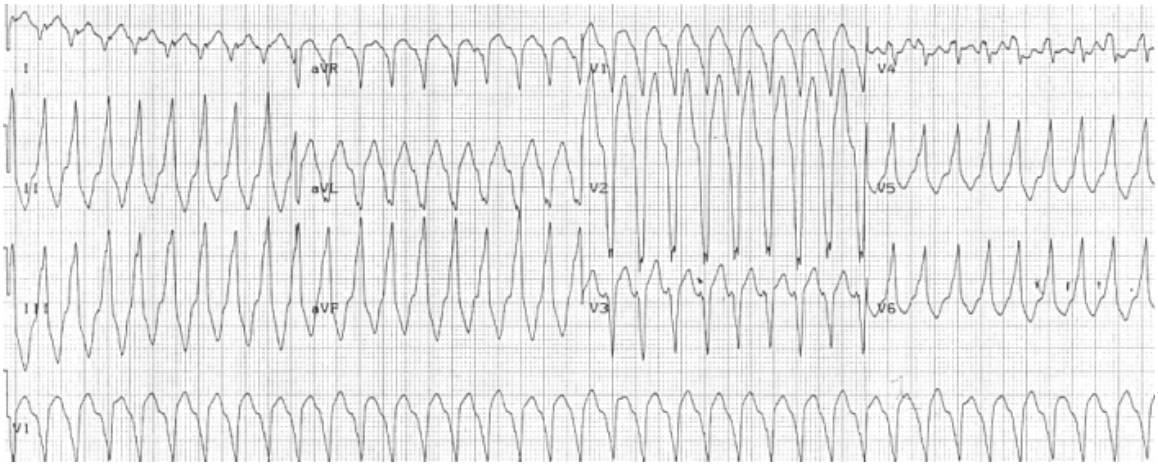
Fatty infiltration

The first, fatty infiltration, is confined to the right ventricle. This involves a partial or near-complete substitution of myocardium with fatty tissue *without* wall thinning. It involves predominantly the apical and infundibular regions of the RV. The left ventricle and ventricular septum are usually spared. No inflammatory infiltrates are seen in fatty infiltration. There is evidence of myocyte (myocardial cell) degeneration and death seen in 50% of cases of fatty infiltration.

Fibro-fatty infiltration

The second, fibro-fatty infiltration, involves replacement of myocytes with fibrofatty tissue. A patchy myocarditis is involved in up to 2/3 of cases, with inflammatory infiltrates (mostly T cells) seen on microscopy. Myocardial atrophy is due to injury and apoptosis. This leads to thinning of the RV free wall (to < 3 mm thickness) Myocytes are replaced with fibrofatty tissue. The regions preferentially involved include the RV inflow tract, the RV outflow tract, and the RV apex. However, the LV free wall may be involved in some cases. Involvement of the ventricular septum is rare. The areas involved are prone to aneurysm formation.

Ventricular arrhythmias



Right ventricular outflow tract tachycardia

Monomorphic ventricular tachycardia originating from the right ventricular outflow tract.

Ventricular arrhythmias due to ARVD typically arise from the diseased right ventricle. The type of arrhythmia ranges from frequent premature ventricular complexes (PVCs) to ventricular tachycardia (VT) to ventricular fibrillation (VF).

While the initiating factor of the ventricular arrhythmias is unclear, it may be due to triggered activity or reentry.

Ventricular arrhythmias are usually exercise-related, suggesting that they are sensitive to catecholamines. The ventricular beats typically have a right axis deviation. Multiple morphologies of ventricular tachycardia may be present in the same individual, suggesting multiple arrhythmogenic foci or pathways.

Right ventricular outflow tract (RVOT) tachycardia is the most common VT seen in individuals with ARVD. In this case, the EKG shows a left bundle branch block (LBBB) morphology with an inferior axis.

Diagnosis

The differential diagnosis for the ventricular tachycardia due to ARVD include:

- Congenital heart disease
  - Repaired tetralogy of Fallot
  - Ebstein's anomaly
  - Uhl's anomaly
  - Atrial septal defect
  - Partial anomalous venous return
- Acquired heart disease
  - Tricuspid valve disease
  - Pulmonary hypertension
  - Right ventricular infarction
  - Bundle-branch re-entrant tachycardia
- Miscellaneous
  - Pre-excited AV re-entry tachycardia
  - Idiopathic RVOT tachycardia
  - Sarcoidosis

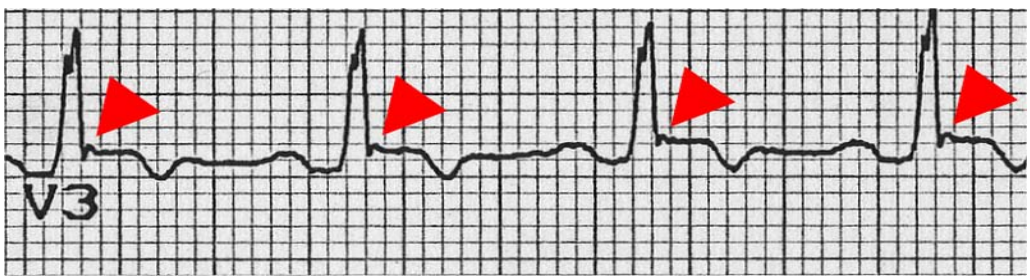
Clinical testing

In order to make the diagnosis of ARVD, a number of clinical tests are employed, including the electrocardiogram (EKG), echocardiography, right ventricular angiography, cardiac MRI, and genetic testing.

Electrocardiogram

90% of individuals with ARVD have some EKG abnormality. The most common EKG abnormality seen in ARVD is T wave inversion in leads V_1 to V_3. However, this is a non-specific finding, and may be considered a normal variant in right bundle branch block (RBBB), women, and children under 12 years old.

RBBB itself is seen frequently in individuals with ARVD. This may be due to delayed activation of the right ventricle, rather than any intrinsic abnormality in the right bundle branch.



The epsilon wave

The epsilon wave (marked by red triangle), seen in ARVD.

The **epsilon wave** is found in about 50% of those with ARVD. This is described as a terminal notch in the QRS complex. It is due to slowed intraventricular conduction. The epsilon wave may be seen on a surface EKG; however, it is more commonly seen on signal averaged EKGs.

Ventricular ectopy seen on a surface EKG in the setting of ARVD is typically of left bundle branch block (LBBB) morphology, with a QRS axis of -90 to +110 degrees. The origin of the ectopic beats is usually from one of the three regions of fatty degeneration (the "triangle of dysplasia"): the RV outflow tract, the RV inflow tract, and the RV apex.

Signal averaged ECG

Signal averaged ECG (SAECG) is used to detect late potentials and epsilon waves in individuals with ARVD.

Echocardiography

Echocardiography may reveal an enlarged, hypokinetic right ventricle with a paper-thin RV free wall. The dilatation of the RV will cause dilatation of the tricuspid valve annulus, with subsequent tricuspid regurgitation. Paradoxical septal motion may also be present.

Cardiac MRI

Fatty infiltration of the RV free wall can be visible on cardiac MRI. Fat has increased intensity in T1-weighted images. However, it may be difficult to differentiate intramyocardial fat and the epicardial fat that is commonly seen adjacent to the normal heart. Also, the sub-tricuspid region may be difficult to distinguish from the atrioventricular sulcus, which is rich in fat.

Cardiac MRI can visualize the extreme thinning and akinesis of the RV free wall. However, the normal RV free wall may be about 3 mm thick, making the test less sensitive.

Right ventricular angiography

Right ventricular angiography is considered the gold standard for the diagnosis of ARVD. Findings consistent with ARVD are an akinetic or dyskinetic bulging localized to the infundibular, apical, and subtricuspid regions of the RV. The specificity is 90%; however, the test is observer dependent.

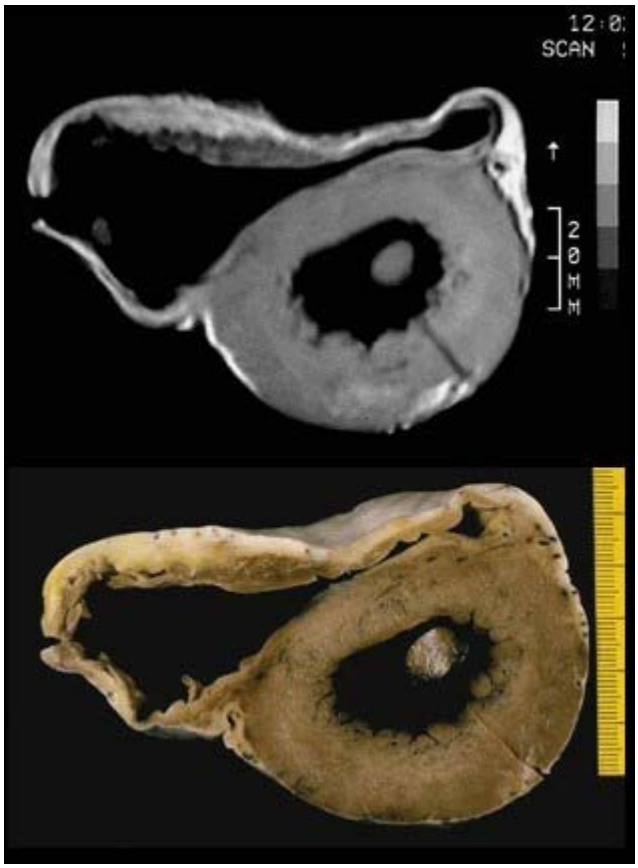
Right ventricular biopsy

Transvenous biopsy of the right ventricle can be highly specific for ARVD, but it has low sensitivity. False positives include other conditions with fatty infiltration of the ventricle, such as chronic alcohol abuse and Duchenne/Becker muscular dystrophy.

False negatives are common, however, because the disease progresses typically from the epicardium to the endocardium (with the biopsy sample coming from the endocardium), and the segmental nature of the disease. Also, due to the paper-thin right ventricular free wall that is common in this disease process, most biopsy samples are taken from the ventricular septum, which is commonly *not* involved in the disease process.

A biopsy sample that is consistent with ARVD would have > 3% fat, >40% fibrous tissue, and <45% myocytes.

Autopsy



In vitro MRI and corresponding cross section of the heart in ARVD show RV dilatation with anterior and posterior aneurysms (17 year old asymptomatic male athlete who died suddenly during a soccer game).

A post mortem histological demonstration of full thickness substitution of the RV myocardium by fatty or fibro-fatty tissue is consistent with ARVD.

Genetic Testing

ARVD is an autosomal dominant trait with reduced penetrance. Approximately 40-50% of ARVD patients have a mutation identified in one of several genes encoding components of the desmosome, which can help confirm a diagnosis of ARVD. Since ARVD is an autosomal dominant trait, children of an ARVD patient have a 50% chance of inheriting the disease causing mutation. Whenever a mutation is identified by genetic testing, family-specific genetic testing can be used to differentiate between relatives who are at-risk for the disease and those who are not. ARVD genetic testing is clinically available.

Diagnostic Criteria

There is no pathognomonic feature of ARVD. The diagnosis of ARVD is based on a combination of major and minor criteria. To make a diagnosis of ARVD requires either 2 major criteria *or* 1 major and 2 minor criteria *or* 4 minor criteria.

Major Criteria

- Right ventricular dysfunction
  - Severe dilatation and reduction of RV ejection fraction with little or no LV impairment
  - Localized RV aneurysms
  - Severe segmental dilatation of the RV
- Tissue characterization
  - Fibrofatty replacement of myocardium on endomyocardial biopsy
- Conduction abnormalities
  - Epsilon waves in V_1 - V_3.
  - Localized prolongation (>110 ms) of QRS in V_1 - V_3
- Family history
  - Familial disease confirmed on autopsy or surgery

Minor Criteria

- Right ventricular dysfunction
  - Mild global RV dilatation and/or reduced ejection fraction with normal LV.
  - Mild segmental dilatation of the RV
  - Regional RV hypokinesis
- Tissue characterization
- Conduction abnormalities
  - Inverted T waves in V_2 and V_3 in an individual over 12 years old, in the absence of a right bundle branch block (RBBB)

    - Late potentials on signal averaged EKG.
    - Ventricular tachycardia with a left bundle branch block (LBBB) morphology
    - Frequent PVCs (> 1000 PVCs / 24 hours)
- Family history
    - Family history of sudden cardiac death before age 35
    - Family history of ARVD

Natural history

There is a long asymptomatic lead-time in individuals with ARVD. While this is a genetically transmitted disease, individuals in their teens may not have any characteristics of ARVD on screening tests.

Many individuals have symptoms associated with ventricular tachycardia, such as palpitations, light-headedness, or syncope. Others may have symptoms and signs related to right ventricular failure, such as lower extremity edema, liver congestion with elevated hepatic enzymes. Unfortunately, sudden death may be the first manifestation of disease.

ARVD is a progressive disease. Over time, the right ventricle becomes more involved, leading to right ventricular failure. The right ventricle will fail before there is left ventricular dysfunction. However, by the time the individual has signs of overt right ventricular failure, there will be histological involvement of the left ventricle. Eventually, the left ventricle will also become involved, leading to bi-ventricular failure. Signs and symptoms of left ventricular failure may become evident, including congestive heart failure, atrial fibrillation, and an increased incidence of thromboembolic events.

Management

The goal of management of ARVD is to decrease the incidence of sudden cardiac death. This raises a clinical dilemma: How to prophylactically treat the asymptomatic patient who was diagnosed during family screening.

A certain subgroup of individuals with ARVD are considered at high risk for sudden cardiac death. Characteristics associated with high risk of sudden cardiac death include:

- Young age
- Competitive sports activity
- Malignant familial history
- Extensive RV disease with decreased right ventricular ejection fraction.
- Left ventricular involvement
- Syncope
- Episode of ventricular arrhythmia

Management options include pharmacological, surgical, catheter ablation, and placement of an implantable cardioverter-defibrillator.

Prior to the decision of the treatment option, programmed electrical stimulation in the electrophysiology laboratory may be performed for additional prognostic information. Goals of programmed stimulation include:

- Assessment of the disease's arrhythmogenic potential
- Evaluate the hemodynamic consequences of sustained VT
- Determine whether the VT can be interrupted via antitachycardia pacing.

Regardless of the management option chosen, the individual is typically suggested to undergo lifestyle modification, including avoidance of strenuous exercise, cardiac stimulants (i.e.: caffeine, nicotine, pseudoephedrine) and alcohol. If the individual wishes to begin an exercise regimen, an exercise stress test may have added benefit.

Pharmacologic management

Pharmacologic management of ARVD involves arrhythmia suppression and prevention of thrombus formation.

Sotalol, a beta blocker and a class III antiarrhythmic agent, is the most effective antiarrhythmic agent in ARVD. Other antiarrhythmic agents used include amiodarone and conventional beta blockers (i.e.: metoprolol). If antiarrhythmic agents are used, their efficacy should be guided by series ambulatory holter monitoring, to show a reduction in arrhythmic events.

While angiotensin converting enzyme inhibitors (ACE Inhibitors) are well known for slowing progression in other cardiomyopathies, they have not been proven to be helpful in ARVD.

Individuals with decreased RV ejection fraction with dyskinetic portions of the right ventricle may benefit from long term anticoagulation with warfarin to prevent thrombus formation and subsequent pulmonary embolism.

Catheter ablation

Catheter ablation may be used to treat intractable ventricular tachycardia. It has a 60-90% success rate. Unfortunately, due to the progressive nature of the disease, recurrence is common (60% recurrence rate), with the creation of new arrhythmogenic foci. Indications for catheter ablation include drug-refractory VT and frequent recurrence of VT after ICD placement, causing frequent discharges of the ICD.

Implantable cardioverter-defibrillator

An ICD is the most effective prevention against sudden cardiac death. Due to the prohibitive cost of ICDs, they are not routinely placed in all individuals with ARVD.

Indications for ICD placement in the setting of ARVD include:

- Cardiac arrest due to VT or VF
- Symptomatic VT that is not inducible during programmed stimulation
- Failed programmed stimulation-guided drug therapy
- Severe RV involvement with poor tolerance of VT
- Sudden death of immediate family member

Since ICDs are typically placed via a transvenous approach into the right ventricle, there are complications associated with ICD placement and follow-up.

Due to the extreme thinning of the RV free wall, it is possible to perforate the RV during implantation, potentially causing pericardial tamponade. Because of this, every attempt is made at placing the defibrillator lead on the ventricular septum.

After a successful implantation, the progressive nature of the disease may lead to fibro-fatty replacement of the myocardium at the site of lead placement. This may lead to undersensing of the individual's electrical activity (potentially causing inability to sense VT or VF), and inability to pace the ventricle.

Cardiac transplant surgery

Cardiac transplant surgery may be performed in ARVD. It may be indicated if the arrhythmias associated with the disease are uncontrollable or if there is severe bi-ventricular heart failure that is not manageable with pharmacological therapy.

Family screening

All first degree family members of the affected individual should be screened for ARVD. This is used to establish the pattern of inheritance. Screening should begin during the teenage years unless otherwise indicated. Screening tests include:

- Echocardiogram
- EKG
- Signal averaged EKG
- Holter monitoring
- Cardiac MRI
- Exercise stress test

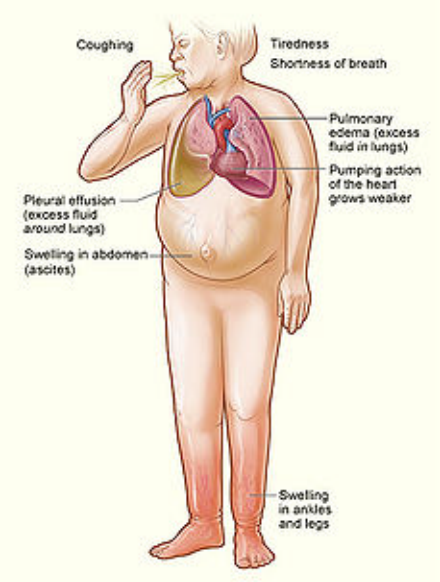
Highly-publicised deaths from arrhythmogenic right ventricular dysplasia

Sevilla FC and Spanish international left wing-back Antonio Puerta died from the condition, at the age of 22, on 28 August 2007, three days after suffering several cardiac arrests, while disputing a La Liga game against Getafe CF. Englishman Matt Gadsby also died from the condition after collapsing on the pitch on 9 September 2006, while playing with his team Hinckley United in a Conference North game against Harrogate Town. Model Krissy Taylor, sister of Niki Taylor died from the disease at age 17 in 1995.

Chapter 7

Heart Failure

Heart failure



The major signs and symptoms of heart failure.

ICD-10	I50.
ICD-9	428.0
DiseasesDB	16209
MedlinePlus	000158
eMedicine	med/3552 emerg/108 radio/189 med/1367150 ped/2636
MeSH	D006333

Heart failure (**HF**) is generally defined as inability of the heart to supply sufficient blood flow to meet the body's needs. It has various diagnostic criteria, and the term *heart failure*

is often incorrectly used to describe other cardiac-related illnesses, such as myocardial infarction (heart attack) or cardiac arrest.

Common causes of heart failure include myocardial infarction (heart attacks) and other forms of ischemic heart disease, hypertension, valvular heart disease, and cardiomyopathy. Heart failure can cause a number of symptoms including shortness of breath (typically worse when lying flat, which is called orthopnea), coughing, chronic venous congestion, ankle swelling, and exercise intolerance. Heart failure is often undiagnosed due to a lack of a universally agreed definition and challenges in definitive diagnosis. Treatment commonly consists of lifestyle measures (such as smoking cessation, light exercise including breathing protocols, decreased salt intake and other dietary changes) and medications, and sometimes devices or even surgery.

Heart failure is a common, costly, disabling, and potentially deadly condition. In developed countries, around 2% of adults suffer from heart failure, but in those over the age of 65, this increases to 6–10%. Mostly due to costs of hospitalization it is associated with a high health expenditure; costs have been estimated to amount to 2% of the total budget of the National Health Service in the United Kingdom, and more than $35 billion in the United States. Heart failure is associated with significantly reduced physical and mental health, resulting in a markedly decreased quality of life. With the exception of heart failure caused by reversible conditions, the condition usually worsens with time. Although some people survive many years, progressive disease is associated with an overall annual mortality rate of 10%.

Terminology

Heart failure is a global term for the physiological state in which cardiac output is insufficient in meeting the needs of the body and lungs.

This occurs most commonly when the cardiac output is low (often termed "congestive heart failure" or CHF, because the body becomes congested with fluid).

It may also occur when the body's requirements for oxygen and nutrients are increased and demand outstrips what the heart can provide, (termed "high output cardiac failure"). This can occur from severe anemia, Gram negative septicaemia, beriberi (vitamin B_1/thiamine deficiency), thyrotoxicosis, Paget's disease, arteriovenous fistulae, or arteriovenous malformations.

Fluid overload is a common problem for people with heart failure but is not synonymous with it. Patients with treated heart failure will often be euvolaemic (a term for normal fluid status), or more rarely, dehydrated.

Medical professionals use the words "acute" to mean of rapid onset and "chronic" of long duration. Chronic heart failure is therefore a long term situation, usually with stable treated symptomatology.

Acute decompensated heart failure is a term used to describe exacerbated or decompensated heart failure, referring to episodes in which a patient can be characterized as having a change in heart failure signs and symptoms resulting in a need for urgent therapy or hospitalization.

There are several terms which are closely related to heart failure, and may be the cause of heart failure, but should not be confused with it:

- Cardiac arrest and asystole refer to situations in which there is *no* cardiac output at all. Without urgent treatment these result in sudden death.
- Myocardial infarction ("Heart attack") refers to heart muscle damage due to insufficient blood supply, usually as a result of a blocked coronary artery.
- Cardiomyopathy refers specifically to problems within the heart muscle, and these problems usually result in heart failure. Ischemic cardiomyopathy implies that the cause of muscle damage is coronary artery disease. Dilated cardiomyopathy implies that the muscle damage has resulted in enlargement of the heart. Hypertrophic cardiomyopathy involves enlargement and *thickening* of the heart muscle.

