Holiday Heart Syndrome

Author: Adam S Budzikowski, MD, PhD; Chief Editor: Jeffrey N Rottman, MD

Background
Alcohol consumed in large quantities for many years has long been recognized to induce an alcoholic cardiomyopathy. Clinically identical to idiopathic dilated cardiomyopathy, alcoholic cardiomyopathy is a major form of secondary dilated cardiomyopathy in the Western world. (See Medscape Reference articles Alcoholic Cardiomyopathy and Dilated Cardiomyopathy.) With this change in cardiac structure and decline in function, there exists the substrate for atrial and ventricular arrhythmias. However, only within the past 20-25 years has the arrhythmogenic potential of short-term alcohol consumption been elucidated in patients without clinically evident heart failure.

In 1978, Ettinger et al conducted a study evaluating 32 separate dysrhythmic episodes in 24 patients. These patients consumed alcohol heavily and regularly; in addition, they took part in a weekend or holiday drinking binge immediately prior to evaluation. Based on the results of this study, the term holiday heart syndrome was coined. It was defined as an acute cardiac rhythm and/or conduction disturbance, most commonly supraventricular tachyarrhythmia, associated with heavy ethanol consumption in a person without other clinical evidence of heart disease. Typically, this resolved rapidly with spontaneous recovery during subsequent abstinence from alcohol use.

Holiday heart syndrome now most commonly refers to the association between alcohol use and rhythm disturbances, particularly supraventricular tachyarrhythmias in apparently healthy people. Similar reports have indicated that recreational use of marijuana may have similar effects. The most common rhythm disorder is atrial fibrillation, which usually converts to normal sinus rhythm within 24 hours. Holiday heart syndrome should be particularly considered as a diagnosis in patients without structural heart disease and with new-onset atrial fibrillation. Although the syndrome can recur, its clinical course is benign, and specific antiarrhythmic therapy is usually not indicated. Interestingly, even modest alcohol intake can be identified as a trigger in some patients with paroxysmal atrial fibrillation.

Pathophysiology
Several mechanisms are theorized to be responsible for the arrhythmogenicity of alcohol. These include an increased secretion of epinephrine and norepinephrine, increased sympathetic output, a rise in the level of plasma free fatty acids, and an indirect effect through acetaldehyde, the primary metabolite of alcohol, or fatty acid ethyl esters, a cardiac alcohol metabolite. Alcohol can also directly decrease sodium current and can affect intracellular pH, either causing acidosis with low doses or alkalosis with higher doses. Interestingly, these effects may be species specific, with rabbits and humans being similarly affected while the dog atria appear unaffected.

Analysis of ECGs performed following resolution of arrhythmias in patients who have consumed a large quantity of alcohol show significant prolongation of the PR, QRS, and QT intervals compared with patients who experienced arrhythmias in the absence of alcohol consumption. The arrhythmogenicity of alcohol has also been examined in the electrophysiology laboratory.
One study evaluated 14 patients with a history of significant alcohol consumption. Initially, the atrial and ventricular extrastimulus technique induced nonsustained ventricular tachycardia in 1 patient, nonsustained atrial fibrillation in 1 patient, paired ventricular responses in 1 patient, and no response in the remaining 11 patients. Following administration of alcohol, 10 of the 14 patients developed sustained or nonsustained tachyarrhythmias in response to the extrastimulus technique, with significant prolongation of His-ventricular conduction.[18]

In another study, ingestion of whiskey resulted in no change in the atrial refractory period but facilitated induction of atrial flutter in individuals who were chronic drinkers and those who were nondrinkers. This evidence strongly suggests that alcohol possesses proarrhythmic properties. These seem to be more pronounced in patients with larger P wave dispersion. Although ventricular repolarization abnormalities on surface ECG were described, whether ventricular myocardium responds similarly to ethanol is uncertain. One case of ventricular fibrillation was described in a patient with heavy alcohol ingestion, but an electrophysiologic study (EPS) revealed only inducibility of atrial fibrillation with rapid ventricular response but no ventricular arrhythmias.

**Epidemiology**

**Frequency**

**United States**

The frequency with which cardiac arrhythmias can be attributed to alcohol use is unclear owing to differing data. One study showed alcohol as the causative agent in 35% of cases of new-onset atrial fibrillation and in 63% of cases in patients younger than 65 years.[11] Conversely, another study showed only about 5-10% of all new episodes of atrial fibrillation to be explainable by alcohol use.

Atrial fibrillation is the most common rhythm disturbance associated with alcohol consumption. Atrial flutter, isolated ventricular premature beats, isolated atrial premature beats, junctional tachycardia, and various other rhythm disturbances may occur with less frequency.

**International**

Worldwide prevalence is not well documented. Prevalence is presumably increased in countries with higher rates of alcohol ingestion and alcoholism.

**Mortality/Morbidity**

Regular consumption of alcohol in modest amounts does not seem to have the same potential to cause arrhythmias as alcohol consumed in heavy amounts. In fact, it has been shown in a sample of patients whose usual daily alcohol intake exceeds 6 drinks that the risk of developing atrial fibrillation, atrial flutter, and atrial premature beats is at least twice that of patients who drink alcohol at least monthly but who on average consume less than a single drink daily.

**Race**

Evidence regarding race is unavailable.

**Sex**

An increased incidence of the holiday heart syndrome has not been clearly documented in males; however, this can be inferred as males have a higher incidence of atrial fibrillation and alcoholism.

**Age**

Although atrial fibrillation increases with age, it is unclear if holiday heart syndrome is more common in elderly patients, since this age group is more likely to have structural heart disease.
Holiday Heart Syndrome Clinical presentation

History

Patients with acute exposure to alcohol can present with a variety of symptoms.

- Palpitations are the most common symptom. These can be intermittent or persistent, depending on the presence or absence of sustained arrhythmia and the ventricular response to atrial fibrillation. Patients with rapid ventricular responses can present with near syncopal symptoms, dyspnea on exertion, and angina.
- Patients often have a history of previous alcohol exposure. This often occurs in binges on weekends, during vacations, and, of course, on holidays. A history of alcoholism should alert physicians to concomitant illnesses such as alcohol-related cardiomyopathy and chronic liver disease. These coexisting illnesses have important prognostic implications and affect patient management.

Physical

On physical examination, the patient may show signs of alcohol intoxication and have alcohol on the breath. Depending on the cardiac rhythm, the patient may have an irregular or thready pulse. Cardiac auscultation is usually normal except for possibly irregular and/or rapid heart tones. Mental status may be impaired consistent with alcohol intoxication.

Holiday Heart Syndrome Differential Diagnoses

Differential Diagnoses

- Alcoholism
- Atrial Fibrillation
- Atrial Flutter
- Hyperthyroidism
- Paroxysmal Supraventricular Tachycardia
- Pulmonary Embolism

Alcoholism

Author: Warren Thompson, MD, FACP; Chief Editor: Iqbal Ahmed, MBBS, FRCPsych (UK)

Practice Essentials

Alcohol use is the third leading cause of preventable death in the United States (after smoking and obesity). Annually, 85,000 deaths are attributable to alcohol at a cost of $185 billion.\textsuperscript{[1,2]}

Essential update: Gabapentin shown to be effective for treating alcohol dependence
In a study of 49 alcohol-dependent individuals randomized to treatment with either 1500 mg of gabapentin nightly (n=25) or placebo (n=24) for 1 week and followed for 3 months, gabapentin improved 2 sleep variables involved in alcohol dependence relapse. Subjects underwent polysomnography on 3 consecutive nights just before starting treatment and again 1 week after treatment was initiated.[3]

Individuals who relapsed by 3-month follow-up had significantly less stage 2 sleep than abstainers (50.3% vs 55.4%; P=.04); those treated with gabapentin had significantly increased stage 2 sleep compared with those who received placebo (P=.008). Patients who relapsed spent more time awake after sleep onset than abstainers (27.6 vs 14.5 minutes; P=.004); the duration of this was also reduced in the gabapentin group (P=.003).[3]

Signs and symptoms

The diagnosis of an alcohol problem is best made by the history. Screening instruments for alcohol problems include the CAGE ([need to] cut down [on drinking], annoyance, guilt [about drinking], [need for] eye-opener) questionnaire and the AUDIT (alcohol use disorders identification test). The CAGE questions should be given face-to-face, whereas AUDIT can be given as a paper-and-pencil test.

The following 4 questions make up the CAGE questionnaire:

- Have you ever felt the need to cut down on your drinking?
- Have people annoyed you by criticizing your drinking?
- Have you ever felt bad or guilty about your drinking?
- Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?

Features of AUDIT are as follows:

- Contains 10 questions, each with 5 possible answers scored 0-4
- The best test for screening because it detects hazardous drinking and alcohol abuse
- Has a greater sensitivity in populations with a lower prevalence of alcoholism

The following are signs and symptoms of alcohol withdrawal:

- Nausea and vomiting
- Diaphoresis
- Agitation and anxiety
- Headache
- Tremor
- Seizures
- Visual and auditory hallucinations: Many patients who are not disoriented—and who therefore do not have delirium tremens—have hallucinations

The following are signs of delirium tremens (ie, alcohol withdrawal delirium):

- Tachycardia and hypertension
• Temperature elevation
• Delirium

The following are signs of chronic alcoholism:

• Gynecomastia
• Spider angiomata
• Dupuytren contractures (also may be congenital)
• Testicular atrophy
• Enlarged or shrunken liver
• Enlarged spleen

Complications of alcoholism manifest as follows:

• Wernicke encephalopathy: Ataxia, ophthalmoplegia (usually lateral gaze palsy), and confusion
• Korsakoff syndrome: Anterograde and retrograde amnesia, often with confabulation and preceded by Wernicke encephalopathy
• Hepatic encephalopathy: Asterixis and confusion

Diagnosis

Alcohol biomarkers are physiologic indicators of alcohol exposure or ingestion and may reflect the presence of an alcohol use disorder. These biomarkers are not meant to be a substitute for a comprehensive history and physical examination. Indirect alcohol biomarkers, which suggest heavy alcohol use by detecting the toxic effects of alcohol, include the following [4]:

• Aspartate aminotransferase (AST)
• Alanine aminotransferase (ALT)
• Gamma glutamyltransferase (GGT)
• Mean corpuscular volume (MCV)
• Carbohydrate-deficient transferrin (CDT)

Features of CDT are as follows:

• Alcohol consumption above 50-80 g/day for 2-3 weeks appears to increase serum concentrations of CDT [5, 6]
• CDT tends to distinguish chronic heavy drinkers from light social drinkers [7]
• The combination of GGT and CDT has greater diagnostic accuracy than either measure alone [5, 6]

Direct alcohol biomarkers include alcohol itself and ethyl glucuronide (EtG). [4] A blood alcohol level detects alcohol intake in the previous few hours and thus is not necessarily a good indicator of chronic excessive drinking. [7] Blood alcohol levels that indicate alcoholism with a high degree of reliability are as follows:

• >300 mg/dL in a patient who appears intoxicated but denies alcohol abuse
- >150 mg/dL without gross evidence of intoxication
- >100 mg/dL upon routine examination

Features of EtG are as follows:
- Becomes positive shortly after intake of alcohol, even in small amounts
- After complete cessation of alcohol intake, EtG can be detected in urine for up to 5 days after heavy binge drinking

Management

The first step in treatment is brief intervention, in which the physician should do the following:
- State unequivocally that the patient has a problem with alcohol
- Emphasize that this determination stems from the consequences of alcohol in that patient's life, not from the quantity of alcohol consumed
- Emphasize the effects on family, friends, and occupation, as well as any physical manifestations
- Point out that loss of control and compulsive use indicate alcohol dependence
- Be empathic and nonjudgmental
- Avoid arguments about the diagnosis
- Avoid use of the word alcoholic
- Indicate the responsibility for change is with the patient
- Listen to the patient's goals and point out discrepancies between his or her goals and actions

Further treatment of alcoholism involves the following:
- Complete abstinence is the only treatment for alcohol dependence
- Emphasize that the most common error is underestimating the amount of help needed to stop drinking
- Hospitalize patients if they have a history of delirium tremens or if they have significant comorbidity
- Consider inpatient treatment if the patient has poor social support, significant psychiatric problems, or a history of relapse after treatment
- Strongly recommend Alcoholics Anonymous (AA)
- Encourage hospitalized patients to call AA from the hospital; AA will send someone to talk to them if the patient makes the contact
- Patients need to attend AA meetings regularly (daily at first) and for a sufficient length of time (usually 2 years or more) because recovery is a difficult and lengthy process
- In the beginning of treatment, and perhaps ongoing, patients should remove alcohol from their homes and avoid bars and other establishments where strong pressures to drink may hinder abstinence
- If the patient has an antisocial personality (ie, severe problems with family, peers, school, and police before age 15 years and before the onset of alcohol problems), recovery is less likely
• If the patient has primary depression, anxiety disorder, or another potentially contributory disorder (the other disorder must antedate the problems with alcohol or it must be a significant problem during long periods of sobriety), treat this primary problem aggressively.

