Stroke and Coronary Heart Diseases, Global and Asian Trend and Risk Factors - A Perspective

Sk. Mamun-Ar-Rashid¹, Sk. Moazzem Hossain²

Abstract

Introduction: Cardiovascular disease (CVD) is the leading cause of death in the world, accounting for 30% of deaths globally. CVD is a group of conditions affecting the functions of the heart, blood vessels or both. The major cardiovascular diseases include coronary heart disease (CHD), stroke, hypertension, heart failure and peripheral vascular diseases. Distribution of CHD and stroke is different in different regions of the world, especially western high-income, Asian and other countries. The Asian prevalence also not homogenous. Estimated number of deaths due to CVD worldwide will projected to 23.4 million, comprising 35% of all deaths in 2030. Significant increase in prevalence of coronary heart diseases (CHD) have been observed in the Asia including Bangladesh, but stroke in some regions of the world. Objectives: (1) Identification of cases and risk factors in different geographical area (2) Reduction of morbidity and mortality by proper treatment and management of modifiable risk factors. Materials and Methods: This observational study was done through using evidence from the published study articles of CVD in national and international journals, electronic databases such as MEDLINE, EMBASE and PUBMED. We also manually checked references of relevant publications of stroke and CHD. Study period: Jan 2019-Dec 2019. Results: Approximately 940 million people in the high income countries, where CHD is the dominant form of CVD which is 2-5 times higher than stroke. In the USA, Canada, Australia, New Zealand, Italy, France and Spain CVD death rates are very low. The highest death CHD rate is in Finland, Ireland, Scotland, Norway, Sweden of the European countries. In Eastern Europe and most of the Asia, the rate of coronary arterial diseases are rapidly increasing. Japan the Asian high income country the death ratio of stroke and CHD is 3:1. The East Asia and the Pacific including China CVD is the major cause of death, where stroke dominating. People in South Asia including India and Bangladesh the coronary diseases are increasing alarmingly, where CVD death increase 30% over the preceding decade and the dominant form is CHD. In the central Asia, specially Uzbekistan, Kazakhstan, Tajikistan both CHD and stroke are very high. In Latin America death from CHD (35%) higher than stroke (29%). In the Middle East and North Africa, CHD responsible for 17% and stroke 7% of all death. Conclusion: Asian countries have disproportionately high morbidity and mortality from stroke with increasing tendency to CHD, but CHD in Western countries which may be due to complex interaction of genetic and environmental factors, smoking, hypertension and metabolic abnormalities. Death rate is higher in male sex from both CHD and stroke worldwide.

Keywords: Cardiovascular diseases (CVD), Stroke, Coronary heart diseases (CHD).

Number of Figures: 06; Number of References: 39; Number of Correspondence: 02.

1. Corresponding Author:
Dr. Sk. Mamun-Ar-Rashid
MD (Internal Medicine)
Senior Consultant
Department of Medicine
Khulna Medical College Hospital, Khulna.
Mobile: 01727 012 190
Email: drmamunmedicine@gmail.com

2. Dr. Sk. Moazzem Hossain
FCPS (Medicine)
Assistant Professor
Department of Medicine
Khulna Medical College, Khulna.

Introduction:
Cardiovascular Diseases (CVD) is the leading cause of death in the world, accounting for 30% of death globally⁶. The major cardiovascular diseases include coronary heart diseases, Cerebrovascular disease or stroke, hypertension, heart failure (CHD), rheumatic, non rheumatic heart diseases and other vascular diseases. Before 1900, infectious diseases and malnutrition were common causes of death when CVD was only<10%⁷. Now a days CVD accounts for nearly 40% in high-income and 28% is low income countries⁸. The estimated number of deaths from CVD in 2008 was 17.3 million and it was 20 million in 2015 throughout the world⁹. Further, global CVD deaths are projected to increase to 23.4 million, comprising 35% of all deaths in 2030⁰. Stroke and CHD are most common causes of mortality and morbidity among CVD cases throughout the world. CVD mortality rate is declining in high income countries like USA, western European countries and Japan but increasing in the developing world, including most Asian countries¹¹. Asian countries have disproportionately high morbidity and mortality from stroke compared with western countries¹². The relationship between traditional risk factors and CVD is different in Asian than Western societies, and there are some unique features about risk factors and metabolic abnormalities for CVD in Asia¹³. There are three main risk factors – smoking, hypertension, serum cholesterol and regional variations of CHD and stroke based on differences in conventional risk factors. Hypertension plays an important role in the development of heart diseases and stroke in Asia than in Western countries. The prevalence of obesity, overweight due to lifestyle changes resulting from industrialization.
and economic development have been increasing in Asia for the last two to three decades. The rate of type-2 DM or insulin resistance syndrome and dyslipidaemia are progressively increasing in most of the Asian countries and Bangladesh. In Bangladesh this trend have been dramatically increasing for last two decades. Mean serum cholesterol levels are lower for adults in most Asian countries than in Western countries, but an increasing trend have been observed. The genetic predisposition, race, awareness, secular trends of stroke and CHD and interaction between genetic and environmental factors may also contribute to the difference in CVD pattern between Asians and people living in other countries. Not only the mortalities, nearly 18% in high income and 10% in low income countries suffers from disability adjusted life year (DALY) resulting from coronary arterial diseases only.

