

## Congenital Heart Disease Patients Opt for Pregnancy

BY BRUCE JANCIN  
Denver Bureau

NEW ORLEANS — Pregnancies and deliveries are on the rise while abortions are declining among women with congenital heart disease, according to a population-based Canadian study.

"These are very provocative findings. As the ACHD [adult congenital heart disease] population increases and ages, we can expect that more women will reach reproductive age. These demographic changes may therefore impact on transmission rates and health services utilization in the future," Dr. Ariane J. Marelli said at the annual scientific sessions of the American Heart Association.

She and her coinvestigators have previously shown, using comprehensive Quebec-wide data, that women accounted for 57% of the province's ACHD population in the year 2000. That study, the first ever in which the prevalence of ACHD has been measured rather than merely estimated, showed that the prevalence of ACHD was 4.09 cases per 1,000 in the year 2000, with 9% consisting of severe forms (*Circulation* 2007;115:163-72). The prevalence of severe ACHD rose in Quebec by 85% from 1985 to 2000, probably because of the major surgical progress in this period.

In the new study of the Quebec population, which has universal access to health care, the investigators found that of 14,828 women with ACHD aged 18-45 years during 1992-2005, a total of

5,858 had 9,970 pregnancies. Thirty-two percent of ACHD patients in this age range had at least one delivery, and 14% had at least one abortion. The proportion of pregnancies resulting in delivery climbed from 61% in 1992 to 78% in 2004. Conversely, the proportion ending in abortion declined from 39% to 22%, according to Dr. Marelli, director of the McGill University adult unit for congenital heart disease, Montreal.

The median age at delivery among women with ACHD was 29, while the median age at abortion was 26.

"Over time, women are getting pregnant at an older age. Our women are following the same trend we're seeing in the normal population," she noted.

The absolute number of deliveries annually among women with ACHD climbed by about 20% between 1992 and 2004. The C-section rate was unexpectedly high at 26.5%, roughly twice that in the general population.

"We were very surprised at the C-section rates," Dr. Marelli said. "They're really very, very high. One has to wonder what the obstetricians are thinking. I can only surmise that it has taken us in cardiology at least a decade to feel a little more reassured [regarding pregnancy in ACHD patients], and they're probably not there yet. I think the responsibility is ours to help them get there."

The study was supported by the Heart and Stroke Foundation of Canada and the Quebec Health Research Foundation. ■

## Genetic Variants Inhibit Response to Clopidogrel

BY MICHELE G. SULLIVAN  
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Variants in genes that control the cytochrome P450 pathway can reduce the beneficial effects of clopidogrel, significantly increasing the rate of cardiovascular death, heart attack, stroke, and stent thrombosis in persons who carry the polymorphisms.

The variants "were associated with adverse clinical outcomes ... more than 50% greater, and a rate of stent thrombosis that was greater by a factor of 3 than the rate in noncarriers," Dr. Jessica L. Mega and her associates reported (*N. Engl. J. Med.* 2009;360:354-62).

The cytochrome P450 pathway transforms clopidogrel into an active metabolite. Genetic variants that reduce the pathway's enzymatic function also decrease this transformation, thus reducing exposure to the active metabolite, wrote Dr. Mega of Brigham and Women's Hospital, Boston, and her colleagues. The reduced-function variant is common, occurring in about 30% of whites, 40% of blacks, and 55% of East Asians.

The two-pronged study analyzed the alleles' pharmacokinetic effects in healthy patients who were included in several drug studies, and its clinical effects in patients who received clopidogrel during the TRITON-TIMI 38 (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel [Clopido-

grel]-Thrombolysis in Myocardial Infarction 38) study.

The pharmacokinetic study measured plasma concentrations of clopidogrel's active metabolite in 162 subjects, and sorted the results according to five genes known to affect the enzymatic pathway. Carriers of at least one of the reduced-function alleles of the CYP2C19 gene had a 32% reduction in the active metabolite, compared with noncarriers, and exhibited a 9% decrease in pharmacodynamic response. The reduced response was seen after a loading dose and during maintenance therapy.

The clinical outcomes analysis included data on 1,477 patients who had been assigned to clopidogrel treatment in TRITON-TIMI 38, and who had provided DNA samples. At least one reduced-function CYP2C19 allele was present in 27% of the study population.