Image library

Deaths while intoxicated. Data from the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

Background

Alcoholism is common, serious, and expensive. Physicians encounter alcohol-related cirrhosis, cardiomyopathy, pancreatitis, and gastrointestinal bleeding, as well as intoxication and alcohol addiction, on a daily basis. Alcoholism is also associated with many cancers. Wernicke encephalopathy and Korsakoff psychosis are also important causes of chronic disability as well as dementia. Fetal alcohol syndrome is a leading cause of mental retardation. In addition, accidents (especially automobile), depression, dementia, suicide, and homicide are important consequences of alcoholism.

Alcohol-related diseases are discussed in separate articles. The focus of this article is screening, diagnosis, treatment, and new research findings on the natural history and heritability of alcoholism.

The following image details deaths while intoxicated.

Pathophysiology

Alcohol affects virtually every organ system in the body and, in high doses, can cause coma and death. It affects several neurotransmitter systems in the brain, including opiates, GABA, glutamate, serotonin, and dopamine. Increased opiate levels help explain the euphoric effect of alcohol, while its effects on GABA cause anxiolytic and sedative effects.
Alcohol inhibits the receptor for glutamate. Long-term ingestion results in the synthesis of more glutamate receptors. When alcohol is withdrawn, the central nervous system experiences increased excitability. Persons who abuse alcohol over the long term are more prone to alcohol withdrawal syndrome than persons who have been drinking for only short periods. Brain excitability caused by long-term alcohol ingestion can lead to cell death and cerebellar degeneration, Wernicke-Korsakoff syndrome, tremors, alcoholic hallucinosis, delirium tremens, and withdrawal seizures. Opiate receptors are increased in the brains of recently abstinent alcoholic patients, and the number of receptors correlates with cravings for alcohol.

**Frequency**

**United States**

These statistics are based on the US National Longitudinal Alcohol Epidemiologic Study. Alcoholism is prevalent in 20% of adult hospital inpatients. One in 6 patients in community-based primary care practices had problem drinking. The following apply to the US adult population:

- Current drinkers - 44%
- Former drinkers - 22%
- Lifetime abstainers - 34%
- Abuse and dependency in the past year - 7.5-9.5%
- Lifetime prevalence - 13.5-23.5%

Alcoholism is slightly more common in lower income and less educated groups. Vaillant studied the natural history of alcoholism and the differences between college-educated and inner-city alcoholic persons. He followed 2 cohorts (over 400 patients) of alcoholic patients over many years.\[9\]

According to Vaillant's research, inner-city men began problem drinking approximately 10 years earlier than college graduates (age 25-30 y vs age 40-45 y). Inner-city men were more likely to be abstinent from alcohol consumption than college graduates (30% vs 10%) but more likely to die from drinking (30% vs 15%). A large percentage of college graduates alternated between controlled drinking and alcohol abuse for many years. Returning to controlled drinking from alcohol abuse is uncommon, no more than 10%; however, this figure is likely to be high because it was obtained from self-reported data. Mortality in both groups was related strongly to smoking. Abstinence for less than 5-6 years did not predict continued abstinence (41% of men abstinent for 2 y relapsed).

The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) study suggests the transition from use to dependence was highest for nicotine users, followed by cocaine, alcohol, and cannabis users.\[10\] An increased risk of transition to dependence among minorities and those with psychiatric or dependence comorbidity highlights the importance of promoting outreach and treatment of these populations.

Binge drinking statistics from the CDC estimate more than 38 million US adults binge drink an average of 4 times a month and the most drinks they consume on average is 8. The report found that binge drinking is more common among households with incomes ≥$75,000, but the largest number of drinks consumed per occasion is highest among households with incomes of <$25,000.\[11\]

**International**
The World Health Organization examined mental disorders in primary care offices and found that alcohol dependence or harmful use was present in 6% of patients. In Britain, 1 in 3 patients in community-based primary care practices had at-risk drinking behavior. Alcoholism is more common in France than it is in Italy, despite virtually identical per capita alcohol consumption.

**Mortality/Morbidity**

Alcohol use is the third leading cause of preventable death in the United States (after smoking and obesity). Annually, 85,000 deaths are attributable to alcohol at a cost of $185 billion. Almost half of these deaths are attributable to alcohol-related injury.

Four percent of the global burden of disease is attributable to alcohol. This figure rises to 7% in North America, Europe, Japan, and Australia and to 12% in Eastern Europe and Central Asia. Worldwide, alcohol is responsible for a percentage of a number of conditions, as follows:

- **Cirrhosis** - 32%
- **Motor vehicle accidents** - 20%
- **Mouth and oropharyngeal cancers** - 19%
- **Esophageal cancer** - 29%
- **Liver cancer** - 25%
- **Breast cancer** - 7%
- **Homicide** - 24%
- **Suicide** - 11%
- **Hemorrhagic stroke** - 10%

An analysis in the United Kingdom in 2010 found that overall, alcohol was found to be the most harmful drug to the person consuming and to others. However, this study does not mean that substances other than alcohol have no harmful consequences; heroin, cocaine, and methamphetamine were found to be the most harmful drugs to individuals themselves. In addition, this study did not address the issue of polydrug abuse, which is a common phenomenon in individuals abusing substances. The combination of alcohol and other substances can lead to serious adverse effects, and such combinations were not explored in this study.

Below are the statistically significant relative risks from a study by the American Cancer Society for men and women who consume 4 or more drinks daily. A drink is defined as one 12-oz beer, one 4- to 5-oz glass of wine, or one mixed drink containing 1.5 oz of spirits (80 proof). The relative risk for the noted maladies with consumption of 4 or more drinks daily is as follows:

- **Cirrhosis** - For men, 7.5; for women, 4.8
- **Injuries** - For men, 1.3
- **Ear, nose, and throat cancer; esophagus cancer; liver cancer** - For men, 2.8; for women, 3

Moderate alcohol consumption (1-2 drinks/d) reduces the risk of cardiovascular disease in men and women by approximately 30%. The effect of heavy alcohol consumption on the risk of cardiovascular disease varies in different studies. The person's drinking pattern appears to have an effect on cardiovascular disease. Drinking with meals may reduce the risk, while binge drinking increases risk (even in otherwise moderate drinkers).
Moderate alcohol consumption appears to increase the risk of breast cancer in women. Total mortality is reduced with moderate alcohol consumption but not with heavy alcohol consumption; the cardiovascular benefit is offset by cirrhosis, cancer, and injuries. The amount of alcohol associated with the lowest mortality appears to be 2 drinks per day in men and 1 drink or fewer per day in women. Moderate alcohol consumption reduces the risk of developing diabetes, but heavy alcohol consumption may increase the risk. The cardiovascular benefit becomes important in men older than 40 years and in women older than 50 years. The risk of hypertension is increased with 3 or more drinks daily.

No benefits are noted in people at low risk for coronary disease (men < 40 y and women < 50 y). Recent data suggest an increase in coronary calcification with moderate alcohol consumption in young adults. [14] This effect was exacerbated by binge drinking.

Of men aged 18-25 years, 60% binge drink. (Binge drinking is defined as 5 alcoholic drinks for men [4 for women] in a row.) Binge drinking significantly increases the risk of injury and contracting sexually transmitted diseases. Women who binge drink at this age are at higher risk of becoming pregnant and potentially harming an unborn child. (Any amount of alcohol consumption during pregnancy is risky.) Cohort data from the Prospective Epidemiological Study of Myocardial Infarction (PRIME) investigated alcohol use patterns on ischemic heart disease in Northern Ireland and France. Regular and moderate alcohol use throughout the week, a typical pattern in middle-aged men in France, was associated with a lower risk of ischemic heart disease, whereas the binge drinking pattern more prevalent in Northern Ireland was associated with a higher risk of ischemic heart disease. [17]

More than three quarters of all foster children in the United States are children of alcohol- or drug-dependent parents. From 60-70% of reported domestic violence incidents involve alcohol. Half of all violent crime is alcohol or drug related.

Overall, morbidity and mortality are related strongly to smoking, and people who drink heavily are less likely to quit smoking. Additionally, persons who begin smoking early are more likely to develop problems with alcohol.

With regard to pregnancy, fetal alcohol syndrome is the leading known cause of mental retardation (1 in 1000 births). More than 2000 infants annually are born with this condition in the United States. Alcohol-related birth defects and neurodevelopmental problems are estimated to be 3 times higher. Even small amounts of alcohol consumption may be risky in pregnancy. A 2001 study by Sood et al reported that children aged 6-7 years whose mothers consumed alcohol even in small amounts had more behavioral problems. [18] In a study from 2003, Baer et al showed that moderate alcohol consumption while pregnant resulted in a higher incidence of offspring problem drinking at age 21 years, even after controlling for family history and other environmental factors. [19] All women who are pregnant or planning to become pregnant should avoid alcohol.

Race

The 2 largest studies, the US National Comorbidity Survey and the Epidemiologic Catchment Area Survey, both showed a lower prevalence of alcoholism in African Americans than in white Americans. The prevalence was equal or higher in Hispanic Americans compared with white Americans.

Studies of Native Americans and Asian Americans are smaller. These studies indicate the prevalence of alcoholism is higher in Native Americans and lower in Asian Americans when compared with white Americans.

Sex
Alcoholism is at least twice as prevalent in men as it is in women. In the National Comorbidity Survey, it was 2.5 times more prevalent in men than in women. The lifetime prevalence was 20% in men and 8% in women. For alcohol abuse or dependence in the past year, the rates were 10% for men and 4% for women.

Women do not metabolize alcohol as efficiently as men. Hazardous drinking (not alcoholism) is greater than 1 drink daily for women and greater than 2 drinks daily for men.

Problem drinking in women is much less common than it is in men, and the typical onset of problem drinking in females occurs later than in males. However, progression is more rapid, and females usually enter treatment earlier than males. Women more commonly combine alcohol with prescription drugs of abuse than do males. Women living with substance-abusing men are at high risk.

Alcohol problems are less likely to be recognized in women, and women with alcohol problems are less likely to be treated. This may be because women are less likely than men to have job, financial, or legal troubles as a result of drinking.