Classification

There are many different ways to categorize heart failure, including:

- the side of the heart involved, (left heart failure versus right heart failure) Left heart failure compromises aortic flow to the body and brain. Right heart failure compromises pulmonic flow to the lungs. Mixed presentations are common, especially when the cardiac septum is involved.
- whether the abnormality is due to insufficient contraction and/or relaxation of the heart (systolic dysfunction vs. diastolic dysfunction)
- whether the problem is primarily increased venous back pressure (behind) the heart Afterload, or failure to supply adequate arterial perfusion (in front of) the heart Preload (backward vs. forward failure)
- whether the abnormality is due to low cardiac output with high systemic vascular resistance or high cardiac output with low vascular resistance (low-output heart failure vs. high-output heart failure)
- the degree of functional impairment conferred by the abnormality (as in the NYHA functional classification)
- the degree of coexisting illness: i.e. heart failure/systemic hypertension, heart failure/pulmonary hypertension, heart failure/diabetes, heart failure/renal failure, etc.

Functional classification generally relies on the New York Heart Association Functional Classification. The classes (I-IV) are:

- Class I: no limitation is experienced in any activities; there are no symptoms from ordinary activities.

- Class II: slight, mild limitation of activity; the patient is comfortable at rest or with mild exertion.
- Class III: marked limitation of any activity; the patient is comfortable only at rest.
- Class IV: any physical activity brings on discomfort and symptoms occur at rest.

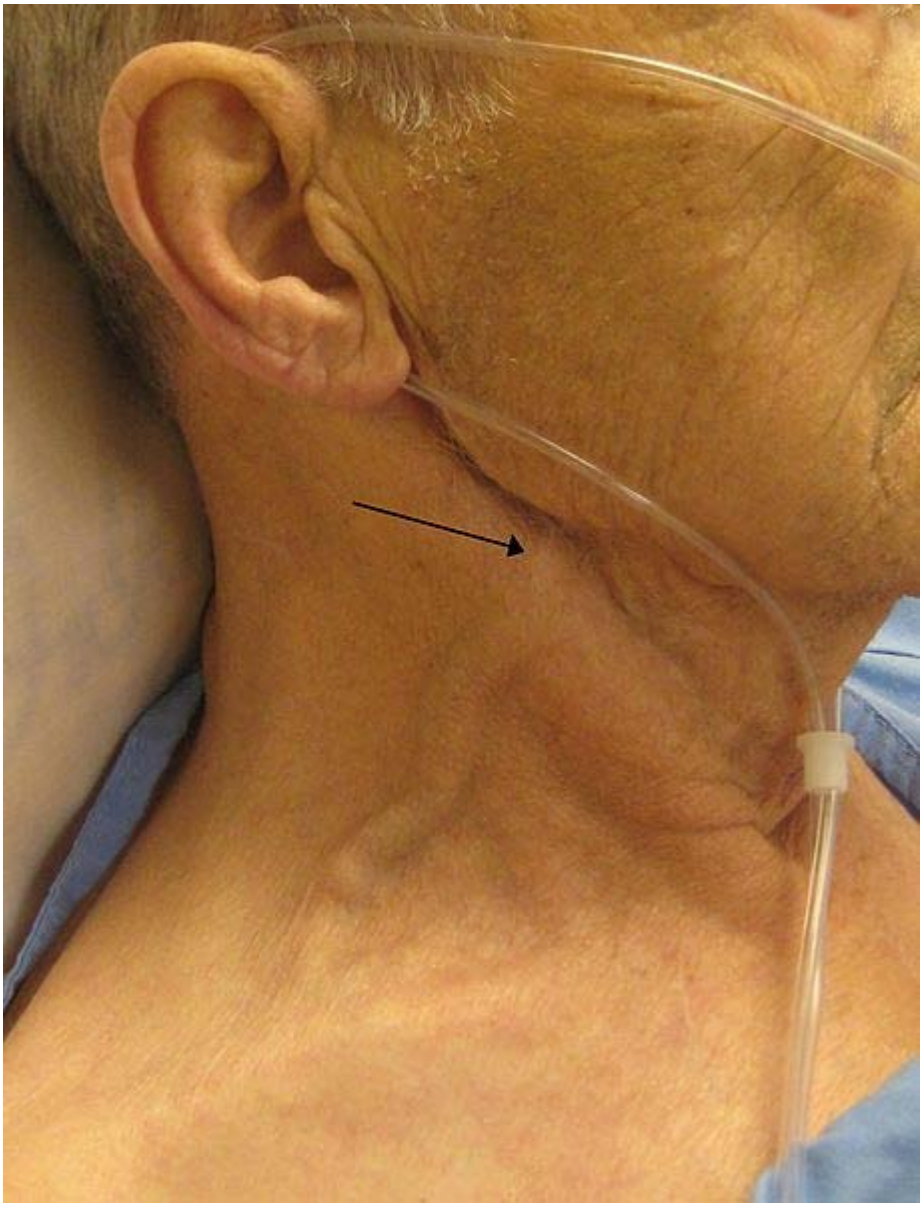
This score documents severity of symptoms, and can be used to assess response to treatment. While its use is widespread, the NYHA score is not very reproducible and doesn't reliably predict the walking distance or exercise tolerance on formal testing.

In its 2001 guidelines the American College of Cardiology/American Heart Association working group introduced four stages of heart failure:

- Stage A: Patients at high risk for developing HF in the future but no functional or structural heart disorder;
- Stage B: a structural heart disorder but no symptoms at any stage;
- Stage C: previous or current symptoms of heart failure in the context of an underlying structural heart problem, but managed with medical treatment;
- Stage D: advanced disease requiring hospital-based support, a heart transplant or palliative care.

The ACC staging system is useful in that Stage A encompasses "pre-heart failure" - a stage where intervention with treatment can presumably prevent progression to overt symptoms. ACC stage A does not have a corresponding NYHA class. ACC Stage B would correspond to NYHA Class I. ACC Stage C corresponds to NYHA Class II and III, while ACC Stage D overlaps with NYHA Class IV.

Signs and symptoms



A man with congestive heart failure and marked jugular venous distension. External jugular vein marked by an arrow.

Signs

Left-sided failure

Common respiratory signs are tachypnea (increased *rate* of breathing) and increased *work* of breathing (non-specific signs of respiratory distress). Rales or crackles, heard initially in the lung bases, and when severe, throughout the lung fields suggest the development of pulmonary edema (fluid in the alveoli). Cyanosis which suggests severe hypoxemia, is a late sign of extremely severe pulmonary edema.

Additional signs indicating left ventricular failure include a laterally displaced apex beat (which occurs if the heart is enlarged) and a gallop rhythm (additional heart sounds) may be heard as a marker of increased blood flow, or increased intra-cardiac pressure. Heart murmurs may indicate the presence of valvular heart disease, either as a cause (e.g. aortic stenosis) or as a result (e.g., mitral regurgitation) of the heart failure.

Right-sided failure

Physical examination can reveal pitting peripheral edema, ascites, and hepatomegaly. Jugular venous pressure is frequently assessed as a marker of fluid status, which can be accentuated by the hepatojugular reflux. If the right ventricular pressure is increased, a parasternal heave may be present, signifying the compensatory increase in contraction strength.

Biventricular failure

Dullness of the lung fields to finger percussion and reduced breath sounds at the bases of the lung may suggest the development of a pleural effusion (fluid collection in between the lung and the chest wall). Though it can occur in isolated left- or right-sided heart failure, it is more common in biventricular failure because pleural veins drain both into the systemic and pulmonary venous system. When unilateral, effusions are often right sided.

Symptoms

Heart failure symptoms are traditionally and somewhat arbitrarily divided into "left" and "right" sided, recognizing that the left and right ventricles of the heart supply different portions of the circulation. However, heart failure is not exclusively *backward failure* (in the part of the circulation which drains to the ventricle).

There are several other exceptions to a simple left-right division of heart failure symptoms. Left sided *forward* failure overlaps with right sided *backward* failure. Additionally, the most common cause of right-sided heart failure is left-sided heart failure. The result is that patients commonly present with both sets of signs and symptoms.

Left-sided failure

Backward failure of the left ventricle causes congestion of the pulmonary vasculature, and so the symptoms are predominantly respiratory in nature. Backward failure can be subdivided into failure of the left atrium, the left ventricle or both within the left circuit. The patient will have dyspnea (shortness of breath) on exertion (*dyspnée d'effort*) and in severe cases, dyspnea at rest. Increasing breathlessness on lying flat, called orthopnea, occurs. It is often measured in the number of pillows required to lie comfortably, and in severe cases, the patient may resort to sleeping while sitting up. Another symptom of heart failure is paroxysmal nocturnal dyspnea a sudden nighttime attack of severe

breathlessness, usually several hours after going to sleep. Easy fatigueability and exercise intolerance are also common complaints related to respiratory compromise.

"Cardiac asthma" or wheezing may occur.

Compromise of left ventricular *forward* function may result in symptoms of poor systemic circulation such as dizziness, confusion and cool extremities at rest.

Right-sided failure

Backward failure of the right ventricle leads to congestion of systemic capillaries. This generates excess fluid accumulation in the body. This causes swelling under the skin (termed peripheral edema or anasarca) and usually affects the dependent parts of the body first (causing foot and ankle swelling in people who are standing up, and sacral edema in people who are predominantly lying down). Nocturia (frequent nighttime urination) may occur when fluid from the legs is returned to the bloodstream while lying down at night. In progressively severe cases, ascites (fluid accumulation in the abdominal cavity causing swelling) and hepatomegaly (enlargement of the liver) may develop. Significant liver congestion may result in impaired liver function, and jaundice and even coagulopathy (problems of decreased blood clotting) may occur.

Causes

Chronic heart failure

The predominance of causes of heart failure are difficult to analyze due to challenges in diagnosis, differences in populations, and changing prevalence of causes with age.

A 19 year study of 13000 healthy adults in the United States (the National Health and Nutrition Examination Survey (NHANES I) found the following causes ranked by Population Attributable Risk score:

1. Ischaemic heart disease 62%
2. Cigarette smoking 16%
3. Hypertension (high blood pressure)10%
4. Obesity 8%
5. Diabetes 3%
6. Valvular heart disease 2% (much higher in older populations)

An Italian registry of over 6200 patients with heart failure showed the following underlying causes:

1. Ischaemic heart disease 40%
2. Dilated cardiomyopathy 32%
3. Valvular heart disease 12%
4. Hypertension 11%

5. Other 5%

Rarer causes of heart failure include:

- Viral myocarditis (an infection of the heart muscle)
- Infiltrations of the muscle such as amyloidosis
- HIV cardiomyopathy (caused by human immunodeficiency virus)
- Connective tissue diseases such as systemic lupus erythematosus
- Abuse of drugs such as alcohol and cocaine
- Pharmaceutical drugs such as chemotherapeutic agents
- Arrhythmias

Obstructive sleep apnea a condition of sleep disordered breathing overlaps with obesity, hypertension, and diabetes and is regarded as an independent cause of heart failure.

Acute decompensated heart failure

Chronic stable heart failure may easily decompensate. This most commonly results from an intercurrent illness (such as pneumonia), myocardial infarction (a heart attack), arrhythmias, uncontrolled hypertension, or a patient's failure to maintain a fluid restriction, diet, or medication. Other well recognized precipitating factors include anemia and hyperthyroidism which place additional strain on the heart muscle. Excessive fluid or salt intake, and medication that causes fluid retention such as NSAIDs and thiazolidinediones, may also precipitate decompensation.

Pathophysiology

Heart failure is caused by any condition which reduces the efficiency of the myocardium, or heart muscle, through damage or overloading. As such, it can be caused by as diverse an array of conditions as myocardial infarction (in which the heart muscle is starved of oxygen and dies), hypertension (which increases the force of contraction needed to pump blood) and amyloidosis (in which protein is deposited in the heart muscle, causing it to stiffen). Over time these increases in workload will produce changes to the heart itself:

- Reduced force of contraction, due to overloading of the ventricle. In health, increased filling of the ventricle results in increased force of contraction (by the Frank–Starling law of the heart) and thus a rise in cardiac output. In heart failure this mechanism fails, as the ventricle is loaded with blood to the point where heart muscle contraction becomes less efficient. This is due to reduced ability to cross-link actin and myosin filaments in over-stretched heart muscle.
- A reduced stroke volume, as a result of a failure of systole, diastole or both. Increased end systolic volume is usually caused by reduced contractility. Decreased end diastolic volume results from impaired ventricular filling – as occurs when the compliance of the ventricle falls (i.e. when the walls stiffen).
- Reduced spare capacity. As the heart works harder to meet normal metabolic demands, the amount cardiac output can increase in times of increased oxygen

demand (e.g. exercise) is reduced. This contributes to the exercise intolerance commonly seen in heart failure. This translates to the loss of one's cardiac reserve. The cardiac reserve refers to the ability of the heart to work harder during exercise or strenuous activity. Since the heart has to work harder to meet the normal metabolic demands, it is incapable of meeting the metabolic demands of the body during exercise.

- Increased heart rate, stimulated by increased sympathetic activity in order to maintain cardiac output. Initially, this helps compensate for heart failure by maintaining blood pressure and perfusion, but places further strain on the myocardium, increasing coronary perfusion requirements, which can lead to worsening of ischemic heart disease. Sympathetic activity may also cause potentially fatal arrhythmias.
- Hypertrophy (an increase in physical size) of the myocardium, caused by the terminally differentiated heart muscle fibres increasing in size in an attempt to improve contractility. This may contribute to the increased stiffness and decreased ability to relax during diastole.
- Enlargement of the ventricles, contributing to the enlargement and spherical shape of the failing heart. The increase in ventricular volume also causes a reduction in stroke volume due to mechanical and contractile inefficiency.

The general effect is one of reduced cardiac output and increased strain on the heart. This increases the risk of cardiac arrest (specifically due to ventricular dysrhythmias), and reduces blood supply to the rest of the body. In chronic disease the reduced cardiac output causes a number of changes in the rest of the body, some of which are physiological compensations, some of which are part of the disease process:

- Arterial blood pressure falls. This destimulates baroreceptors in the carotid sinus and aortic arch which link to the nucleus tractus solitarius. This center in the brain increases sympathetic activity, releasing catecholamines into the blood stream. Binding to alpha-1 receptors results in systemic arterial vasoconstriction. This helps restore blood pressure but also increases the total peripheral resistance, increasing the workload of the heart. Binding to beta-1 receptors in the myocardium increases the heart rate and make contractions more forceful, in an attempt to increase cardiac output. This also, however, increases the amount of work the heart has to perform.
- Increased sympathetic stimulation also causes the hypothalamus to secrete vasopressin (also known as antidiuretic hormone or ADH), which causes fluid retention at the kidneys. This increases the blood volume and blood pressure.
- Reduced perfusion (blood flow) to the kidneys stimulates the release of renin – an enzyme which catalyses the production of the potent vasopressor angiotensin. Angiotensin and its metabolites cause further vasocontriction, and stimulate increased secretion of the steroid aldosterone from the adrenal glands. This promotes salt and fluid retention at the kidneys, also increasing the blood volume.
- The chronically high levels of circulating neuroendocrine hormones such as catecholamines, renin, angiotensin, and aldosterone affects the myocardium directly, causing structural remodelling of the heart over the long term. Many of

these remodelling effects seem to be mediated by transforming growth factor beta (TGF-beta), which is a common downstream target of the signal transduction cascade initiated by catecholamines and angiotensin II, and also by epidermal growth factor (EGF), which is a target of the signaling pathway activated by aldosterone
- Reduced perfusion of skeletal muscle causes atrophy of the muscle fibres. This can result in weakness, increased fatigueability and decreased peak strength - all contributing to exercise intolerance.

The increased peripheral resistance and greater blood volume place further strain on the heart and accelerates the process of damage to the myocardium. Vasoconstriction and fluid retention produce an increased hydrostatic pressure in the capillaries. This shifts the balance of forces in favour of interstitial fluid formation as the increased pressure forces additional fluid out of the blood, into the tissue. This results in edema (fluid build-up) in the tissues. In right-sided heart failure this commonly starts in the ankles where venous pressure is high due to the effects of gravity (although if the patient is bed-ridden, fluid accumulation may begin in the sacral region.) It may also occur in the abdominal cavity, where the fluid build-up is called ascites. In left-sided heart failure edema can occur in the lungs - this is called cardiogenic pulmonary edema. This reduces spare capacity for ventilation, causes stiffening of the lungs and reduces the efficiency of gas exchange by increasing the distance between the air and the blood. The consequences of this are shortness of breath, orthopnea and paroxysmal nocturnal dyspnea.

The symptoms of heart failure are largely determined by which side of the heart fails. The left side pumps blood into the systemic circulation, whilst the right side pumps blood into the pulmonary circulation. Whilst left-sided heart failure will reduce cardiac output to the systemic circulation, the initial symptoms often manifest due to effects on the pulmonary circulation. In systolic dysfunction, the ejection fraction is decreased, leaving an abnormally elevated volume of blood in the left ventricle. In diastolic dysfunction, end-diastolic ventricular pressure will be high. This increase in volume or pressure backs up to the left atrium and then to the pulmonary veins. Increased volume or pressure in the pulmonary veins impairs the normal drainage of the alveoli and favors the flow of fluid from the capillaries to the lung parenchyma, causing pulmonary edema. This impairs gas exchange. Thus, left-sided heart failure often presents with respiratory symptoms: shortness of breath, orthopnea and paroxysmal nocturnal dyspnea.

In severe cardiomyopathy, the effects of decreased cardiac output and poor perfusion become more apparent, and patients will manifest with cold and clammy extremities, cyanosis, claudication, generalized weakness, dizziness, and syncope

The resultant hypoxia caused by pulmonary edema causes vasoconstriction in the pulmonary circulation, which results in pulmonary hypertension. Since the right ventricle generates far lower pressures than the left ventricle (approximately 20 mmHg versus around 120 mmHg, respectively, in the healthy individual) but nonetheless generates cardiac output exactly equal to the left ventricle, this means that a small increase in pulmonary vascular resistance causes a large increase in amount of work the right

ventricle must perform. However, the main mechanism by which left-sided heart failure causes right-sided heart failure is actually not well understood. Some theories invoke mechanisms that are mediated by neurohormonal activation. Mechanical effects may also contribute. As the left ventricle distends, the intraventricular septum bows into the right ventricle, decreasing the capacity of the right ventricle.

Systolic dysfunction

Heart failure caused by systolic dysfunction is more readily recognized. It can be simplistically described as failure of the pump function of the heart. It is characterized by a decreased ejection fraction (less than 45%). The strength of ventricular contraction is attenuated and inadequate for creating an adequate stroke volume, resulting in inadequate cardiac output. In general, this is caused by dysfunction or destruction of cardiac myocytes or their molecular components. In congenital diseases such as Duchenne muscular dystrophy, the molecular structure of individual myocytes is affected. Myocytes and their components can be damaged by inflammation (such as in myocarditis) or by infiltration (such as in amyloidosis). Toxins and pharmacological agents (such as ethanol, cocaine, and amphetamines) cause intracellular damage and oxidative stress. The most common mechanism of damage is ischemia causing infarction and scar formation. After myocardial infarction, dead myocytes are replaced by scar tissue, deleteriously affecting the function of the myocardium. On echocardiogram, this is manifest by abnormal or absent wall motion.

Because the ventricle is inadequately emptied, ventricular end-diastolic pressure and volumes increase. This is transmitted to the atrium. On the left side of the heart, the increased pressure is transmitted to the pulmonary vasculature, and the resultant hydrostatic pressure favors extravassation of fluid into the lung parenchyma, causing pulmonary edema. On the right side of the heart, the increased pressure is transmitted to the systemic venous circulation and systemic capillary beds, favoring extravassation of fluid into the tissues of target organs and extremities, resulting in dependent peripheral edema.

Diastolic dysfunction

Heart failure caused by diastolic dysfunction is generally described as the failure of the ventricle to adequately relax and typically denotes a stiffer ventricular wall. This causes inadequate filling of the ventricle, and therefore results in an inadequate stroke volume. The failure of ventricular relaxation also results in elevated end-diastolic pressures, and the end result is identical to the case of systolic dysfunction (pulmonary edema in left heart failure, peripheral edema in right heart failure.)

