

1.4 ► Malignant Heart Disease in Young Indians

ONE NIGHT in March 1971, Jagdish, a young Indian physician interning at one of Chicago's major teaching hospitals, was taken to the Emergency Room (ER) complaining of chest pain. Given how young he was—he was 25—he was sent home after a few tests and a brief examination. Over the next few days, he returned twice more with the same complaint. Each time, he was discharged after a relatively cursory examination. His youth, and his apparent condition—

How Young is Young?

Premature heart disease is heart disease that occurs *before you start getting old*. It is defined as heart disease diagnosed under the age of 55 years in men and under 65 years for women.

Extremely premature heart disease is heart disease that occurs *in the young*—most often defined in someone under 45 or under 40. In this book, it is defined as under 45.

some sort of cardiac event—were at odds with each other. On his fourth visit to the ER in five days, Jagdish was diagnosed with an acute heart attack and admitted. Over the years, however, the treatment and management of his heart disease were insufficiently aggressive, again perhaps because of his young age. Fifteen years after that heart attack in 1971, Jagdish suddenly died while awaiting a heart transplant.

In 1972, barely a year after Jagdish had first come to the ER with chest pain, my beeper went off in the middle of the night, summoning me to the Cardiac Care Unit (CCU) of the same hospital to take over another physician's shift. Ravi, a 26-year-old first-year medical resident on duty in the CCU, once again Indian, had been admitted in the same unit following a heart attack. Not long thereafter, a *third* Indian, a 39-year-old engineer, was rushed in after suffering a massive heart attack that had severely damaged the heart muscle. Tests showed that Patel's heart disease was so far advanced that it was inoperable. He died five years later.

Compared to whites in the study, the Indians were younger and smoked less and fewer had hypertension. Yet their heart disease was more severe, diffuse, and more likely to be multi-vessel.

And this was all in one Chicago-area hospital over a 15 or 16 month period. The stories admittedly are anecdotal, but telling. Coronary heart disease among Indians

strikes early, strikes hard, and strikes unexpectedly. In Section 2, we looked at the high rates of premature, severe, malignant heart disease among Indian immigrants in many different countries. In Section 3, we discovered strong parallels to this among Indians on the Indian subcontinent itself. Chapter IV, Section 1 attempts to explain this epidemic and why it has taken the particular contours it has taken. The current section moves the discussion forward by examining three cardinal features that make heart disease in Indians truly distinctive, and to some degree even unique:

- Its extreme prematurity (as all three cases, above, indicate)
- Its severity and extensiveness (as indicated in the third case)
- Its occurrence in persons with *few or no* major traditional risk factors

Let's look at the first: prematurity.

I. PREMATUREITY: INDIAN HEART DISEASE STRIKES EARLY

Advanced heart disease is generally more common among older people. Heart disease is described as premature when a man under 55, or a woman under 65, suffers of one or more coronary events—such as a heart attack, death, coronary angioplasty, or bypass surgery. Like most heart disease, premature heart disease is caused by atherosclerosis (the hardening and narrowing of the arteries), which begins early in life. In the case of premature heart disease, however, the process accelerates and progresses much more rapidly.

On average, Indians develop heart disease about *10 years earlier* than other populations, and young Indians often have heart disease as severe as older Indians. Alarmingly, even Indian doctors, who know

about the dangers of heart disease and the importance of prevention, on an average *die 15 years earlier* than non-Indian doctors in the UK. In the west (the US and Europe together), 15% of men and 12% of women who die from heart disease die before reaching 65. In India, the figure is 35%—more than double the figure for Europeans and Americans. Still, heart disease *is* the most common cause of premature death in both Europe and the US, but it is primarily a disease of senior citizens, with more than 60% of heart attacks and bypass surgeries in the US occurring in people older than 65 years of age. The median age of a first heart attack among Europeans is 59 years, and 60 years among Chinese. Among people from the Indian subcontinent, it is 50 years—fully 10 years earlier.