Age

The prevalence of alcoholism declines with increasing age. The prevalence in elderly populations is unclear but is probably approximately 3%. A study of the US Medicare population found that alcohol-related hospitalizations were as common as hospitalizations for myocardial infarction.

Among older patients with alcoholism, from one third to one half develop alcoholism after age 60 years. This group is harder to recognize. A recent population-based study found that problem drinking (>3 drinks/d) was observed in 9% of older men and in 2% of older women. Alcohol levels are higher in elderly patients for a given amount of alcohol consumed than in younger patients.

Among younger individuals (such as college students), weekly or daily consumption of energy drinks (highly caffeinated beverages) has been strongly associated with alcohol dependence. This population is an important target population for alcohol use disorder prevention.\(^{20}\)
Atrial Fibrillation

Practice Essentials

Atrial fibrillation (AF) has strong associations with other cardiovascular diseases, such as heart failure, coronary artery disease (CAD), valvular heart disease, diabetes mellitus, and hypertension. It is characterized by an irregular and often rapid heartbeat. The exact mechanisms by which cardiovascular risk factors predispose to AF are not understood fully but are under intense investigation. Catecholamine excess, hemodynamic stress, atrial ischemia, atrial inflammation, metabolic stress, and neurohumoral cascade activation are all purported to promote AF.

Essential update: Newer anticoagulants show benefits versus warfarin

In patients with atrial fibrillation, the newer oral anticoagulants dabigatran (Pradaxa), rivaroxaban (Xarelto), apixaban (Eliquis), and edoxaban (Lixiana) protected against stroke or systemic embolism better than warfarin and had comparable safety profiles, according to a meta-analysis of 4 randomized trials involving 42,411 patients who received the newer anticoagulants and 29,272 who received warfarin. The newer anticoagulants also significantly reduced all-cause mortality and intracranial hemorrhage, but increased gastrointestinal bleeding.

Median follow-ups ranged from 1.8 years to 2.8 years. The risk of stroke or systemic embolic events was reduced by 19% with the newer anticoagulants compared with warfarin; hemorrhagic strokes accounted for a large proportion of the reduction. Compared with warfarin, low-dose new anticoagulant regimens showed similar overall reductions in stroke or systemic embolic events and a more favorable bleeding profile, but significantly more ischemic strokes.

Signs and symptoms

The clinical presentation of AF spans the entire spectrum from asymptomatic AF with rapid ventricular response to cardiogenic shock or devastating cerebrovascular accident (CVA). Unstable patients requiring immediate direct current (DC) cardioversion include the following:

- Patients with decompensated congestive heart failure (CHF)
- Patients with hypotension
- Patients with uncontrolled angina/ischemia

Initial history and physical examination include the following:

- Documentation of clinical type of AF (paroxysmal, persistent, or permanent)
- Assessment of type, duration, and frequency of symptoms
- Assessment of precipitating factors (eg, exertion, sleep, caffeine, alcohol use)
- Assessment of modes of termination (eg, vagal maneuvers)
- Documentation of prior use of antiarrhythmics and rate-controlling agents
- Assessment of presence of underlying heart disease
- Documentation of any previous surgical or percutaneous AF ablation procedures
Airway, breathing, and circulation (ABCs)
Vital signs (particularly heart rate, blood pressure, respiratory rate, and oxygen saturation)
Evaluation of head and neck, lungs, heart, abdomen, lower extremities, and nervous system

Diagnosis

Findings from 12-lead electrocardiography (ECG) usually confirm the diagnosis of AF and include the following:

- Typically irregular ventricular rate
- Absence of discrete P waves, replaced by irregular, chaotic F waves, in the setting of irregular QRS complexes
- Aberrantly conducted beats after long-short R-R cycles (ie, Ashman phenomenon)
- Heart rate (typically 110-140 beats/min, rarely >160-170 beats/min)
- Preexcitation
- Left ventricular hypertrophy
- Bundle-branch block
- Acute or prior myocardial infarction (MI)

Transthoracic echocardiography (TTE) is helpful for the following applications:

- To evaluate for valvular heart disease
- To evaluate atrial and ventricular chamber and wall dimensions
- To estimate ventricular function and evaluate for ventricular thrombi
- To estimate pulmonary systolic pressure (pulmonary hypertension)
- To evaluate for pericardial disease

Transesophageal echocardiography (TEE) is helpful for the following applications:

- To evaluate for left atrial thrombus (particularly in the left atrial appendage)
- To guide cardioversion (if thrombus is seen, cardioversion should be delayed)

Management

The cornerstones of AF management are rate control and anticoagulation, as well as rhythm control for those symptomatically limited by AF. The clinical decision to use a rhythm-control or a rate-control strategy requires integrated consideration of the following:

- Degree of symptoms
- Likelihood of successful cardioversion
- Presence of comorbidities
- Candidacy for AF ablation

The 2006 American College of Cardiology (ACC)/American Heart Association (AHA)/European Society of Cardiology (ESC) guidelines on anticoagulation for patients with nonvalvular AF include the following:

- No risk factors: Aspirin 81-325 mg/day
- 1 moderate risk factor: Aspirin 81-325 mg/day or warfarin (international normalized ratio [INR] 2-3)
- Any high-risk factor or >1 moderate-risk factor: Warfarin (INR 2-3)

Risk factors are as follows:
High-risk factors: Prior stroke or transient ischemic attack (TIA), systemic thromboembolism
Moderate-risk factors: Age >75 years, hypertension, heart failure, left ventricular function < 35%, diabetes mellitus
Risk factors of unknown significance: Female sex, age 65-74 years, coronary artery disease, thyrotoxicosis

New-onset AF:

ACC/AHA/ESC 2006 guidelines for new-onset AF include the following [6]:

- An initial rate-control strategy is “reasonable” for asymptomatic or minimally symptomatic older patients with hypertension and comorbid cardiovascular disease
- For younger individuals, especially those without significant comorbid cardiovascular disease, an initial rhythm-control strategy may be better

Agents used for rate control in new-onset AF include the following:

- Diltiazem
- Metoprolol
- Digoxin (rarely as monotherapy)
- Amiodarone (mainly for patients who are intolerant of or unresponsive to other agents)

Anticoagulation is indicated as follows:

- Patients with newly diagnosed AF and those awaiting electrical cardioversion can be started on intravenous (IV) heparin or low-molecular-weight heparin (LMWH)
- Concomitantly, patients can be started on warfarin in an inpatient setting while awaiting a therapeutic INR value (2-3)
- Oral direct thrombin inhibitors may present an alternative to warfarin in a higher-risk population with nonvalvular AF

Newer oral anticoagulants that have been approved by the US Food and Drug Administration (FDA) and may be considered as alternatives to warfarin include the following:

- Dabigatran (direct thrombin inhibitor)
- Rivaroxaban (highly selective direct factor Xa inhibitor)
- Apixaban (factor Xa inhibitor)

Long-term management of AF:

Optimal long-term strategies for AF management should be based on a thoroughly integrated consideration of patient-specific factors and likelihood of success. Selection of an appropriate antithrombotic regimen should be balanced between the risk of stroke and the risk of bleeding. Factors that increase the risk of bleeding with warfarin therapy include the following:

- History of bleeding (the strongest predictive risk factor)
- Age older than 75 years
- Liver or renal disease
- Malignancy
- Thrombocytopenia or aspirin use
- Hypertension
- Diabetes mellitus
- Anemia
- Prior stroke
- Fall risk
• Genetic predisposition
• Supratherapeutic INR

Alternatives to warfarin:

• If warfarin will not be used, adding clopidogrel to aspirin may be considered[7]
• Updated ACC/AHA/Heart Rhythm Society (HRS) guidelines on AF include a class Ib recommendation for dabigatran[8] for preventing stroke and systemic thromboembolism in patients with paroxysmal-to-permanent atrial fibrillation and risk factors for stroke or systemic embolization

Agents used for rate control include the following:

• Oral beta-blockers
• Nondihydropyridine calcium channel blockers
• Digoxin
• Amiodarone

Agents used for rhythm control include the following:

• Flecainide
• Propafenone
• Dofetilide
• Amiodarone
• Dronedarone
• Sotalol

Catheter ablation performed in experienced centers is recommended in the 2011 update to the ACCF/AHA/HRS AF guidelines for the following indications[7]:

• It is recommended as an alternative to pharmacologic therapy to prevent recurrent paroxysmal AF in significantly symptomatic patients with little or no structural heart disease or severe pulmonary disease[9]
• It is reasonable as a treatment for symptomatic persistent AF
• It may be reasonable as a treatment for symptomatic paroxysmal AF in patients with some structural heart disease

Image library

Classification scheme for patients with atrial fibrillation.

Background

Classification of atrial fibrillation (AF) begins with distinguishing a first detectable episode, irrespective of whether it is symptomatic or self-limited. Published guidelines from an American College of Cardiology
(ACC)/American Heart Association (AHA)/European Society of Cardiology (ESC) committee of experts on the treatment of patients with atrial fibrillation recommend classification of AF into the following 3 patterns (also see the image below)\textsuperscript{[10]}:

- **Paroxysmal AF** – Episodes of AF that terminate spontaneously within 7 days (most episodes last less than 24 hours)
- **Persistent AF** - Episodes of AF that last more than 7 days and may require either pharmacologic or electrical intervention to terminate
- **Permanent AF** - AF that has persisted for more than 1 year, either because cardioversion has failed or because cardioversion has not been attempted

This classification schema pertains to cases that are not related to a reversible cause of AF (eg, thyrotoxicosis, electrolyte abnormalities, acute ethanol intoxication). Atrial fibrillation secondary to acute myocardial infarction, cardiac surgery, pericarditis, pulmonary embolism, or acute pulmonary disease is considered separately because, in these situations, AF is less likely to recur once the precipitating condition has been treated adequately and has resolved.

### Paroxysmal AF

Atrial fibrillation is considered to be recurrent when a patient has 2 or more episodes. If recurrent AF terminates spontaneously, it is designated as paroxysmal.

Some patients with paroxysmal AF, typically younger patients, have been found to have distinct electrically active foci within their pulmonary veins. These patients generally have many atrial premature beats noted on Holter monitoring. Isolation or elimination of these foci can lead to elimination of the trigger for paroxysms of AF.

Paroxysmal AF may progress to permanent AF, and aggressive attempts to restore and maintain sinus rhythm may prevent comorbidities associated with AF.

### Persistent AF

If recurrent AF is sustained, it is considered persistent, irrespective of whether the arrhythmia is terminated by either pharmacologic therapy or electrical cardioversion.

Persistent AF may be either the first presentation of AF or the result of recurrent episodes of paroxysmal AF. Patients with persistent AF also include those with longstanding AF in whom cardioversion has not been indicated or attempted, often leading to permanent AF.

Patients can also have AF as an arrhythmia secondary to cardiac disease that affects the atria (eg, congestive heart failure, hypertensive heart disease, rheumatic heart disease, coronary artery disease). These patients tend to be older, and AF is more likely to be persistent.
Persistent AF with an uncontrolled, rapid ventricular heart rate response can cause a dilated cardiomyopathy and can lead to electrical remodeling in the atria (atrial cardiomyopathy). Therapy, such as drugs or atrioventricular nodal ablation and permanent pacemaker implantation, to control the ventricular rate can improve left ventricular function and improve quality-of-life scores.

**Permanent AF**

Permanent AF is recognized as the accepted rhythm, and the main treatment goals are rate control and anticoagulation. While it is possible to reverse the progression from paroxysmal to persistent and to permanent, this task can be challenging.

