

The Safer Sex?

Probing a cardiac gender gap

By KATHY A. FACKELMANN

"Fifteen years ago, my mother died quite prematurely of heart disease. Looking back, I have to feel that there was failure, from every corner, to help her," said Constance Horner, under secretary at the Department of Health and Human Services, addressing a 1989 conference on women and heart disease.

Horner's story offers a poignant reminder of the traditional and often dangerous tendency to consider heart disease an affliction of men. That assumption was especially prevalent several decades ago, when physicians largely ignored women who complained of chest pain (angina), a potential sign of impending heart attack.

Most people know that heart disease represents the number-one killer of men in the United States. But many don't realize that it's also the number-one killer of women. Although the hormone estrogen apparently helps many women ward off coronary artery disease during their reproductive years, this protective edge begins to vanish with menopause. From then on, a woman's risk of developing heart disease mounts rapidly, soon equaling that of men. Statistics clearly bear this out: Between age 45 and 65, approximately one in nine U.S. women shows symptoms of heart disease, compared with about one in seven men; after age 65,

that ratio jumps to one in three, roughly matching the ratio in men.

But while the *disease* gap eventually disappears, another gap lurks in the statistics: a disquieting difference between men's and women's cardiac *mortality* rates. During the first few weeks after a heart attack, women face twice the risk of death of men, and their heightened relative risk persists well into the following year. In addition, female candidates for coronary artery bypass surgery must confront the stark fact that the operation itself — a risky but potentially lifesaving procedure — puts women in greater jeopardy of death than men.

Does this mortality gap reflect some innate, biological difference in the female body? Are the statistical discrepancies due to known risk factors, such as women's tendency to suffer heart attacks at a later (and presumably frailer) age than men? To what extent do women or their physicians overlook early symptoms of heart disease, delaying important treatment?

Recently published research and findings presented in November at the American Heart Association (AHA) scientific sessions in Dallas provide conflicting data and few answers. Nevertheless, many investigators view these collectively murky results as a first step toward understanding the vagaries of heart disease in women.

In the 1980s, several research reports attributed women's higher death rate from heart attacks to the fact that women typically suffer attacks about a decade later in life than men, and thus may not recover as readily as a younger person of either sex. But new data from the University of Massachusetts Medical School in Worcester indicate that the deadly difference doesn't spring solely from age.

Cardiologist Richard C. Becker and his colleagues studied 2,742 men and 597 women who were hospitalized for a first or second heart attack, caused by a clot that restricted blood flow to the heart. All patients received a clot-busting drug (recombinant tissue plasminogen activator) within four hours after the attack. At the AHA meeting, Becker reported that 9 percent of the women and 4 percent of the men died during the initial hospital stay. And among those who survived the attack, 12 percent of the women died during the following year (primarily from cardiovascular disease), compared with 6 percent of the men.

The researchers found that the women in the study were more than twice as likely as the men to develop chronic heart failure after the attack. In people with this potentially lethal condition, lingering damage from the acute attack permanently impairs the heart's pumping ability. During the first few weeks after their

heart attacks, 5.7 percent of the women and 2.1 percent of the men developed chronic heart failure, Becker reports.

The patients' ages in this study followed a familiar pattern: 24 percent of the women, and only 9 percent of the men, were more than 70 years old. And the age distribution did make a difference in mortality risk, Becker says — but it didn't account for the entire gender gap.

In their statistical assessment of risk factors, the researchers also isolated pre-existing, chronic conditions that could complicate a heart patient's recovery. Compared with the men in the study, the women had a higher prevalence of high blood pressure and diabetes, they found. But even when the team statistically controlled for these conditions, lumping them in with the age factor, a significant mortality gap remained.

Becker says he can't explain this risk remnant, but he and others speculate that differences in female physiology might somehow tip the scales. "The heart of a woman doesn't tolerate a myocardial infarction [heart attack] as well as that of a man," he suggests.

Another report, however, argues against the notion of a built-in risk for women. Nicholas H. Fiebach and his colleagues at Yale University studied 332 female and 790 male heart attack sufferers, finding that 14 percent of the women and 9 percent of the men died during the initial hospitalization. When the researchers controlled not only for the risks associated with age, diabetes and hypertension, but also for the severity of heart disease, they managed to account for all but 1.5 percent of the gender gap — an insignificant remnant, Fiebach says.

The Yale researchers conclude that the severity factor merits special attention in efforts to explain women's heightened mortality risk.

Several of their findings suggest that women tend to reach the cardiac care unit with more serious heart conditions than men, they report in the Feb. 23, 1990 *JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION*. For example, hospital admitting exams showed that the women in this sample, compared with the men, had more severely impaired left ventricular function — an important measure of heart attack severity.

Fiebach believes some physicians may overlook cardiac warning signs in women, especially if those patients are relatively young. "If a middle-aged woman is having chest pain, one doesn't think of a heart attack. If a middle-aged man is having chest pain, one automatically thinks of a heart attack," he told *SCIENCE NEWS*. He also suggests that heart disease may be more difficult to diagnose in women than in men. In any case, a failure to diagnose and treat coronary

artery disease until it becomes more severe could lead to more damaging heart attacks, which in turn carry a higher risk of death, he says.

