

# Despite Higher 1st-Year Death Risk, LVADs Are Urged for Older Patients

BY MITCHEL L. ZOLER  
Philadelphia Bureau

PHILADELPHIA — Older patients are much less likely to survive their first year on a ventricular assist device than are younger patients, according to a review of 1,365 patients who have received such devices.

Despite this, many patients who are at least 60 years old can often benefit from a left ventricular assist device, Peer M. Portner, Ph.D., said at the annual meeting of the International Society for Heart and Lung Transplantation.

"Age is likely a surrogate marker for comorbid conditions at the time of the implant. Left ventricular assist systems [LVAS] can produce a strong survival benefit, even in the oldest patients. This underscores the importance of patient selection for destination therapy," said Dr. Portner, of the department of cardiothoracic surgery at Stanford University in Palo Alto, Calif., and developer of the Novacor LVAS.

"We have an idea of which patients will do better [after receiving an LVAS], but we don't have strong data" to document this, he said. "It's been hard to collect the data that could help" identify the patients who will have the best outcomes after receiving an LVAS.

The analysis reported by Dr. Portner came from a registry of patients who received the Novacor LVAS during 1984-2003. During that period, 1,461 patients received the device at 98 centers worldwide. This analysis excluded 70 patients who received the device as destination therapy and 26 patients with inadequate follow-up data, which left 1,365 patients who received the device as a bridge to transplant. The average period of implantation prior to receiving a heart transplant was 144 days for the entire group, but today the average period during which the im-

plant is in place is about 1 year.

Outcomes data were analyzed by the patients' age, and the database was divided into four groups that had roughly similar numbers of patients: those aged 12-39 years (316 patients), those aged 40-49 years (353), those aged 50-59 years (451), and those aged 60 years and older (245).

A logistic regression analysis showed that death during the first year with the device was directly linked to age. Patients who were in the oldest subgroup (at least 60 years old) had a 2.4-fold increased risk of death compared with all other patients. In contrast, patients in the youngest subgroup (younger than 40 years) had a 50% lower risk of death compared with the other patients. The two intermediate age groups had mortality risks that were between these two extremes.

Expressed another way, the survival rate at 1 year was 75% in patients younger than 40 years, 70% in those aged 40-49 years, 60% in patients aged 50-59 years, and 40% in patients aged 60 years or older. Although mortality was high in older patients, the data also showed that a significant number of older patients could survive beyond 1 year on a LVAS.

"I think that there is a significant opportunity [for treating older patients] beyond what is commonly done now," said Dr. Portner.

"The number of patients who receive destination therapy is very small. It's unfortunate that we're stuck in the United States with having a separate indication for destination therapy. The decision on the ultimate outcome of a recipient of an assist device should depend on how they progress. The device technology is underused. No device is perfect, but they have improved and there is an opportunity to give patients better outcomes and improved quality of life." ■

## VERBATIM

*'Young physicians are moving as quickly as they can to study fields that do not require emergency work at all. They are moving toward boutique practices, which I abhor.'*

Dr. James Nepola, on the shortage of physicians willing to be on call in emergency departments, p. 72

## ALTERNATIVE MEDICINE

AN EVIDENCE-BASED APPROACH

### Pycnogenol for Preventing Traveler's DVT

#### History of Use

According to naturopath Michael T. Murray of Bastyr University, Seattle, the earliest recorded medicinal use of pine bark extracts was in 1534, when French explorer Jacques Cartier became trapped in ice during an expedition up the St. Lawrence River. His crew subsisted on salted meat and dry biscuits but began showing signs of scurvy, the cause of which was not then known. Local Native Americans recommended that the explorers consume tea made from pine bark and needles, and the men survived the ordeal.

In the 1970s, Jacques Masquelier, a professor at the University of Bordeaux (France), heard of Cartier's story and concluded that pine bark must contain vitamin C and other antioxidants. He subsequently analyzed the active proanthocyanidin components, which are similar to those in grape seed extract, and termed them collectively pycnogenol. Today, pycnogenol, formulated from extracts of the French maritime pine tree *Pinus pinaster*, is a registered trademark of Horphag Ltd., Guernsey, England.