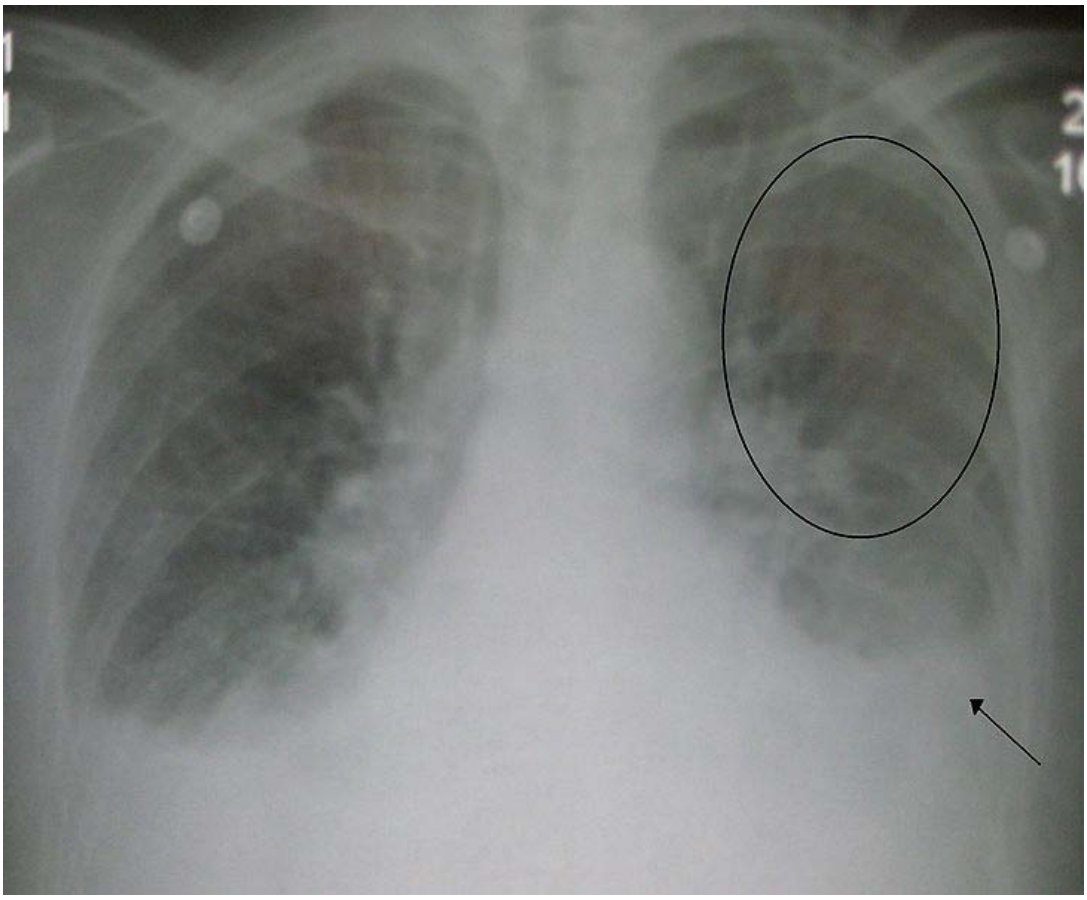
Diastolic dysfunction can be caused by processes similar to those that cause systolic dysfunction, particularly causes that affect cardiac remodeling.

Diastolic dysfunction may not manifest itself except in physiologic extremes if systolic function is preserved. The patient may be completely asymptomatic at rest. However,

they are exquisitely sensitive to increases in heart rate, and sudden bouts of tachycardia (which can be caused simply by physiological responses to exertion, fever, or dehydration, or by pathological tachyarrhythmias such as atrial fibrillation with rapid ventricular response) may result in flash pulmonary edema. Adequate rate control (usually with a pharmacological agent that slows down AV conduction such as a calcium channel blocker or a beta-blocker) is therefore key to preventing decompensation.

Left ventricular diastolic function can be determined through echocardiography by measurement of various parameters such as the E/A ratio (early-to-atrial left ventricular filling ratio), the E (early left ventricular filling) deceleration time, and the isovolumic relaxation time.

Diagnosis



Acute pulmonary edema. Note enlarged heart size, apical vascular redistribution (circle), and small bilateral pleural effusions (arrow).

No system of diagnostic criteria has been agreed as the gold standard for heart failure. Commonly used systems are the "Framingham criteria" (derived from the Framingham Heart Study), the "Boston criteria", the "Duke criteria", and (in the setting of acute myocardial infarction) the "Killip class".

Imaging

Echocardiography is commonly used to support a clinical diagnosis of heart failure. This modality uses ultrasound to determine the stroke volume (SV, the amount of blood in the heart that exits the ventricles with each beat), the end-diastolic volume (EDV, the total amount of blood at the end of diastole), and the SV in proportion to the EDV, a value known as the *ejection fraction* (EF). In pediatrics, the shortening fraction is the preferred measure of systolic function. Normally, the EF should be between 50% and 70%; in systolic heart failure, it drops below 40%. Echocardiography can also identify valvular heart disease and assess the state of the pericardium (the connective tissue sac surrounding the heart). Echocardiography may also aid in deciding what treatments will help the patient, such as medication, insertion of an implantable cardioverter-defibrillator or cardiac resynchronization therapy. Echocardiography can also help determine if acute myocardial ischemia is the precipitating cause, and may manifest as regional wall motion abnormalities on echo.

Chest X-rays are frequently used to aid in the diagnosis of CHF. In the compensated patient, this may show cardiomegaly (visible enlargement of the heart), quantified as the *cardiothoracic ratio* (proportion of the heart size to the chest). In left ventricular failure, there may be evidence of vascular redistribution ("upper lobe blood diversion" or "cephalization"), Kerley lines, cuffing of the areas around the bronchi, and interstitial edema.

Electrophysiology

An electrocardiogram (ECG/EKG) may be used to identify arrhythmias, ischemic heart disease, right and left ventricular hypertrophy, and presence of conduction delay or abnormalities (e.g. left bundle branch block). Although these findings are not specific to the diagnosis of heart failure a normal ECG virtually excludes left ventricular systolic dysfunction.

Blood tests

Blood tests routinely performed include electrolytes (sodium, potassium), measures of renal function, liver function tests, thyroid function tests, a complete blood count, and often C-reactive protein if infection is suspected. An elevated B-type natriuretic peptide (BNP) is a specific test indicative of heart failure. Additionally, BNP can be used to differentiate between causes of dyspnea due to heart failure from other causes of dyspnea. If myocardial infarction is suspected, various cardiac markers may be used.

According to a meta-analysis comparing BNP and N-terminal pro-BNP (NTproBNP) in the diagnosis of heart failure, BNP is a better indicator for heart failure and left ventricular systolic dysfunction. In groups of symptomatic patients, a diagnostic odds ratio of 27 for BNP compares with a sensitivity of 85% and specificity of 84% in detecting heart failure.

Angiography

Heart failure may be the result of coronary artery disease, and its prognosis depends in part on the ability of the coronary arteries to supply blood to the myocardium (heart muscle). As a result, coronary catheterization may be used to identify possibilities for revascularisation through percutaneous coronary intervention or bypass surgery.

Monitoring

Various measures are often used to assess the progress of patients being treated for heart failure. These include fluid balance (calculation of fluid intake and excretion), monitoring body weight (which in the shorter term reflects fluid shifts).

Algorithms

There are various algorithms for the diagnosis of heart failure. For example, the algorithm used by the Framingham Heart Study adds together criteria mainly from physical examination. In contrast, the more extensive algorithm by the European Society of Cardiology (ESC) weights the difference between supporting and opposing parameters from the medical history, physical examination, further medical tests as well as response to therapy.

Framingham criteria

By the Framingham criteria, diagnosis of congestive heart failure (heart failure with impaired pumping capability) requires the simultaneous presence of at least 2 of the following major criteria or 1 major criterion in conjunction with 2 of the following minor criteria:

Major criteria:

- Cardiomegaly on chest radiography
- S3 gallop (a third heart sound)
- Acute pulmonary edema
- Paroxysmal nocturnal dyspnea
- Crackles on lung auscultation
- Central venous pressure of more than 16 cm H2O at the right atrium
- Jugular vein distension
- Positive abdominojugular test
- Weight loss of more than 4.5 kg in 5 days in response to treatment (sometimes classified as a minor criterium)

Minor criteria:

- Tachycardia of more than 120 beats per minute
- Nocturnal cough

- Dyspnea on ordinary exertion
- Pleural effusion
- Decrease in vital capacity by one third from maximum recorded
- Hepatomegaly
- Bilateral ankle edema

Minor criteria are acceptable only if they can not be attributed to another medical condition such as pulmonary hypertension, chronic lung disease, cirrhosis, ascites, or the nephrotic syndrome. The Framingham Heart Study criteria are 100% sensitive and 78% specific for identifying persons with definite congestive heart failure.

ESC algorithm

The ESC algorithm weights the following parameters in establishing the diagnosis of heart failure:

Parameter	Influence + - to some degree ++ - to intermediate degree +++ - to high degree	Supports if present	Opposes if normal or absent
Compatible symptoms		++	++
Compatible signs		++	+
Cardiac dysfunction on echocardiography		+++	+++
Response of symptoms or signs to therapy		+++	++
ECG			
Normal			++
Abnormal		++	+
Dysrhythmia		+++	+
Laboratory			
BNP > 400 pg/mL and/or NT-proBNP > 2000 pg/mL		+++	+
BNP < 100 pg/mL and NT-proBNP < 400 pg/mL		+	+++
Hyponatraemia		+	+
Renal dysfunction		+	+
Mild elevations of troponin		+	+
Chest X-ray			
Pulmonary congestion		+++	+
Reduced exercise capacity		+++	++

Abnormal pulmonary function tests	+	+
Abnormal haemodynamics at rest	+++	++

Management

Treatment focuses on improving the symptoms and preventing the progression of the disease. Reversible causes of the heart failure also need to be addressed: (e.g. infection, alcohol ingestion, anemia, thyrotoxicosis, arrhythmia, hypertension). Treatments include lifestyle and pharmacological modalities.

Acute decompensation

In acute decompensated heart failure (ADHF), the immediate goal is to re-establish adequate perfusion and oxygen delivery to end organs. This entails ensuring that airway, breathing, and circulation are adequate. Immediated treatments usually involve some combination of vasodilators such as nitroglycerin, diuretics such as furosemide, and possibly non invasive positive pressure ventilation (NIPPV).

Chronic management

The goal is to prevent the development of acute decompensated heart failure, to counteract the deleterious effects of cardiac remodeling, and to minimize the symptoms that the patient suffers. First-line therapy for all heart failure patients is angiotensin-converting enzyme (ACE) inhibition. ACE inhibitors (i.e., enalapril, captopril, lisinopril, ramipril) improve survival and quality of life in heart failure patients, and have been shown to reduce mortality in patients with left ventricular dysfunction in numerous randomized trials. In addition to pharmacologic agents (oral loop diuretics, beta-blockers, ACE inhibitors or angiotensin receptor blockers, vasodilators, and in severe cardiomyopathy aldosterone receptor antagonists), behavioral modification should be pursued, specifically with regards to dietary guidelines regarding salt and fluid intake. Exercise should be encouraged as tolerated, as sufficient conditioning can significantly improve quality-of-life.

In patients with severe cardiomyopathy, implantation of an automatic implantable cardioverter defibrillator (AICD) should be considered. A select population will also probably benefit from ventricular resynchronization.

In select cases, cardiac transplantation can be considered. While this may resolve the problems associated with heart failure, the patient generally must remain on an immunosuppressive regimen to prevent rejection, which has its own significant downsides.

Palliative care and hospice

Without transplantation, heart failure caused by ischemic heart disease is not reversible, and cardiac function typically deteriorates with time. (In particular, diastolic function

worsens as a function of age even in individuals without ischemic heart disease.) The growing number of patients with Stage D heart failure (intractable symptoms of fatigue, shortness of breath or chest pain at rest despite optimal medical therapy) should be considered for palliative care or hospice, according to American College of Cardiology/American Heart Association guidelines.

Prognosis

Prognosis in heart failure can be assessed in multiple ways including clinical prediction rules and cardiopulmonary exercise testing. Clinical prediction rules use a composite of clinical factors such as lab tests and blood pressure to estimate prognosis. Among several clinical prediction rules for prognosing acute heart failure, the 'EFFECT rule' slightly outperformed other rules in stratifying patients and identifying those at low risk of death during hospitalization or within 30 days. Easy methods for identifying low risk patients are:

- ADHERE Tree rule indicates that patients with blood urea nitrogen < 43 mg/dl and systolic blood pressure at least 115 mm Hg have less than 10% chance of inpatient death or complications.
- BWH rule indicates that patients with systolic blood pressure over 90 mm Hg, respiratory rate of 30 or less breaths per minute, serum sodium over 135 mmol/L, no new ST-T wave changes have less than 10% chance of inpatient death or complications.

A very important method for assessing prognosis in advanced heart failure patients is cardiopulmonary exercise testing (CPX testing). CPX testing is usually required prior to heart transplantation as an indicator of prognosis. Cardiopulmonary exercise testing involves measurement of exhaled oxygen and carbon dioxide during exercise. The peak oxygen consumption (VO2 max) is used as an indicator of prognosis. As a general rule, a VO2 max less than 12-14 cc/kg/min indicates a poor survival and suggests that the patient may be a candidate for a heart transplant. Patients with a VO2 max<10 cc/kg/min have clearly poorer prognosis. The most recent International Society for Heart and Lung Transplantation (ISHLT) guidelines also suggest two other parameters that can be used for evaluation of prognosis in advanced heart failure, the heart failure survival score and the use of a criterion of VE/VCO2 slope > 35 from the CPX test. The heart failure survival score is a score calculated using a combination of clinical predictors and the VO2 max from the cardiopulmonary exercise test.

Epidemiology

Heart failure is the leading cause of hospitalization in people older than 65. In developed countries, the mean age of patients with heart failure is 75 years old. In developing countries, two to three percent of the population suffers from heart failure, but in those 70 to 80 years old, it occurs in 20—30 percent.

Heart failure affects close to 5 million people in the USA and each year close to 500,000 new cases are diagnosed. What is of more concern is that more than 50% of patients seek re-admission within 6 months after treatment and the average duration of hospital stay is 6 days.

In tropical countries, the most common cause of HF is valvular heart disease or some type of cardiomyopathy. Moreover as underdeveloped countries become more affluent, there has also been an increase in diabetes, hypertension and obesity which has resulted in heart failure.

In USA, HF is much higher in African Americans, Hispanics, Native Americans and recent immigrants from the eastern bloc countries like Russia. This high prevalence in these ethnic populations has been linked to high incidence of diabetes and hypertension. In many new immigrants to the USA the high prevalence of heart failure has largely been attributed to lack of preventive health care or substandard treatment.

Gender

Both men and women have similar incidence of HF. However, there are distinct differences between the two genders.

- Women generally develop heart failure after menopause.
- Women tend to become more depressed than men following diagnosis.
- Women have similar symptoms but the intensity is more pronounced.
- Women usually survive a lot longer with heart failure than men.

Race

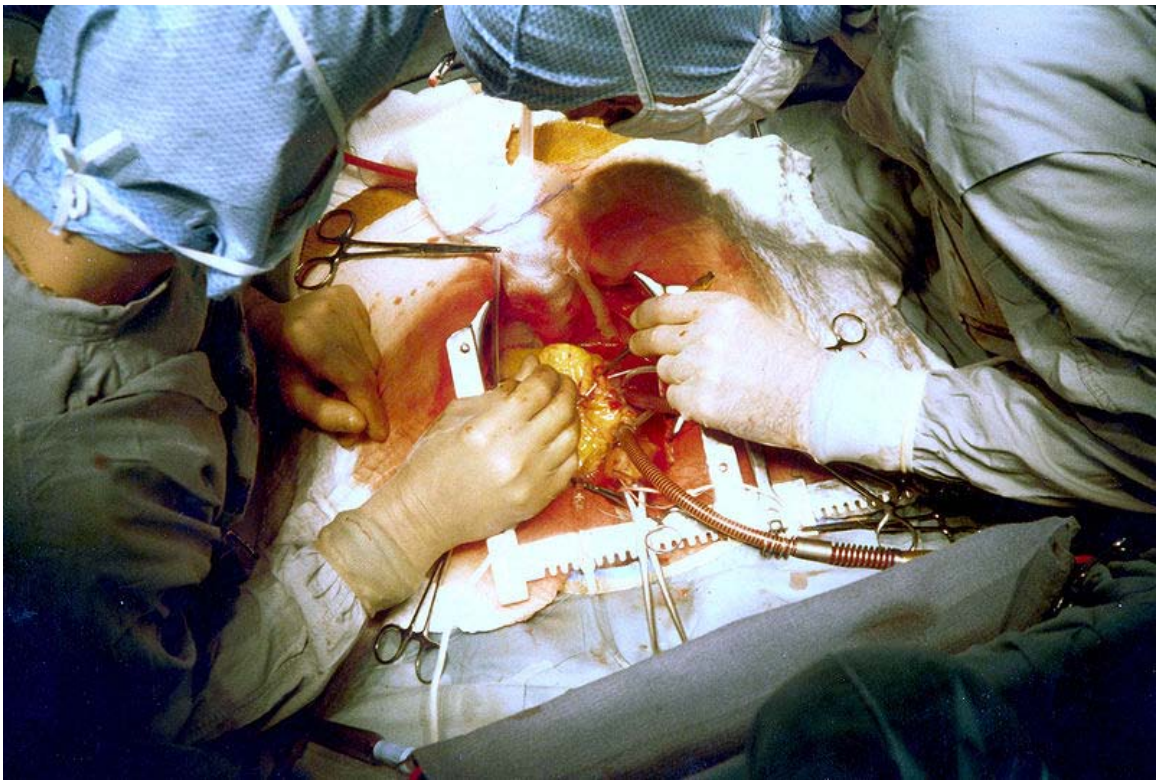
New information suggests that elements of heart failure in African Americans and Caucasians may be different and therapy for heart failure has different efficacies depending on racial, ethnic, and genetic backgrounds.

Age

Heart failure basically means that the heart muscles have become weak and do not function as normal. Heart failure is a progressive medical disorder. As the heart gets weaker, symptoms and signs become prominent. Heart failure can affect the entire heart or only the right or left side. In the majority of cases, both sides of the heart are affected. HF can occur at any age depending on the cause. In general heart failure does increase with age.

Chapter 8

Cardiac Surgery



Two cardiac surgeons performing a cardiac surgery known as coronary artery bypass surgery. Note the use of a steel retractor used to forcefully maintain the exposure of the patient's heart.

Cardiovascular surgery is a surgery on the heart and/or great vessels performed by cardiac surgeons. Frequently, it is done to treat complications of ischemic heart disease (for example, coronary artery bypass grafting), correct congenital heart disease, or treat valvular heart disease caused by various causes including endocarditis. It also includes heart transplantation.

History

The earliest operations on the pericardium (the sac that surrounds the heart) took place in the 19th century and were performed by, Francisco Romero Dominique Jean Larrey, Henry Dalton, and Daniel Hale Williams. The first surgery on the heart itself was performed by Norwegian surgeon Axel Cappelen on the 4th of September 1895 at Rikshospitalet in Kristiania, now Oslo. He ligated a bleeding coronary artery in a 24 year old man who had been stabbed in the left axillae and was in deep shock upon arrival. Access was through a left thoracotomy. The patient awoke and seemed fine for 24hrs, but became ill with increasing temperature and he ultimately died from what the post mortem proved to be mediastinitis on the 3rd postoperative day. The first successful surgery of the heart, performed without any complications, was by Dr. Ludwig Rehn of Frankfurt, Germany, who repaired a stab wound to the right ventricle on September 7, 1896.

Surgery in great vessels (aortic coarctation repair, Blalock-Taussig shunt creation, closure of patent ductus arteriosus), became common after the turn of the century and falls in the domain of cardiac surgery, but technically cannot be considered heart surgery.

Heart Malformations – Early Approaches

In 1925 operations on the valves of the heart were unknown. Henry Souttar operated successfully on a young woman with mitral stenosis. He made an opening in the appendage of the left atrium and inserted a finger into this chamber in order to palpate and explore the damaged mitral valve. The patient survived for several years but Souttar's physician colleagues at that time decided the procedure was not justified and he could not continue.

Cardiac surgery changed significantly after World War II. In 1948 four surgeons carried out successful operations for mitral stenosis resulting from rheumatic fever. Horace Smithy (1914–1948) of Charlotte, revived an operation due to Dr Dwight Harken of the Peter Bent Brigham Hospital using a punch to remove a portion of the mitral valve. Charles Bailey (1910–1993) at the Hahnemann Hospital, Philadelphia, Dwight Harken in Boston and Russell Brock at Guy's Hospital all adopted Souttar's method. All these men started work independently of each other, within a few months. This time Souttar's technique was widely adopted although there were modifications.

In 1947 Thomas Holmes Sellors (1902–1987) of the Middlesex Hospital operated on a Fallot's Tetralogy patient with pulmonary stenosis and successfully divided the stenosed pulmonary valve. In 1948, Russell Brock, probably unaware of Sellor's work, used a specially designed dilator in three cases of pulmonary stenosis. Later in 1948 he designed a punch to resect the infundibular muscle stenosis which is often associated with Fallot's Tetralogy. Many thousands of these "blind" operations were performed until the introduction of heart bypass made direct surgery on valves possible.

Open heart surgery

This is a surgery in which the patient's heart is opened and surgery is performed on the internal structures of the heart.

It was soon discovered by Dr. Wilfred G. Bigelow of the University of Toronto that the repair of intracardiac pathologies was better done with a bloodless and motionless environment, which means that the heart should be stopped and drained of blood. The first successful intracardiac correction of a congenital heart defect using hypothermia was performed by Dr. C. Walton Lillehei and Dr. F. John Lewis at the University of Minnesota on September 2, 1952. The following year, Soviet surgeon Aleksandr Aleksandrovich Vishnevskiy conducted the first cardiac surgery under local anesthesia.

Surgeons realized the limitations of hypothermia – complex intracardiac repairs take more time and the patient needs blood flow to the body (and particularly the brain); the patient needs the function of the heart and lungs provided by an artificial method, hence the term cardiopulmonary bypass. Dr. John Heysham Gibbon at Jefferson Medical School in Philadelphia reported in 1953 the first successful use of extracorporeal circulation by means of an oxygenator, but he abandoned the method, disappointed by subsequent failures. In 1954 Dr. Lillehei realized a successful series of operations with the controlled cross-circulation technique in which the patient's mother or father was used as a 'heart-lung machine'. Dr. John W. Kirklin at the Mayo Clinic in Rochester, Minnesota started using a Gibbon type pump-oxygenator in a series of successful operations, and was soon followed by surgeons in various parts of the world.