Overall, carriers were 50% more likely than noncarriers to experience one of the study's primary outcomes. On individual outcomes, carriers were nearly five times more likely to die from cardiovascular causes, 38% more likely to have had a nonfatal heart attack, and four times more likely to have had a nonfatal stroke.

Carriers were also three times more likely to experience stent thrombosis than were noncarriers. The CYP2C19\*2 allele was present in 95% of patients who were classified as having a reduced-function allele. ■

## Many Elective Angiographies Are Deemed Unnecessary, Data Show

BY BRUCE JANCIN  
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NEW ORLEANS — Nearly two-thirds of 400,000 patients who underwent elective diagnostic coronary angiography recently at 601 U.S. hospitals turned out not to have obstructive coronary artery disease.

This is not an efficient use of health care resources, and a clear factor in this poor performance is the low positive predictive value of current noninvasive stress testing methods for myocardial ischemia, Dr. Manesh R. Patel said at the annual scientific sessions of the American Heart Association.

Clinical guidelines advise documenting ischemia through noninvasive stress testing before considering diagnostic coronary angiography. That was done in 84% of the cases in this series, which was taken from the American College of Cardiology National Cardiovascular Data Registry. However, the positive predictive value of noninvasive testing was a mere 41%, according to Dr. Patel of Duke University, Durham, N.C.

He reported on 397,954 stable patients without a history of acute coronary syndrome or coronary revascularization who underwent diagnostic coronary angiography during 2004-

2008 and were entered into the comprehensive national registry.

Obstructive coronary artery disease (CAD) was detected in 38% of patients based on at least a 50% stenosis of the left main artery or a 70% or greater stenosis of other major vessels.

Of the patients with obstructive CAD, 14% had a low Framingham risk score, 59% were at moderate Framingham risk, and 27% were at high risk. Among those patients found not to have significant CAD, 39% had a low Framingham risk score, 52% had a moderate risk score, and the rest had a high Framingham score.

Among the 69% of subjects who were referred for angiography following a positive stress test, 41% proved to have obstructive CAD. Of the 12% of patients who were sent for diagnostic angiography after a negative stress test, 28% were found to have obstructive CAD.

A total of 16% of patients in this large series were referred for diagnostic angiography without a prior stress test, presumably because something in their clinical evaluation caused their physician to believe they had a high likelihood of significant CAD. Yet upon angiography, only 35% of this group proved to have obstructive CAD.

Complications of diagnostic angiography occurred in 1.6% of cases. ■

## Hospitalization for Heart Events Trended Downward 2000-2005

NEW ORLEANS — The total number of hospitalizations for cardiovascular events and procedures in the United States declined by 17% during the first 6 years of this decade, according to data from the Healthcare Cost and Utilization Project's Nationwide Inpatient Sample.

Hospitalizations for coronary heart disease fell by an age- and sex-adjusted 24% from 2000 to 2005, while stroke-related hospitalizations declined by 18%. Meanwhile, heart failure admissions remained essentially constant, Craig S. Roberts, Pharm.D., reported at the annual scientific sessions of the American Heart Association.

The rate of elective coronary artery bypass graft (CABG) surgery plummeted by 46%. The total number of CABG procedures decreased by 40% from more than 385,500 performed in 2000.

In contrast, primary angioplasties increased by over 13%,

from 2.2 per 1,000 persons in 2000 to 2.5 in 2005, while the elective angioplasty rate remained flat over that period, according to Dr. Roberts of Pfizer Inc. in New York.

The total cardiovascular hospitalization rate was 13.8 per 1,000 in 2000, dropping to 11.5 in 2005.

The nearly 3.4 million total cardiovascular hospitalizations in 2005 were more than 704,000 fewer than in 2000.

Coronary heart disease hospitalizations declined from 3.3 to 2.5 per 1,000 during 2000-2005. Stroke-related hospitalizations dropped from 2.0 to 1.7 per 1,000. The heart failure hospitalization rate was 3.8 per 1,000 at the beginning of the decade and 3.7 in 2005.

The cardiovascular hospitalization decreases were consistent from year to year and were similar in men and women across all age groups.

—Bruce Jancin