Table 1.2. Three Types of Heart Disease

Classification	Characteristics
Type I: extremely premature, malignant heart disease	Typical age of onset: Younger than 45 years of age Develops in the presence or absence of traditional risk factors Triggered by high levels of emerging risk factors Highly prevalent on Indian subcontinent and among people of Indian descent living in other countries Severe atherosclerosis and narrowing, with diffuse, multi-site distribution of plaque all along several coronary arteries
Type II: standard heart disease	Typical age of onset: Older than 65 years of age Triggered by high levels of traditional risk factors Patients typically have low levels of the emerging risk factors Prevalent in most parts of the world and in most sub-populations. Wide range of severity of atherosclerosis, from mild to very severe.
Type III: a mixed type	Typical age of onset: Between 45 and 65 years of age Triggered by moderate levels of emerging risk factors, such as Lp(a), along with varying levels of traditional risk factors

Classifying heart disease among Indians

Another way to grasp just how premature and malignant Indian heart disease can be is to place heart disease within a classification system. Like diabetes, heart disease can be classified into two fundamental types—I and II. With heart disease, there is a third category, type III, which is a composite mix of the first two. The numerical breakdown of heart disease around the world into the three types has not been studied well thus far. Indians, however, may have a predominance of type I. Approximately 35-40% of Indians with heart disease have type I disease compared to 5-10% among other populations.

Like Type 1 diabetes, which develops very early in a person's life and is not triggered by lifestyle choices the way type II diabetes is, type I heart disease similarly occurs in the young—defined as persons younger than 45. Hence its name, extremely premature malignant heart disease. Again, like type 1 diabetes, it is not triggered by lifestyle choices or by high levels of the traditional heart disease risk factors, such as smoking, obesity, hypertension, inactivity, or a diet too rich in saturated fat and cholesterol—although the presence of these factors certainly makes type I worse.

The key fact about type I heart disease is that it can develop in the presence or absence of high levels of the traditional risk factors. In fact, among Indians, it typically develops in their absence, because Indians tend to have rates of smoking, general obesity, high blood pressure, and high cholesterol that are similar to or lower than, for example, whites. Indians who develop Type 1 heart disease, however, tend to have a family history of premature heart disease, along with multiple emerging risk factors (*see* Chapter III). Indians, as we have seen previously, also have a higher prevalence of diabetes, metabolic syndrome, abdominal obesity, and low levels of HDL. Of this, diabetes and metabolic syndrome may well account for perhaps one quarter to one third of heart disease among Indians.

In Type 1 disease, there is usually severe narrowing of multiple arteries, often at multiple sites on the same artery. A study in the United Kingdom found four Indians, who had suffered a heart attack between 18 and 22 years of age—either an extraordinary coincidence or yet another

Table 1.3. Age-specific death rates from heart disease in the UK in Indians and in the general population (1988-1992), per 100,000 people per year

Age	Men		Women	
	General population	Indian	General population	Indian
20-39	7	15	1	1
40-49	74	133	12	16
50-59	295	442	72	101
60-69	869	1059	331	450

Note that more than twice as many Indian men die from heart disease at young ages. Indian women also consistently have higher rates at older ages. Source: Balrajan, R. Ref. 1.05.

manifestation of the uniquely high prevalence of extremely premature heart disease among Indians worldwide. No members of other ethnic groups were found to have suffered a heart attack at such a young age.

Diffuse heart disease means that the buildup of plaque has spread all along the coronary artery, occurring at multiple sites instead of just one or two specific locations where the artery is narrowed or thickened by plaque.

(Revisit, also, the three anecdotes with which this section began.) Table 1.3, summarizes the death rates from heart disease among Indians compared to whites at different ages.

A British study found that the rate of first heart attacks among Indian men under the age of 40 was *10 times* that for whites of a similar age. Similar findings were observed in Malaysia and Qatar. In Malaysia, Indians, who make up less than 10% of the general population, accounted for 56% of heart attacks in people younger than 40. In Qatar, where Indians are again less than 10% of the

population, the figure was 71%. A Singapore study found that 10 times as many Indian men under 30 died from heart disease as Chinese men of the same age. Other studies in the UK have shown a death rate from heart disease among under-30 Indians two to three times higher than for whites, but only 50% higher in the 60-69 age range. In short, the excess risk of heart disease among Indians over and above the rates found in others is most pronounced at younger ages. This gap decreases with advancing age, partly explained by the fact that many Indians who would have died from heart disease after age 60 have already died by then.

From the heart attack registries of Western countries, we can estimate that only 2% to 6% of all heart attacks are sustained by individuals younger than 40, compared to about 25% of heart attacks in India. Studies undertaken at Calicut Medical College in Kerala, India showed that, from 1971 to 1991, the rate of first heart attacks among patients younger than 40 increased **20-fold**. In 1971, for example, one in more than 80 heart attack patients at Calicut was under 40, compared to **one in every four** in 1991. Similar observations have been made at other medical institutions in Kerala and in other states in India.