Dr. Nazih Zuhdi worked for four years under Drs. Clarence Dennis, Karl Karlson, and Charles Fries, who built an early pump-oxygenator. Zuhdi and Fries worked on several designs and re-designs of Dennis' earlier model from 1952–1956 at the Brooklyn Center. Zuhdi then went to work with Dr. C. Walton Lillehei at the University of Minnesota. Lillehei had designed his own version of a cross-circulation machine, which came to become known as the DeWall-Lillehei heart-lung machine. Zuhdi worked on perfusion and blood flow trying to solve the problem of air bubbles while bypassing the heart so the heart could be stopped for the operation. Zuhdi moved to Oklahoma City, OK, in 1957, and began working at the Oklahoma University College. Zuhdi, the heart surgeon, teamed up with Dr. Allen Greer, a lung surgeon and Dr. John Carey, forming a three man open heart surgery team. With the advent of Dr. Zuhdi's heart-lung machine which was modified in size, being much smaller than the DeWall-Lillehei heart-lung machine, and with other modifications, reduced the need for blood down to a minimal amount, and the cost of the equipment down to $500.00 and also reduced the prep time from two hours to 20 minutes. Dr. Zuhdi performed the first Total Intentional Hemodilution open heart surgery on Terry Gene Nix, age 7, on February 25, 1960, at Mercy Hospital, Oklahoma City, OK. The operation was a success; however, Nix died three years later in 1963. In March, 1961, Zuhdi, Carey, and Greer, performed open heart surgery on a child, age 3½, using the Total Intentional Hemodilution machine, with success. That patient is still alive.

In 1985 Dr. Zuhdi performed Oklahoma's first successful heart transplant on Nancy Rogers at Baptist Hospital. The transplant was successful, but Rogers, a cancer sufferer, died from an infection 54 days after surgery.

Modern beating-heart surgery

Since the 1990s, surgeons have begun to perform "off-pump bypass surgery" – coronary artery bypass surgery without the aforementioned cardiopulmonary bypass. In these operations, the heart is beating during surgery, but is stabilized to provide an almost still work area. Some researchers believe this approach results in fewer post-operative complications (such as postperfusion syndrome) and better overall results (study results are controversial as of 2007, the surgeon's preference and hospital results still play a major role).

Minimally invasive surgery

A new form of heart surgery that has grown in popularity is robot-assisted heart surgery. This is where a machine is used to perform surgery while being controlled by the heart surgeon. The main advantage to this is the size of the incision made in the patient. Instead of an incision being at least big enough for the surgeon to put his hands inside, it does not have to be bigger than 3 small holes for the robot's much smaller hands to get through.

Pediatric Cardiovascular Surgery

Pediatric Cardiovascular Surgery is surgery of the heart of children. Russell M. Nelson performed the first successful pediatric cardiac operation at the Salt Lake General Hospital in March 1956, a total repair of tetralogy of Fallot in a four-year-old girl.

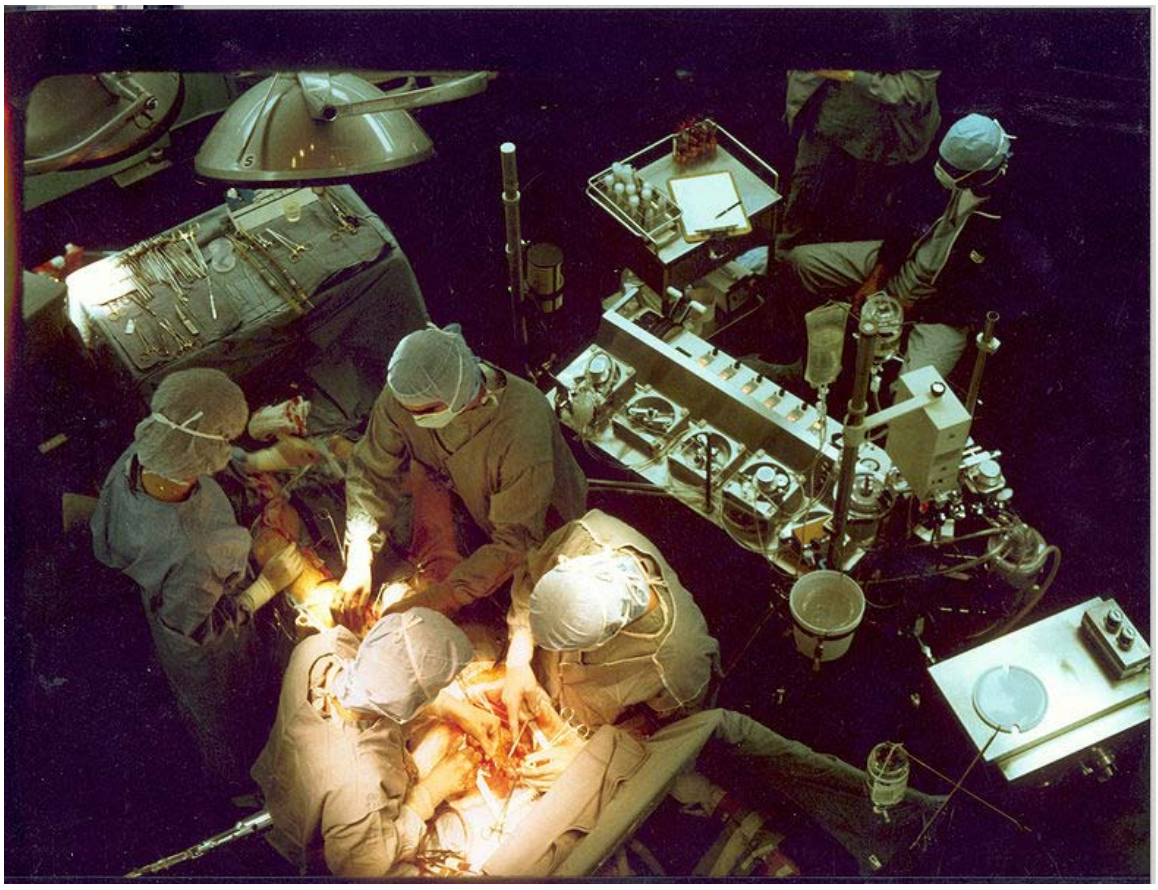
Risks

The development of cardiac surgery and cardiopulmonary bypass techniques has reduced the mortality rates of these surgeries to relatively low ranks. For instance, repairs of congenital heart defects are currently estimated to have 4–6% mortality rates.

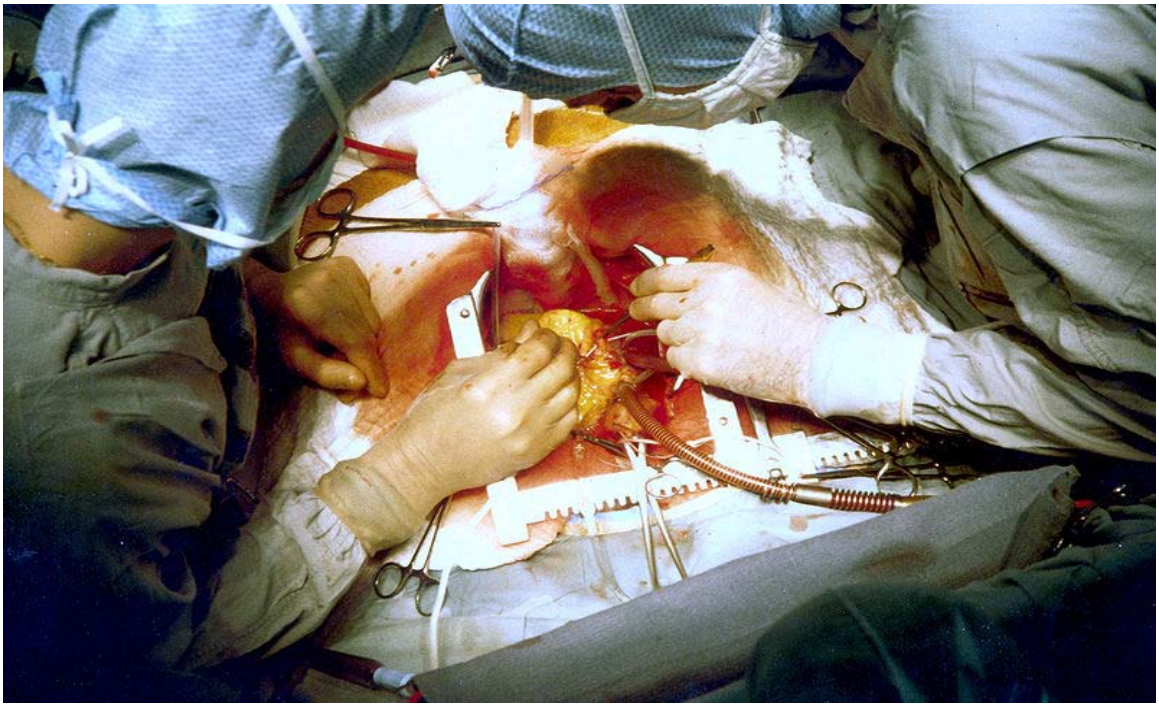
A major concern with cardiac surgery is the incidence of neurological damage. Stroke occurs in 2–3% of all people undergoing cardiac surgery, and is higher in patients at risk for stroke. A more subtle constellation of neurocognitive deficits attributed to cardiopulmonary bypass is known as postperfusion syndrome (sometimes called 'pumphead'). The symptoms of postperfusion syndrome were initially felt to be permanent, but were shown to be transient with no permanent neurological impairment.

Chapter 9

Coronary Artery Bypass Surgery



Early in a **coronary artery bypass surgery** during vein harvesting from the legs (left of image) and the establishment of bypass (placement of the aortic cannula) (bottom of image). The perfusionist and heart-lung machine (HLM) are on the upper right. The patient's head (not seen) is at the bottom.



Coronary artery bypass surgery during mobilization (freeing) of the right coronary artery from its surrounding tissue, adipose tissue (yellow). The tube visible at the bottom is the aortic cannula (returns blood from the HLM). The tube above it (obscured by the surgeon on the right) is the venous cannula (receives blood from the body). The patient's heart is stopped and the aorta is cross-clamped. The patient's head (not seen) is at the bottom.

Coronary artery bypass surgery, also **coronary artery bypass graft (CABG pronounced cabbage) surgery**, and colloquially **heart bypass** or **bypass surgery** is a surgical procedure performed to relieve angina and reduce the risk of death from coronary artery disease. Arteries or veins from elsewhere in the patient's body are grafted to the coronary arteries to bypass atherosclerotic narrowings and improve the blood supply to the coronary circulation supplying the myocardium (heart muscle). This surgery is usually performed with the heart stopped, necessitating the usage of cardiopulmonary bypass; techniques are available to perform CABG on a beating heart, so-called "off-pump" surgery.

History

The first coronary artery bypass surgery was performed in the United States on May 2, 1960, at the Albert Einstein College of Medicine-Bronx Municipal Hospital Center by a team led by Dr. Robert Goetz and the thoracic surgeon, Dr. Michael Rohman with the assistance of Dr. Jordan Haller and Dr. Ronald Dee. In this technique the vessels are held together with circumferential ligatures over an inserted metal ring. The internal mammary artery was used as the donor vessel and was anastomosed to the right coronary artery. The actual anastomosis with the Rosenbach ring took fifteen seconds and did not require

Cardio-Pulmonary bypass. The disadvantage of using the internal mammary artery was that, at autopsy nine months later, the anastomosis was open, but an atheromatous plaque had occluded the origin of the internal mammary that was used for the bypass.

Russian cardiac surgeon, Dr. Vasilii Kolesov, performed arguably the first successful internal mammary artery–coronary artery anastomosis in 1964.

However, Goetz's has been cited by others, including Kolesov, as the first successful human coronary artery bypass. Goetz's case has frequently been overlooked. Confusion has persisted for over 40 years and seems to be due to the absence of a full report and to misunderstanding about the type of anastomosis that was created. The anastomosis was intima-to-intima, with the vessels held together with circumferential ligatures over a specially designed metal ring. Kolesov did the first successful coronary bypass using a standard suture technique in 1964, and over the next five years he performed 33 sutured and mechanically stapled anastomoses in St. Petersburg, Russia.

Dr. René Favaloro, an Argentine surgeon, achieved a physiologic approach in the surgical management of coronary artery disease—the bypass grafting procedure—at the Cleveland Clinic in May 1967. His new technique used a saphenous vein autograft to replace a stenotic segment of the right coronary artery. Later, he successfully used the saphenous vein as a bypassing channel, which has become the typical bypass graft technique we know today. Soon Dr. Dudley Johnson extended the bypass to include left coronary arterial systems. In 1968, Doctors Charles Bailey, Teruo Hirose and George Green used the internal mammary artery instead of the saphenous vein for the grafting.

Terminology

There are many variations on terminology, in which one or more of "artery", "bypass" or "graft" is left out. The most frequently used acronym for this type of surgery is **CABG** (pronounced 'cabbage'), pluralized as **CABGs** (pronounced 'cabbages'). More recently the term **aortocoronary bypass (ACB)** has come into popular use. **CAGS** (Coronary Artery Graft Surgery, pronounced phonetically) should not be confused with Coronary Angiography (CAG).

Arteriosclerosis is a common arterial disorder characterized by thickening, loss of elasticity, and calcification of arterial walls, resulting in a decreased blood supply.

Atherosclerosis is a common arterial disorder characterized by yellowish plaques of cholesterol, lipids, and cellular debris in the inner layer of the walls of large and medium-sized arteries.

Number of bypasses

The terms *single bypass*, *double bypass*, *triple bypass*, *quadruple bypass* and *quintuple bypass* refer to the number of coronary arteries bypassed in the procedure. In other words, a double bypass means two coronary arteries are bypassed (e.g. the left anterior

descending (LAD) coronary artery and right coronary artery (RCA)); a triple bypass means three vessels are bypassed (e.g. LAD, RCA, left circumflex artery (LCX)); a quadruple bypass means four vessels are bypassed (e.g. LAD, RCA, LCX, first diagonal artery of the LAD) while quintuple means five. Bypass of more than four coronary arteries is uncommon.

A greater number of bypasses does not imply a person is "more sick", nor does a lesser number imply a person is "healthier." A person with a large amount of coronary artery disease (CAD) may receive fewer bypass grafts owing to the lack of suitable "target" vessels. A coronary artery may be unsuitable for bypass grafting if it is small (< 1 mm or < 1.5 mm depending on surgeon preference), heavily calcified (meaning the artery does not have a section free of CAD) or intramyocardial (the coronary artery is located within the heart muscle rather than on the surface of the heart). Similarly, a person with a single stenosis ("narrowing") of the left main coronary artery requires only two bypasses (to the LAD and the LCX). However, a left main lesion places a person at the highest risk for death from a cardiac cause.

The surgeon reviews the coronary angiogram prior to surgery and identifies the lesions (or "blockages") in the coronary arteries. The surgeon will estimate the number of bypass grafts prior to surgery, but the final decision is made in the operating room upon examination of the heart.

Indications for CABG

Several alternative treatments for coronary artery disease exist. They include:

- Medical management (anti-anginal medications plus statins, antihypertensives, smoking cessation, tight blood sugar control in diabetics)
- Percutaneous coronary intervention (PCI)

Both PCI and CABG are more effective than medical management at relieving symptoms, (e.g. angina, dyspnea, fatigue). CABG is superior to PCI for some patients with multivessel CAD

The Surgery or Stent (SoS) trial was a randomized controlled trial that compared CABG to PCI with bare-metal stents. The SoS trial demonstrated CABG is superior to PCI in multivessel coronary disease.

The SYNTAX trial was a randomized controlled trial of 1800 patients with multivessel coronary disease, comparing CABG versus PCI using drug-eluting stents (DES). The study found that rates of major adverse cardiac or cerebrovascular events at 12 months were significantly higher in the DES group (17.8% versus 12.4% for CABG; P=0.002). This was primarily driven by higher need for repeat revascularization procedures in the PCI group with no difference in repeat infarctions or survival. Higher rates of strokes were seen in the CABG group.

The FREEDOM (Future Revascularization Evaluation in Patients With Diabetes Mellitus—Optimal Management of Multivessel Disease) trial will compare CABG and DES in patients with diabetes. The registries of the nonrandomized patients screened for these trials may provide as much robust data regarding revascularization outcomes as the randomized analysis.

A study comparing the outcomes of all patients in New York state treated with CABG or percutaneous coronary intervention (PCI) demonstrated CABG was superior to PCI with DES in multivessel (more than one diseased artery) coronary artery disease (CAD). Patients treated with CABG had lower rates of death and of death or myocardial infarction than treatment with a coronary stent. Patients undergoing CABG also had lower rates of repeat revascularization. The New York State registry included all patients undergoing revascularization for coronary artery disease, but was not a randomized trial, and so may have reflected other factors besides the method of coronary revascularization.

The 2004 ACC/AHA CABG guidelines state CABG is the preferred treatment for:

- Disease of the left main coronary artery (LMCA).
- Disease of all three coronary vessels (LAD, LCX and RCA).
- Diffuse disease not amenable to treatment with a PCI.

The 2005 ACC/AHA guidelines further state: CABG is the likely the preferred treatment with other high-risk patients such as those with severe ventricular dysfunction (i.e. low ejection fraction), or diabetes mellitus.

Prognosis

Prognosis following CABG depends on a variety of factors, and successful grafts typically last 8–15 years. In general, CABG improves the chances of survival of patients who are at high risk (generally triple or higher bypass), though statistically after about five years the difference in survival rate between those who have had surgery and those treated by drug therapy diminishes. Age at the time of CABG is critical to the prognosis, younger patients with no complicating diseases doing better, while older patients can usually be expected to suffer further blockage of the coronary arteries.

Controversy

The value of coronary artery bypass surgery in rescuing someone having a heart attack (by immediately alleviating an obstruction) is clearly defined in multiple studies, but studies have failed to find benefit for bypass surgery vs. medical therapy in stable angina patients. The artery bypass can temporarily alleviate chest pain, but does not increase longevity. The "vast majority of heart attacks do not originate with obstructions that narrow arteries".

Loss of mental function is a common complication of bypass surgery, and should influence procedure cost benefit considerations. One published study using MRI imaging just after coronary bypass surgery found significant brain damage in 51% of patients.

Several factors may contribute to immediate cognitive decline. The heart-lung blood circulation system and the surgery itself release a variety of debris, including bits of blood cells, tubing, and plaques. For example, when surgeons clamp and connect the aorta to tubing, resulting emboli block blood flow and cause mini strokes. Other heart surgery factors related to mental damage may be events of hypoxia, high or low body temperature, abnormal blood pressure, irregular heart rhythms, and fever after surgery.

A safer, more permanent and successful way to prevent heart attacks in patients at high risk is to give up smoking, exercise, eat a more whole plant food based diet and take "drugs to get blood pressure under control, drive cholesterol levels down and prevent blood clotting". Longer term, behavioral and medication treatment may be the only way to avoid vascular related loss of mental function.

Procedure (Simplified)

1. The patient is brought to the operating room and moved on to the operating table.
2. An anaesthetist places a variety of intravenous lines and injects a painkilling agent (usually fentanyl) followed within minutes by an induction agent (usually propofol) to render the patient unconscious.
3. An endotracheal tube is inserted and secured by the anaesthetist or assistant (e.g. respiratory therapist or nurse anaesthetist) and mechanical ventilation is started. General anaesthesia is maintained by a continuous very slow injection of Propofol.
4. The chest is opened via a median sternotomy and the heart is examined by the surgeon.
5. The bypass grafts are harvested - frequent conduits are the internal thoracic arteries, radial arteries and saphenous veins. When harvesting is done, the patient is given heparin to prevent the blood from clotting.
6. In the case of "off-pump" surgery, the surgeon places devices to stabilize the heart.
7. If the case is "on-pump", the surgeon sutures cannulae into the heart and instructs the perfusionist to start cardiopulmonary bypass (CPB). Once CPB is established, the surgeon places the aortic cross-clamp across the aorta and instructs the perfusionist to deliver cardioplegia (a special Potassium-mixture, cooled) to stop the heart and slow its metabolism. Usually the patient's machine-circulated blood is cooled to around 84 °F (29 °C)
8. One end of each graft is sewn on to the coronary arteries beyond the blockages and the other end is attached to the aorta.
9. The heart is restarted; or in "off-pump" surgery, the stabilizing devices are removed. In cases where the aorta is partially occluded by a C-shaped clamp, the heart is restarted and suturing of the grafts to the aorta is done in this partially occluded section of the aorta while the heart is beating.

10. Protamine is given to reverse the effects of heparin.
11. The sternum is wired together and the incisions are sutured closed.
12. The patient is moved to the intensive care unit (ICU) to recover. After awakening and stabilizing in the ICU (approximately one day), the person is transferred to the cardiac surgery ward until ready to go home (approximately four days).

Minimally Invasive CABG

Alternate methods of minimally invasive coronary artery bypass surgery have been developed. Off-pump coronary artery bypass (OPCAB) is a technique of performing bypass surgery without the use of cardiopulmonary bypass (the heart-lung machine). Further refinements to OPCAB have resulted in minimally invasive direct coronary artery bypass surgery (MIDCAB), a technique of performing bypass surgery through a 5 to 10 cm incision.

Conduits used for bypass

The choice of conduits is highly dependent upon the particular surgeon and institution. Typically, the left internal thoracic artery (LITA) (previously referred to as *left internal mammary artery* or *LIMA*) is grafted to the left anterior descending artery and a combination of other arteries and veins is used for other coronary arteries. The right internal thoracic artery (RITA), the great saphenous vein from the leg and the radial artery from the forearm are frequently used. The right gastroepiploic artery from the stomach is infrequently used given the difficult mobilization from the abdomen.

Graft patency

Grafts can become diseased and may occlude in the months to years after bypass surgery is performed. Patency is a term used to describe the chance that a graft remain open. A graft is considered patent if there is flow through the graft without any significant (>70% diameter) stenosis in the graft.

Graft patency is dependent on a number of factors, including the type of graft used (internal thoracic artery, radial artery, or great saphenous vein), the size or the coronary artery that the graft is anastomosed with, and, of course, the skill of the surgeon(s) performing the procedure. Arterial grafts (e.g. LITA, radial) are far more sensitive to rough handling than the saphenous veins and may go into spasm if handled improperly.