**Lone atrial fibrillation**

In addition to the above schema, the term "lone atrial fibrillation" has been used to identify AF in younger patients without structural heart disease, who are at a lower risk for thromboembolism. The definition of lone AF remains controversial, but it generally refers to paroxysmal, persistent, or permanent AF in younger patients (< 60 y) who have normal echocardiographic findings.\[11\]

**Pathophysiology**

Atrial fibrillation (AF) shares strong associations with other cardiovascular diseases, such as heart failure, coronary artery disease (CAD), valvular heart disease, diabetes mellitus, and hypertension.\[12\] These factors have been termed upstream risk factors, but the relationship between comorbid cardiovascular disease and AF is incompletely understood and more complex than this terminology implies. The exact mechanisms by which cardiovascular risk factors predispose to AF are not understood fully but are under intense investigation. Catecholamine excess, hemodynamic stress, atrial ischemia, atrial inflammation, metabolic stress, and neurohumoral cascade activation are all purported to promote AF.

Because diabetes mellitus and obesity are increasing in prevalence and are associated with an elevated risk of AF, Fontes et al examined whether insulin resistance is an intermediate step for the development of AF. In a community-based cohort that included 279 patients who developed AF within 10 years of follow-up, no significant association was observed between insulin resistance and incident AF.\[13\]

Although the precise mechanisms that cause atrial fibrillation are incompletely understood, AF appears to require both an initiating event and a permissive atrial substrate. Significant recent discoveries have highlighted the importance of focal pulmonary vein triggers, but alternative and nonmutually exclusive mechanisms have also been evaluated. These mechanisms include multiple wavelets, mother waves, fixed or moving rotors, and macro-reentrant circuits. In a given patient, multiple mechanisms may coexist at any given time. The automatic focus theory and the multiple wavelet hypothesis appear to have the best supporting data.

**Automatic focus**

A focal origin of AF is supported by several experimental models showing that AF persists only in isolated regions of atrial myocardium. This theory has garnered considerable attention, as studies have demonstrated that a focal source of AF can be identified in humans and that isolation of this source can eliminate AF.
The pulmonary veins appear to be the most frequent source of these automatic foci, but other foci have been demonstrated in several areas throughout the atria. Cardiac muscle in the pulmonary veins appears to have active electrical properties that are similar, but not identical, to those of atrial myocytes. Heterogeneity of electrical conduction around the pulmonary veins is theorized to promote reentry and sustained AF. Thus, pulmonary vein automatic triggers may provide the initiating event, and heterogeneity of conduction may provide the sustaining conditions in many patients with AF.

Multiple wavelet

The multiple wavelet hypothesis proposes that fractionation of wave fronts propagating through the atria results in self-perpetuating "daughter wavelets." In this model, the number of wavelets is determined by the refractory period, conduction velocity, and mass of atrial tissue. Increased atrial mass, shortened atrial refractory period, and delayed intra-atrial conduction increase the number of wavelets and promote sustained AF. This model is supported by data from patients with paroxysmal AF demonstrating that widespread distribution of abnormal atrial electrograms predicts progression to persistent AF.[14] Intra-atrial conduction prolongation has also been shown to predict recurrence of AF.[15] Together, these data highlight the importance of atrial structural and electrical remodeling in the maintenance of AF—hence the phrase "atrial fibrillation begets atrial fibrillation."

Etiology

Atrial fibrillation (AF) is strongly associated with the following risk factors:

- Hemodynamic stress
- Atrial ischemia
- Inflammation
- Noncardiovascular respiratory causes
- Alcohol and drug use
- Endocrine disorders
- Neurologic disorders
- Genetic factors
- Advancing age

Hemodynamic stress

Increased intra-atrial pressure results in atrial electrical and structural remodeling and predisposes to AF. The most common causes of increased atrial pressure are mitral or tricuspid valve disease and left ventricular dysfunction. Systemic or pulmonary hypertension also commonly predisposes to atrial pressure overload, and intracardiac tumors or thrombi are rare causes.

Atrial ischemia

Coronary artery disease infrequently leads directly to atrial ischemia and AF. More commonly, severe ventricular ischemia leads to increased intra-atrial pressure and AF.

Inflammation
Myocarditis and pericarditis may be idiopathic or may occur in association with collagen vascular diseases; viral or bacterial infections; or cardiac, esophageal, or thoracic surgery.

**Noncardiovascular respiratory causes**

Pulmonary embolism, pneumonia, lung cancer, and hypothermia have been associated with AF.

**Drug and alcohol use**

Stimulants, alcohol, and cocaine can trigger AF. Acute or chronic alcohol use (ie, holiday or Saturday night heart, also known as alcohol-related cardiomyopathy) and illicit drug use (ie, stimulants, methamphetamines, cocaine) have been specifically found to be related to AF.

**Endocrine disorders**

Hyperthyroidism, diabetes, and pheochromocytoma have been associated with AF.

**Neurologic disorders**

Intracranial processes such as subarachnoid hemorrhage or stroke can precipitate AF.

**Familial AF**

A history of parental AF appears to confer increased likelihood of AF (and occasional family pedigrees of AF are associated with defined ion channel abnormalities, especially sodium channels). One cohort study suggests that familial AF is associated with an increased risk of AF. This increase was not lessened by adjustment for genetic variants and other AF risk factors.

**Advancing age**

AF is strongly age-dependent, affecting 4% of individuals older than 60 years and 8% of persons older than 80 years.

**Epidemiology**

Atrial fibrillation affects more than 2.2 million persons in the United States. AF is strongly age-dependent, affecting 4% of individuals older than 60 years and 8% of persons older than 80 years. Approximately 25% of individuals aged 40 years and older will develop AF during their lifetime.

The prevalence of AF is 0.1% in persons younger than 55 years, 3.8% in persons 60 years or older, and 10% in persons 80 years or older. With the projected increase in the elderly population in the United States, the prevalence of AF is expected to more than double by the year 2050. AF is uncommon in childhood except after cardiac surgery.

The incidence of AF is significantly higher in men than in women in all age groups. AF appears to be more common in whites than in blacks, with blacks have less than half the age-adjusted risk of developing AF.
In 10-15% of cases of AF, the disease occurs in the absence of comorbidities (lone atrial fibrillation). However, AF is often associated with other cardiovascular diseases, including hypertension; heart failure; diabetes-related heart disease; ischemic heart disease; and valvular, dilated, hypertrophic, restrictive, and congenital cardiomyopathies. The Atherosclerosis Risk in Communities (ARIC) Study suggests reduced kidney function and presence of albuminuria are strongly associated with AF.

The rate of ischemic stroke in patients with nonrheumatic AF averages 5% a year, which is somewhere between 2 and 7 times the rate of stroke in patients without AF. The risk of stroke is not due solely to AF; it increases substantially in the presence of other cardiovascular diseases. The prevalence of stroke in patients younger than 60 years is less than 0.5%; however, in those older than 70 years, the prevalence doubles with each decade. The attributable risk of stroke from AF is estimated to be 1.5% for those aged 50-59 years, and it approaches 30% for those aged 80-89 years. Women are at a higher risk of stroke due to AF than men and some have suggested this may be due to undertreatment with warfarin. However, one study of patients 65 years or older with recently diagnosed AF found warfarin use played no part in the increased risk of stroke among female patients.

**Prognosis**

AF is associated with a 1.5- to 1.9-fold higher risk of death, which is in part due to the strong association between AF and thromboembolic events, according to data from the Framingham heart study.

Medical therapies aimed at rhythm control offered no survival advantage over rate control and anticoagulation, according to the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial. The study addressed whether rate control and anticoagulation are sufficient goals for asymptomatic, elderly patients. Atrial fibrillation (AF) is associated with increased morbidity and mortality, in part due to the risk of thromboembolic disease, particularly stroke, in AF and in part due to its associated risk factors. Studies have shown that individuals in sinus rhythm live longer than individuals with AF. Disruption of normal atrial electromechanical function in AF leads to blood stasis. This, in turn, can lead to development of thrombus, most commonly in the left atrial appendage. Dislodgement or fragmentation of a clot can then lead to embolic phenomena, including stroke.

Development of AF predicts heart failure and is associated with a worse New York Heart Association Heart Failure classification. AF may also worsen heart failure in individuals who are dependent on the atrial component of the cardiac output. Those with hypertensive heart disease and those with valvular heart disease are particularly at high risk for developing heart failure when AF occurs. In addition, AF may cause tachycardia-mediated cardiomyopathy if adequate rate control is not established.

The risk of stroke from AF that lasts longer than 24 hours is a major concern and is usually addressed by prescribing a blood thinner (Coumadin or dabigatran). Prognostic score systems, such as CHADS2, appear to underestimate the risk of embolic stroke in patients older than 75 years; thus, some studies recommend treating all patients older than 75 years unless a compelling contraindication is noted. The CHADS2 score predicts ischemic stroke not only for patients with a history of atrial fibrillation but also for patients without atrial fibrillation who have a history of coronary heart disease. In the latter group, net benefit of prophylactic anticoagulation has yet to be established.

An analysis of the AFNET (Central Registry of the German Competence NETwork on Atrial Fibrillation) registry of 8847 patients with nonvalvular atrial fibrillation indicated that the CHA2DS2-VASc score is more sensitive
than the CHADS<sub>2</sub> score for risk stratification of thromboembolic events (ischemic stroke, transient ischemic attack [TIA], systemic embolism), particularly in patients at low or intermediate risk for stroke (CHADS<sub>2</sub> score of 0 or 1)—who therefore do not require oral anticoagulation.\textsuperscript{[28, 29]}

During a mean follow-up of 5 years, the investigators found 36.5% (144 of 395) of strokes or other thromboembolic events occurred in patients given a CHADS<sub>2</sub> score of 0 or 1, groups in which there is no definitive recommendation for oral anticoagulation.\textsuperscript{[28, 29]} However, CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring—which adds age 65-74 years, vascular disease, and female sex as stroke risk factors to the CHADS<sub>2</sub> score\textsuperscript{[29]}—placed 30.3% of those classified as CHADS<sub>2</sub> 0 or 1 into CHA<sub>2</sub>DS<sub>2</sub>-VASc 1 or 2 and higher, groups in which oral anticoagulation is recommended.\textsuperscript{[28]}

A post-hoc analysis of the ONTARGET and TREND studies, which evaluated the efficacy of treatment with ramipril plus telmisartan or telmisartan alone in reducing cardiovascular disease, used the Mini–Mental State Examination (MMSE) to measure the cognitive function of participants at baseline and after two and five years. Results show that AF is associated with an increased risk of cognitive decline, new dementia, loss of independence in performing activities of daily living and admission to long-term care facilities.\textsuperscript{[30]}

**Atrial fibrillation in association with acute myocardial infarction**

AF is a common finding in patients presenting with an acute myocardial infarction. A meta-analysis pooled data from 43 studies and more than 278,800 patients.\textsuperscript{[31]} The study found that AF in the setting of acute myocardial infarction was associated with 40% increase in mortality compared to patients in sinus rhythm with acute myocardial infarction. The causes of death were unclear, but may be related to triple anticoagulation therapy with aspirin, clopidogrel, and warfarin, or may be related to hemodynamic consequences associated with the loss of atrial contraction. Whether AF is a complication of myocardial infarction or a marker for myocardial infarction severity is unclear.