East Asian countries have lower mortalities from CHD, but central Asian countries have higher mortality from both stroke and CHD. Because more than half of the world’s population lives and half of the CVD burden is estimated to occur in the Asia, so prevention of CVD is a critical issue here. Japan, China, Korea, Thailand, Singapore and some other Asian countries have adequate disease specific mortality data, but very limited in most other Asian countries. In Bangladesh both stroke and CHD are progressively increasing. By 2030 in the world of all death and disability, 14.9% men and 13.1% female death will be due to CHD and Stroke will be responsible for 14.4% of all male and 11.8% of all female death. So prevention and management of stroke and coronary heart disease is essential to reduce morbidity and mortality.

**Materials and Methods:**
This observational study was done through using evidence from the published study articles of CVD in national and international journals, electronic databases such as MEDLINE, EMBBASE and PUBMED. We also manually checked references of relevant publications of stroke and CHD. Study period: Jan 2019-Dec 2019.

**Brief Vascular pathology in relation to different profiles of CHD and stroke:**
It is the risk factors and genetic interactions causing variable presentation of CHD and stroke at different regions of the world, but vascular pathology is very important. There are 2 major types of vascular pathology leading to stroke, stroke subtypes and CHD. One is atherosclerosis and other is arteriosclerosis. Major risk factors for atherosclerosis are dyslipidaemia, glucose abnormality, hypertension and smoking. Arteriosclerosis, a small vascular pathology typically occurring in small penetrating arterioles, especially basal gangliaions of brain, resulting from necrosis or apoptosis of smooth muscle cells of tunica media of blood vessels leading to micro-aneurysm formation causing intraparenchymal haemorrhage and fibrous proliferative changes to lacunar stroke. Risk factors for arteriosclerosis are primarily hypertension and secondarily glucose abnormality and metabolic syndrome. Aging is a common risk factor for arteriosclerosis throughout the world.

**Results:** Data obtained from different sources presented as bar and dot diagram in relation to region, country to time for CHD and stroke used for descriptive observational study.

![Figure 1: Age-standardized death rates per 100,000 for stroke (left) and CHD (right) across countries in different regions of Asia in 2002. Data from the World Health Organization, Department of Measurement and Health Information. Patterns on the bars represent different regions: Middle Eastern countries (●), Central Asian countries (■), South Asian countries (▲), Southeast Asian countries (▲), East Asian countries (▲), and non-Asian countries (open bars). USA indicates United Arab Emirates, USA, United State of America; and UK, United Kingdom.](image-url)
The Bar diagram shows—Japan, the high income country of Asia the diagram shows 45 deaths due to stroke and nearly 30 deaths from CHD.100 deaths from stroke and 45 deaths from CHD respectively in South Korea. Philippines had 65 stroke death and 130 in CHD. Thailand had nearly 100 in stroke and 50 in CHD in 2004, which was nearly 60 both stroke and CHD in study result of 2002. Singapore, another rich country of Asia the age standardized death rate shows 100 for CHD, but less than 50 deaths due to stroke. China, the highest populated country of Asia as well as in the world the age standardized death rate due to stroke was nearly 160 and 70 in CHD shown in 2002, which was almost same in the study result 2004. The distribution of death rate due to stroke and CHD in central Asian countries are— In Kazakhstan it was 225 due to stroke and nearly 410 in CHD in 2004 which was 200 and nearly 380 in 2002. 150 deaths from stroke and approximately 370 death occurred in CHD in Uzbekistan in the year 2004 in relation to165 and 380 deaths respectively in 2002. In Tajikistan death rate from stroke was >100 and 280 from CHD in 2004 which was nearly 90 and 340 respectively in 2002. In the Middle East countries of Asia, the result shows Jordan, Oman, Saudi Arabia and United Arab Emirates had >200, 180,175 and < 150 deaths respectively due to CHD, whereas 80, >50, 50 and >60 deaths from stroke in 2002. Kuwait had death rate of 100 for coronary heart disease and 40 for stroke in the study result of 2004. The bar diagram result in age standardized death rates in Iran was 220 from CHD and 99 in stroke shown in 2004 and it was 290 due to CHD and nearly 100 due to stroke in 2002.