Generally the best patency rates are achieved with the in-situ left internal thoracic artery (the proximal end is left connected to the subclavian artery) with the distal end being anastomosed with the coronary artery (typically the left anterior descending artery or a diagonal branch artery). Lesser patency rates can be expected with radial artery grafts and "free" internal thoracic artery grafts (where the proximal end of the thoracic artery is excised from its origin from the subclavian artery and re-anastomosed with the ascending aorta). Saphenous vein grafts have worse patency rates, but are more available, as the

patients can have multiple segments of the saphenous vein used to bypass different arteries.

Veins that are used either have their valves removed or are turned around so that the valves in them do not occlude blood flow in the graft. LITA grafts are longer-lasting than vein grafts, both because the artery is more robust than a vein and because, being already connected to the arterial tree, the LITA need only be grafted at one end. The LITA is usually grafted to the left anterior descending coronary artery (LAD) because of its superior long-term patency when compared to saphenous vein grafts.

Sternal precautions

Patients undergoing coronary artery bypass surgery will have to avoid certain things for eight to 12 weeks to reduce the risk of opening the incision. These are called sternal precautions. First, patients need to avoid using their arms excessively, such as pushing themselves out of a chair or reaching back before sitting down. To avoid this, patients are encouraged to build up momentum by rocking several times in their chair before standing up. Second, patients should avoid lifting anything in excess of 5–10 pounds. A gallon (U.S.) of milk weighs approximately 8.5 pounds, and is a good reference point for weight limitations. Finally, patients should avoid overhead activities with their hands, such as reaching for sweaters from the top shelf of a closet or reaching for plates or cups from the cupboard.

Complications

People undergoing coronary artery bypass are at risk for the same complications as any surgery, plus some risks more common with or unique to CABG.

CABG associated

- Postperfusion syndrome (pumphead), a transient neurocognitive impairment associated with cardiopulmonary bypass. Some research shows the incidence is initially decreased by off-pump coronary artery bypass, but with no difference beyond three months after surgery. A neurocognitive decline over time has been demonstrated in people with coronary artery disease regardless of treatment (OPCAB, conventional CABG or medical management). However, a 2009 research study suggests that longer term (over 5 years) cognitive decline is not caused by CABG but is rather a consequence of vascular disease.
- Nonunion of the sternum; internal thoracic artery harvesting devascularizes the sternum increasing risk.
- Myocardial infarction due to embolism, hypoperfusion, or graft failure.
- Late graft stenosis, particularly of saphenous vein grafts due to atherosclerosis causing recurrent angina or myocardial infarction.
- Acute renal failure due to embolism or hypoperfusion.
- Stroke, secondary to embolism or hypoperfusion.
- Vasoplegic syndrome, secondary to cardiopulmonary bypass and hypothermia

- Grafts last 8 – 15 years, and then need to be replaced.

General surgical

- Infection at incision sites or sepsis.
- Deep vein thrombosis (DVT)
- Anesthetic complications such as malignant hyperthermia.
- Keloid scarring
- Chronic pain at incision sites
- Chronic stress related illnesses
- Death

Chapter 10

Heart Valve Repair and Mitral Valve Repair

Heart valve repair

Heart valve repair is a surgical technique used to fix defects in heart valves in valvular heart diseases, and provides an alternative to valve replacement. Without further specification, it refers to **native heart valve repair**, rather than repair of an artificial heart valve.

General techniques

Valvuloplasty

Valvuloplasty is the widening of a stenotic valve using a balloon catheter. Types include:

- Aortic valvuloplasty in repair of a stenotic aortic valve
- Mitral valvuloplasty in the correction of an uncomplicated mitral stenosis

Valvulotomy

Commissurotomy of cardiac valves is called *valvulotomy*, and consists of making one or more incisions at the edges of the commissure formed between two or three valves, in order to relieve constriction such as occurs in valvular stenosis, especially mitral valve stenosis.

By valve

Mitral valve repair

Mitral valve repair is mainly used to treat stenosis (narrowing) or regurgitation (leakage) of the mitral valve.

Aortic valve repair

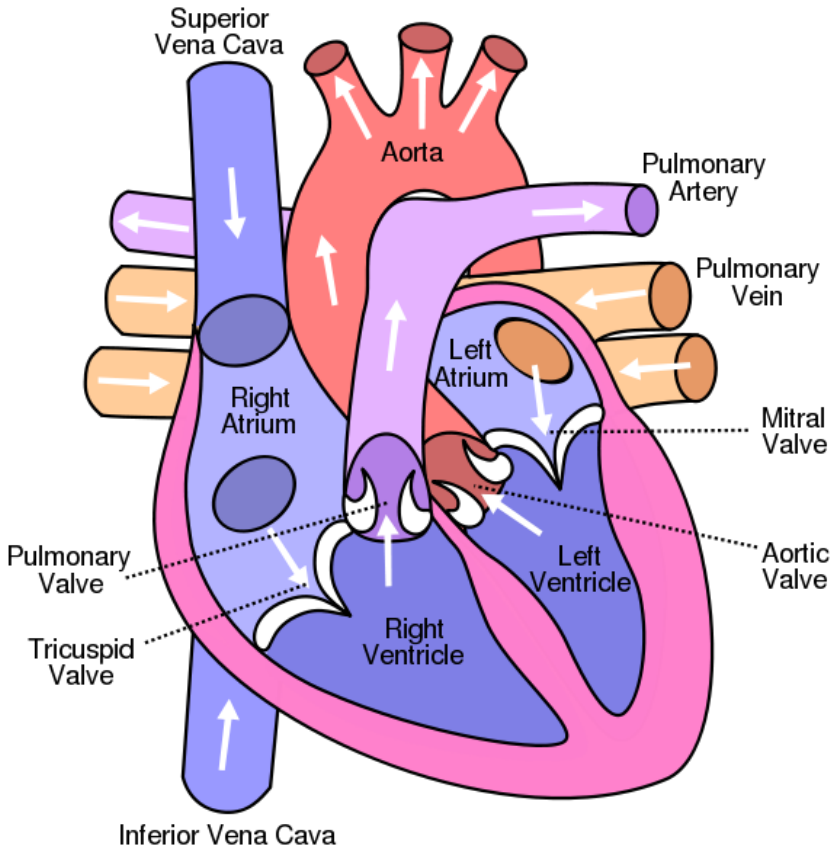
Aortic valve repair is a surgical procedure used to correct some aortic valve disorders as an alternative to aortic valve replacement. Aortic valve repair is performed less often and is more technically difficult than mitral valve repair. There are two surgical techniques of aortic-valve repair:

- The Reimplantation-Technique (David-Procedure)
- The Remodeling-Technique (Yacoub-Procedure)

Tricuspid valve repair

Tricuspid valve repair is used to correct tricuspid regurgitation.

Mitral valve repair



Anterior (frontal) view of the opened heart. White arrows indicate normal blood flow. (Mitral valve labeled at center right.)

Mitral valve repair is a cardiac surgery procedure performed by cardiac surgeons to treat stenosis (narrowing) or regurgitation (leakage) of the mitral valve. The mitral valve is the "inflow valve" for the left side of the heart. Blood flows from the lungs, where it picks up oxygen, through the pulmonary veins, to the left atrium of the heart. After the left atrium fills with blood, the mitral valve allows blood to flow from the left atrium into the heart's main pumping chamber called the left ventricle. It then closes to keep blood from leaking back into the left atrium or lungs when the ventricle contracts (squeezes) to push blood out to the body. It has two flaps, or leaflets.

The techniques of mitral valve repair include inserting a cloth-covered ring around the valve to bring the leaflets into contact with each other (annuloplasty), removal of redundant/loose segments of the leaflets (quadrangular resection), re-suspension of the leaflets with artificial (Gore-Tex) cords. More recently the Alfieri stitch (or "bow-tie") has been adapted to allow percutaneous repair in select patients.

Procedures on the mitral valve usually require a median sternotomy, but advances in non-invasive methods (such as keyhole surgery) allow surgery without a sternotomy (and resulting pain and scar). Minimally invasive mitral valve surgery is much more technically demanding and may involve higher risk.

Occasionally, the mitral valve is abnormal from birth (congenital). More often the mitral valve becomes abnormal with age (degenerative) or as a result of rheumatic fever. In rare instances the mitral valve can be destroyed by infection or a bacterial endocarditis. Mitral regurgitation may also occur as a result of ischemic heart disease (coronary artery disease).

A history of mitral valve repair

In 1923 Dr. Elliott Cutler of the Peter Bent Brigham Hospital performed the world’s first successful heart valve surgery - a mitral valve *repair*. The patient was a 12-year-old girl with rheumatic mitral stenosis.

The development of the heart-lung machine in the 1950s paved the way for *replacement* of the mitral valve with an artificial valve in the 1960s. For decades after, mitral valve replacement was the only surgical option for patients with a severely diseased mitral valve. However, there are some significant downsides to an prosthetic mitral valve. Infection of the valve can occur, which is dangerous and difficult to treat. Patients with mechanical heart valves are required to take blood thinners for the rest of their lives which presents a risk of bleeding complications. The artificial mitral valve has an elevated risk of stroke. Finally, artificial tissue valves will wear out - on average lasting between 10 and 15 years, requiring further surgery at an advanced age.

In the past two decades, some surgeons have embraced surgical techniques to repair the damaged native valve, rather than replace it. These techniques were pioneered by a French heart surgeon, Dr. Alain F. Carpentier. A repair still involves major cardiac surgery but for many patients presents the significant advantage of avoiding blood

thinners and may provide a more durable result. Not all damaged valves are suitable for repair; in some, the state of valve disease is too advanced and replacement is necessary. Often, a surgeon must decide during the operation itself whether a *repair* or *replacement* is the best course of action.

There has been great debate about timing of surgery in patients with asymptomatic mitral valve regurgitation. There are minimally invasive (port access) options available pioneered by Hugo Vanerman in Belgium. These methods may be safer, and allow the patient to return to their normal activity much sooner than the standard approach. Robotic mitral valve repair operations are also being tested at some medical centers.

In the 2000s there have been several trials of a newer strategy of mitral valve repair that does not require major cardiac surgery. Through a catheter inserted in the groin, the valve leaflets are clipped together. This technique - percutaneous mitral valve repair - remains under trial, is very specialized and is only available at a select number of hospitals worldwide.

Chapter 11

Aortic Valve Replacement

Aortic valve replacement is a cardiac surgery procedure in which a patient's failing aortic valve is replaced with an alternate healthy valve. The aortic valve can be affected by a range of diseases; the valve can either become leaky (aortic insufficiency / regurgitation) or partially blocked (aortic stenosis). Aortic valve replacement is open heart surgery. A new catheter-based approach (percutaneous aortic valve replacement or PAVR), which obviates the need for open heart surgery, is being used in some places of the world and is being tested in clinical trials in the United States and Europe.

Types of heart valves

There are two basic types of artificial heart valve: mechanical valves and tissue valves.

Tissue valves

Tissue heart valves are usually made from animal tissues, either animal heart valve tissue or animal pericardial tissue. The tissue is treated to prevent rejection and calcification.

There are alternatives to animal tissue valves. In some cases a homograft - a human aortic valve -- can be implanted. Homograft valves are donated by patients and harvested after the patient dies. The durability of homograft valves is comparable to porcine and bovine tissue valves. Another procedure for aortic valve replacement is the Ross procedure (or pulmonary autograft). In a Ross procedure, the aortic valve is removed and replaced with the patient's own pulmonary valve. A pulmonary homograft (pulmonary valve taken from a cadaver) is then used to replace the patient's own pulmonary valve. This procedure was first used in 1967 and is used primarily in children, because the procedure allows the patient's own pulmonary valve (now in the aortic position) to grow with the child.

Mechanical valves

Mechanical valves are designed to outlast the patient, and have typically been stress-tested to last several hundred years. Although mechanical valves are long-lasting and generally only one surgery is needed, there is an increased risk of blood clots forming with mechanical valves. As a result, mechanical valve recipients must generally take anti-coagulant (blood thinning) drugs such as warfarin for the rest of their lives, which makes

the patient more prone to bleeding. Recent advances in mechanical valve materials (pyrolytic carbon) have the promise of reducing and possibly eliminating the need for anti-coagulants. One such valve is the On-X. The material used resists the formation of blood clots. Research is on-going. Warfarin is the traditional drug used as an anti-coagulant. There is a study underway into the use of Plavix instead of Warfarin which will significantly simplify blood clotting control. Estimated Study Completion Date: March 2015

Valve selection

Tissue valves tend to wear out faster with increased flow demands - such as with a more active (typically younger) person. Tissue valves typically last 10-15 years in less active (typically elderly) patients, but wear out faster in younger patients. When a tissue valve wears out and needs replacement, the person must undergo another valve replacement surgery. For this reason, younger patients are often recommended mechanical valves to prevent the increased risk (and inconvenience) of another valve replacement. There is a promising new valve replacement procedure called a Trans-catheter Aortic Valve (TCAV). It is currently only available for high risk patients and still in the research stage. In the future it may be possible for the recipient of a prosthetic tissue valve to have a much less invasive surgery performed to insert a new valve once the replacement valve wears out. A new valve is compressed and positioned orthoscopically and then it is expanded within the first replacement valve forcing it open and allowing the TCAV to operate. The current expected life span of the TCAV is approximately 10 -15 years. It is also expected that yet another TCAV can be implanted within the first TCAV. As technology advances the lifespan of the TCAV may be extended.

Surgical procedure

Aortic valve replacement is most frequently done through a median sternotomy, meaning the incision is made by cutting through the sternum. Once the pericardium has been opened, the patient is placed on cardiopulmonary bypass machine, also referred to as the heart-lung machine. This machine takes over the task of breathing for the patient and pumping their blood around while the surgeon replaces the heart valve.

Once the patient is on bypass, an incision is made in the aorta and a crossclamp applied. The surgeon then removes the patient's diseased aortic valve and a mechanical or tissue valve is put in its place. Once the valve is in place and the aorta has been closed, the patient is taken off the heart-lung machine. Transesophageal echocardiogram (TEE, an ultra-sound of the heart done through the esophagus) can be used to verify that the new valve is functioning properly. Pacing wires are usually put in place, so that the heart can be manually paced should any complications arise after surgery. Drainage tubes are also inserted to drain fluids from the chest and pericardium following surgery. These are usually removed within 36 hours while the pacing wires are generally left in place until right before the patient is discharged from the hospital.

Hospital stay and recovery time

After aortic valve replacement, the patient will frequently stay in an intensive care unit for 12-36 hours. The patient is often able to go home after this, unless complications arise. Common complications include heart block, which typically requires the permanent insertion of a cardiac pacemaker.

Recovery from aortic valve replacement will take a year, if the patient is in good health. Patients are advised not to do any heavy lifting for 6-8 months after surgery, to avoid damage to the sternum (the breast bone).

Surgical outcome and risk of procedure

The risk of death or serious complications from aortic valve replacement is typically quoted as being between 1-3%, depending on the health and age of the patient, as well as the skill of the surgeon. Older patients, as well as more fragile ones, are sometimes ineligible for surgery because of elevated risks.

Percutaneous aortic valve replacement

Percutaneous aortic valve replacement allows the implantation of valves using a catheter without open heart surgery. It is routinely being used in Europe and other regions in patients who are at high risk to undergo open heart surgery, but is still in clinical trials in North America. The Edwards SAPIEN valve, commercially approved in Europe since 1997, is being evaluated in a multi-center clinical trial in the United States, with Cedars-Sinai Medical Center being the leading test site.

Chapter 12

Pulmonary Thromboendarterectomy and Valve-Sparing Aortic Root Replacement

Pulmonary thromboendarterectomy

In thoracic surgery, a **pulmonary thromboendarterectomy**, **PTE**, is an operation that removes organized clotted blood (thrombus) from the pulmonary arteries.

Indication

PTE is a treatment for chronic thromboembolic pulmonary hypertension (pulmonary hypertension induced by recurrent/chronic pulmonary emboli).

Description of the surgery

A PTE has significant risk; mortality for the operation is typically 5%. PTEs are risky because of what is done and how it is done. PTEs involve a full cardiopulmonary bypass (CPB), deep hypothermia and full cardiac arrest, with the critical procedure carried out in a standstill operation. . The reason for the complexity of procedure comes from the anatomy. The obvious part is that a pulmonary bypass is required. Surgeons cannot operate on something they cannot see; the blood going to the lungs has to be diverted from the pulmonary vasculature and lung function taken care of by a machine. Less obvious is that hypothermia is required. This goes back to the pathophysiology of emboli; they are organized, somewhat delicate, essentially part of the vessel wall, and hard to remove completely, unlike in an acute pulmonary embolectomy (for acute pulmonary embolism, which is done without hypothermia). Making this task more difficult is the anatomy of the lung and pathophysiology of chronic thromboembolic pulmonary hypertension (CTEPH); lungs also get blood from the bronchial arteries are often enlarged. The practical implication is that a conventional cardiopulmonary bypass (CPB) is not sufficient to do the surgery because

1. too much blood would be in the surgical field and
2. the delicate thrombi would be difficult to remove completely.

The solution is a full cardiac arrest, which can be done with hypothermia. So, after going on to CPB and they induce a deep hypothermia (18-20 degrees Celsius), to preserve the patient's brain. Once the patient is cooled off sufficiently the CPB machine is turned off and the surgeon has time to do the delicate work, which takes about 40 minutes, and consists of carefully removing the organized thrombus. The most challenging part of the surgery is finding the optimal plane to dissect the pulmonary artery. If the surgeon dissects too deeply into the vessel wall the pulmonary vessels may rupture. If the surgeon does not dissect deep enough the clot breaks proximally during extraction and the distal part of the pulmonary vasculture will not have its pulmonary blood flow restored. The right lung is typically done first as it is easier. Video cameras (angioscopes) are used to see deeper into the pulmonary vasculture. At the end an almost beautiful negative of the pulmonary arteries exists—as the emboli over time fill the larger vessels that feed the smaller occluded vessel.. It is not uncommon that collectively this negative almost represents the whole pulmonary tree—the only part missing being what the person was living off before the surgery. Bypass time is typically 345 minutes.

Recovery/ICU

The ICU recovery involves several challenges. Most patients get significant reperfusion pulmonary edema, at places where thrombi were removed, [Levinson et al., 1986] and thus have less than ideal oxygen saturation values. This results because with the thrombus removal the surgeon strips out the pulmonary endothelium. The challenge for the ICU physician thus is getting the extra water out of the lungs, (for which they make use of the strong diuretic furosemide) to get decent oxygen saturation values, yet maintain the blood pressure. Maintaining these two parameters can be a challenge. Maintaining a good oxygen saturation can be accomplished by run the patient dry (with a diuretic) and set a high BiPAP (bidirectional positive airway pressure). Problem is that a high BiPAP leads to a poor venous return, which means the blood pressure suffers. Adding volume would help with the blood pressure, but would make the edema worse so it is generally avoided. Adding albumin does not help; the pulmonary arteries are too porous post-operation. So, a balancing act is required between blood pressure and oxygen saturation that is controlled with the BiPAP and the diuretic.

Post-surgery

The benefits of PTEs are significant. Most patients after surgery no longer suffer from shortness of breath and therefore have a much improved quality of life. Further, pulmonary vascular resistance usually drops back to close normal levels. Since the pulmonary resistance is proportional to the pressure driving the pulmonary flow ($P=Q*R$), it follows that the pulmonary pressure decreases. This in turn means that the work per time (power) decreases because it is equal to the pressure gradient times the volumetric flow, which in this case is the cardiac output. As a result of the operation, patients are spared from pulmonary hypertension and further right ventricular hypertrophy. Most pleasing is that patients who previously had right heart dysfunction often recover function.

History and development

The UCSD Medical Center's cardiothoracic surgery department is widely recognized as a pioneer in the relatively new surgery, having performed more PTEs than the rest of the world combined (over 2100 since 1970 out of a total of 3500 worldwide) with the lowest mortality rate (less than 5%).

Relation to pulmonary thrombectomies

PTEs and pulmonary thrombectomies are both operations that removed thrombus from the lung's arterial vasculature. Aside from this similarity they differ in many ways.

- PTEs are done non-emergently whilst pulmonary thrombectomies are typically done as an emergency procedure.
- PTEs typically are done using hypothermia and full cardiac arrest.
- PTEs are done for chronic pulmonary embolism, thrombectomies for severe acute pulmonary embolism.
- PTEs are generally considered a very effective treatment, surgical thrombectomies are an area of some controversy and their effectiveness a matter of some debate in the medical community.

Valve-sparing aortic root replacement

Valve-sparing aortic root replacement (also known as the **David procedure**) is a cardiac surgery procedure involving replacement of the aortic root without replacement of the aortic valve. Two similar procedures were developed, one by Sir Magdi Yacoub, and another by Tirone David.

Techniques

Remodeling Technique

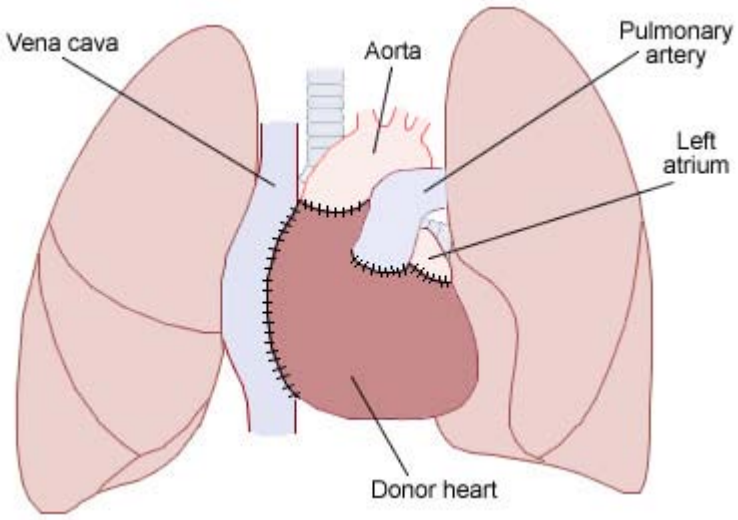
Established by Sir Magdi Yacoub.