**Patient Education**

A study by van Diepen et al suggests that patients with heart failure or atrial fibrillation have a significantly higher risk of noncardiac postoperative mortality than patients with coronary artery disease; thus, patients and physicians should consider this risk, even if a minor procedure is planned.\textsuperscript{[32]}

For excellent patient education resources, visit eMedicineHealth’s [Heart Center](https://emedicinehealth.com/heart-center) and [Stroke Center](https://emedicinehealth.com/stroke-center). Also, see eMedicineHealth’s patient education articles [Atrial Fibrillation](https://emedicinehealth.com/atrial-fibrillation), [Heart Rhythm Disorders](https://emedicinehealth.com/heart-rhythm-disorders), [Stroke](https://emedicinehealth.com/stroke), and [Supraventricular Tachycardia](https://emedicinehealth.com/supraventricular-tachycardia).
Atrial Fibrillation Clinical Presentation

Author: Lawrence Rosenthal, MD, PhD, FACC, FHRS; Chief Editor: Jeffrey N Rottman, MD

History

Clinical presentation spans the entire spectrum from asymptomatic atrial fibrillation (AF) with rapid ventricular response to cardiogenic shock or devastating cerebrovascular accident (CVA).

Initial evaluation of the patient with new-onset atrial fibrillation should focus on the patient's hemodynamic stability. Care of hemodynamically unstable patients is guided by Advanced Cardiac Life Support (ACLS) protocols, including immediate direct current (DC) cardioversion. Symptomatic patients may benefit from intravenous (IV) rate-controlling agents, either calcium-channel blockers or beta-adrenergic blockers.

While up to 90% of AF episodes may not cause symptoms, many patients experience a wide variety of symptoms, including palpitations, dyspnea, fatigue, dizziness, angina, and decompensated heart failure. In addition, AF can be associated with hemodynamic dysfunction, tachycardia-induced cardiomyopathy, and systemic thromboembolism.

Unstable patients requiring immediate DC cardioversion include the following:

- Patients with decompensated congestive heart failure (CHF)
- Patients with hypotension
- Patients with uncontrolled angina/ischemia

Less severe symptoms and patient complaints include the following:

- Palpitations
- Fatigue or poor exercise tolerance
- Presyncope or syncope
- Generalized weakness, dizziness, fatigue

In addition to eliciting the symptoms above, history taking of any patient presenting with suspected AF should include questions relevant to temporality, precipitating factors (including hydration status, recent infections, alcohol use), history of pharmacologic or electric interventions and responses, and presence of heart disease. An effort should also be made to evaluate for potential comorbid diseases that contribute to initiation or maintenance of AF. Occasionally, a patient may have a clear and strong belief about the onset of symptoms that may be helpful in determining a course of action.

Initial history includes the following:

Documentation of clinical type of AF (paroxysmal, persistent, or permanent) (See Diagnostic Considerations.)

- Assessment of type, duration, and frequency of symptoms
- Assessment of precipitating factors (eg, exertion, sleep, caffeine, alcohol use)
- Assessment of modes of termination (eg, vagal maneuvers)
- Documentation of prior use of antiarrhythmics and rate-controlling agents
- Assessment of presence of underlying heart disease

Documentation of any previous surgical or percutaneous AF ablation procedures

**Physical Examination**

Physical examination always begins with airway, breathing, and circulation (ABCs) and vital signs, as these guide the pace of the intervention. The physical examination also provides information on underlying causes and sequelae of atrial fibrillation.

**Vital signs**

Heart rate, blood pressure, respiratory rate, and oxygen saturation are particularly important in evaluating hemodynamic stability and adequacy of rate control in AF.

Patients will have an irregularly irregular pulse and will commonly be tachycardic, with heart rates typically in the 110- to 140-range, but rarely over 160-170. Patients who are hypothermic or who have cardiac drug toxicity may present with bradycardic atrial fibrillation.

**Head and neck**

Examination of the head and neck may reveal exophthalmos, thyromegaly, elevated jugular venous pressures, or cyanosis. Carotid artery bruits suggest peripheral arterial disease and increase the likelihood of comorbid coronary artery disease.

**Pulmonary**

The pulmonary examination may reveal evidence of heart failure (eg, rales, pleural effusion). Wheezes or diminished breath sounds are suggestive of underlying pulmonary disease (eg, chronic obstructive pulmonary disease [COPD], asthma).

**Cardiac**

The cardiac examination is central to the physical examination of the patient with AF. Thorough palpation and auscultation are necessary to evaluate for valvular heart disease or cardiomyopathy. A displaced point of maximal impulse or S₃ suggests ventricular enlargement and elevated left ventricular pressure. A prominent P₂ points to the presence of pulmonary hypertension.

**Abdomen**

The presence of ascites, hepatomegaly, or hepatic capsular tenderness suggests right ventricular failure or intrinsic liver disease. Left upper quadrant pain may suggest splenic infarct from peripheral embolization.

**Lower extremities**
Examination of the lower extremities may reveal cyanosis, clubbing, or edema. A cool or cold pulseless extremity may suggest peripheral embolization, and assessment of peripheral pulses may lead to the diagnosis of peripheral arterial disease or diminished cardiac output.

**Neurologic**

Signs of a transient ischemic attack or cerebrovascular accident may be discovered. Evidence of prior stroke and increased reflexes is suggestive of hyperthyroidism.

**Holiday Heart Syndrome Workup**

Author: Adam S Budzikowski, MD, PhD; Chief Editor: Jeffrey N Rottman, MD

**Laboratory Studies**

- Assess serum electrolyte levels, particularly potassium, in all patients with acute arrhythmias.

**Imaging Studies**

- Echocardiography has become the standard diagnostic modality to assess chamber enlargement, left ventricular (LV) wall motion abnormalities, hypertrophy, valvular disease, and systolic dysfunction.
- In patients at risk for coronary artery disease, additional cardiac imaging (eg, perfusion imaging, echocardiography) may be required.

**Other Tests**

- Twelve-lead ECG is essential to exclude other cardiac pathology such as ischemia, infarction, pulmonary embolism, or hypertrophy.
- Upon resolution of holiday heart syndrome and return to sinus rhythm, treadmill stress testing is reasonable in some patients to look for exercise-related arrhythmia after the acute effects of alcohol have resolved.

**Holiday Heart Syndrome Treatment & Management**

Author: Adam S Budzikowski, MD, PhD; Chief Editor: Jeffrey N Rottman, MD

**Medical Care**

Patients presenting to the emergency department with sustained tachyarrhythmia secondary to acute alcohol toxicity usually can be observed with ECG monitoring. Treatment with an AV nodal blocking agent (eg, beta-blocker, verapamil, diltiazem) may be needed if the ventricular rate is excessive. If the duration of atrial fibrillation approaches 24-48 hours, cardioversion should be considered to obviate the need for anticoagulation. In general, pericardioversion anticoagulation is required for atrial fibrillation lasting more than 48 hours.
Most patients with structural heart disease should be admitted for observation and treatment if the arrhythmia persists.

Young patients with no evidence of structural heart disease sometimes can be discharged without further treatment once their arrhythmia has stabilized.

Advise all patients against the excessive use of alcohol in the future.

**Consultations**

Patients presenting with new-onset tachyarrhythmias and structural heart disease, such as myocardial ischemia and/or LV dysfunction, often require a more extensive evaluation, and consultation with a cardiologist may be necessary.

**Diet**

The use of alcohol is contraindicated. Stimulants such as caffeine should be avoided initially; the interaction of alcohol and caffeine on atrial fibrillation has not been determined.

**Activity**

Following alcohol-related arrhythmia, it usually is advisable for patients to refrain from significant exertion because excessive catecholamines can precipitate recurrent episodes in some cases. Most patients without underlying heart disease should be able to gradually resume full physical activity over the next few days.

---

**Holiday Heart Syndrome Medication**

Author: Adam S Budzikowski, MD, PhD; Chief Editor: Jeffrey N Rottman, MD

**Medication Summary**

Symptoms of acute alcohol toxicity often resolve spontaneously. Arrhythmia monitoring and observation are adequate in many patients. In patients with atrial tachyarrhythmias and a rapid ventricular response (eg, atrial fibrillation or flutter), ventricular rate control is important for those who are symptomatic. The use of intravenous beta-antagonists, diltiazem, or verapamil is appropriate. Digoxin has a slow onset of action, and chronic therapy with this drug is rarely indicated. As always, patients who are hemodynamically unstable patients should be treated with direct current cardioversion.

**Beta-antagonists**

**Class Summary**

In patients with atrial tachyarrhythmias and a rapid ventricular response (eg, atrial fibrillation or flutter), ventricular rate control is important for those who are symptomatic.

[View full drug information]
**Metoprolol (Lopressor, Toprol XL)**

Beta-antagonists are useful agents because of their rapid onset of action and sympatholytic effects. They are the treatment of choice if acute myocardial ischemia or myocardial infarction is present.

**Calcium channel blockers (nondihydropyridine)**

**Class Summary**

In specialized conducting and automatic cells in the heart, calcium is involved in the generation of the action potential. The calcium channel blockers inhibit movement of calcium ions across the cell membrane, thus depressing both impulse formation (automaticity) and conduction velocity.

**Verapamil (Calan, Covera-HS, Verelan)**

Can diminish PVCs associated with perfusion therapy and decrease the risk of ventricular fibrillation and ventricular tachycardia.

**Diltiazem (Cardizem CD, Dilacor, Tiazac)**

For symptomatic supraventricular tachycardias. In many situations, this may be the drug of choice if used IV, since it is relatively short acting and can be stopped if there is resolution of arrhythmia following recovery from acute alcohol toxicity. This is an excellent approach in patients without evidence of underlying cardiac disease.

**Digoxin (Lanoxin, Lanoxicaps)**

Cardiac glycoside with direct inotropic effects in addition to indirect effects on the cardiovascular system. Acts directly on cardiac muscle, increasing myocardial systolic contractions. Its indirect actions result in increased carotid sinus nerve activity and enhanced sympathetic withdrawal for any given increase in mean arterial pressure.

**Further Inpatient Care**

Upon resolution of holiday heart symptoms and return to sinus rhythm, treadmill stress testing is reasonable in some patients to look for exercise-related arrhythmia when the acute effects of alcohol have resolved. This is also important in patients at risk for coronary artery disease; occasionally, additional cardiac imaging (eg, perfusion imaging, echocardiography) is required.

**Further Outpatient Care**

Alcohol-induced atrial fibrillation without other unrelated episodes would not typically be considered a current indication for atrial fibrillation surgical or catheter ablation.

**Inpatient & Outpatient Medications**
Upon resolution of the alcohol-related arrhythmia, most patients do not require further therapy if they refrain from alcohol use. Patients with underlying heart disease or those with severe symptoms on presentation (eg, syncope, hypotension) may be candidates on discharge for oral agents such as beta-antagonists.

Transfer

Persons with alcoholism should be considered for transfer to facilities for detoxification/rehabilitation.

Deterrence/Prevention

Advise patients to refrain from alcohol and stimulants and to avoid excessive fatigue.

Prognosis

Prognosis depends on the presence of underlying heart disease. Long-term alcohol use increases the risk of cardiomyopathy and chronic liver disease.

References

AVAILABLE ON REQUEST

Caffeine: No Downside, Hint of Benefit in Atrial Fibrillation

Fran Lowry

January 10, 2014

Heartwire © 2014 Medscape, LLC

Cite this article: Caffeine: No Downside, Hint of Benefit in Atrial Fibrillation. Medscape. Jan 10, 2014.

A meta-analysis from Chinese researchers has concluded that there is an inverse relationship between regular caffeine consumption and atrial fibrillation risk[1].

"It is unlikely that habitual caffeine intake increases AF risk," write Dr Min Cheng (State Key Laboratory of Cardiovascular Disease, Beijing, China) and colleagues in their study, published online January 6, 2014 in the Canadian Journal of Cardiology.

In fact, they conclude, habitual caffeine consumption may actually reduce AF risk.

