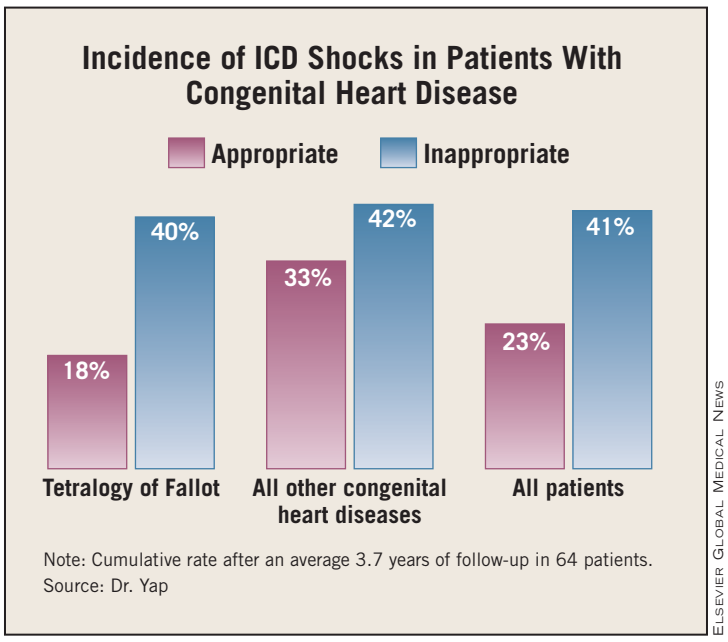
Inappropriate Shocks Higher in Adults With Congenital Disease

BY MITCHEL L. ZOLER
Philadelphia Bureau

CHICAGO — Adults with congenital heart disease face an increased risk of ventricular arrhythmias and sudden cardiac death, but that doesn't mean they should all get an implantable cardioverter defibrillator.

"We must be very careful using ICDs [implantable cardioverter defibrillators] for primary prevention" of ventricular arrhythmias in adults with congenital heart disease, Dr. Sing-Chien Yap said at the annual scientific sessions of the American Heart Association. That's despite the fact that in these patients the risk of sudden cardiac death is 25-100 times greater than in the general population.



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The major limitation on using ICDs in these patients is their rate of inappropriate shocks, which are primarily triggered by supraventricular arrhythmias in adults with congenital heart disease. In a series of 64 Dutch adults with congenital heart disease who had an ICD, the incidence of inappropriate shocks was 41% during 3.7 years of follow-up, an annual rate of about 11%, said Dr. Yap, a cardiologist at the Thoraxcenter of Erasmus University in Rotterdam, the Netherlands. This is a "very high number," Dr. Yap said. In more typical patients with ICDs, the annual rate of inappropriate shocks is less than 5%.

"Inappropriate shocks are the dark side of ICD therapy," said Dr. Yap. The problem is the relatively high rate of supraventricular arrhythmias in adults with congenital heart disease. In the 64 patients that he reviewed, about 30% had a history of atrial arrhythmias. "We're becoming more and more conservative when implanting ICDs" in these patients.

A different perspective on the role of ICDs in adults with congenital heart disease was offered by cardiologists at Ohio State University and Columbus Children's Hospital, both in Columbus. Since January 2005, they have managed 41 adults with congenital heart disease who met their criteria for undergoing a surveillance electrophysiology study. An inducible ventricular arrhythmia was found in 17 patients (41%), of whom 15 had an arrhythmia that was immediately inducible without need for treatment with isoproterenol. Ten of these patients received an ICD, said Dr. Shane F. Tsai, a cardiologist at Ohio State. So far during intermediate-term follow-up, none of the ICDs has delivered a shock.

"We're not recommending ICDs for all of these patients, but it's been our choice to be very aggressive," Dr. Tsai said. It's not yet clear which adults with congenital heart disease need surveillance by electrophysiology studies and what benefit they might gain from an ICD, he cautioned. "The real issue is do we reduce deaths," but proving that will require longer follow-up, he said.

In the Dutch study, the cumulative rate of appropriate shocks during 3.7 years of follow-up was 23%, about 6% per year, which means the usefulness of ICDs in these patients is roughly comparable to the 7% annual rate that was reported for patients with hypertrophic cardiomyopathy, Dr. Yap said.