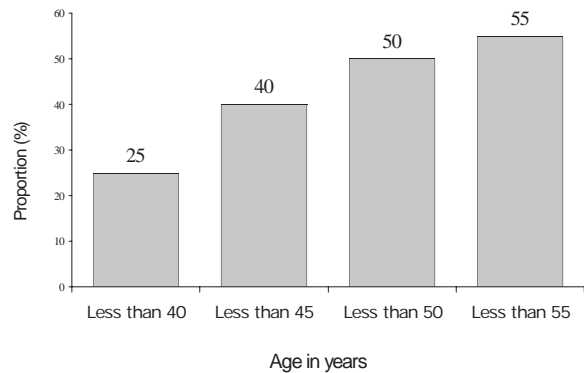


Figure 1.18 The percentage of first heart attacks among Indians that occur before a particular age. The leftmost column, for example, tells us that, of all the Indians who sustain a first heart attack, about 25% suffer this at an age younger than 40. In western countries, only about 5% of first heart attacks occur in people younger than 40. Source: Enas, EA. Ref. 1.07.

II. SEVERITY: INDIAN HEART DISEASE STRIKES HARD

Causes of Inoperable Heart Disease

- Severe diffuse disease involving the entire artery
- Total occlusion (obstruction) of several coronary arteries
- Severe muscle damage leading to an ejection fraction less than 25%
- Inadequate healthcare facilities or other issues of affordability leading to late detection of heart disease

Let's now look at the second trait of Indian heart disease: its severity. Any way you examine it, heart disease among Indians strikes hard when it occurs. Severe heart disease is virtually non-existent among young Asians except on the Indian subcontinent; and in other populations, young heart attack patients have either a normal coronary angiogram or single-vessel disease. Approximately 75% of Indians who have had coronary angiograms showed severe narrowing of two or more of their coronary arteries. In all populations, severe heart disease tends to result in a massive heart attack, with a greater propensity for death, disability, and heart failure, which means the heart has lost some of its blood-pumping ability perhaps because of damage to the heart muscle.

In another indication of Indian heart disease severity, a British study found that, among patients with acute heart attack, Indians suffered a higher rate of cardiac arrest before reaching the hospital than patients

from other ethnic groups. Among those Indians who survived the crisis and hospitalization, the death rates were twice as high over the ensuing six months, compared to other groups. This was true despite the fact that these Indians were on average younger and smoked less than the other heart attack patients in the study. They had equal access to medical care and there was no

The CADI study subjects did everything right, yet developed high rates of heart disease. This points to a genetic component to Indian heart disease, in addition to the environmental and nutritional factors.

difference in medical management compared to whites. Several Canadian studies have shown heart disease of greater severity among Indians than Native Canadians and Chinese. Additionally, Indian women in Canada undergoing coronary angiograms are twice as likely to have left-main or three-vessel heart disease than white women. This results in a higher rate of referral for bypass surgery. Compared to whites, Indians in Canada who suffer a heart attack also have higher rates of in-hospital mortality, and a greater need for bypass surgery. In one study, compared to other groups, Indians were five times more likely to die or to experience a recurrent heart attack within one year, despite a three-fold higher rate of bypass surgery.

Severe heart disease is also associated with a high rate of death, following bypass surgery (see Chapter VII, Section 5). In a Canadian study of nearly 3,000 patients undergoing coronary angiograms, 15% were Indians, although Indians make up only 2% of the Canadian population. In addition, compared to whites, these Indians were

The major determinants of heart disease severity are diabetes, low HDL, a high total cholesterol to HDL ratio, and high levels of Lp(a). Indians may be the only population with an excess of all four.

younger, smoked less, and fewer had hypertension; yet their heart disease was more severe, diffuse, and more likely to be multi-vessel.

Inoperable heart disease

Although severe disease may mandate the need for bypass surgery, very severe and diffuse disease makes it difficult and sometimes impossible to operate (see **Color Plate 1.12 Localized versus diffuse plaque buildup**). In addition, coronary angiograms and bypass surgery are in any case performed less frequently in many countries than in the US. Even in highly industrialized western countries

What is Severity, How Do You Measure It, and Why Does It Matter?