Reimplantation Technique

Established by Tirone David and Christopher Feindel at the Toronto General Hospital.

Chapter 13

Heart Transplantation



(Diagram illustrating the placement of a donor heart in an **orthotopic procedure**. Notice how the back of the patient's left atrium and great vessels are left in place).

Hearts transplants, or **cardiac transplantation**, is a surgical transplant procedure performed on patients with end-stage heart failure or severe coronary artery disease. The most common procedure is to take a working heart from a recently deceased organ donor (cadaveric allograft) and implant it into the patient. The patient's own heart may either be removed (orthotopic procedure) or, less commonly, left in to support the donor heart (heterotopic procedure); both are controversial solutions to one of the most enduring human ailments. Post-operation survival periods now average 15 years.

The world's first human heart transplant was performed by Christiaan Barnard on December 3, 1967 in Cape Town South Africa on a man called Louis Washkansky. The first successful human heart transplant in the United States was performed at Maimonides Medical Center. Worldwide there are 3,500 heart transplants performed every year; about 800,000 people have a Class IV heart defect and need a new organ. This disparity has spurred considerable research into the use of non-human hearts since 1993. It is now possible to take a heart from another species (xenograft), or implant a man-made artificial one, although the outcome of these two procedures has been less successful in

comparison to the far more commonly performed allografts. Engineers want to fix the remaining problems with the manufactured options in the next 15 years.

Contraindications

Some patients are less suitable for a heart transplant, especially if they suffer from other circulatory conditions unrelated to the heart. The following conditions in a patient would increase the chances of complications occurring during the operation:

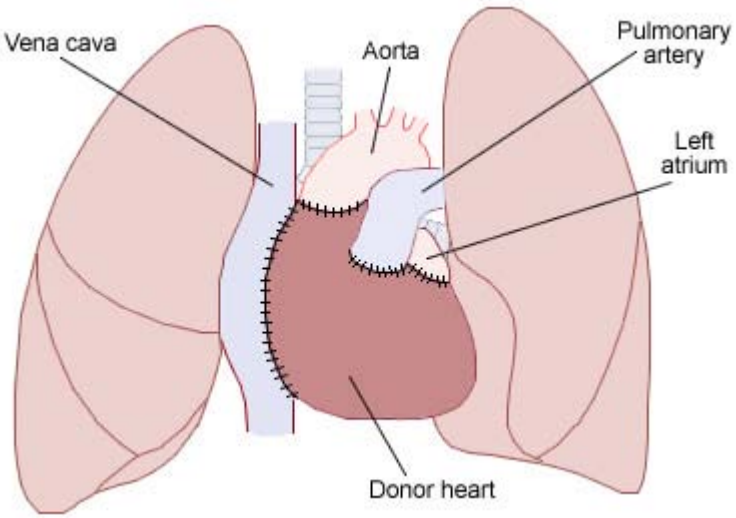
- Kidney, lung, or liver disease
- Insulin-dependent diabetes with other organ dysfunction
- Life-threatening diseases unrelated to heart failure
- Vascular disease of the neck and leg arteries.
- High pulmonary vascular resistance
- Recent thromboembolism
- Age over 60 years (some variation between centres)
- Alcohol, tobacco or drug abuse

Procedures

Pre-operative

A typical heart transplantation begins with a suitable donor heart being located from a recently deceased or brain dead donor, also called a beating heart cadaver. The transplant patient is contacted by a nurse coordinator and instructed to attend the hospital in order to be evaluated for the operation and given pre-surgical medication. At the same time, the heart is removed from the donor and inspected by a team of surgeons to see if it is in a suitable condition to be transplanted. Occasionally it will be deemed unsuitable. This can often be a very distressing experience for an already emotionally unstable patient, and they will usually require emotional support before being sent home. The patient must also undergo many emotional, psychological, and physical tests to make sure that they are in good mental health and will make good use of their new heart. The patient is also given immunosuppressant medication so that their immune system will not reject the new heart.

Operative



Schematic of a transplanted heart with native lungs and the great vessels

Once the donor heart has passed its inspection, the patient is taken into the operating room and given a general anesthetic. Either an **orthotopic** or a **heterotopic** procedure is followed, depending on the condition of the patient and the donor heart.

Orthotopic procedure

The **orthotopic procedure** begins with the surgeons performing a median sternotomy to expose the mediastinum. The pericardium is opened, the great vessels are dissected and the patient is attached to cardiopulmonary bypass. The failing heart is removed by transecting the great vessels and a portion of the left atrium. The pulmonary veins are not transected; rather a circular portion of the left atrium containing the pulmonary veins is left in place. The donor heart is trimmed to fit onto the patient's remaining left atrium and the great vessels are sutured in place. The new heart is restarted, the patient is weaned from cardiopulmonary bypass and the chest cavity is closed.

Heterotopic procedure

In the **heterotopic procedure**, the patient's own heart is not removed before implanting the donor heart. The new heart is positioned so that the chambers and blood vessels of both hearts can be connected to form what is effectively a 'double heart'. The procedure can give the patients original heart a chance to recover, and if the donor's heart happens to fail (e.g. through rejection), it may be removed, allowing the patient's original heart to start working again. Heterotopic procedures are only used in cases where the donor heart is not strong enough to function by itself (due to either the patient's body being considerably larger than the donor's, the donor having a weak heart, or the patient suffering from pulmonary hypertension).

Post-operative

The patient is taken into ICU to recover. When they wake up, they will be transferred to a special recovery unit in order to be rehabilitated. How long they remain in hospital post-transplant depends on the patient's general health, how well the new heart is working, and their ability to look after their new heart. Doctors typically like the new recipients to leave hospitals soon after surgery because of the risk of infection in a hospital (typically 1 – 2 weeks without any complications). Once the patient is released, they will have to return to the hospital for regular check-ups and rehabilitation sessions. They may also require emotional support. The number of visits to the hospital will decrease over time, as the patient adjusts to their transplant. The patient will have to remain on immunosuppressant medication to avoid the possibility of rejection. Since the vagus nerve is severed during the operation, the new heart will beat at around 100 beats per minute unless nerve regrowth occurs.

The patient will be monitored to detect rejection of the heart by the body. This surveillance can be performed via frequent biopsy or a gene expression blood test known as AlloMap Molecular Expression Testing. Typically, biopsy is performed immediately post transplant and then AlloMap blood testing is performed once the patient is stable. The transition from biopsy to AlloMap could occur as soon as 55 days post transplant.

'Living organ' transplant

Doctors made medical history in February 2006, at Bad Oeynhausen Clinic for Thorax- and Cardiovascular Surgery, Germany, when they successfully transplanted a 'beating heart' into a patient. Normally a donor's heart is injected with potassium chloride in order to stop it beating, before being removed from the donor's body and packed in ice in order to preserve it. The ice can usually keep the heart fresh for a maximum of four to six hours with proper preservation, depending on its starting condition. Rather than cooling the heart, this new procedure involves keeping it at body temperature and connecting it to a special machine called an Organ Care System that allows it to continue beating with warm, oxygenated blood flowing through it. This can maintain the heart in a suitable condition for much longer than the traditional method.

Complications

Post-operative complications include infection, sepsis, organ rejection, as well as the side-effects of the immunosupressive medication. Since the transplanted heart originates from another organism, the recipient's immune system may attempt to reject it. Immunosupressive drugs reduce that risk, but may have some unwanted side effects, such as increased likelihood of infections or nephrotoxic effects.

Prognosis

The prognosis for heart transplant patients following the orthotopic procedure has greatly increased over the past 20 years, and as of June 5, 2009, the survival rates were as follows.

- 1 year: 88% (males), 77.2% (females)
- 3 years: 79.3% (males), 77.2% (females)
- 5 years: 73.1% (males), 67.4% (females)

In a November 2008 study conducted on behalf of the U.S. federal government by Dr. Eric Weiss of the Johns Hopkins University School of Medicine, it was discovered that heart transplants — all other factors being accounted for — work better in same-sex transplants (male to male, female to female). However, due to the present acute shortage in donor hearts, this may not always be feasible.

As of August 2009, Tony Huesman was the world's longest living heart transplant recipient, having survived for 31 years with a transplanted heart. Huesman received a heart in 1978 at the age of 20 after viral pneumonia severely weakened his heart. Huesman died on August 10, 2009 of cancer. The operation was performed at Stanford University under American heart transplant pioneer Dr. Norman Shumway. Another noted heart transplant recipient, Kelly Perkins, climbs mountains around the world to promote positive awareness of organ donation. Perkins is the first heart transplant recipient to climb to the peaks of Mt. Fuji, Mt. Kilimanjaro, the Matterhorn, Mt. Whitney, and Cajon de Arenales in Argentina in 2007, 12 years after her transplant surgery. Dwight Kroening is yet another noted recipient promoting positive awareness for organ donation. Twenty two years after his heart transplant, he is the first to finish an Ironman competition. Fiona Coote was the second Australian to receive a heart transplant in 1984 (at age 14) and the youngest Australian. At 24 years since her transplant she is also a long term survivor and is involved in publicity and charity work for the Red Cross, and promoting organ donation in Australia.

Economic aspect

Typical expenses during the first year (everything included from surgery, hospitalization, lab testing, medications) averaged of $787,700 in 2008.

Chapter 14

Septal Myectomy and Alcohol Septal Ablation

Septal myectomy

Septal myectomy is a cardiac surgery treatment for hypertrophic cardiomyopathy (HCM). The surgery entails removing a portion of the septum that is obstructing the flow of blood from the left ventrical to the aorta. Septal myectomies have been successfully performed for more than 25 years. The alternatives to septal myectomies are treatment with medication (usually beta or calcium blockers) or non-surgical removal of tissue with alcohol ablation. Ordinarily, septal myectomies are performed only after attempts at treatment with medication fail. The choice between septal myectomy and alcohol ablation is a complex medical decision.

Outcomes

Septal myectomy is associated with a low perioperative mortality and a high late survival rate. A study at the Mayo Clinic found surgical myectomy performed to relieve outflow obstruction and severe symptoms in HCM was associated with long-term survival equivalent to that of the general population, and superior to obstructive HCM without operation. The results are shown below:

Survival (all-cause mortality) *			Survival (HCM-related death)			Survival (sudden cardiac death)		
Years	**With surgery**	**Without surgery**	**Years**	**With surgery**	**Without surgery**	**Years**	**With surgery**	**Without surgery**
1	98%	90%	1	99%	94%	1	100%	97%
5	96%	79%	5	98%	89%	5	99%	93%
10	83%	61%	10	95%	73%	10	99%	89%

* Includes 0.8% operative mortality.

Comparison with alcohol ablation

Either alcohol septal ablation or myectomy offers substantial clinical improvement for patients with hypertrophic obstructive cardiomyopathy. One non-randomized comparison suggested that hemodynamic resolution of the obstruction and its sequelae are more complete with myectomy. Whether one or the other treatment is preferable for certain patient types is debated among cardiovascular scientists.

Alcohol septal ablation

Alcohol septal ablation is a percutaneous, minimally-invasive treatment performed by an interventional cardiologist to relieve symptoms and improve functional status in severely symptomatic patients with hypertrophic cardiomyopathy (HCM) who meet strict clinical, anatomic and physiologic selection criteria. In carefully selected patients, when performed by an experienced interventional cardiologist, the procedure is successful in relieving symptoms in over 90% of patients.

Hypertrophic cardiomyopathy is a condition of the heart muscle which grows abnormally thick, in the absence of a physiologic cause such as hypertension (high blood pressure) or aortic valve disease. In a subset of patients with hypertrophic obstructive cardiomyopathy, thickening of the heart muscle in a particular part of the interventricular septum causes obstruction to blood being ejected from the left ventricle.

Alcohol septal ablation is a technique designed to reduce the obstruction to blood being ejected from the heart; the technique creates a small controlled heart attack, killing the area of heart muscle responsible for the obstruction, and eventually causing it to become less thick.

History

Alcohol septal ablation was first performed in Britain at the Royal Brompton Hospital by Ulrich Sigwart in 1994. Since that time, it has quickly gained favor among physicians and patients alike due to its minimally-invasive nature, avoiding general anesthesia, lengthy recuperation and other complications associated with open heart surgery (septal myectomy).

Technique

Alcohol septal ablation is performed in the cardiac catheterization laboratory, and should only be performed by interventional cardiologists with specific training in the procedure. As such, it is only available in a few institutions. The technique is similar to coronary angioplasty, and utilizes similar equipment. Using wires and balloons to localize the

septal artery feeding the diseased muscle, a small amount of absolute alcohol is infused into the artery to produce a small heart attack. Patients typically experience mild chest discomfort during the procedure, which takes approximately 30 minutes to complete. Analgesics and mild sedatives are administered as needed. Patients typically are maintained in the hospital for three to four days to monitor for any complications, including need for permanent pacemaker in 5-10%.

Outcomes

Relief of obstruction is noted immediately in the majority of appropriately selected patients. Clinical success is defined as a 50% or more reduction in peak gradient across the outflow tract, predicting continued improvement in gradient and cardiac remodeling over the ensuing 1 to 2 years. Over 90% of patients experience a successful procedure, with improvement in outflow tract gradient and mitral regurgitation. Patients typically report progressive reduction in symptoms, including improved shortness of breath, lightheadedness and chest pain. Serial echocardiograms are routinely obtained to follow the cardiac remodeling over time, and document reduction in outflow tract gradient.

When compared to surgical myectomy, similar outcomes are noted out to approximately 5 years. However, a prospective, randomized trial has not been performed. Despite initial concerns regarding long-term arrhythmic potential of alcohol septal ablation, no increased risk has been noted to date. It is important to note that patients who fail to respond to alcohol septal ablation may still be candidates for surgical myectomy. Likewise, patients who fail surgical myectomy may still respond to alcohol septal ablation. Which patients are best served by surgical myectomy, alcohol septal ablation, or medical therapy is an important topic and one which is intensely debated in medical scientific circles.

Chapter 15

Atrial Septostomy and Blalock–Taussig Shunt

Atrial septostomy

Atrial septostomy is a surgical procedure in which a small hole is created between the upper two chambers of the heart, the atria. This procedure is primarily used to treat dextro-Transposition of the great arteries or d-TGA (often imprecisely called transposition of the great arteries), a life-threatening cyanotic congenital heart defect seen in infants. Atrial septostomy has also seen limited use as a surgical treatment for pulmonary hypertension. This technique was developed in 1966 by American surgeons William Rashkind and William Miller at the Children's Hospital of Philadelphia.

There are two types of this procedure: **balloon atrial septostomy** (also called **endovascular atrial septostomy**, **Rashkind atrial balloon septostomy**, or simply **Rashkind's procedure**) and **blade atrial septostomy** (also called **static balloon atrial septostomy**).

Indications

In a normal heart, oxygen-depleted blood ("blue") is pumped from the right side of the heart, through the pulmonary artery, to the lungs where it is oxygenated. This is the pulmonary circulation part of blood flow. The oxygen-rich ("red") blood then returns to the left heart, via the pulmonary veins, and is pumped through the aorta to the rest of the body, including the heart muscle itself. This is the systemic circulation part of blood flow, the other loop of an interconnected normal cardio-pulmonary system.

With d-TGA, certain major blood vessels are connected improperly, so oxygen-poor blood from the right heart is pumped immediately through the aorta and circulated to the body and the heart itself, bypassing the lungs altogether, while the left heart pumps oxygen-rich blood continuously back into the lungs through the pulmonary artery. This is a life-threatening situation due to the resultant low oxygen levels throughout the body. Atrial septostomy allows more of the oxygen-rich blood to circulate throughout the body. The procedure is a temporary measure meant to help the patient survive until further corrective surgery can be done.

In the separate case of pulmonary hypertension, abnormally high blood pressure in the blood vessels within and connected to the lungs puts stress on the right side of the heart, potentially leading to right heart failure. Atrial septostomy relieves some of this pressure, but at the cost of lower oxygen levels in the blood (hypoxia). As with d-TGA, this surgery is not a definitive solution to the underlying medical problem.

Procedure

The majority of atrial septostomies are performed on infants with d-TGA or other cyanotic heart defects. In these cases, a balloon catheter is guided through a large vein into the right atrium, during cardiac catheterization. The catheter is threaded into the foramen ovale, a naturally-existing hole between the atria that normally closes shortly after birth. The balloon at the end of the catheter is inflated so as to enlarge the foramen ovale enough that it will no longer become sealed. This allows more oxygenated blood to enter the right heart (especially in the case of d-TGA) where it can be pumped to the rest of the body. The balloon is deflated and the catheter is removed.

Sometimes the initial surgery is not entirely successful, or there are other factors that make a simple balloon atrial septostomy impossible, such as an older patient whose foramen ovale has already closed. This is when a blade atrial septostomy is performed. The details of the procedure are largely the same, except that a small blade on the end of the catheter is first used to create an opening between the right and left atria, before the insertion of the balloon.

Risks

As with any surgery, there are certain risks to atrial septostomy, including tearing of the cardiac tissue, arrythmias, and rarely, death.

Blalock–Taussig shunt

The **Blalock-Taussig shunt** (also referred to as a **Blalock-Thomas-Taussig shunt**) is a surgical procedure to give palliation to cyanotic heart defects which are common causes of blue baby syndrome. In modern surgery, this procedure is temporarily used to direct blood flow to the lungs and relieve cyanosis while the infant is waiting for corrective or palliative surgery.

One branch of the subclavian artery or carotid artery is separated and connected with the pulmonary artery. The lung receives more blood with low oxygenation from the body. The first area of application was tetralogy of Fallot.

Alternatives

The procedure is no longer in use in its original form. Now a length of artificial tubing, 3 to 4 millimeters in diameter, is sewn between either the subclavian or the carotid artery and the corresponding side branch of the pulmonary artery, thus obviating the need to cut off blood supply and making it easier to regulate the blood flow to the lungs. Some centers now use a shunt directly from the right ventricle to the pulmonary artery, a Sano shunt. This is done to avoid the reduced diastolic blood flow in the coronary circulation associated with the Blalock-Taussig shunt.

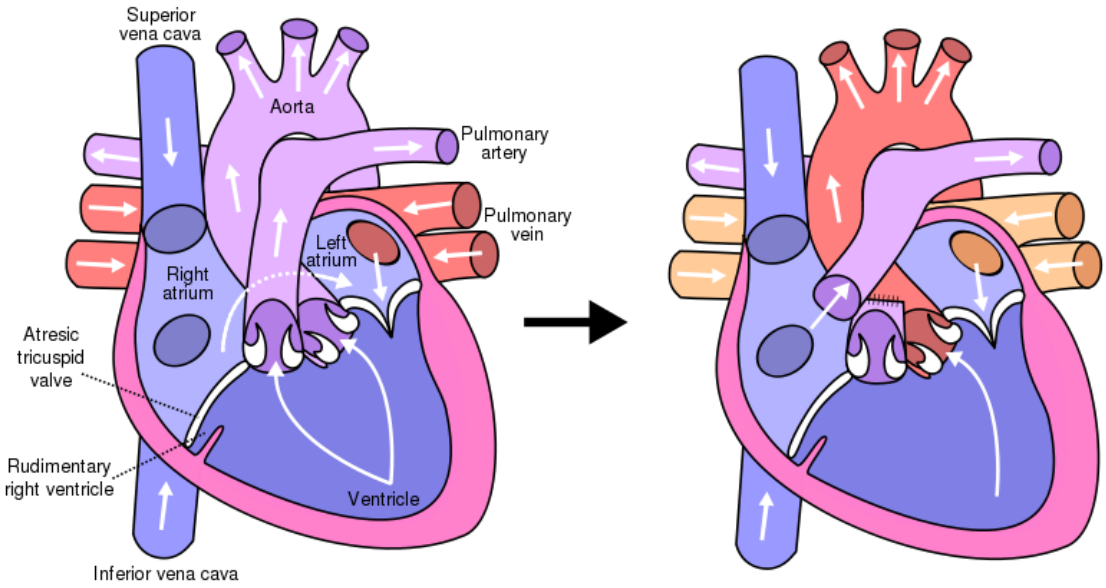
History

The original procedure was named for Alfred Blalock, surgeon, Baltimore, (1899–1964) and Helen B. Taussig, cardiologist, Baltimore/Boston, (1898–1986) who, along with Blalock's laboratory technician Vivien Thomas (1910–1985), developed the procedure. Taussig, who treated hundreds of infants and children with this disorder, had observed that children with a cyanotic heart defect and a patent ductus arteriosus (PDA) lived longer than those without the PDA. It therefore seemed to her that a shunt which mimicked the function of a PDA might relieve the tetralogy patients' poor oxygenation. In 1943, having broached the possibility of a surgical solution to Dr. Robert Gross of Boston without success, Dr. Taussig approached Blalock and Thomas in their Hopkins laboratory in 1943. According to the account of the original consultation between the three provided in Vivien Thomas' 1985 autobiography *Partners of the Heart*, Taussig carefully described the anomaly of Tetralogy of Fallot, but made no suggestion about the specific surgical correction required, observing merely that it should be possible to get more blood to the lungs, "as a plumber changes pipes around." Although Dr. Taussig was not aware of it at that time, Blalock and Thomas had already experimented with such an anastomosis, one that Blalock had conceived years earlier for a different purpose but which had the unanticipated effect of re-routing blood to the lungs. The operation involved the joining of the subclavian artery to the pulmonary artery. After meeting with Taussig, the two men set about perfecting the operation in the animal lab, with Thomas performing the subclavian-to-pulmonary anastomosis alone in some 200 laboratory dogs, then adapting the instruments for the first human surgery from those used on the experimental animals and coaching Blalock through the first 100 operations on infants.