In Pakistan >235 death in CHD and 120 due to stroke, in India 238 in CHD and 125 in stroke, but in Bangladesh 215 in CHD and 115 stroke death in the result 2002. Indian death trend shown almost unchanged in the study result of 2004 in relation to 2002. Among the South East Asian countries Indonesia, Malaysia is nearly 165,>100 in CHD and 100, 80 in stroke respectively in the data in 2002. In 2004, Malaysia had nearly same mortality pattern. In Mongolia nearly 195 death from stroke, whereas >100 death of CHD in the study result in 2004.

**Cardiovascular Disease Epidemiology in Asia**

![Bar diagram showing age-standardized death rates per 100,000 for cardiovascular disease in different regions of Asia and western countries, pattern on the bars represent different regions. 2004](image)

*Figure 2. Age-standardized death rates per 100,000 for cardiovascular disease in different regions of Asia and western countries, pattern on the bars represent different regions. 2004*

Source: Adopted from Cardiovascular Disease Epidemiology in Asia; circulation: 2013.
Figure 3. Age-standardized death rates per 100,000 for cerebrovascular disease 2004, in different regions of Asia & Western Countries.

Source: Adopted from Cardiovascular Disease Epidemiology in Asia; circulation: 2013.

Figure 4. Age-standardized death rates per 100,000 for Ischaemic heart disease 2004, in different regions of Asia & Western Countries.

Source: Adopted from Cardiovascular Disease Epidemiology in Asia; circulation: 2013.
Increased haemorrhagic stroke in the present study may be due to the interaction between ischemic and hemorrhagic groups. In the USA, the richest and most health facilitated country of the world, the bar diagram shows 27% death from stroke, more than 102 due to CHD shown in 2002. Nearly 30% death from stroke and 98% death recorded from CHD in 2004. In Canada only 23% death from stroke and nearly 80% death due to CHD recorded in 2004.

Death rate in some other European countries not shown in bar diagram have much regional variations. Russia, Poland, Sweden, Denmark and Iceland had death rate much more higher in CHD than stroke per 100000/yr.

### Discussion

Cardiovascular diseases (CVD) accounts for approximately 30% death worldwide, nearly 40% in high income countries and about 28% in low and middle income countries. The global rise of CVD is the result of unprecedented transformation in the cause known as epidemiologic transition and this shift is driven by industrialization, urbanization and associated lifestyle changes which are taking place in every part of the world. Data from 2002 and 2004 reflects stroke and CHD in Asian regions and Western country.

Japan, the high income country of Asia between 1951–1980 stroke was the leading cause of death, it is now 4th. In Japan stroke rates increased dramatically, but CHD did not rise sharply over the last century.

Higher sodium, lower calcium and higher alcohol consumption may contribute to the higher prevalence of hypertension and stroke for Japanese. On the other hand, lower saturated fat (meat) and higher n-3polyunsaturated fat (fish) intake may contribute to the lower prevalence of hypercholesterolemia and lower risk of CHD for Japanese. After 2010, the trend of stroke death in Japan is decreasing, may be due comprehensive hypertension prevention and control. Several Cohort studies reported that CHD increases in men living in urban and sub urban areas of Japan in the past decades. The age adjusted mortality from CVD in Japan is decreasing from 1984.

In 1999, the age adjusted mortality from stroke for men and women was 41.6 and 42.8 respectively per 100000/yr in South Korea, accounting for approximately 40% decrease in stroke for men and approximately 25% decrease for women. In South Korea death from stroke was more than double from CHD in 2002 and almost same in 2004. Hypertension, high salt intake and genetic factors may be responsible for stroke death here. Smoking is strong risk factor for stroke and CHD. Recent trend in South Korea is to decrease of stroke, but increase tendency to CHD in both male and female.

Philippines, another East Asian country age adjusted mortality from CHD was highest among East Asian countries. In the Eastern Asian countries Japan and South Korea, the age adjusted mortality per 100000/yr. stroke dominating, whereas in Philippines CHD. Hypertension is more prevalent in East Asia than South and other regions of Asia.