Cardiovascular researcher Kathleen B. King agrees that the traditional diagnostic bias still influences medical thinking. "There's definitely an attitude that heart disease is a man's problem," says King, of the University of Rochester in New York.

And physicians may not be alone in their delayed response to early warning signs, or even an outright heart attack, in women. Fiebach found that the women in his study generally waited longer than the men to head for the hospital after their chest pains began. "It may be that the longer you wait, the more chances are that you're going to have a severe complication," he suggests, while cautioning that the link between such delays and a poor clinical outcome remains speculative.

The Yale report also hints that physicians may treat male and female heart attack patients differently once their stay in the hospital has ended. The researchers noted that physicians prescribed beta-blocker drugs — which slow the heartbeat and may improve survival outlook for some people — more often for men than for women at the time of hospital discharge. Fiebach emphasizes, however, that this finding did not reach statistical significance in the study. Further research is needed, he says, to determine whether such gender-based treatment differences exist.

The heart attack itself is only part of the story. Researchers also see disturbing differences between the sexes when they look at mortality rates during and after coronary artery bypass surgery, in which surgeons attempt to restore blood flow to the heart by attaching a vein above and below the site of a coronary artery blockage to shunt blood around it. Whether undertaken before or after a heart attack, bypass surgery can sometimes save lives — but statistics show that the operation entails a greater gamble for women than for men.

A research team led by cardiologist Steven S. Khan at the University of California, Los Angeles, has uncovered evidence suggesting that women with heart disease tend to get bypass surgery later in the course of their disease. Khan attributes such delays, which may increase the riskiness of the surgery, to a "referral bias" on the part of physicians.

"Women pretty much have to have a heart attack or very severe symptoms — life-threatening symptoms of their heart disease — before they are sent to surgery," Khan says. Like other researchers, he suspects that some women who complain of chest pain get the brush-off by physicians who think the pain is psychosomatic. He also notes that heart disease

may be trickier to diagnose in women, whose reports of chest pain don't always match the traditional description of angina. Moreover, physicians may worry about advising some women — especially those debilitated by old age or suffering serious complicating conditions — to undergo the rigorous bypass procedure unless their heart condition seems dire.

Kahn and his colleagues assessed the mortality rates of 1,815 men and 482 women who had bypass surgery between 1982 and 1987. They report in the April 15, 1990 *ANNALS OF INTERNAL MEDICINE* that 4.6 percent of the women, compared with 2.6 percent of the men, died during surgery or the postoperative recovery period. But when the researchers statistically controlled for age and severity of illness, the mortality gap vanished.

In general, they found, the women were sicker than the men when wheeled into the operating room, showing more severe signs of heart disease, including a particularly risky type of chest pain called unstable angina. Regardless of gender, says Kahn, a patient's odds of dying during or after bypass surgery increase with the severity of his or her heart condition.

The notion that physicians refer only the sickest women for surgery finds no support in a study conducted at Downstate Medical Center in Brooklyn, N.Y. Thierry A. Folliguet and his co-workers assessed several measures of heart disease severity — including chest pain and the number of blocked arteries — in 858 men and 439 women who underwent bypass surgery at three New York hospitals in 1989. At the AHA meeting, Folliguet reported a total lack of evidence indicating that the women were more severely ill than the men when they reached the operating room. He says he cannot explain the discrepancy between his finding and Khan's.

Folliguet favors a long-standing explanation of women's higher mortality rate from bypass surgery: body size. Because women typically are smaller than men, he says, their bypass operations pose more technical difficulties. Many cardiovascular surgeons espouse this view, asserting that smaller arteries reduce a woman's chance of surviving the surgery and recovery period.

Other researchers have uncovered data contradicting the body-size theory. King, for instance, focused on 464 women who had bypass surgery between 1983 and 1988, finding that 4.3 percent of them died during or soon after the operation. At the AHA meeting, she reported that a statistical analysis comparing the women who died with those who survived showed no link between bypass risk and body surface area.

King quickly points out that body surface area, calculated from height and

weight, may not correlate with the size of coronary arteries. She and her colleagues want to conduct a follow-up study measuring blood vessel size and tracking mortality rates, in the hope of establishing whether or not small vessel size puts women — and smaller men — at extra risk during bypass surgery.

The Rochester results also punch holes in a theory attributing women's higher bypass risk to their tendency to suffer heart attacks at an older age than men. King's all-female sample showed no correlation between age and bypass mortality. "Our study showed that age really didn't make a difference," she told *SCIENCE NEWS*.

Potential complicating factors, such as diabetes or high blood pressure, similarly failed to explain these women's risk, she says.

Many heart researchers today suspect that a complex interplay of factors — including age, severity of illness and perhaps some innate biological differences — works against women who suffer heart attacks. But that risk equation remains largely unsolved.

"We're just beginning to explain how all these things contribute," Fiebach says.

While no amount of research can save her mother now, Horner points out that some 247,000 U.S. women face the prospect of a deadly heart attack in the coming year. Given the magnitude and urgency of that threat, she urges researchers to pursue their investigations with vigor.

In the meantime, one fact is clear: Men have no monopoly on hazards of the heart. □