#### Rationale for Use

Like grape seed extract, green tea, and other polyphenol-flavonoid compounds, pycnogenol is a powerful antioxidant. It interferes with cell proliferation, modulates chronic inflammation, and inhibits xanthine oxidase. It acts in a capillary-protective fashion via effects on the lysosomal enzyme system.

Pycnogenol also inhibits platelet aggregation, which suggests that it may have potential for prevention of blood clots. Smokers tend to have elevations in platelet activity levels, and a German study found that smoking-induced platelet reactivity was prevented by the intake of 500 mg aspirin or 125 mg pycnogenol (Thromb. Res. 1999;95:155-61).

#### The Economy Class Syndrome

Much attention has been paid in recent years to the economy class syndrome, in which passengers in cramped conditions on long flights have subsequently developed deep vein thrombosis (DVT) and pulmonary embolism.

A report from the emergency medical service of the Paris airports found that, of the 70 cases of acute thromboembolism treated between 1984 and 1998, 76.5% were in patients who had been on flights lasting longer than 12 hours (Bull. Acad. Natl. Med. 1999;183:985-97). This report also acknowledged that it reflected only acute, symptomatic cases, such as patients who fainted upon leaving the airplane.

The true scope of the problem was highlighted by the LONFLIT study, which showed that 3% of travelers developed clots on long flights, most of which were silent or asymptomatic but still potentially dangerous (Angiology 2001;52:369-74).

With some 600 million Americans flying each year—50% on flights longer than 4 hours—one estimate is that up to 1.8 million travelers may develop clots (Phytother. Res. 2004;18:687-95).

Routine advice for travelers at risk for these

conditions, such as those with varicose veins and chronic venous insufficiency, has included the use of compression stockings and prophylaxis with low-molecular-weight heparin or aspirin. Travelers are also advised to drink non-alcoholic fluids, avoid salty food, and stand and stretch frequently, but exercising can be difficult on a crowded airplane. Advocates of the use of pycnogenol suggest that it is safer than aspirin, as it does not increase bleeding time or cause GI side effects.

#### Clinical Study Findings

A group of Italian researchers recently reported their data comparing pycnogenol with placebo for the prevention of edema and venous stasis in a group of 169 asymptomatic subjects at mild to moderate risk of thrombosis following flights lasting 7-12 hours. The study involved ultrasound scans of the legs before and within 12 hours after the flights to evaluate the femoral, popliteal, and tibial veins. Assessment of edema was done on an analog scale, with composite scores ranging from 0 to 12. The rate of ankle swelling was measured with a strain gauge.

Participants received two capsules of 100 mg pycnogenol or placebo 2-3 hours before their flight, with two more capsules 6 hours later and one the next day. After the flights, patients in the pycnogenol group had an increase in edema score of 17.9%, compared with an increase of 58.3% in the placebo group, a difference that was statistically significant (Clin. Appl. Thromb. Hemost. 2005;11:289-94).

The change in ankle circumference from before to after the flight also was significantly smaller in the active treatment group, at 6%, compared with 11% in the placebo group. The rate of ankle swelling, evaluated in a subgroup of 45 patients, increased an average of 91% in the placebo group but only 36% in the pycnogenol group. No patients in the study reported side effects from the treatment.

The researchers noted a number of factors that may contribute to flight-associated edema and release of thrombogenic factors, including compression of the popliteal vein on the edge of the seat, immobility, decreased fluid intake, water loss in the dry atmosphere, decreased air pressure, and relative hypoxia.

They also pointed out that edema is not limited to the visible lower limbs. "The effects of edema could be more important than expected as retinal and brain edema have been episodically described and can be associated with vision problems and ... sleep and behavioral pattern alterations, which may be associated or confused with jet-lag symptoms. Actually, in our experience, in several subjects and patients with high levels of edema after long flights, the presence of subclinical edema has been detected with cerebral MRI or CT scans."

The subclinical cerebral edema was, in some cases, associated with severe alterations in speech and sleep. This phenomenon should be studied more specifically, particularly in older patients who are prone to the development of edema, they said.

—Nancy Walsh

▶ *Travelers on long flights are at risk for the "economy class syndrome," involving edema, venous stasis, and possible deep vein thrombosis.*

▶ *Extracts of the French maritime pine tree exhibit antioxidant and antiplatelet effects, and have been shown to reduce edema following air travel.*