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High Impact

by Susan Sample

Cardiologist's Studies Pump Research on Chronic Heart Failure

The number of times each research paper has been cited-165-reads like the systolic blood pressure of patients Edward M. Gilbert, M.D., treats at University of Utah Hospital. In fact, many of his patients participated in the clinical studies that earned the Utah cardiologist the distinction last summer of being ranked 12th in the nation for publishing "high-impact" papers in cardiovascular research.

From 1993-97, Gilbert contributed to seven articles published in top peer-reviewed journals, which were then cited 1,157 times, or an average of 165.3 times per paper, during the five-year span, according to Science Watch, a research service group of the Institute for Scientific Information.

When Gilbert heard the news, "it kind of blew me away." He acknowledged that the articles, clinical trials of new drugs to treat chronic heart failure, "are pivotal findings. Usually though, the older the paper, the more likely it is to be cited. These were referred to almost as soon as they were published."

As gratifying as the accolades are, Gilbert is proudest of the clinical impact: "Patients now are getting these drugs prescribed because of these papers."

About 5 million Americans have chronic heart failure, sometimes referred to as congestive heart failure. Although the word failure might suggest a heart attack or sudden death, chronic heart failure is a condition resulting from an injury to the heart muscle, impairing the ability of the left ventricle to eject blood. The causes vary. Some are identifiable: coronary artery disease (responsible for the condition in two-thirds of the patients); valvular heart disorders; hypertension; thyroid disease or alcoholism. Other causes, referred to as idiopathic dilated cardiomyopathy, are unknown. The symptoms, however, are the same in all patients: dyspnea or shortness of breath, fatigue, fluid retention and an enlarged heart.

Chronic heart failure usually is a progressive condition. The heart dilates and hypertrophies, becoming more spherical. This

"pathological remodeling" causes the strength of the contraction, or squeezing motion, to decrease, which increases a patient's risk for sudden death.

"Heart failure gets worse because of the body's nerve and hormone responses to the progressive enlargement. Over the long term, the hormones are harmful," said Gilbert. "The analogy I use is: if you put a Volkswagen in second gear to drive up a hill, it'll be okay. But if you drive it to Las Vegas, the car will burn out.

"Even heart failure patients with the most stable condition have a 50 percent chance of dying within five years."

While the rate of heart attacks is declining in the United States, chronic heart failure is on the rise. "It's the most common cause of hospitalization in the elderly," said Gilbert. According to the Advisory Council to Improve Outcomes Nationwide in Heart Failure, the condition is "responsible for more than 11 million physician office visits and causes or contributes to over 3.5 million hospitalizations in people more than 65 years old." These hospitalizations cost a total of $8-15 million each year, more than twice the cost of hospitalizations for all forms of cancer. "From a public health perspective, heart failure is very important," noted the Utah cardiologist.

Fortunately, as reported in the high-impact papers, angiotensin-converting enzyme (ACE) inhibitors and beta-adrenergic receptor (beta) blockers not only treat the symptoms of chronic heart failure, but also reverse the progression. "Traditionally, beta-blockers were contraindicated. They were avoided, because it was felt the acute effects were harmful to the patient: lowering the heart rate and decreasing the squeezing function," explained Gilbert. "By starting at low doses, then increasing, we found patients would not only tolerate the drug, but over time, it had a protective factor."

As the pumping function improved, the heart returned to normal size and shape, reducing patients' risk of hospitalization and death.

In 1975, a group of Swedish researchers introduced the concept of using beta-blockers to treat heart failure, although it wasn't until 1985 that the U of U conducted the first randomized clinical trial. Researchers measured the pressure in patients' hearts and lung veins, and used questionnaires to assess symptoms in an effort to measure the drugs' effect on mortality and morbidity. These endpoints later were assessed in multi-center clinical trials across the country; Utah had one of the largest patient enrollments.

Despite the proven ability of beta-blockers and ACE inhibitors to stop the progression of chronic heart failure, the drugs still aren't widely prescribed. "Taken together, these drugs will reduce the annual rate of death from heart failure by 50 percent," said Gilbert. "But we know that only 50 percent of the people who could use ACE inhibitors receive them, and just 5 percent receive beta-blockers.

Many generalists don't recognize chronic heart failure in their patients unless they're retaining fluid."

A definitive diagnosis can be made with an echo-cardiogram, an ultrasound image of the heart's chambers, although physicians don't routinely order this test unless the patient's history suggests he or she is suffering from dyspnea or fatigue. Often, these symptoms aren't reported. "Many older people don't climb stairs anymore; they don't mow their lawns," said Gilbert. "They've moved into a one-floor condo and modified their lifestyles, so no one recognizes the symptoms of heart failure. Their symptoms are mistaken for the aging process.

"One of the challenges is figuring out how we can identify patients with chronic heart failure early on," he said. Finding blood test markers is one possibility Gilbert would like to investigate. He's also looking at the bigger picture: "We need to help patients control diabetes, hypertension, cholesterol and obesity. These lead to more than half of the causes of heart failure in the United States."

He acknowledged that obesity can be a "tricky" topic to discuss with patients, but emphasized that "it isn't a pejorative matter. We're not talking about it on an aesthetic level. Rather, what can we do to help you feel better and live longer."

The cardiologist works with a health-care team that includes a dietitian, nurse and exercise physiologist. "We acknowledge that losing weight will be hard. We don't tell patients to starve themselves; they'll lose muscle mass. And it's not practical to tell them to run a marathon. They can walk. With certainty, we can say that exercise will improve the symptoms of heart failure, and it's safe."

As Gilbert explains to his patients, "If you have an old horse and a full wagon load, it's hard for the horse to pull. Unload the wagon, and it's easier. Obesity and high blood pressure are like heavy loads.

"Beta-blockers are like a whip," he adds. "If you use them occasionally, they help get the horse going. If you rely on the whip all the time, you'll kill the horse."

High-impact Cardiovascular Research Papers

Beneficial effects of Metoprolol in idiopathic dilated cardiomyopathy. The Lancet 1993, 342:1441.

The effect of Carvedilol on morbidity and mortality in patients with chronic heart failure. New England Journal of Medicine 1996, 334:1349.

Effects of Vesnarinone on morbidity and mortality in patients with heart failure. New England Journal of Medicine 1993, 329:149.

Dose-response of chronic beta-blocker treatment in heart failure from either idiopathic dilated or ischemic cardiomyopathy. Circulation 1994, 89:1632.

Carvedilol improves left-ventricular function and symptoms in chronic heart failure-a double-blind randomized study. Journal of American College of Cardiology 1995, 25:1225.

Carvedilol produces dose-related improvements in left-ventricular function and survival in subjects with chronic heart failure. Circulation 1996, 94:2807.

Carvedilol inhibits clinical progression in patients with mild symptoms of heart failure. Circulation 1996, 94:2800.

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