An analysis of the 64 patients who got ICDs failed to identify any feature that helped to predict an increased or decreased risk of receiving inappropriate shocks. The only feature able to identify patients with a significantly reduced risk of receiving appropriate shocks was having tetralogy of Fallot as the congenital disease. ■

Optimal Clopidogrel Dose in Children Found

BY BRUCE JANCIN
Denver Bureau

CHICAGO — Clopidogrel at a dose of 0.2 mg/kg in infants and toddlers achieves a platelet inhibition level similar to the 75 mg/day that's standard in adults for prevention and treatment of major cardiac events, Dr. Jennifer S. Li said at the annual scientific sessions of the American Heart Association.

This was the main finding of the phase II Platelet Aggregation In Children (PICOLO) study, the first randomized, double-blind, multicenter clinical trial to look at the pharmacokinetics of clopidogrel in children age 0-24 months at increased risk of thrombotic events because of congenital heart disease, explained Dr. Li of the Duke Clinical Research Institute, Durham, N.C.

The antiplatelet drug isn't at present approved for use in young children, although it's often used off-label in those at increased thrombotic risk. PICOLO was undertaken in order to identify the optimal dose for platelet inhibition in such patients. Pinning down the correct dose was a priority because extrapolating adult dosing to children at roughly 1 mg/kg has been reported to result in life-threatening hemorrhage.

"This may be because extrapolated dosing doesn't account for physiologic or metabolic differences in children," she said.

PICOLO involved 73 evaluable 0- to 24-month-olds at increased thrombotic risk due to a systemic-to-pulmonary artery shunt, stent placement, or Kawasaki disease. They were randomized to 7-28 days of clopidogrel at 0.01, 0.1, or 0.2 mg/kg per day or placebo.

The goal was to find the dose that achieved 30%-50% platelet inhibition by light transmission aggregometry. That's what 75 mg/day accomplishes in adults, for whom there is extensive evidence to show that this degree of platelet inhibition results in a marked reduction in thrombotic events.

The optimal dose in children proved to be 0.2 mg/kg. It achieved 49% inhibition of the maximum extent of platelet aggregation and 44% inhibition of the rate of aggregation. Lesser doses didn't even come close to the target.

Clopidogrel at all doses was well tolerated. No hemorrhagic events occurred.

Effective platelet inhibition can't be assumed to be a surrogate for clinical efficacy in children. Clinical outcomes are being assessed in the ongoing Clopidogrel To Lower Arterial Thrombotic Risk For Neonates and Infants Trial (CLARINET). Both PICOLO and CLARINET are sponsored by Sanofi-Aventis and Bristol-Myers Squibb. ■

Renal Impairment Worsens Ventricular Function

BY MITCHEL L. ZOLER
Philadelphia Bureau

CHICAGO — More than a third of adults with congenital heart disease also had significant renal dysfunction in a review of 201 patients.

Impaired renal function in patients with congenital heart disease was also linked with worse ventricular function and a dramatically increased risk of death, Dr. Sanaz Piran said at the annual scientific sessions of the American Heart Association.

The implications of these findings for managing patients are not yet clear. What's needed now is a study that examines whether treatment of these patients with an ACE inhibitor has a positive impact on renal function and clinical outcomes, said Dr. Piran, a physician at McMaster University in Hamilton, Ont.

The analysis that she reported was done on 201 consecutive patients older than 18 years with single or systemic right ventricles seen at the Toronto Congenital Cardiac Centre for Adults. The group included 73 patients with detransposition of the great arteries (DTGA), 69 who had a Fontan procedure, and 59 with congenitally corrected transposition of the great arteries (CCTGA). Their average age was 34 years. The analysis also included 30 normal, healthy, age-matched controls.

The ejection fraction was significantly lower in patients with renal dysfunction (37%) than in those without (44%).

The overall prevalence of renal dysfunction—defined as a calculated creatinine clearance rate of less than 60 mL/min—was 36%, with prevalence rates of 56% in patients who had a Fontan procedure, 37% in those who had CCTGA, and 18% in patients following DTGA.

The ventricular ejection fraction was also significantly lower (37%) in patients with a creatinine clearance rate of less than 60 mL/min, compared with patients with a creatinine clearance of 60 mL/min or greater, who had an average ejection fraction of 44%.

During follow-up of up to 30 years, 22 patients died. The mortality was 24% among the patients with renal dysfunction at baseline, compared with a 2% death rate among those with a creatinine clearance rate of more than 60 mL/min at baseline, Dr. Piran said. ■

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