Thomas' autobiographical account, corroborated by the participants in the early tetralogy operations (Drs. Denton Cooley and the late William P. Longmire, Jr., intern and resident respectively during the surgery) has led to the recent conclusion that Thomas' contribution, both experimentally and clinically, was so critical that he should have received credit for the procedure along with Drs. Blalock and Taussig. However, because of the racial prejudices of the time, and the academic custom which generally precluded mention of non-degreed lab assistants (Thomas had no formal education beyond high school), he did not receive the honor of having the shunt named after him. The 2004 HBO television movie *Something the Lord Made*, based on *Washingtonian* writer Katie McCabe's 1989 article of the same name, was made about his role in the historic Blue Baby surgery, as was the 2003 public television documentary *Partners of the Heart.*

Chapter 16

Fontan Procedure



Fontan procedure for tricuspid atresia

Intervention:
Fontan procedure

ICD-10 code:
ICD-9 code: 35.94
MeSH D018729
Other codes:

The **Fontan procedure**, or **Fontan/Kreutzer procedure**, is a palliative surgical procedure used in children with complex congenital heart defects. It involves diverting the venous blood from the right atrium to the pulmonary arteries without passing through the morphologic pulmonary ventricle. It was initially described in 1971 by Dr Fontan and Dr Kreutzer separately as a surgical treatment for tricuspid atresia.

Indications

The Fontan procedure has more recently been used in pediatric situations where an infant only has a single effective ventricle, either due to heart valve defects (e.g. tricuspid or pulmonary atresia) or an abnormality of the pumping ability of the heart (e.g. hypoplastic left heart syndrome, hypoplastic right heart syndrome), or has complex congenital heart disease where a bi-ventricular repair is impossible or inadvisable.

Children with hypoplastic left heart syndrome have a single effective ventricle supplying blood to the lungs and the body (either from birth or after an initial surgery e.g. Norwood procedure). They are delicately balanced between inadequate blood supply to the lungs (causing cyanosis) and oversupply to the lungs (causing heart failure). In addition, the single ventricle is doing nearly twice the expected amount of work (because it has to pump blood for both lungs and body). As a result, these children can have trouble gaining weight, and are also vulnerable to decompensation in the face of otherwise minor illnesses (even a common cold). Sometimes medications (e.g. diuretics) can help them through this stage.

Therefore, when either they are large enough, and if the pressure in the pulmonary arteries is low enough, these children are referred for Fontan procedure commonly after 2 years of life.

Contraindications

After Fontan, blood must flow through the lungs without being pumped by the heart. Therefore children with high pulmonary vascular resistance may not tolerate a Fontan procedure. Often cardiac catheterization is performed to check the resistance before proceeding with the surgery. (This is also the reason a Fontan procedure cannot be done immediately after birth; the pulmonary vascular resistance is high in utero and takes months to drop.)

Types

There are three different types of Fontan procedure:

- Atriopulmonary connection (the original) Described by Fontan and Kreutzer.
- Intracardiac total cavopulmonary connection (lateral tunnel)
- Extracardiac total cavopulmonary connection

Approach

The Fontan is usually done as a two staged repair.

The first stage, also called a **Bidirectional Glenn procedure** or **Hemi-Fontan** involves redirecting oxygen-poor blood from the top of the body to the lungs. That is, the pulmonary arteries are disconnected from their existing blood supply (e.g. a shunt created

during a Norwood procedure, a patent ductus arteriosus, etc). The superior vena cava (SVC), which carries blood returning from the upper body, is disconnected from the heart and instead redirected into the pulmonary arteries. The inferior vena cava (IVC), which carries blood returning from the lower body, continues to connect to the heart.

At this point, patients are no longer in that delicate balance, and the single ventricle is doing much less work. They usually can grow adequately, and are less fragile. However, they still have marked hypoxia (because of the IVC blood that is not fed into the lungs to be oxygenated). Therefore most patients are referred for another surgery.

The second stage, also called **Fontan completion**, involves redirecting the blood from the IVC to the lungs as well. At this point, the oxygen-poor blood from upper and lower body flows through the lungs without being pumped (driven only by the pressure that builds up in the veins). This corrects the hypoxia, and leaves the single ventricle responsible only for supplying blood to the body.

Post-operative complications

In the short term, children can have trouble with pleural effusions, fluid building up around the lungs. This can require a longer stay in the hospital for drainage with chest tubes. To address this risk, some surgeons make a fenestration (a small hole) from the venous circulation into the atrium. When the pressure in the veins is high, some of the oxygen-poor blood can escape through the fenestration to relieve the pressure. However, this results in hypoxia, so the fenestration may eventually need to be closed by an interventional cardiologist.

In the long term, children can have trouble with atrial flutter and atrial fibrillation because of scarring in the atrium, especially if the connection of IVC to pulmonary arteries involved an intracardiac baffle (instead of an extracardiac conduit). This sometimes requires treatment such as radiofrequency ablation. There are other long-term risks, including protein-losing enteropathy and chronic renal insufficiency, although understanding of these risks is still incomplete. Some patients require long-term blood thinners.

The Fontan procedure is palliative, not curative. But in many cases it can result in normal or near-normal growth, development, exercise tolerance, and good quality of life. In some cases, patients will eventually require heart transplantation.

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Chapter 17

Norwood Procedure and Jatene Procedure

Norwood procedure

Intervention:
Norwood procedure

ICD-10 code:

ICD-9 code:

Other codes:

The **Norwood Procedure** is a surgery performed on the heart, the first successful use of the procedure was reported by Norwood and colleagues in 1981. This procedure is most often performed to treat Hypoplastic Left Heart Syndrome, certain types of mitral atresia, or other conditions that result in single ventricle circulation.

In these conditions, the most urgent problem is that the heart is unable to pump blood to the systemic circulation (i.e. to the body). The goal of the Norwood procedure is to connect the single ventricle to the systemic circulation. To accomplish this, blood flow to the lungs is disrupted, and therefore an alternative path must be created to supply the lungs.

Entry to the body cavity for the Norwood Procedure is gained by a vertical incision above the sternum. Separation of the sternum is necessary.

This surgery is complex and may vary slightly depending on the diagnosis and overall condition of the heart. The main pulmonary artery is separated from the left and right portions of the pulmonary artery and joined with the upper portion of the aorta. Widening of the pulmonary artery is often necessary, and may be accomplished by using the patient's existing biological tissue, or appropriate animal tissue. This allows the blood, a mixture of oxygenated and deoxygenated, to be pumped to the body via the pulmonary valve.

Since the remainder of the pulmonary artery is now disconnected from the heart, one of a few techniques must be used to supply blood to the lungs:

- With a modified Blalock-Taussig Shunt, a Gore-Tex conduit (a kind of plastic tubing) is used to connect the subclavian artery to the pulmonary artery. In this case, blood comes from the single ventricle, through the pulmonary valve, the reconstructed aorta, the subclavian artery, and the conduit, to the lungs. There are variations on this procedure where the origin of the shunt is elsewhere in the systemic circulation (e.g. from the aorta itself) rather than the subclavian artery.
- With a Sano Shunt, a hole is made in the wall of the single ventricle, and a Gore-Tex conduit is used to connect the ventricle to the pulmonary artery. The key difference here is that the blood flow is more pulsatile than with the Blalock-Taussig version.

After this first step (*switching the right ventricle in functional position of the absent left ventricle*) children generally proceed down the path to a Fontan procedure.

Jatene procedure

The **Jatene procedure**, or **arterial switch**, is an open heart surgical procedure used to correct dextro-transposition of the great arteries (**d-TGA**); its development was pioneered by Canadian cardiac surgeon William Mustard and it was named for Brazilian cardiac surgeon Adib Jatene, who was the first to use it successfully. It was the first method of d-TGA repair to be attempted, but the last to be put into regular use because of technological limitations at the time of its conception. Use of the arterial switch is historically preceded by two atrial switch methods: the Senning and Mustard procedures.

This surgery may be used in combination with other procedures for treatment of certain cases of double outlet right ventricle (**DORV**) in which the great arteries are dextro-transposed.

Timing

The Jatene procedure is ideally performed during the second week of life, before the left ventricle adjusts to the lower pulmonary pressure and is therefore unable to support the systemic circulation. In the event of sepsis or delayed diagnosis, a combination of pulmonary artery banding (**PAB**) and shunt construction may be used to increase the left ventricular mass sufficiently to make an arterial switch possible later in infancy.

Prognosis

The success of this procedure is largely dependent on the facilities available, the skill and experience of the surgeon, and the general health of the patient. Under preferable conditions, the intra-operative and post-operative success rate is 96% or more, with a comparable survival rate after 5 years. Approximately 10% of arterial switch recipients develop residual pulmonary stenosis post-operatively, which can lead to right heart failure if left untreated; treatment usually involves endovascular stenting and/or xenograft patching.

Method

Overview

- General anaesthesia and cardiopulmonary bypass are used.
- The aorta and pulmonary artery are detached from their native roots and reattached to the opposite root; thus, the pulmonary root becomes the neo-aorta, and the aortic root becomes the neo-pulmonary artery.
- The coronary arteries are transplanted from the aorta/neo-pulmonary artery to the pulmonary artery/neo-aorta.
- Length of procedure, from initiation of anaesthesia to post-operative cease thereof, is approximately 6-8 hours.

Preparatory

If the procedure is anticipated far enough in advance (with prenatal diagnosis, for example), and the individual's blood type is known, a family member with a compatible blood type may donate some or all of the blood needed for transfusion during the use of a heart-lung machine (**HLM**). The patient's mother is normally unable to donate blood for the transfusion, as she will not be able to donate blood during pregnancy (due to the needs of the fetus) or for a few weeks after giving birth (due to blood loss), and the process of collecting a sufficient amount of blood may take several weeks to a few months. However, in cases where the individual has been diagnosed but surgery must be delayed, maternal (or even autologous, in certain cases) blood donation may be possible, as long as the mother has a compatible blood type. In most cases, though, the patient receives a donation from a blood bank. A blood transfusion is necessary for the arterial switch because the HLM needs its "circulation" filled with blood and an infant does not have enough blood on their own to do this (in most cases, an adult would not require blood transfusion).

The patient will require a number of imaging procedures in order to determine the individual anatomy of the great arteries and, most importantly, the coronary arteries. These may include angiography, magnetic resonance imaging (**MRI**), and/or computed tomography (**CT scan**). The coronary arteries are carefully mapped out in order to avoid unexpected intra-operative complications in transferring them from the native aorta to the neo-aorta.

Pre-operative

As with any procedure requiring general anaesthesia, arterial switch recipients will need to fast for several hours prior to the surgery to avoid the risk of choking on vomit while unconscious.

After the patient is anesthetized, they receive the following drugs via intravenous drip, which continue as necessary throughout the procedure:

- Aprotinin, to prevent excessive bleeding
- Solumedrol, to reduce swelling and inflammation
- Regitine, to prevent hypertension
- Prophylactic antibiotics, to prevent infection

Intra-operative

The heart is accessed via median sternotomy, and the patient is given heparin to prevent the blood from clotting. A generous section of pericardium is harvested, then disinfected and sterilized with a weak solution of glutaraldehyde; and the coronary and great artery anatomy are examined. The ductus arteriosus and right pulmonary branch, up to and including the first branches in the hilum of the right lung, are separated from the surrounding supportive tissue to allow mobility of the vessels. Silk marking sutures may be placed in the pulmonary trunk at this time, to indicate the commissure of the aorta to the neo-aorta; alternatively, this may be done later in the procedure.

The cardiopulmonary bypass is then initiated by inserting a cannula into the ascending aorta as distally from the aortic root as possible while still supplying all arterial branches, another cannula is inserted into the right atrium, and a vent is created for the left ventricle via catheterization of the right superior pulmonary vein. The HLM is started at a low-flow and the patient's body is cooled to a rectal temperature of 20 °C (68 °F), which prevents the brain damage otherwise associated with the temporary circulatory arrest necessary during the procedure; the patient must be cooled for a minimum of 20 minutes prior to beginning the repair.

While the patient is cooling, the ductus arteriosus is ligated at both the aortic and pulmonary ostia, then transected at its center; the left pulmonary branch, including the first branches in the hilum of the left lung, is separated from the supportive tissue; and the aorta is marked at the site it will be transected, which is just below the pulmonary bifurcation, proximal to where the pulmonary artery will be transected.

When the patient is fully cooled, the ascending aorta is clamped as close as possible below the HLM cannula, and cryocardioplegia is achieved by delivering cold blood to the heart via the ascending aorta (below the cross clamp). The aorta is then transected at the marked spot, and the pulmonary artery is transected a few millimetres below the bifurcation. The vessels are again examined, and the pulmonary root is inspected for left ventricular outflow tract obstruction (**LVOTO**). If a ventricular septal defect (**VSD**) is

present, it may be repaired, at this point via either the aortic or pulmonary valve; it may alternatively be repaired later in the procedure.

The great arteries are usually arranged using the Lecompte maneuver, with the aortic cross clamp positioned to hold the pulmonary artery anterior to the ascending aorta; though with some congenital arrangements of the great arteries, such as side-by-side, this is not possible and the arteries will be transplanted in the non-anatomic 'anterior aorta' arrangement. If the aortic commissure has not yet been marked, it may be done at this point, using the same method as would be used prior to bypass; however, there is a third opportunity for this still later in the procedure.

Coronary arteries are examined closely, and the ostia and proximal arterial course are identified, as are any infundibular branches, if they exist. The coronary ostia and a large "button" of surrounding aortic wall are then excised from the aorta, well into the sinus of Valsalva; and the proximal sections of the coronary arteries are separated from the surface of the heart, which prevents tension or distortion after anastomosis to the neo-aorta. Infundibular branches are sometimes unable to be spared, but this is a very rare occurrence. If the aortic commissure has not previously been marked, the excised coronary arteries will be used to determine the implantation position of the aorta.

The aorta is then transplanted onto the pulmonary root, using either absorbable or permanent continuous suture. The aortic clamp is temporarily removed while small sections of the neo-aorta are cut away to accommodate the coronary ostia, and a continuous absorbable suture is then used to anastomose each coronary "button" into the prepared space. In most cases, the coronary implantation sites will be at left and right anterior positions at the base of the neo-aorta; however, if the circumflex coronary artery branches from the right coronary artery, the circumflex coronary artery will be distorted if the pair are not implanted higher than normal on the neo-aorta, and in some cases they may need to be implanted above the aortic commissure, on the native aorta itself. The circumflex coronary artery may originate from the same coronary sinus as, rather than directly from, the right coronary artery, in which case they may still be excised on the same "button" and transplanted similarly to if they had a shared ostium, unless one or both have intramural communication with another coronary vessel. Sometimes, one or more coronary ostia are located very close to the valvular opening and a small portion of the native aortic valve must be removed when the coronary artery is excised, which causes a generally mild, and usually well-tolerated, neo-pulmonary valve regurgitation.

The HLM is turned off and the aortic and atrial cannula are removed, then an incision is made in the right atrium, through which the congenital or palliative atrial septal defect (**ASD**) is repaired; where a Rashkind balloon atrial septostomy was used, the ASD should be able to be closed with sutures, but cases involving large congenital ASDs or Blalock-Hanlon atrial septectomy, a pericardial, xenograft, or Dacron patch may be necessary. If there is a VSD which has not yet been repaired, this is performed via the atrial incision and tricuspid valve, using sutures for a small defect or a patch for a large defect.

When the septal defects have been repaired and the atrial incision is closed, the previously removed cannula are replaced and the HLM is restarted. The left ventricle is then vented and the cross clamp removed from the aorta, enabling full-flow to be re-established and rewarming to begin; at this point the patient will receive an additional dose of Regatine to keep blood pressure under control. The previously harvested pericardium is then used to patch the coronary explantation sites, and to extend - and widen, if necessary - the neo-pulmonary root, which allows the pulmonary artery to be anastamosed without residual tension; the pulmonary artery is then transplanted to the neo-pulmonary root.

Final stages

The patient is fitted with chest tubes, temporary pacemaker leads, and ventilated before weaning from the HLM is begun; and administration of post-operative drugs is initiated, these include:

- muscle relaxant, to induce temporary paralysis
- opioid analgesic, to manage pain, cause sedation and induce serenity
- inotrope, to assist the heart in contracting adequately

The rib cage is relaxed and the external surgical wound is bandaged, but the sternum and chest incision are left open to provide extra room in the pleural cavity, allowing the heart room to swell and preventing pressure caused by pleural effusion.

Post-operative

The sternum and chest can usually be closed within a few days; however, the chest tubes, pacemaker, ventilator, and drugs may still be required after this time. The patient will continue to fast for up to a few days, and breastmilk or infant formula can then be gradually introduced via nasogastric tube (**NG tube**); the primary goal after a successful arterial switch, and before hospital discharge, is for the infant to gain back the weight they have lost and continue to gain weight at a normal or near-normal rate.

History

Scottish pathologist Matthew Baillie first described **TGA** in 1797, presumably as a posthumous diagnosis. Early mortality rates at this time are estimated to have been as high as 90%; the survivors would have been those with one or more concomitant intracardiac shunts (ASD, patent ductus arteriosus (**PDA**), patent foramen ovale (**PFO**), and/or VSD), and are unlikely to have survived past adolescence.

In 1950, American surgeons Alfred Blalock and C. Rollins Hanlon introduced the *Blalock-Hanlon atrial septectomy*, which was then routinely used to palliate patients. This would have effectively reduced early mortality rates, particularly in cases with no concomitant shunts, but is unlikely to have reduced late mortality rates.

Mustard first conceived of, and attempted, the anatomical repair (arterial switch) for d-TGA in the early 1950s. His few attempts were unsuccessful due to technical difficulties posed by the translocation of the coronary arteries, and the idea was abandoned.

Swedish cardiac surgeon Åke Senning described the first corrective surgery for d-TGA (the *Senning procedure*) in 1959, which involved using the atrial septum to create an intratrial baffle that redirected bloodflow at the atrial level; Senning yielded a high success rate using this procedure, significantly lowering both early and late mortality rates.

Due to the technical complexity of the Senning procedure, others could not duplicate his success rate; in response, Mustard developed a simpler alternative method (the *Mustard procedure*) in 1964, which involved constructing a baffle from autologous pericardium or synthetic material, such as Dacron. This procedure yielded early and late mortality rates comparable to the Senning procedure; however, a late morbidity rate was eventually discovered in relation to the use of synthetic graft material, which does not grow with the recipient and eventually causes obstruction.

In 1966, American surgeons William Rashkind and William Miller transformed the palliation of d-TGA patients with the innovative *Rashkind balloon atrial septostomy*, which, unlike the thoracotomy required by a septectomy, is performed through the minimally invasive surgical technique of cardiac catheterization.

Although the atrial switch procedures dramatically reduced both early and late mortality rates, these statistics remained high, partly due to the wait time required between birth and surgery (pre-operative mortality: 5-10%; early mortality: 0-15%; late mortality: 20-25%). A concomitant VSD raises the early mortality rate for atrial switch to 10-60%, even in cases where the VSD is repaired. The late morbidity rate is also very high in atrial switch recipients, with 13-100% developing post-operative complications related to intra-operative damage caused to the sinus node and/or the inherent unsuitability of the heart chambers for role reversal.

These statistics, combined with advances in microvascular surgery, created a renewed interest in Mustard's original concept of an arterial switch procedure. The first successful arterial switch was performed on a forty-two day old d-TGA + VSD infant by Jatene in 1975. Egyptian cardiac surgeon Magdi Yacoub was subsequently successful in treating TGA with intact septum when preceded by pulmonary artery banding and systemic-to-pulmonary shunt palliation. Austrian surgeon B. Eber was the first to recount a small series of successful arterial switch procedures, and the first large successful series was reported by Guatemalan surgeon Aldo R. Casteneda.

By 1985, the arterial switch had become the procedure of choice, and remains the standard modern procedure for d-TGA repair. Atrial switches are still occasionally used as a standby when coronary artery patterns contraindicate coronary anastomoses, in cases of delayed diagnosis where pulmonary artery banding is not possible, and when a d-TGA + VSD patient also has left ventricular outflow tract obstruction.

The world's smallest infant to survive an arterial switch was Jerrick De Leon, born 13 weeks premature. At the time of the operation on February 6, 2005, he weighed just over 1.5 pounds (700 grams).

Chapter 18

Cox Maze Procedure and Minimaze Procedure

Cox maze procedure

The **Cox maze procedure** is a type of heart surgery for atrial fibrillation.

"Maze" refers to the series of incisions arranged in a maze-like pattern in the atria. Today, various methods of minimally invasive maze procedures, collectively named minimaze procedures, are used.

History

James Cox, MD, and associates developed the "maze" or "Cox maze" procedure, an "open-heart" cardiac surgery procedure intended to eliminate atrial fibrillation (AF), and performed the first one at St. Louis' Barnes Hospital -- now Barnes-Jewish Hospital -- in 1987. The intention was to eliminate AF by using incisional scars to block abnormal electrical circuits (atrial macroreentry) that AF requires. This required an extensive series of full-thickness incisions through the walls of both atria, a median sternotomy (vertical incision through the sternum) and cardiopulmonary bypass (heart-lung machine; extracorporeal circulation). A series of improvements were made, culminating in 1992 in the Cox maze III procedure, which is now considered to be the "gold standard" for effective surgical cure of AF. It was quite successful in eliminating AF, but had drawbacks as well. The Cox maze III is sometimes referred to as the "Traditional maze", the "cut and sew maze", or simply the "maze".

During the past 10 years, several energy sources such as unipolar radiofrequency, bipolar radiofrequency, microwave, laser, high-intensity focused ultrasound, and cryothermia were incorporated into various devices in order to create some of the lesions of the Cox Maze-III procedure without actually cutting into the atrial walls. Microwave and Laser therapy have both been withdrawn from the market but the other devices continue to be utilized to treat atrial fibrillation surgically. Most of them, however, are used to create lesion patterns that are not as extensive as those of the Cox Maze-III procedure and have not proven to be as successful. Whether the failures when using these devices are due to a

failure of the energy source or to the fact that an incomplete lesion set was employed remains an unresolved matter.