"The finding of this study is meaningful. First, there is no need for concern that habitual caffeine intake may increase AF risk. Second, as atrial fibrosis is an important substrate for AF and caffeine has an antifibrosis property, the finding may pave the way for seeking effective antifibrosis agents for AF management or prompt development of caffeine as an agent for preventing AF," Cheng et al write.

Commenting on this study, Dr Stanley Nattel (University of Montreal, QC) called the findings "reassuring" for patients, many of whom have felt they need to steer clear of coffee and other caffeinated drinks.

Caffeine and AF: Link Unclear

Caffeine is a major component of some of the most widely consumed beverages, and the link between regular caffeine intake with incident AF was unknown. The aim of this meta-analysis was to investigate the association
between chronic exposure to caffeine and AF risk and also to evaluate the potential dose-response relationship.

Cheng et al's analysis consisted of six prospective cohort studies that included 228,465 participants. Three of these studies were done in the US, two in Sweden, and one in Denmark.

During a mean follow-up of from four to 25.2 years, 4,261 participants suffered from AF.

Participants' mean age at baseline ranged from 53 to 63 years. The prevalence of smoking ranged from 5.8% among participants with the lowest caffeine intake to 76.8% among participants with the highest caffeine intake.

All of the studies documented the incidence of AF by electrocardiography; three studies estimated daily caffeine intake by the frequency of caffeine or coffee consumption during the previous year, and three studies estimated caffeine consumption according to reported daily coffee consumption. In addition, three studies summed the daily intake of coffee, tea, cola, cocoa, or chocolate for each subject.

The pooled relative risk (RR) for the incidence of AF from habitual caffeine exposure was 0.90 (95% CI 0.81–1.01; p=0.07) in the primary analysis. There was also significant heterogeneity among the six studies ($I^2=73\%$; p=0.002).

The researchers also found an inverse relationship between the amount of caffeine consumed and the risk of AF.

Pooled results from studies that adjusted for potential confounders showed an 11% reduction for low doses of caffeine (RR 0.89, 95% CI 0.80–0.99; p=0.032), and a 16% reduction for high doses (RR 0.84, 95% CI 0.75–0.94; p=0.002).

Similarly, an inverse relation was found between habitual caffeine intake and AF risk (p=0.015 for overall trend), and the incidence of AF decreased by 6% (RR 0.94, 95% CI 0.90–0.99) for every 300-mg/day increment in habitual caffeine intake.

A Second Cup?

In their discussion, the authors suggest that habitual caffeine consumption may offer a moderate protective effect against AF for a variety of reasons.

The studies in this meta-analysis showed that 400 mg of caffeine did not induce change in P-wave indices compared with the baseline electrocardiography, and one showed that 400 mg of caffeine did not change PR interval, QRS duration, corrected QT interval, RR interval, or corrected QT-interval dispersion.

Nor, in another study, did 300 mg of caffeine increase the occurrence or severity of ventricular arrhythmias during the healing phase of acute MI. Even in patients with clinical ventricular arrhythmias, caffeine did not significantly alter inducibility or severity of arrhythmias, the authors noted.

Further, in people who habitually consumed caffeine, the adrenergic effects of caffeine were greatly attenuated and its possible acute proarrhythmia effect reduced.

Habitual caffeine intake may also reduce AF risk because of its antifibrosis effect, Cheng et al write.

Harm vs Benefit
"AF is a very common condition, affecting about one in four people over their lifespan. Patients with AF are often told to avoid stimulants like caffeine, but the evidence for deleterious effects of caffeine is quite weak," Nattel, who was not part of the current study, pointed out. He also applauded the rigorous criteria investigators used in their meta-analysis.

But, unlike the authors, Nattel stopped short of saying that patients should actually consider "using" caffeine to treat AF.

"Even though the study suggested a dose-related protective effect of caffeine against AF, I would not recommend using caffeine to treat AF on this basis. But the results do reassure us that AF patient can enjoy their cup of coffee with a clear conscience," he said.

The study was supported by the National Natural Science Foundation of China and the National Basic Research Program of China. Cheng reports no relevant financial relationships. Nattel is editor in chief of the Canadian Journal of Cardiology.

References


Alcohol May Trigger AF Episodes

Reed Miller

June 06, 2012

Heartwire © 2012 Medscape, LLC

Cite this article: Alcohol May Trigger AF Episodes. Medscape. Jun 06, 2012

June 6, 2012 (San Francisco, California) — Results of a new study suggest that patients with paroxysmal atrial fibrillation (PAF) should avoid consuming alcohol to reduce the risk of AF episodes, but the exact link between alcohol and arrhythmias is still poorly understood [1].

Dr Gregory Marcus (University of California, San Francisco) and colleagues previously reported trial results showing that daily consumption of alcohol by patients younger than 60 increases the risk of atrial fibrillation and flutter and that the risk of atrial flutter especially increases with greater alcohol consumption. "It looked like that might be related to a shorter atrial refractory period, which theoretically could have some causal mechanisms related to atrial fibrillation, but there's been very little research on understanding those mechanisms," Marcus told heartwire.

"There's generally a perception out there that alcohol is good for your heart, but it looks like there's something going on that's probably important and could be detrimental electrically, so that's pertinent to everyone who drinks alcohol. Second, if we could really understand how alcohol triggers atrial fibrillation, we might learn something important about atrial fibrillation itself." He also suggested that this question is "ripe
for a randomized study," comparing arrhythmia episodes of patients consuming alcohol with those not consuming alcohol.

Marcus and medical student Mala Mandyman (University of California, San Francisco) are the lead authors of a study, scheduled for the August 1, 2012 issue of the American Journal of Cardiology, comparing the self-reported frequency of PAF episodes in patients with previously documented PAF with the frequency of episodes of patients with other types of supraventricular tachycardia (SVT).

At a single center, 223 patients with a documented arrhythmia (133 with PAF and 90 with SVT) completed a survey detailing their alcohol-consumption pattern and arrhythmia episodes. Episodes were considered triggered by vagal activation if the subject's episodes usually began while the patient was resting or eating or if the symptoms terminated with exercise. If the episode was triggered after the patient was exercising, stressed, or consuming caffeine, the episode was considered triggered by sympathetic activation.

After multivariable adjustment, the patients with PAF had a 4.42 greater odds of reporting alcohol consumption (p=0.014) and a 2.02 greater odds (95% CI 1.02–4.00) as the arrhythmia trigger compared with patients with SVT. Younger age (odds ratio 0.68, p=0.022) and a family history of AF (OR 5.73, p=0.028) each were independently associated with vagal activation of episodes. Patients with PAF and alcohol triggers were more likely to report vagal triggers of arrhythmias (OR 10.32, p=0.045).

In patients with PAF, beer was the type of alcohol most commonly cited as a trigger (odds ratio 4.49, p=0.011), although the authors note that the questionnaire only asked what type of alcohol the subject drank the most, rather than what they were drinking before each episode. This association may be due to beer drinkers generally drinking more alcohol overall compared with those who prefer wine or spirits, but this association persisted after adjustment for average consumption and bingeing, Mandyam et al point out.

"It does appear that certain patients are more or less prone to alcohol triggering their symptoms. I don't think we know--there are conflicting data from large epidemiological studies--if alcohol actually causes atrial fibrillation," Marcus said. "So there are insufficient data to give a strong recommendation, [but] certainly in people in whom alcohol has triggered atrial fibrillation, I recommend abstinence [in the future]." With everyone else, Marcus advises moderation.

This study was supported by the National Center for Research Resources, the National Center for Advancing Translational Sciences, and the office of the director, National Institutes of Health.

References


Coffee Consumption and Chronic Liver Disease: The New Best Prescription?
Review Article: Coffee Consumption, the Metabolic Syndrome and Non-alcoholic Fatty Liver Disease

Yesil A, Yilmaz Y
*Aliment Pharmacol Ther.* 2013;38:1038-1044

**Study Summary**

Coffee consumption is a part of daily life in most areas of the world. As such, a number of studies have evaluated the chemical composition and related effects that this enjoyable beverage may have on health and disease.

For many years, healthcare providers have advised patients to avoid excessive consumption because of a concern about caffeine dependence. Several recent studies, however, suggest that regular coffee consumption may modulate the risk for fibrosis in chronic liver disease.

Yesil and Yilmaz analyzed the experimental, epidemiologic, and clinical studies and the modulation of the metabolic syndrome and nonalcoholic fatty liver disease (NAFLD). Animal studies showed a reduction in the metabolic syndrome with improvements in glycemic and lipid regulation, as well as reductions in transaminases and proinflammatory cytokine hepatic gene expression. Other studies showed reductions in hepatic fat and collagen proinflammatory tumor necrosis factor, as well as increases in anti-inflammatory interleukins. Epidemiologic and clinical studies demonstrated a significant inverse association between coffee consumption and prevalence of metabolic syndrome, as well as a reduced risk for NAFLD.

**Coffee Reduces Risk for Hepatocellular Carcinoma: An Updated Meta-analysis**

Bravi F, Bosetti C, Tavani A, Gallus S, La Vecchia C
*Clin Gastroenterol Hepatol.* 2013;11:1413-1421

**Study Summary**
The meta-analysis by Bravi and colleagues is a logical extension of the data demonstrating the beneficial effects of coffee on NAFLD, now showing a reduction in associated risk for hepatocellular carcinoma (HCC). Sixteen studies were identified. Overall, compared with no coffee consumption, the risk for HCC was reduced by 28% with low-level consumption, and by 36% with high-level consumption (3 or more cups/day). It is likely that this favorable effect is the result of reduced cirrhosis evident in coffee drinkers, as well as improvement in the metabolic syndrome, because diabetes is another known risk factor for HCC. The researchers adjusted for other major risk factors for HCC, including hepatitis B virus, hepatitis C virus, cirrhosis, alcohol use, and tobacco use.

**Viewpoint**

The data on beneficial effects of coffee consumption are impressive. These effects extend across all geographic areas as well as evidence from animals and retrospective and prospective clinical studies.

There are differences in coffee bean composition as well as extractions used in preparation, but these findings seem to be specifically related to brewed, roasted, regular (not decaffeinated) coffee. Of interest, the beneficial effects have not been evident in nonfiltered, boiled (Turkish), or French press preparations.

Reportedly, there are more than 1500 chemical components of coffee, which are subject to agricultural and preparation-related influences. Although caffeine is the major active ingredient, many other components have significant antioxidant activity. Caffeine was thought previously to have antioxidant effects, but this has not been demonstrated subsequently in animal or human models.

The specific mechanisms by which coffee exerts these beneficial effects have not been clearly defined. What is apparent is that these effects extend across the spectrum of liver disease, ranging from hepatic steatosis to fibrosis, cirrhosis, and HCC. Of interest, these beneficial effects do not seem to extend to risk reduction for pancreatic cancer.\(^1\) On the basis of the evidence, however, moderate consumption of brewed regular coffee seems to have clinical benefit for patients at risk for NAFLD or viral-related hepatic fibrosis. As clinicians who often recommend avoidance or reduction of delectables that contribute to disease states, it is nice to be able to give one back to patients.

**References**

Best Evidence Review of Health Effects of Coffee

Coffee is one of the most frequently consumed beverages on earth, yet there remain many questions regarding its effects on health. A recent observational study made headlines for finding a positive association between heavy coffee consumption and an increased risk for death among men, but the research had some substantial limitations. Other research certainly suggests that coffee can reduce the risk for diabetes and cardiovascular events. Overall, however, patients will probably have far more to gain by addressing other lifestyle and diet issues besides coffee drinking in their quest for a longer, happier life.