In China stroke death was nearly two times than CHD. A Large Cohort study in China confirmed that age adjusted stroke mortality was 3 times higher than CHD. Approximately 3 million Chinese died from CVD annually which accounted 41% of deaths from any causes in 2009. The recent age adjusted stroke mortality rate in China is reported to be decreasing in urban areas, whereas in rural areas it is increasing or is stable. Hypertension, high salt and moderate cholesterol intake and
smoking may be responsible for stroke. In China, approximately 90% of urban population walks or rides a bi-cycle in their daily life32. Increase physical activities, low fatty diet and genetics may be responsible for decrease incidence of CHD in China.

The South East Asian country Indonesia, coronary heart disease death rate was higher than stroke, Malaysia had same death pattern in both study results, but much lower than Indonesia. Thailand another country of this region stroke death was much more higher than CHD.

In Singapore, there was a 3-5% decline in mortality from stroke annually from 1976 – 199410. Among Asian countries intake of total and saturated fat is highest (31%) in Singapore28. High fat intake, smoking and changes of life style results is increase CHD in Singapore but death rate reasonably lower due to better treatment facilities.

In south East Asian countries Singapore, Indonesia and Malaysia had higher death rate in CHD, but stroke in Thailand. Indonesia had highest death rate from CHD in this region. Mongolia had much higher death rate in stroke and CHD.

In the central Asian countries prevalence of both stroke and CHD is very high. Increased death rate in Kazakhstan due to CHD, but unchanged in Uzbekistan and modest decline in Tajikistan.

Stroke death rate with increasing tendency both in Kazakhstan and Tajikistan, but was unchanged in Uzbekistan. Central Asian region with the highest death rates (58%) due to CVD in the world, nearly double the rate of high income countries32. Smoking, obesity, genetic and environmental factors may be responsible.

Islamic republic of Iran had high mortality due to CHD and relatively low due to stroke, but modest increasing in stroke rate.

In India, CVD accounted for 32% of all deaths in 2000 and 2 million death by CHD in 2010, representing 30% increase over the preceding decade and the dominant form was CHD4. The Urban prevalence is more than the rural areas4. India, the second most populated country of the world CHD is increasing alarmingly because of smoking, increasing tendency to fatty diet, lack of physical exercise and DM among urban populations.

Pakistan, another South Asian country CHD death rate is much more higher than stroke.

Bangladesh, the densely populated country CVD death rate is rising for previous 2-3 decades with prevalence of CHD death rate higher than stroke, but stroke death rate also rising7. CVD death rate is rising in Banglaeshi population and it is about 5% regardless of type for the last few years28. Prevalence is higher in urban (8%) to rural areas (2%)28. The high CVD prevalence along with an upward trend of both CHD and stroke here may be due to smoking, hypertension with poor drug compliances, DM or IGT and dyslipidemia resulting from sedentation and high carbohydrate diet.

It is clearly evident that Iran, India, Bangladesh, Pakistan the south Asian countries CHD is the dominant form of CVD.

south Asian regions has the highest overall prevalence of DM with a rate as high as 14%15. The middle East countries of Asia Jordan, Oman, Saudi Arabia and United Arab Emirates CHD death rates are relatively high than stroke. Kuwait had low death rate in CHD and very low in stroke death.

Daily fat consumption increases ranging 13.6% in Sudan and 143.3% in Saudi Arabia33. Over 75% Egyptians are obese or over weight and 67%in Iraq and Jordan34. In the middle East and North Africa CVD death rates just below those of developed countries, CHD responsible for 17% of all deaths and stroke for 7%3. Traditional high fibre containing and low fatty diet changed to fatty diet recently. Fatty diet, lack of physical exercise and obesity are risk factors for coronary heart diseases over last few decades.

The most part of sub-Saharan Africa CVD is the leading cause of death (46%) among adults age more than 35 years3.

In USA, CVD death rate was low, but CHD was relatively high to stroke and upward trend is obvious. Better medical facilities, hypertension control and low salt diet results lower death from stroke. High total and LDL cholesterol are associated with CHD and 40% large artery atherosclerotic stroke in USA3. Obesity, smoking, alcohol and lack of physical exercise are common risk factors for CHD and stroke in USA.

Canada had the lowest stroke death rate and low death rate from CHD in 2004. Australia had reasonably low death rate both from stroke and CHD which was nearly unchanged in data shown 2004 and 2002.