The **severity** of heart disease is an important indicator of a patient's chances of future health. In clinical practice, the two main factors used in measuring it are (i) the number of arteries that show narrowing, and (ii) the amount of narrowing as determined by a coronary angiogram. The distribution of plaque along the artery is another factor. Plaque buildup that is diffuse—meaning that it affects the entire, or almost the entire, length of the artery, rather than just one localized area—is regarded as more severe. Indians show severity on all of these dimensions, often presenting at the hospital with multi-vessel, diffuse and even inoperable heart disease.

Another criterion of severity is post-procedure outcomes. Severe heart disease leads to poorer outcomes. The more severe the disease, the greater the need for bypass surgery, angioplasty, or other procedures, and the more likely it is that there will be complications following the procedure. The likelihood of a recurrence—for example, of heart attack—is also higher. In a 15-year follow-up study of heart attack survivors who had their first attack when they were on average 48 years old, those with three-vessel disease were three times more likely to have one or more additional heart attacks, and eight times less likely to have an event-free survival compared with those with only single-vessel disease.

How do you measure or confirm severity? Angiograms are widely used to reveal the extent of heart disease, but an angiogram may appear normal unless the disease is already advanced. This is especially true in the case of many Indians who have diffuse, spread-out plaque build-up that is not visibly concentrated at any one point (see **Color Plate 1.12**). Ultimately, however, nothing beats a postmortem autopsy as the most accurate way of ascertaining severity. In fact, it was a definitive study of 9,568 autopsies undertaken in Singapore between 1950 and 1954 that conclusively showed, for the very first time in history, that Indians do have high rates of severe premature heart disease. Heart disease is not an abstract concept; pathologists and medical examiners can see it with their own eyes. That Singapore study showed a rate of coronary atherosclerosis seven times higher in Indians than in Chinese, as well as more severe disease.

such as Canada or the UK (both of which have national health insurance programs), the wait period to see a cardiologist can be very long; and compared to the practice in the United States both countries are less

Ejection fraction is a measure of how much blood your heart can pump out with each heartbeat, versus how much it leaves behind. It measures your heart's pumping power. If your heart's ejection fraction is too low, the surgeon may consider it too risky to perform bypass surgery on you.

aggressive in doing angiograms. This sometimes means that, by the time a patient gets an angiogram, there is a greater chance that their heart disease has become advanced, particularly if, like Indians, they are already predisposed to having severe heart disease. A study in Birmingham, UK, for example, found a disproportionate number of Indians with advanced inoperable disease. Upon follow-up, it was found that four times as many Indians with inoperable heart disease died from heart disease as whites.

Another reason why your heart disease may be considered inoperable is if your heart is not pumping powerfully enough, perhaps because of damage to the heart muscle. If you have what is known as a low **ejection fraction** (less than 25%), you will usually not be accepted as a candidate for bypass surgery. Ejection fraction measures how hard the heart can pump. It is the percentage of blood your heart can pump out of the left ventricle, versus how much is left behind in the ventricle after the heartbeat. A healthy left ventricle pumps out at least 55% of the blood in it with each beat, yielding an ejection fraction of more than 55%.

Bypass surgery can be performed but it may provide little benefit if the muscle supplied by the arteries is significantly damaged. In addition, the likelihood of death during or following surgery (perioperative mortality) may be unacceptably high. Total occlusion is rarely seen in whites but not uncommon in Indians.

III. FEW OR NO TRADITIONAL RISK FACTORS: INDIAN HEART DISEASE STRIKES UNEXPECTEDLY

A major puzzle is that, with the exception of diabetes, the prematurity, severity, and high rates of heart disease found among Indians are not accompanied by particularly high rates of traditional risk factors. This was especially clear among the Indians in the CADI Study (*see also section 2*). The prevalence of high cholesterol, hypertension, and tobacco use among Indians is similar to or lower than that among whites and other populations. In fact, in the CADI study, the rates of smoking and obesity among Indians were below 5%, compared to above 25% for whites, as shown in Figure 1.19. The high rate of heart disease in the presence of low rates of traditional cardiac risk factors is called the “Indian