The Study


The Background

"Doctor, I made some of those changes we talked about last time!" my patient relates with enthusiasm. I am genuinely excited. Ten tortillas per day, lots of Hogan's Heroes reruns, and problem alcohol drinking is no way to go through life, son.

"I stopped drinking coffee!" And my hopes vanish faster than the Baconator® my patient inhaled immediately before his appointment with me. Coffee?! That was never part of the conversation. I can't help but look at my e-chart; yep, 1 cup of coffee each morning. In my analysis, he's safe as kittens regarding any health risk from coffee consumption.

This scene has played out time and again in my practice, and it has reinforced to me that many adults consider coffee drinking a guilty pleasure. If so, there are many guilty individuals out there. According to trade association reports, 83% of US adults now drink coffee, a 5% increase since 2012 and part of an upward trend over the past 2 decades. The majority of Americans drink coffee on a daily basis, and the average number of cups per day among daily drinkers is 3.1.

But what are the health risks associated with that cup of joe? A new study will give anyone in line at their favorite coffee shop something serious to consider.

Study Synopsis
This prospective study recruited adults between the ages of 20 and 87 years for over 30 years, ending in 2002. Patients with a history of cardiovascular disease, cancer, or abnormal exercise stress testing were excluded from the current analysis.

Participants completed health questionnaires that included questions regarding coffee consumption. They also underwent a baseline examination that included laboratory analyses and an exercise stress test. Mortality data were culled from national and state databases.

The main study outcome was the relationship between coffee consumption and mortality risk. These results were adjusted to account for demographics, chronic disease, and other health habit information. They were not stratified according to lab results.

Data for study analysis came from 43,727 adults; 77% of the cohort was male, and the average age at the time of enrollment was 43 years. Participants were predominantly white, at the higher end of the socioeconomic spectrum, and well educated. Approximately one quarter of the study cohort had hypertension or hyperlipidemia.

A minority of participants (19% of men and 21% of women) never drank coffee, while approximately a third (35.2% of men and 33.5% of women) drank 22 or more cups of coffee per week. Coffee consumption was associated with higher rates of smoking and lower levels of cardiorespiratory fitness.

The most surprising finding from the multivariate adjustment analysis was that men who drank at least 28 cups of coffee per week experienced a hazard ratio of 1.21 for all-cause mortality (95% confidence interval, 1.04-1.40) when compared with men who did not drink coffee. There were also nonsignificant increases in the risk for mortality associated with drinking any amount of coffee, from 1 to 28 cups per week among men. However, there was no significant effect of coffee consumption on the risk for mortality among women.

An association between heavy coffee consumption and a higher risk for cardiovascular mortality specifically was found on initial analysis among men, but this association was rendered nonsignificant after adjustment for cardiorespiratory fitness. Subgroup analysis found that any mortality risk associated with coffee was most pertinent for men and women younger than 55 years of age. Adjustment for body mass index did not significantly alter the study's main findings, and coffee did not promote a higher risk for mortality among smokers.

The strengths of this study are its size and length of follow-up. It would be difficult to create meaningful results for mortality outcomes from a smaller study. The natural limitation to an observational study is confounding data, and the researchers made adjustments to account for important confounders, including an objective test to measure exercise tolerance. They did not adjust their results based on laboratory data such as lipid levels.

This research has other major limitations. Participants' coffee consumption was measured only at baseline and changes were not assessed. While the researchers noted that adults' coffee-drinking habits change little over time, certainly the culture of coffee and coffee consumption has undergone a revolution during the study period between 1971 and 2002. It is hard to believe that there have not been changes in the ways that people prepare and consume coffee over 3 decades.

This leads to another major study limitation: a failure to define their main variable. Not only was the type of coffee -- caffeinated vs decaffeinated, for example -- not evaluated as part of the study methods, but the authors failed to define the measurement of a cup of coffee in the first place. In America's "Supersize It!" culture, there are some massive cups of coffee out there (the average coffee mug holds 9 ounces), so any reasonable analysis should account for the exact volume of coffee consumed.1
Discussion

This is not the first study performed on the health effects of coffee, and the subject remains controversial. It is interesting that the results of this study buck the trend of recent, high-quality research that suggests that coffee improves health outcomes.

Coffee can raise blood pressure acutely, but the consensus appears to be that it has a negligible role in promoting hypertension. In one systematic review of observational studies, only mild coffee consumption of 1-3 cups per day was associated with a higher risk for hypertension compared with no coffee consumption.\([3]\)

A more recent review found that the cumulative effect of coffee consumption on blood pressure was less than 1 mm Hg, and coffee did not promote hypertension.\([4]\)

Coffee has more mixed effects on other important cardiovascular risk factors. A meta-analysis of 12 studies found that coffee increased serum levels of total cholesterol, low-density lipoprotein cholesterol, and triglycerides, with a dose-response effect.\([5]\) In contrast, a meta-analysis of 18 studies with over 400,000 participants in total found that each additional cup of coffee consumed daily was associated with a 7% reduction in the risk for incident type 2 diabetes.\([6]\)

Given these variable effects on cardiovascular disease risk factors, how does coffee consumption affect the rates of actual cardiovascular events? Previous research found a positive association between coffee intake and the risk for either myocardial infarction or cardiovascular death.\([7]\) However, a recent review found that moderate coffee consumption reduced the risk for heart failure, with a peak protective effect at 4 servings per day.\([8]\) This same review also found that high levels of coffee consumption might increase heart failure risk. A review of 9 cohort studies found that at least 4 cups of coffee per day reduced the risk for stroke by 17% compared with abstinence from coffee.\([9]\)

What about mortality outcomes among coffee drinkers vs nondrinkers? Research is mixed in this area as well. In an observational study of 37,742 Japanese women, coffee consumption had no significant effect on the overall risk for mortality, but there was a clear reduction in the risk for death due to coronary heart disease among coffee drinkers.\([10]\) Another study examined mortality outcomes associated with coffee among 3837 patients with diabetes.\([11]\) Like the current study by Liu and colleagues, it featured a broad age range among its subjects. However, in contrast to the current research, coffee consumption was associated with a lower risk for mortality, even at levels of greater than 6 cups per day. Finally, data from the Health Professionals Follow-Up Study and Nurses' Health Study, which featured similar largely white and well-educated populations in comparison with the current study, demonstrated no effect of coffee consumption on the risk for mortality among men and a lower risk for mortality among women who drank coffee.\([12]\) Again, the benefit among women was principally for cardiovascular mortality.

Conclusion

The results of the current study made national headlines but really provide more questions than answers when it comes to the major health effects of coffee consumption. It should be emphasized that the higher risk for death in this study was limited to men at the highest levels of coffee consumption. Other good evidence suggests that coffee is not deleterious to health and does not promote early mortality.

Moderation is key to most things in life, and individuals who are heavy coffee drinkers should consider reining in their rampant coffee habit. However, patients may also overestimate the risks of drinking coffee. If they choose to cut back on moderate consumption of coffee, physicians should inform them that they may not be reducing their risk for diabetes or improving their for mortality. At the same time, such changes in and of
themselves can be empowering and can serve as teachable moments to encourage other salutary behaviors that have a better chance of improving morbidity and mortality.

Clinical Pearls

• The current study finds that coffee is associated with a higher risk for mortality but only among men who drank an average of at least 4 cups of coffee per day. There were significant limitations in this observational study.

• Previous research has found that coffee consumption can increase serum lipid levels. Coffee appears to have a negligible effect on the risk for hypertension.

• In contrast, coffee consumption appears to reduce the risk for incident diabetes.

• The overall record of coffee on cardiovascular and mortality outcomes is mixed. The evidence appears strongest for a reduction in the risk for cardiovascular death among women who drink coffee.

• There is insubstantial evidence to recommend against moderate consumption of coffee among adults.

References

1. Available on request
**INSTRUCTIONS**
- Read through the article and answer the multiple choice questions provided at the back of the article.
- Please note that some questions may have more than one answer; in the case of the latter please “tick” every correct answer.
- When done only fax through your answer sheet to the fax number given on the answer sheet.

**QUESTIONNAIRE**

**G1 (14)**

**HOLIDAY HEART SYNDROME**

**Background**

**Question 1:** Is it TRUE or FALSE that although alcohol consumed in large quantities for many years can induce an alcoholic cardiomyopathy it is not clinically identical to idiopathic dilated cardiomyopathy?

- A TRUE
- B FALSE

**Question 2:** Can the subsequent abstinence from alcohol use lead to spontaneous recovery from holiday heart syndrome?

- A YES
- B NO

**Pathophysiology**

**Question 3:** Which of the following mechanisms are theorized to be responsible for the arrhythmogenicity of alcohol?

- A Decreased secretion of epinephrine and nor epinephrine
- B A fall in the level of plasma free fatty acids
- C Increased sympathetic output
- D An indirect effect through acetaldehyde or fatty acid ethyl esters

**Epidemiology**

**Question 4:** Which of the following is the most common rhythm disturbance associated with alcohol?

- A IST
- B AF
- C AVNRT
- D ART

**Clinical presentation**

**Question 5:** Which one of the following is the most common symptom associated with acute exposure to alcohol?

- A Near syncopal episodes
- B Dyspnea on exertion
- C Angina
- D Palpitations

**Alcoholism**

**Question 6:** Which one of the following is the leading cause of preventable death in the US?

- A Alcoholism
- B Obesity
- C Traffic collisions
- D Drug abuse
- E Smoking tobacco

**Question 7:** With regard to screening instruments for alcohol problems, which one of the following should be given face-to-face?

- A CAGE
- B AUDIT

**Question 8:** Which of the following are signs of alcohol withdrawal?

- A Gynecomastia
- B Seizures
- C Headache
- D Testicular atrophy
- E Delirium

**Question 9:** Is it TRUE or FALSE that alcohol biomarkers can be a substitute for a comprehensive history and physical examination?

- A TRUE
- B FALSE

**Question 10:** With regard to the brief intervention, as a first step in treatment of alcoholism, which of the following should a physician do?

- A Place emphasis on the effects on family, friends, and occupation as well as any physical manifestations
- B Be judgmental to scare the patient
- C Make use of the word alcoholic
- D Indicate the responsibility for change is with the patient
- E Avoid arguments about the diagnosis
Question 11: Which of the following is the only treatment for alcohol dependence?

A Only drink on weekends
B Drink only one alcoholic drink per week
C Complete abstinence
D One or two drinks monthly

Question 12: For how long should an alcohol dependent patient attend AA meetings?

A Daily for one month
B Twice weekly for three months
C Once a month for one year
D Daily at first and then for two years or more
E Sporadically as the patients feels a need to go

Question 13: Can fetal alcohol syndrome cause mental retardation?

A YES
B NO

Question 14: Which of the following neurotransmitter systems in the brain that is affected by alcohol, cause anxiolytic and sedative effects?

A Opiates
B GABA
C Dopamine
D Serotonin
E Glutamate

Question 15: Brain excitability caused by long-term alcohol ingestion, can lead to which of the following?

A Alcoholic hallucinosis
B Cell death and cerebellar degeneration
C Delirium tremens and tremors
D Wernicke-Korsakoff syndrome
E Withdrawal seizures

Question 16: According to the NESARC study, the transition from use to dependence was highest in which group?

A Cocaine users
B Alcohol users
C Nicotine users
D Cannabis users

Question 17: What percentage of the global burden of disease is attributable to alcohol?

A 12%
B 8%
C 7%
D 4%
E 2%

Question 18: Percentage wise, which of the following conditions have the highest incidence as a cause of alcohol abuse?