In UK, CHD is much more prevalent than stroke and the trend is stable. Death from AMI is very high in male sex in Ireland and Scotland.

France, Spain, Italy the Mediterranean countries have both CHD and stroke lowest of the world and the trend is stable. France have lowest death rate both due to stroke and CHD.

Finland has the highest death rate from AMI in male sex in northern Western Europe then Belfast of UK followed by Norway and Sweden7.

In Germany both stroke and CHD death rate was reasonably low in study result of 2002 and 2004.

In a study conducted 1989 – 1993 Russia, Sweden, Denmark, Iceland had very high rate of coronary arterial death specially Acute myocardial infarction (AMI) and reasonably high stroke death.

The Eastern Europe and central Asia region with the highest death rates (58%) due to CVD in the world, nearly double the rate of high income countries32. Both stroke and CHD are common in Poland, Hungary, Czech Republic, Slovenia, and Slovakia. Age adjusted death rate is much more high in adult male than female. Obesity, dyslipidaemia, type-2 DM, smoking are common risk factors. In Poland, the age adjusted mortality of CVD decreased approximately 30% during1990 and Slovenia, Hungary, the Czech Republic and Slovakia had similar decline32,4.

In Latin America, approximately 28% of all deaths are attributable to CHD higher (35%) than stroke (29%). During
1970 – 2007 Mexico, Costa Rica, Venezuela continued an overall increase in age adjusted CHD mortality 3 – 10%, whereas Argentina, Brazil, Chile and Columbia rates have been declined by 2%/yr.

In North Africa coronary heart diseases (CHD) is responsible for 17% of all deaths and stroke for 7%. For the most part, Sub-Saharan Africa CVD is the leading cause of death (46%) among adults age more than 35 yrs.

85% of the world’s population lives in low-income and medium income countries1. In 2001, only 3 million CVD death occurred in high income countries compared to 13 million in low-income countries31. People live in high-income countries, where CHD is the dominant form of CVD, which is 2-5 times higher than stroke2. USA, Canada, Western European countries, Australia, New Zealand are high-income countries where CVD rates are almost same. Atherosclerosis is very common in Western populations and is reflected in high CHD4.

The highest CVD death rate among high-income countries are Finland, Ireland, and Scotland and low in the France, Spain and Italy5.

In Latin America, approximately 28% of all deaths in this region are attributable to CVD with CHD higher (35%) than stroke (29%)32. Mexico, Costa Rica, Venezuela continued on overall increase in age adjusted CHD mortality 3-10%, where as Argentina, Brazil, Chile and Colombia rates have been declined by 2%/yr between 1970-200233.4.

Similar to well established traditional risk factors for stroke and CHD in western countries hypertension, smoking and DM are main risk factors for stroke in Asia2. APCSC results show that the hazard ratios of DM for ischemic stroke and CHD are similar for both Asian and western countries18.

High BP was identified as a strong risk factor for CVD, especially for stroke, and both systolic and diastolic BP levels were associated with CVD risk in a dose response fashion19. Serum total cholesterol is a risk factor for CHD in Asian countries46. A consistent positive association of total and LDL cholesterol level and the risk of CHD is found in some Asian countries46.

Smoking is a potent risk factor not only for CHD, but also for stroke20. The impact of smoking is much stronger in men than women (13-27%) versus (2.7%) in respect to CHD20. Although the prevalence of current smoking has declined from 82% in 1965 to 32% in 2010 for men and 16% to 8% for women, the prevalence among men is still higher in Japan and some other Asian countries than in Western countries24.

Atherosclerosis is very common in Western populations and is reflected in high CHD4. Increased industrialization, mechanization and computerization have shifted physically demanding agriculture based work to sedentary office based works leads to overweight and obesity. Only 22% Americans engaging in sustained physical activities for at least 30minutes on 5 or more days in a week32. Consumption of calorie rich fatty food, specially saturated animal fat and hydrogenated plant fatty food resulting in atherosclerosis leads to CHD and stroke in large arteries. In 1996-1999 fat intake in USA was 34% and 33% in the UK including Ireland and Scotland of the total calorie intake4. Genetic and environmental factors play an important role in atherosclerosis and CHD. Smoking, hypertension and dyslipidaemia causes endothelial injury and ultimately atherosclerosis in 2nd – 3rd decade of life, but clinical presentation may occur in sixth, seven or eight decade32. Age and increase life expectancy are common risk factors for CHD and stroke due to lacunar infarction in Japan and some regions of the world.

