TWO STUDIES: LONG-TERM COGNITIVE DECLINE AFTER BYPASS SURGERY; ALZHEIMER’S GENE LINKED TO EARLIER BYPASS

CHICAGO – How well a patient responds to heart bypass surgery may depend as much on the brain as the heart.

In two studies, researchers from Duke University Medical Center have shown that heart surgery can affect mental functioning, and that a gene involved in a brain disease may predispose patients to early surgery.

One study concluded that although coronary artery bypass graft (CABG) surgery is intended to improve blood flow to the hearts of more than 600,000 Americans each year, it is less beneficial to the brains of some of those patients. One-third of the patients studied had measurable cognitive declines five years after surgery, and the researchers suspect that is due to the use of the heart-lung machine.

Another study found that having a common gene that predisposes people to Alzheimer’s disease may predict early heart problems. In the Duke study, patients with the APOE-4 gene received surgery up to 10 years earlier than the population as a whole.

The results of the Duke studies were prepared for presentation today (April 26) by Dr. Mark Newman, chief of cardiothoracic anesthesia, during a poster session at the annual meeting of the Society for Cardiovascular Anesthesiologists.

Both studies were supported by grants from the National Heart, Lung and Blood Institute (part of the National Institutes of Health) and the American Heart Association.

Cognitive decline after bypass surgery

Duke researchers, like other physicians, have been aware that CABG surgery can cause mental dysfunction in some patients. To find out just how many patients are affected, they designed a test that each patient took before surgery, at discharge, at six weeks and five years following surgery. The test assessed such factors as memory, concentration and attention.

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To their surprise, the researchers concluded that after a five-year follow-up of 313 patients, nearly one-third (31.1 percent) of these patients had measurable cognitive declines.

“Little is more devastating than for patients and their families to have a successful operation that prolongs life, but diminishes the quality of that prolonged life,” Newman said. “Our results confirm long-term persistence of cognitive dysfunction and the importance of prevention of these deficits.”

It is highly likely that the source of the problem is the heart-lung bypass machine commonly used in CABG surgery, Newman said. This machine essentially acts as the body’s heart and lungs while surgeons operate on the stopped heart.

“While we have known for some time that the heart-lung machine is probably a cause, we don’t know for certain exactly what the mechanism is,” Newman said. “It is likely that tiny emboli, or clots, are formed and travel to the brain. Other factors, such as inflammation and the lowered blood pressures, could play a part as well.

“There needs to be further investigation into operative neuroprotection to allow us to reduce the short- and long-term consequences of cognitive decline after surgery,” Newman said.

One of the ways heart surgeons are trying to lessen the impact of CABG surgery is to perform the surgery on a beating heart, which doesn’t require the heart-lung machine, though it presents technical challenges of its own.

“As in everything in medicine, you must balance the benefits with the risks,” Newman explained. “By operating on a beating heart, you don’t need a bypass machine; however, you must factor in whether or not the quality of the suturing and connections, and the additional time in the operating room, would be the same as the conventional approach.”

Joining Newman in the study were Jerry Kirchner, Barbara Phillips-Bute, Elizabeth Phillips, Duke Han, Bruno Baudet, Dr. Alina Grigore, Dr. J.G. Reves and James Blumenthal, all from Duke.

The Alzheimer’s gene link to heart disease

The gene apolipoprotein (APO) comes in three variants, E-2, E-3 and E-4. Researchers have known that not only is the E-4 variant linked to Alzheimer’s disease, but that it is a risk factor for the development of atherosclerosis, the buildup of plaques within coronary arteries that cause heart disease. Since the APO gene is involved in the regulation of cholesterol and triglycerides in the blood, it is believed the E-4 variant leads to a buildup of these lipids, high levels of which are considered risk factors for heart disease.

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The Duke study was the first to look at the relationship between APOE-4 status and the timing of a patient’s first CABG surgery, Newman said. Based on a genetic analysis of 576 CABG patients, the researchers found that those with the APOE-4 variant were much younger when they received their surgeries.

“We found a significant difference in the average age at surgery between people who have the variant gene and those who don’t,” Newman said. “While there are probably other factors involved, APOE-4 status appears to be an important determinant of when a heart patient receives bypass surgery.”

The average age for CABG surgery in the general population is 65. However, the Duke study found that patients who inherited a copy of the defective gene from one parent got the operation at the average age of 60.6. Those who inherited a defective copy from each parent received the operation at the average age of 54.2.

Although the APOE-4 link is statistically significant, Newman said, the mechanisms underlying the association are still unclear. He does believe, however, that APOE-4 is involved somehow in the inflammation process that can occur when a plaque ruptures or is damaged.

“When a plaque ruptures, platelets in the blood arrive at the scene of the injury and clots can form, which can lead to an acute cardiac event,” Newman said. “It may be that in people with the E-4 variant, these plaques are more susceptible to rupture or other injury.”

While a simple genetic test can help physicians spot patients who might be at risk for heart disease, Newman said it is still too early for these findings to be translated into a drug or treatment that can be used to treat heart patients. However, since many researchers are already investigating the role of APOE-4 in Alzheimer’s disease and stroke, a potential treatment might not be that far away, Newman said.

To better understand the genetics behind heart disease, Newman and his team plan to collect genetic samples from all consenting CABG surgery patients at Duke.

Also involved in the study were Dr. Alina Grigore, William White, Dr. Daniel Laskowitz, Ann Saunders, Dr. Hilary Grocott, Dr. Mark Stafford-Smith and Dr. J.G. Reves, all from Duke.

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