A Liver cancer
B Esophageal cancer
C Homicide
D Motor vehicle accidents
E Cirrhosis

Question 19: Is it TRUE or FALSE that women, consuming four or more drinks daily, statistically have a slightly higher risk for getting ear, nose, and throat cancer, esophagus cancer and liver cancer?

A TRUE
B FALSE

Question 20: In which case may moderate alcohol consumption reduce the risk of cardiovascular disease?

A While binge drinking
B When drinking with meals

Question 21: When does the cardiovascular benefit become important?

A For men younger than 30 years
B For women younger than 40 years
C For men older than 40 years
D For women older than 50 years
Question 22: Is it TRUE or FALSE that people who begin smoking early are more likely to develop problems with alcohol?

A TRUE
B FALSE

Question 23: Which of the following are TRUE with regard to alcohol prevalence?

A The lifetime alcohol prevalence was 20% for women and 8% for men
B Problem drinking in women is much less common than in men
C The prevalence of alcoholism increases with the increase in age
D Women living with substance-abusing men are at high risk
E Daily or weekly consumption of energy drinks by younger individuals has been strongly associated with alcohol dependence

Atrial fibrillation

Question 24: Which of the following are FALSE with regard to newer anticoagulants compared with warfarin?

A In patients with AF the newer anticoagulants protected against stroke or systemic embolism better than warfarin
B The newer anticoagulants significantly reduced all-cause mortality and intracranial hemorrhage
C The newer anticoagulants also decreased gastrointestinal bleeding
D Compared with warfarin, low-dose new anticoagulant regimens showed significantly more ischemic strokes
E With the embolic newer anticoagulants the risk of stroke or systemic events was reduced to 39% as compared to warfarin

Question 25: Is it TRUE that patients with hypotension need immediate direct current cardioversion?

A YES
B NO

Question 26: For which of the following applications is TEE helpful?

A To evaluate for valvular heart disease
B To evaluate for left atrial thrombus
C To evaluate for pericardial disease
D To guide cardioversion
E To estimate pulmonary systolic pressure

Question 27: Which one of the following are moderate risk factors for AF?

A Prior stroke or transient ischemic attack
B Coronary artery disease
C Diabetes mellitus
D Female sex
E Hypertension

Question 28: Which one of the following agents used for rate control in new-onset AF is prescribed mainly for patients who are intolerant of or unresponsive to other agents?

A Amiodarone
B Digoxin
C Metoprolol
D Diltiazem

Question 29: With regard to the long-term management of AF, which of the following agents are used for rhythm control?

A Oral beta-blockers
B Flecainide
C Digoxin
D Sotalol
E Amiodarone

Question 30: Persistent AF is classified as which of the following?

A AF that has persisted for more than 1 year
B Episodes of AF that terminate spontaneously within 7 days
C Episodes of AF that last more than 7 days and may require either pharmacologic or electrical intervention to terminate

Question 31: Is it possible for paroxysmal AF to progress to permanent AF?

A YES
B NO

Question 32: Lone atrial fibrillation has been used to classify AF in which group?

A Females over 60 years with normal echocardiographic findings
B Older males (> 65 years) with abnormal echocardiographic findings
C Younger patients (< 60 years) with normal echocardiographic findings
D Patients with abnormal echocardiographic findings
<table>
<thead>
<tr>
<th>Question 33:</th>
<th>Is it TRUE or FALSE that the precise mechanisms that cause atrial fibrillation are fully understood and as such AF requires an initiating event or a permissive atrial substrate?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A TRUE</td>
<td>B FALSE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 34:</th>
<th>AF is not associated with which of the following risk factors?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Atrial ischemia</td>
<td>B Genetic factors</td>
</tr>
<tr>
<td>C Smoking</td>
<td>D Alcohol and drug abuse</td>
</tr>
<tr>
<td>E Advancing age</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 35:</th>
<th>Which of the following are common causes of increased atrial pressure?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Mitral or tricuspid valve disease</td>
<td>B Intracardiac tumors</td>
</tr>
<tr>
<td>C Intracardiac thrombi</td>
<td>D Systemic or pulmonary hypertension</td>
</tr>
<tr>
<td>E Left ventricular dysfunction</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 36:</th>
<th>Which percentage of individuals aged 40 and older will develop AF during their lifetime?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A 40%</td>
<td>B Approximately 25%</td>
</tr>
<tr>
<td>C Between 4% and 15%</td>
<td>D 10%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 37:</th>
<th>Is it TRUE that the incidence for AF is significantly higher in men than in women in all age groups?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A YES</td>
<td>B NO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 38:</th>
<th>Did medical therapies aimed at rhythm control offer a survival advantage over rate control and anticoagulation, according to the AFFIRM trial?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A YES</td>
<td>B NO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 39:</th>
<th>The risk of stroke from AF becomes a major concern when it lasts longer than how many hours?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A 8 hours</td>
<td>B 12 hours</td>
</tr>
<tr>
<td>C 24 hours</td>
<td>D 48 hours</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 40:</th>
<th>What percentage of AF episodes does not cause symptoms?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Less than 20%</td>
<td>B Approximately 40%</td>
</tr>
<tr>
<td>C Between 30% and 60%</td>
<td>D Nearly 70%</td>
</tr>
<tr>
<td>E Up to 90%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 41:</th>
<th>Which of the following are particularly important in evaluating hemodynamic stability and adequacy of rate control in AF?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Heart rate</td>
<td>B Respiratory rate</td>
</tr>
<tr>
<td>C Blood pressure</td>
<td>D Oxygen saturation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 42:</th>
<th>The presence of which of the following suggest tight ventricular failure or intrinsic liver disease?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Left upper quadrant pain</td>
<td>B Ascites</td>
</tr>
<tr>
<td>C A cool or cold pulseless extremity</td>
<td>D Hepatomegaly</td>
</tr>
<tr>
<td>E Hepatic capsular tenderness</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 43:</th>
<th>Should serum electrolyte levels in all patients with acute arrhythmias be assessed, and in particular that of potassium?</th>
</tr>
</thead>
<tbody>
<tr>
<td>B YES</td>
<td>C NO</td>
</tr>
</tbody>
</table>
Question 44: Which one of the following has become the standard diagnostic modality to assess chamber enlargement, left ventricular wall motion abnormalities, hypertrophy, valvular disease and systolic dysfunction?

A Perfusion imaging  
B Ventilation-perfusion scintigraphy  
C Echocardiography  
D Cardiac MR imaging

Question 45: When would a patient, presenting with sustained tachyarrhythmia secondary to acute alcohol toxicity, be treated with an AV nodal blocking agent?

A Never  
B When the ventricular rate is very low  
C Only if the duration of atrial fibrillation approaches 24-28 hours  
D When the ventricular rate is excessive

Question 46: Since the holiday heart syndrome occurs mainly among healthy young patients, mainly over a holiday period and is not an adverse condition, patients do not have to be advised against excessive use of alcohol in the future. Is this statement TRUE or FALSE?

A TRUE  
B FALSE

Question 47: Is it TRUE that, following alcohol-related arrhythmia, most patients without underlying heart disease should be able to gradually resume full physical activity over the next few days?

A YES  
B NO

Question 48: Which one of the following drugs is rarely indicated for chronic therapy because of its slow onset of action?

A Diltiazem  
B Verapamil  
C Digoxin  
D Metoprolol

Question 49: Can the administration of the drug diltiazem, if used in IV, be stopped if there is resolution of arrhythmia following recovery from acute alcohol toxicity?

A YES  
B NO

Question 50: Which of the following statements are FALSE with regard to patients with alcohol-induced AF?

A Patients without other unrelated episodes would not typically be considered a current indication for atrial fibrillation surgical or catheter ablation  
B Upon resolution of the alcohol-related arrhythmia most patients still require further therapy even if they refrain from alcohol use  
C Persons with alcoholism should be considered for transfer to facilities for detoxification or rehabilitation  
D Patients should be advised to refrain from alcohol and stimulants  
E Patients do not have to avoid excessive fatigue
Question 51: Which of the following findings of a meta-analysis by Chinese researchers are TRUE?

- A The researchers found an inverse relationship between the amount of caffeine consumed and the risk of AF
- B An adverse relation was found between habitual caffeine intake and AF risk
- C The incidence of AF decreased by 6% for every 300-mg/day increment in habitual caffeine intake
- D Pooled relative risk for the incidence of AF from habitual caffeine exposure was 0.90 in the primary analysis

Question 52: According to one study, did caffeine significantly alter inducibility or severity of arrhythmias in patients with clinical ventricular arrhythmias?

- A YES
- B NO

Question 53: AF is a common condition that affects approximately which ratio of people over their lifespan?

- A One in 40 000 people
- B One in 4000 people
- C One in 400 people
- D One in 40 people
- E One in 4 people

Alcohol may trigger AF episodes

Question 54: Is it TRUE or FALSE that we still do not really understand how alcohol triggers atrial fibrillation?

- A TRUE
- B FALSE

Question 55: Which of the following episodes was considered triggered by vagal activation?

- A While the patient was eating
- B While the patient was resting
- C While the patient was stressed
- D While the patient was consuming caffeine
- E If the symptoms terminated with exercise

Question 56: Is it TRUE that patients with alcohol triggers but not patients with PAF, were more likely to report vagal triggers of arrhythmias?

- A TRUE
- B FALSE

Question 57: Epidemiologic and clinical studies demonstrated a significant inverse association between coffee consumption and prevalence of metabolic syndrome, as well as a reduced risk for NAFLD. Is this statement TRUE?

- A YES
- B NO

Question 58: According to a meta-analysis, overall, compared with no coffee consumption, the risk for HCC was reduced by what percentage with high-level consumption of coffee?

- A 11%
- B 18%
- C 28%
- D 36%
- E 58%

Question 59: The specific mechanisms by which coffee exerts the beneficial effects it has, have not been clearly defined, but it is apparent that these effects extend to which of the following?

- A Hepatic steatosis
- B Cirrhosis
- C HTT
- D Pancreatic cancer
- E Fibrosis
ANSWER FORM

<table>
<thead>
<tr>
<th>Professional Board</th>
<th>Postal address</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surname</th>
<th>E-mail Address</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ID Number</th>
<th>Fax Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FOH Number</th>
<th>Contact Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time spent on activity</th>
<th>Is this for an audit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How would you like to receive your IAR?</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMS</td>
</tr>
<tr>
<td>FAX</td>
</tr>
<tr>
<td>EMAIL</td>
</tr>
<tr>
<td>POST</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>G1 (14) General Activity 1 of 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holiday Heart Syndrome</td>
</tr>
<tr>
<td>Caffeine: No downside, hint of benefit in atrial fibrillation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>21</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>41</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>22</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>42</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>23</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>43</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>44</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>45</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>26</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>46</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>27</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>47</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>28</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>48</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>29</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>49</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>31</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>51</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>32</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>52</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>33</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>53</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>54</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>55</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>37</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>57</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>38</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>58</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>39</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>59</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I hereby declare that the completion of this document is my own effort without any assistance.
Signed: _______________________________ Date: ___________________________

Please rate the article:

<table>
<thead>
<tr>
<th>POOR</th>
<th>FAIR</th>
<th>AVERAGE</th>
<th>GOOD</th>
<th>EXCELLENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

FAX TO 0866144200 OR 012 653 2073 AFTER COMPLETION

This article is accredited for SIX Clinical (6 CEU’s)

<table>
<thead>
<tr>
<th>Mark</th>
<th>/59</th>
<th>PERCENTAGE</th>
<th>% (PASS RATE 70%)</th>
<th>PASSED</th>
<th>FAILED</th>
</tr>
</thead>
</table>

MODERATED BY: __________________ DATE: ________________