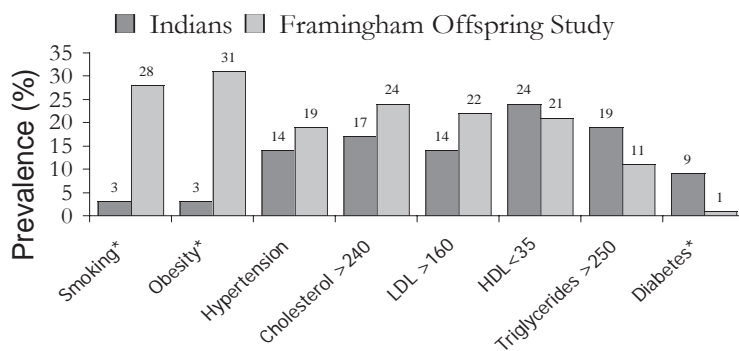


Figure 1.19. Differences in the prevalence of risk factors between Indian participants in the CADI Study and Americans in the Framingham Offspring Study. Compared to Framingham participants, the prevalence of standard risk factors such as smoking, obesity and high blood pressure among the Indians in CADI Study was far lower. The prevalence of high total cholesterol and high LDL was also quite a bit less among the Indians. Indians did have a greater prevalence of diabetes, however, as well as a greater prevalence of high triglyceride levels. Source: Enas, EA. Ref. 1.13.

Paradox” and is explained in detailed in Chapter IV Section 1.

The results of the CADI Study are particularly significant in framing the puzzle of why Indians develop severe heart disease even when they have low rates of obesity, smoking, and high blood pressure. The CADI subjects did everything right: Half were vegetarians; all of them ate a diet low in saturated fats and exercised an average of 134 minutes a week—at a time when the level of exercising recommended by health authorities was only 60 minutes a week. Despite all this, we found high levels of heart disease. (Although the CADI subjects, like other Indians generally, did have higher rates of diabetes, that alone

was insufficient to explain their higher rates of heart disease, particularly given the low prevalence of other traditional risk factors among them.) The study's findings, therefore, point strongly to a genetic component, underscoring the need to keep searching for non-traditional risk factors that may be responsible for this anomaly.

In all populations, including Indians, the major factors that determine how severe your heart disease will be are diabetes, high levels of lipoprotein(a), low levels of HDL cholesterol, and a high ratio of total cholesterol to HDL. Indians, it appears, may be the only population with an excess of all four of the above-mentioned factors associated with severity. (For further details, see Chapter II, Sections 3, 4, and 7, and Chapter III, Section 10.) These four factors—diabetes, high Lp(a), low HDL, and high total cholesterol to HDL—may account for almost all of the greater severity of heart disease we see among Indians (see Chapter IV, Section 1).

Premature, severe heart disease often causes death or disability in the prime of life. When a person develops severe heart disease before the age of 40 and dies from it, never having made their full contribution to society, and often leaving behind a young dependent spouse and young children, the consequences can be truly tragic. Early testing, aggressive treatment, and diligent management of risk factors through lifestyle alterations is imperative among Indians to reduce the devastating economic, emotional, and social consequences to the individual and society that premature, severe, malignant heart disease currently poses to Indians everywhere.

Did you know...

Some traditional risk factors, such as high blood pressure and high total cholesterol, does not strongly correlate by them self with the severity of heart disease. Smoking, paradoxically, is usually associated with less severe heart disease, because smokers get heart attacks on average 10 years earlier than non-smokers.

KEY • POINTS • IN • A • NUTSHELL

- ♥ Coronary heart disease among Indians strikes early, strikes hard, and strikes unexpectedly.
- ♥ Heart disease among young Indians (young defined as under 45) is often severe and diffuse, and it follows a malignant course that may be classified as Type I heart disease.
- ♥ Indians typically develop a heart attack 10 years earlier than other populations.
- ♥ Young Indians have a much higher risk of heart attack than similarly aged people in other populations.
- ♥ Approximately one-third of all first heart attacks among Indians occur in Indians younger than 45, and their heart disease is often comparable in severity to that of older Indians.
- ♥ Serious forms of coronary artery disease, especially left main coronary artery disease and three-vessel disease are twice as common among Indians as in whites, and even more common among Indian women.
- ♥ Diabetes only partially explains the prematurity and severity of Indian heart disease. In addition to traditional risk factors such as diabetes (see Chapter II, section 6), Indians have high levels of newly discovered "emerging" risk factors such as homocysteine, CRP and LP(a). Together, these constitute the most likely cause of the prematurity and severity of heart disease among Indians.