Minimaze procedure

Intervention:
Minimaze procedure

ICD-10 code:
ICD-9 code: 37.33
Other codes:

The **mini-maze procedures** are cardiac surgery procedures intended to cure atrial fibrillation (AF), a common disturbance of heart rhythm. They are procedures derived from the original maze procedure developed by James Cox, MD.

The origin of the mini-maze procedures: The Cox maze procedure

James Cox, MD, and associates developed the "maze" or "Cox maze" procedure, an "open-heart" cardiac surgery procedure intended to eliminate atrial fibrillation, and performed the first one in 1987. “Maze” refers to the series of incisions arranged in a maze-like pattern in the atria. The intention was to eliminate AF by using incisional scars to block abnormal electrical circuits (atrial macroreentry) that AF requires. This required an extensive series of endocardial (from the inside of the heart) incisions through both atria, a median sternotomy (vertical incision through the breastbone) and cardiopulmonary bypass (heart-lung machine; extracorporeal circulation). A series of improvements were made, culminating in 1992 in the Cox maze III procedure, which is now considered to be the "gold standard” for effective surgical cure of AF. It was quite successful in eliminating AF, but had drawbacks as well. The Cox maze III is sometimes referred to as the “Traditional maze”, the “cut and sew maze”, or simply the "maze".

Minimally invasive epicardial surgical procedures for AF (minimaze)

Efforts have since been made to equal the success of the Cox maze III while reducing surgical complexity and likelihood of complications. During the late 1990s, operations similar to the Cox maze, but with fewer atrial incisions, led to the use of the terms "minimaze", "mini maze" and “mini-maze”, although these were still major operations.

A primary goal has been to perform a curative, "maze-like" procedure *epicardially* (from the outside of the heart), so that it could be performed on a normally beating heart,

without cardiopulmonary bypass. Until recently this was not thought possible; as recently as 2004, Dr. Cox defined the mini-maze as requiring an endocardial approach:

“In summary, it would appear that placing the following lesions can cure most patients with atrial fibrillation of either type: pulmonary vein encircling incision, left atrial isthmus lesion with its attendant coronary sinus lesion, and the right atrial isthmus lesion. We call this pattern of atrial lesions the “mini-maze Procedure” ... None of the present energy sources—including cryotherapy, unipolar radiofrequency, irrigated radiofrequency, bipolar radiofrequency, microwave, and laser energy—are capable of creating the left atrial isthmus lesion from the epicardial surface, because of the necessity of penetrating through the circumflex coronary artery to reach the left atrial wall near the posterior mitral annulus. Therefore, the mini-maze procedure cannot be performed epicardially by means of any presently available energy source.”

Although Dr. Cox's 2004 definition specifically excludes an epicardial approach to eliminate AF, he and others pursued this important goal, and the meaning of the term changed as successful epicardial procedures were developed. In 2002 Saltman performed a completely endoscopic surgical ablation of AF and subsequently published their results in 14 patients. These were performed epicardially, on the beating heart, *without cardiopulmonary bypass or median sternotomy*. Their method came to be known as the minimaze or microwave minimaze procedure, because microwave energy was used to make the lesions that had previously been performed by the surgeon's scalpel.

Shortly thereafter, Randall K. Wolf, MD and others developed a procedure using radiofrequency energy rather than microwave, and different, slightly larger incisions. In 2005, he published his results in the first 27 patients. This came to be known as the Wolf minimaze procedure.

Today, the terms “minimaze”, "mini-maze", and "mini maze" are still sometimes used to describe open heart procedures requiring cardiopulmonary bypass and median sternotomy, but more commonly they refer to minimally invasive, epicardial procedures not requiring cardiopulmonary bypass, such as those developed by Saltman, Wolf, and others. These procedures are characterized by:

1. No median sternotomy incision; instead, an endoscope and/or “mini-thoracotomy” incisions between the ribs are used.
2. No cardiopulmonary bypass; instead, these procedures are performed on the normally beating heart.
3. Few or no actual incisions into the heart itself. The "maze" lesions are made *epicardially* by using radiofrequency, microwave, or ultrasonic energy, or by cryosurgery.
4. The part of the left atrium in which most clots form (the “appendage”) is usually removed, in an effort to reduce the long-term likelihood of stroke.

Microwave minimaze

Completely Endoscopic Microwave Ablation of Atrial Fibrillation on the Beating Heart Using Bilateral Thoracoscopy: The microwave minimaze requires three 5 mm to 1cm incisions on each side of the chest for the surgical tools and the endoscope. The pericardium is entered, and two sterile rubber tubes are threaded behind the heart, in the transverse and oblique sinuses. These tubes are joined together, then used to guide the flexible microwave antenna energy source through the sinuses behind the heart, to position it for ablation. Energy is delivered and the atrial tissue heated and destroyed in a series of steps as the microwave antenna is withdrawn behind the heart. The lesions form a "box-like" pattern around all four pulmonary veins behind the heart. The left atrial appendage is usually removed. A very thorough description of the procedure is available.

Wolf minimaze

Video-assisted Bilateral Epicardial Bipolar Radiofrequency Pulmonary Vein Isolation and Left Atrial Appendage Excision: The Wolf minimaze requires one 5cm and two 1cm incisions on each side of the chest. These incisions allow the surgeon to maneuver the tools, view areas through an endoscope, and to see the heart directly. The right side of the left atrium is exposed first. A clamp-like tool is positioned on the left atrium near the right pulmonary veins, and the atrial tissue is heated between the jaws of the clamp, cauterizing the area. The clamp is removed. The autonomic nerves (ganglionated plexi) that may cause AF may be eliminated as well. Subsequently the left side of the chest is entered. The ligament of Marshall (a vestigial structure with marked autonomic activity) is removed. The clamp is subsequently positioned on the left atrium near the left pulmonary veins for ablation. Direct testing to demonstrate complete electrical isolation of the pulmonary veins, and that the ganglionated plexi are no longer active, may be performed.

High Intensity Focused Ultrasound (HIFU) minimaze

Surgical ablation of atrial fibrillation with off-pump, epicardial, high-intensity focused ultrasound: Although the HIFU minimaze is performed epicardially, on the normally beating heart, it is also usually performed in conjunction with other cardiac surgery, and so would not be minimally invasive in those cases. An ultrasonic device is positioned epicardially, on the left atrium, around the pulmonary veins, and intense acoustic energy is directed at the atrium to destroy tissue in the appropriate regions near the pulmonary veins.

Mechanism of Elimination of Atrial Fibrillation

The mechanism by which AF is eliminated by curative procedures such as the maze, minimaze, or catheter ablation is controversial. All successful methods destroy tissue in the areas of the left atrium near the junction of the pulmonary veins, hence these regions are thought to be important. A concept gaining support is that paroxysmal AF is mediated in part by the autonomic nervous system and that the intrinsic cardiac nervous system,

which is located in these regions, plays an important role. Supporting this is the finding that targeting these autonomic sites improves the likelihood of successful elimination of AF by catheter ablation.

Patient Selection

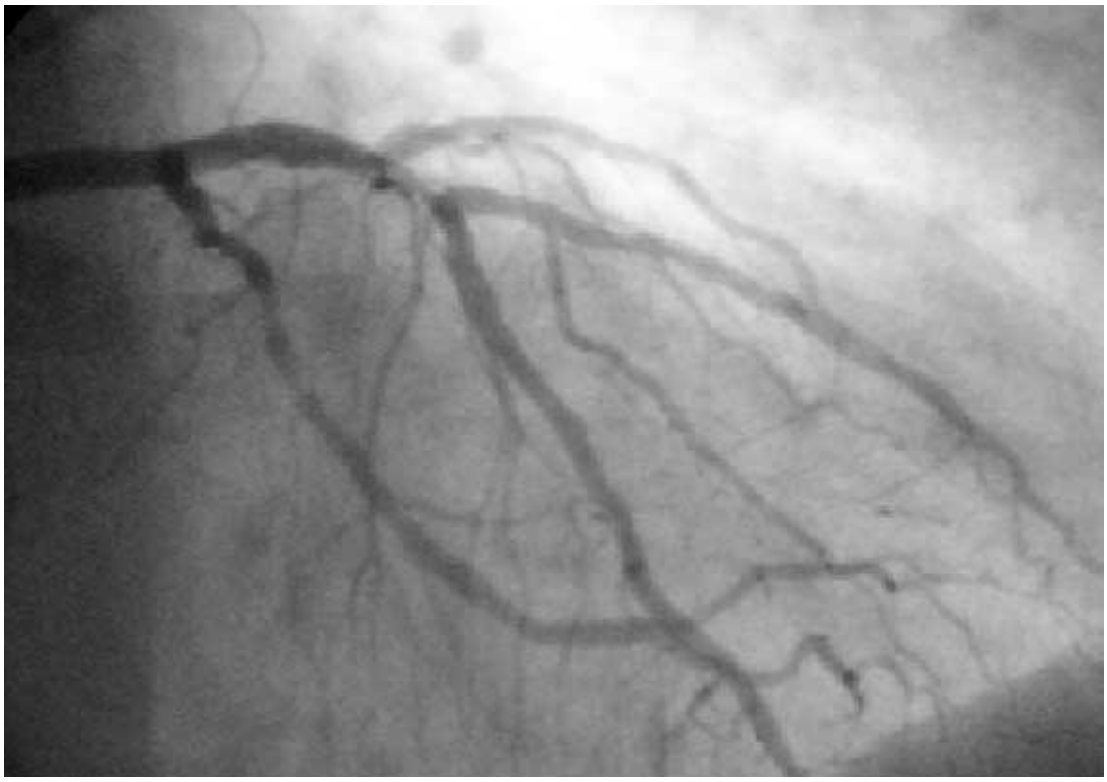
The minimaze procedures are alternatives to catheter ablation of AF, and the patient selection criteria are similar. Patients are considered for minimaze procedures if they have moderate or severe symptoms and have failed medical therapy; asymptomatic patients are generally not considered. Those most likely to have a good outcome have paroxysmal (intermittent) AF, and have a heart that is relatively normal. Those with severely enlarged atria, marked cardiomyopathy, or severely leaking heart valves are less likely to have a successful result; these procedures are generally not recommended for such patients. Previous cardiac surgery provides technical challenges due to scarring on the outside of the heart, but does not always preclude minimaze surgery.

Surgical Results

Long-term success of the minimaze procedures awaits a consensus. Attaining a consensus is hindered by several problems; perhaps the most important of these is incomplete or inconsistent post-procedure follow-up to determine if atrial fibrillation has recurred, although many reasons have been considered. It has been clearly demonstrated that longer or more intensive follow-up identifies much more recurrent atrial fibrillation, hence a procedure with more careful follow-up will appear to be less successful. In addition, procedures continue to evolve rapidly, so long follow-up data do not accurately reflect current procedural methods. For more recent minimaze procedures, only relatively small and preliminary reports are available. With those caveats in mind, it can be said that reported short-term freedom from atrial fibrillation following the radiofrequency ("Wolf") procedure ranges from 67% to 91% with longer-term results in a similar range, but limited primarily to patients with paroxysmal atrial fibrillation.

Chapter 19

Coronary Catheterization



A coronary angiogram (an X-ray with radio-opaque contrast in the coronary arteries) that shows the left coronary circulation. The distal left main coronary artery (LMCA) is in the left upper quadrant of the image. Its main branches (also visible) are the left circumflex artery (LCX), which courses top-to-bottom initially and then toward the centre/bottom, and the left anterior descending (LAD) artery, which courses from left-to-right on the image and then courses down the middle of the image to project underneath of the distal LCX. The LAD, as is usual, has two large diagonal branches, which arise at the centre-top of the image and course toward the centre/right of the image.

A **coronary catheterization** is a minimally invasive procedure to access the coronary circulation and blood filled chambers of the heart using a catheter. It is performed for both diagnostic and interventional (treatment) purposes.

Coronary catheterization is one of the several cardiology diagnostic tests and procedures. Specifically, coronary catheterization is a visually interpreted test performed to recognize occlusion, stenosis, restenosis, thrombosis or aneurysmal enlargement of the coronary artery lumens; heart chamber size; heart muscle contraction performance; and some aspects of heart valve function. Important internal heart and lung blood pressures, not measurable from outside the body, can be accurately measured during the test. The relevant problems that the test deals with most commonly occur as a result of advanced atherosclerosis – atheroma activity within the wall of the coronary arteries. Less frequently, valvular, heart muscle, or arrhythmia issues are the primary focus of the test.

Coronary artery luminal narrowing reduces the flow reserve for oxygenated blood to the heart, typically producing intermittent angina. Very advanced luminal occlusion usually produces a heart attack. However, it has been increasingly recognized, since the late 1980s, that coronary catheterization does not allow the recognition of the presence or absence of coronary atherosclerosis itself, only significant luminal changes which have occurred as a result of end stage complications of the atherosclerotic process.

History

The technique of angiography was first developed in 1927 by the Portuguese physician Egas Moniz to provide contrasted x-ray in order to diagnose nervous diseases, such as tumors, coronary heart disease and arteriovenous malformations. He is recognized as one of the pioneers in this field.

Coronary catheterization was further explored in 1929 when the German physician Werner Forssmann inserted a plastic tube in his cubital vein and guided it to the right chamber of the heart. He took an x-ray to prove his success and published it on November 5 1929 with the title "Über die Sondierung des rechten Herzens" (About probing of the right heart). The coronarography of the left heart was introduced in 1953 with the report by a Portuguese group, published in Cardiologia, International Archives of Cardiology volume 22, pages 45–61, by E. Coelho et al., entitled L'artériographie des coronaires chez l'homme vivant. They were the first to non-selectively inject radiocontrast in the coronary arteries.

In 1960 F. Mason Sones, a pediatric cardiologist at the Cleveland Clinic, accidentally injected radiocontrast in a coronary artery instead of the left ventricle. Although the patient had a reversible cardiac arrest, Sones and Shirey developed the procedure further, and are credited with the discovery (Connolly 2002); they published a series of 1,000 patents in 1966 (Proudfit *et al.*).

Since the late 1970s, building on the pioneering work of Charles Dotter in 1964 and especially Andreas Gruentzig starting in 1977, coronary catheterization has been extended to therapeutic uses: (a) the performance of less invasive physical treatment for angina and some of the complications of severe atherosclerosis, (b) treating heart attacks before complete damage has occurred and (c) research for better understanding of the pathology of coronary artery disease and atherosclerosis.

In the early 1960s, cardiac catheterization frequently took several hours and involved significant complications for as many as 2–3% of patients. With multiple incremental improvements over time, simple coronary catheterization examinations are now commonly done more rapidly and with significantly improved outcomes.

Patient participation

The patient being examined or treated is usually awake during coronary catheterization, ideally with only local anaesthesia such as lidocaine and minimal general sedation, throughout the procedure. Performing the procedure with the patient awake is safer as the patient can immediately report any discomfort or problems and thereby facilitate rapid correction of any undesirable events. Medical monitors fail to give a comprehensive view of the patient's immediate well-being; how the patient feels is often a most reliable indicator of procedural safety.

Death, myocardial infarction, stroke, serious ventricular arrhythmia, and major vascular complications each occur in less than 1% of patients undergoing catheterization. However, though the imaging portion of the examination is often brief, because of setup and safety issues the patient is often in the lab for 20–45 minutes. Any of multiple technical difficulties, while not endangering the patient (indeed added to protect the patient's interests) can significantly increase the examination time.

Equipment

Coronary catheterization is performed in a cardiac catheterization lab, usually located within a hospital. With current designs, the patient must lay relatively flat on a narrow, minimally padded, radiolucent (transparent to X-ray) table. The X-Ray source and imaging camera equipment are on opposite sides of the patient's chest and freely move, under motorized control, around the patient's chest so images can be taken quickly from multiple angles. More advanced equipment, termed a bi-plane cath lab, uses two sets of X-Ray source and imaging cameras, each free to move independently, which allows two sets of images to be taken with each injection of radiocontrast agent.

The equipment and installation setup to perform such testing typically represents a capital expenditure of US$2–5 million (2004), sometimes more, partially repeated every few years.

Diagnostic procedures

During coronary catheterization (often referred to as a **cath** by physicians), blood pressures are recorded and X-Ray motion picture shadow-grams of the blood inside the coronary arteries are recorded. In order to create the X-ray pictures, a physician guides a small tube-like device called a catheter, typically ~2.0 mm (6-French) in diameter, through the large arteries of the body until the tip is just within the opening of one of the coronary arteries. By design, the catheter is smaller than the lumen of the artery it is

placed in; internal/intraarterial blood pressures are monitored through the catheter to verify that the catheter does not block blood flow.

The catheter is itself designed to be radiodense for visibility and it allows a clear, watery, blood compatible radiocontrast agent, commonly called an X-ray dye, to be selectively injected and mixed with the blood flowing within the artery. Typically 3–8 cc of the radiocontrast agent is injected for each image to make the blood flow visible for about 3–5 seconds as the radiocontrast agent is rapidly washed away into the coronary capillaries and then coronary veins. Without the X-ray dye injection, the blood and surrounding heart tissues appear, on X-ray, as only a mildly-shape-changing, otherwise uniform water density mass; no details of the blood and internal organ structure are discernible. The radiocontrast within the blood allows visualization of the blood flow within the arteries or heart chambers, depending on where it is injected.

If atheroma, or clots, are protruding into the lumen, producing narrowing, the narrowing may be seen instead as increased haziness within the X-ray shadow images of the blood/dye column within that portion of the artery; this is as compared to adjacent, presumed healthier, less stenotic areas.

For guidance regarding catheter positions during the examination, the physician mostly relies on detailed knowledge of internal anatomy, guide wire and catheter behavior and intermittently, briefly uses fluoroscopy and a low X-ray dose to visualize when needed. This is done without saving recordings of these brief looks. When the physician is ready to record diagnostic views, which are saved and can be more carefully scrutinized later, he activates the equipment to apply a significantly higher X-ray dose, termed cine, in order to create better quality motion picture images, having sharper radiodensity contrast, typically at 30 frames per second. The physician controls both the contrast injection, fluoroscopy and cine application timing so as to minimize the total amount of radiocontrast injected and times the X-Ray to the injection so as to minimize the total amount of X-ray used. Doses of radiocontrast agents and X-ray exposure times are routinely recorded in an effort to maximize safety.

Though not the focus of the test, calcification within the artery walls, located in the outer edges of atheroma within the artery walls, is sometimes recognizable on fluoroscopy (without contrast injection) as radiodense halo rings partially encircling, and separated from the blood filled lumen by the interceding radiolucent atheroma tissue and endothelial lining. Calcification, even though usually present, is usually only visible when quite advanced and calcified sections of the artery wall happen to be viewed on end tangentially through multiple rings of calcification, so as to create enough radiodensity to be visible on fluoroscopy.

Therapeutic procedures

By changing the diagnostic catheter to a guiding catheter, physicians can also pass a variety of instruments through the catheter and into the artery to a lesion site. The most

commonly used are 0.014-inch-diameter (0.36 mm) guide wires and the balloon dilation catheters.

By injecting radiocontrast agent through a tiny passage extending down the balloon catheter and into the balloon, the balloon is progressively expanded. The hydraulic pressures are chosen and applied by the physician, according to how the balloon within the stenosis responds. The radiocontrast filled balloon is watched under fluoroscopy (it typically assumes a "dog bone" shape imposed on the outside of the balloon by the stenosis as the balloon is expanded), as it opens. As much hydraulic brute force is applied as judged needed and visualized to be effective to make the stenosis of the artery lumen visibly enlarge.

Typical normal coronary artery pressures are in the <200 mmHg range (27 kPa). The hydraulic pressures applied within the balloon may extend to as high as 19000 mmHg (2,500 kPa). Prevention of over-enlargement is achieved by choosing balloons manufactured out of high tensile strength clear plastic membranes. The balloon is initially folded around the catheter, near the tip, to create a small cross-sectional profile to facilitate passage though luminal stenotic areas and designed to inflate to a specific pre-designed diameter. If over inflated, the balloon material simply tears and allows the inflating radiocontrast agent to simply escape into the blood.

Additionally, several other devices can be advanced into the artery via a guiding catheter. These include laser catheters, stent catheters, IVUS catheters, Doppler catheter, pressure or temperature measurement catheter and various clot and grinding or removal devices. Most of these devices have turned out to be niche devices, only useful in a small percentage of situations or for research.

Stents, which are specially manufactured expandable stainless steel mesh tubes, mounted on a balloon catheter, are the most commonly used device beyond the balloon catheter. When the stent/balloon device positioned within the stenosis, the balloon is inflated which, in turn, expands the stent and the artery. The balloon is removed and the stent remains in place, supporting the inner artery walls in the more open, dilated position. Current stents generally cost around $1,000 to 3,000 each (US 2004 dollars), the drug coated ones being the more expensive.

Advances in catheter based physical treatments

Interventional procedures have been plagued by restenosis due to the formation of endothelial tissue overgrowth at the lesion site. Restenosis is the body's response to the injury of the vessel wall from angioplasty and to the stent as a foreign body. As assessed in clinical trials during the late 1980 and 1990s, using only balloon angioplasty (POBA, plain old balloon angioplasty), up to 50% of patients suffered significant restenosis but that percentage has dropped to the single to lower two digit range with the introduction of drug-eluting stents. Sirolimus, paclitaxel and everolimus are the three drugs used in coatings which are currently FDA approved in the United States. As opposed to bare metal, drug eluting stents are covered with a medicine that is slowly dispersed with the

goal of suppressing the restenosis reaction. The key to the success of drug coating has been (a) choosing effective agents, (b) developing ways of adequately binding the drugs to the stainless surface of the stent struts (the coating must stay bound despite marked handling and stent deformation stresses) and (c) developing coating controlled release mechanisms that release the drug slowly over about 30 days. One of the newest innovations in coronary stents is the development of a dissolving stent. Abbott laboratories has used a dissolvable material, polylactic acid, that will completely absorb within 2 years of being implanted.