Serum total cholesterol, LDL or non High Density Lipoprotein (HDL) cholesterol levels or the LDL/HDL ratio have been positively associated with risk of IHD, whereas HDL cholesterol levels were inversely associated with the risk25. Many epidemiological studies in the United States have reported a positive association between serum total and LDL cholesterol levels and the risk of ischemic stroke4. The Atherosclerosis risk in communities (ARIC) study reported that total cholesterol levels were positively associated with the risk of non Lacunar stroke, but not lacunar stroke23.

Obesity with dyslipidaemia, lack of exercise, type-2 DM, smoking and hypertension are main modifiable risk factors for CHD and stroke in western Europe and USA. These are common risk factors though population attributable risk fraction (PAF) is variable in different regions of the world.

The global rise in CVD is the result of epidemiologic transition life style changes taking place in every part of the world among all races, ethnic groups and cultures. Global trend of CVD by 2001, was responsible for 29% of all deaths and 14% DALYS. By 2030, 33% of all deaths will be the result of CVD. Of these, 14.9% of deaths in man and 13.1% of deaths in women will be due to CHD23. Stroke will be responsible for 10.4% of all male deaths and 11.8% of all female death22. Evidence of coronary heart disease in premenopausal women is less than men, but almost same in post menopausal women.

The modest decline of CVD death rate specially stroke and CHD in high –income countries will continue, but the rate of decline will be slow. It is due to competing trends of common risk factors. In one hand well-recognized increase in the prevalence of diabetes mellitus and obesity, rate of decline of smoking and a leveling off in the rate of detection, treatment and control of hypertension are in the negative column. On the other hand, cholesterol levels continue to decline in the face of increased statin use.

Treatment of hypertension and elevated cholesterol along with wide spread Use of aspirin have contributed significantly reducing death from stroke and CHD. Public health campaigns promoting life style modifications, cessation of smoking also contributed to reduce death rates. Advance treatment facilities such as angioplasty, CABG, Implantable defibrillators and other invasive procedures reduces death rates specially due to CHD.

Improvement and availability of therapeutic approaches, follow up along with implementation of preventing measures effectively reduces death rates from CHD and stroke in the developed countries. Poor therapeutic approach, inadequate treatment and rehabilitations in the low-medium income
countries results in increase in death rates from stroke and CHD. Risk factors have potentiating rather than additive effect on stroke and CHD.

Nationwide approaches to hypertension management, smoking prevention, control of metabolic risk factors would be of value to reduce mortality from Asia, Africa, Eastern Europe and other low-medium income countries. Improvement of surveillance and affer care of treatment of stroke and CHD in these regions will effectively reduce death rates.

**Conclusion:**
Asian countries have disproportionately high morbidity and mortality from stroke with increasing tendency to CHD, but CHD in Western countries which may be due to complex interaction of genetic and environmental factors, smoking, hypertension and metabolic abnormalities. Urbanization, industrialization, office based sedentary work lack of physical exercise and high fatty diet play important role causing CVD. Death rate is higher in male sex from both CHD and stroke worldwide.

**Conflict of Interest:** None.

**References:**
3. WHO statistical information system, cause of death: mortality and health status. Available at: http://www.who.int/research/en
https://doi.org/10.1016/j.atherosclerosis.2006.08.022
PMid:16970954

https://doi.org/10.1001/jama.2009.1619
PMid:19903920 PMCID:PMC3284229

https://doi.org/10.1093/aje/kwf166
PMid:12505888

https://doi.org/10.1016/j.jacc.2008.02.075
PMid:18582638

https://doi.org/10.1093/heapro/dag03
PMid:14695368

https://doi.org/10.1136/tc.2005.013284
PMid:16728748 PMCID:PMC2564655

https://doi.org/10.1161/01.CIR.41.451.1-162


https://doi.org/10.5551/jat.12.295
PMid:16394610

https://doi.org/10.1016/s0140-6736(04)17018-9

https://doi.org/10.1596/978-0-8213-6262-4


https://doi.org/10.1161/01.STR.24.7.954
PMid:8322395

https://doi.org/10.1161/01.ATV.10.4.535
PMid:2369364

https://doi.org/10.1093/ajcn/88.1.195
PMid:18614741

https://doi.org/10.3945/ajcn.2008.27109
PMid:19515740

https://doi.org/10.1016/j.jacc.2008.06.018
PMid:18786479

https://doi.org/10.2147/VHRM.S166111
PMid:30174432 PMCID:PMC6110270