Studies Need More Hispanics to Unravel Paradox

BY PATRICE WENDLING

CHICAGO — Although Hispanics are grossly underrepresented in heart failure trials, emerging evidence suggests they have unique risk factors and heart failure outcomes that must be taken into clinical consideration.

The evidence also underscores the importance of recognizing the vast heterogeneity of Hispanics, Dr. Ileana Piña said at a meeting sponsored by the International Society on Hypertension in Blacks.

"Hispanics represent a cultural group, not a racially identifiable group," said the Cuban-born cardiologist. "You can't lump them all together."

But that's exactly what has happened. Until the Medicare enrollment files were changed in 1994, Hispanics or Native Americans were simply classified as either "white" or "black." It wasn't until the 2000 U.S. census that the term "Hispanic" was changed to "Spanish, Hispanic, or Latino" to describe persons of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.

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Several studies have made the observation—coined the "Hispanic paradox"—that Hispanics have lower all-cause and cardiovascular mortality, despite increased obesity and diabetes, and lower socioeconomic status, said Dr. Piña, professor of medicine at Case Western Reserve University in Cleveland, and a Veterans Affairs National Quality Scholar.

A study of Medicare enrollees aged 65 years or older found that Hispanics were 1.2 times more likely to be hospitalized for heart failure than were whites, while blacks were 1.5 times more likely. But after adjustment for sex and age, in-hospital mortality was significantly lower among Hispanics and blacks than among whites (Am. Heart J. 2005;150:448-54).

Sociocultural factors are often used to explain the Hispanic paradox, but more recent data are causing some to rethink the paradox or at least to differentiate Hispanics by birthplace. Among diabetics in the San Antonio Heart Study, age- and sex-adjusted hazard ratios indicated that U.S.-born Mexican Americans have a 66% greater risk of all-cause mortality and of cardiovascular mortality, compared with non-Hispanic whites, while Mexico-born Mexican Americans appeared to be at similar risk (Diabetes Care 2002;25:1557-63).

A recently published "state-of-the-art" paper on the subject notes that Hispanic ethnicity is marked by a disproportionate cardiometabolic risk burden, largely because of exceedingly high rates of insulin resistance. The authors hypothesize that "the central concept of insulin resistance—compounded by inflammation and neuroendocrine overactivity—may be a predominant etiologic factor for cardiomyopathy in Hispanics" (J. Am. Coll. Cardiol. 2009;53;1167-75).

The authors called for greater representation in patient registries, research studies, and clinical trials, a call echoed by Dr. Piña. She noted that Hispanic or Latino patients made up just 3% of HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) , even though they make up about 15% of the total U.S. population. Still, among nine other recent heart failure trials, it was the only one to specifically differentiate Hispanics, instead of lumping them together with other ethnicities as "nonwhites" or "other."

Dr. Piña disclosed serving as a speaker for AstraZeneca, Novartis, and Merck, and as a consultant for the Food and Drug Administration. ■

Albuminuria Levels Appear to Predict Heart Failure Outcomes

BY MITCHEL L. ZOLER

Albuminuria was a powerful, independent predictor of poor prognosis in heart failure in a prospective study of more than 2,000 patients.

Because diagnosis of albuminuria using a patient's spot urinary albumin to creatinine ratio (UACR) is a "simple and readily available clinical test that is widely used in primary and secondary care, it might be of value in risk stratification of patients with heart failure," Dr. Colette E. Jackson of the University of Glasgow, and her associates wrote in their report (Lancet 2009;374:543-50).

But the finding came with two important caveats: First, the new analysis did not establish whether reducing albumin excretion by treatment improves clinical outcomes. The study also did not establish whether calculating a patient's UACR adds incremental prognostic information to other new, prognostic biomarkers such as natriuretic peptides.

This uncertainty about the role of UACR in managing heart failure patients was echoed in a comment that accompanied the report, which asked whether albuminuria should be used as a (surrogate) treatment target in heart failure, and if so how it should it be treated. "Until a properly designed, adequately powered study is done, the question is open to debate," Dr. Kevin Damman and his associates at the University Medical Centre in Groningen, the Netherlands, wrote in their comment (Lancet 2009;374:506-7).

The new analysis was a preplanned, investigator-originated substudy of the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) study, which found that treatment with the angiotensin receptor blocker candesartan was significantly better than placebo for preventing cardiovascular death and heart failure hospitalization in patients with New York Heart Association class II-IV heart failure who were intolerant of an angiotensin-converting enzyme inhibitor (Lancet 2003;362:759-66).

The new analysis focused on 2,310 patients in CHARM who had their UACR measured. Overall, 58% of these patients had a normal UACR at baseline, 30% had microalbuminuria, and 11% had macroalbuminuria. Patients with high UACRs were older and had more cardiovascular comorbidity, worse renal function, and a higher prevalence of diabetes than did those with normal UACRs, but some patients had micro- or macroalbuminuria without having diabetes, hypertension, or renal dysfunction.

After adjustment for prognostic variables, including renal function, diabetes, and blood level of hemoglobin A_{1c}, the hazard ratio for the incidence of cardiovascular death or hospitalization for heart failure was 43% higher in patients with microalbuminuria and 75% higher in patients with macroalbuminuria, compared with those with normal UACRs. These differences were statistically significant. For every 100 mg/mmol increase in the UACR the risk for cardiovascular death or heart failure hospitalization rose by 7%, a statistically significant effect.

Dr. Jackson said that she had no conflicts of interest, but several of her coauthors reported receiving research funding, and lecture and consulting fees, from AstraZeneca, the company that markets candesartan (Atacand). Dr. Damman and his coauthors said they had no conflicts. ■

Four-Hour Flight Can Raise VTE Risk Nearly Threefold

BY NEIL OSTERWEIL

BOSTON — Air travel can put frequent or casual flyers at significantly increased risk for a venous thromboembolic event for up to a month after the end of a trip, British investigators reported at a meeting of the International Society on Thrombosis and Haemostasis.

Flying for more than 4 hours at a stretch—or a total flying time of more than 12 hours in the past 4 weeks—was associated with a two- to nearly threefold greater risk for VTE, compared with nontraveling controls, reported Dr. Peter K. MacCallum of Barts and The London at the University of London.

"In this community-based case-control study, we found that air travel was a mild risk factor for venous thrombosis in the subsequent 4 weeks. The risk seen at 4 weeks was no longer apparent at the 12-week time-frame, so the dose response and the declining risk with the passage of time tend to support a causal relationship between air travel and subsequent thrombosis," Dr. MacCallum said.

The size of the air-travel effect on VTE risk was comparable to that of low-risk surgery. Other factors associated with increased risk for VTE were body mass index from 25 kg/m^2 to 30 or greater than 30, he reported.

Cases series linking air travel to VTE risk date to the 1950s, and by 1977 the phenomenon had earned the nickname "Economy class syndrome." Over the last decade, researchers have taken a more systematic approach, with case-control, observational, follow-up, intervention, and laboratory studies.

The findings echo those of a recently published meta-analysis, which suggested that air travel was associated with about a threefold risk for VTE (Ann. Intern. Med. 2009 Aug. 4 [Epub ahead of print]).

Dr. MacCallum and his colleagues conducted a community-based, case-control study looking at venous thromboembolic events among patients in 123 general practices in the United Kingdom. They identified patients who had received a prescription for warfarin over the previous 12 months, performed a record search to identify those patients who had confirmed deep vein thromboembolism/pulmonary embolism (DVT/PE), and assigned six age- and sex-matched controls for each case.

All cases and controls were contacted by mail with consent forms and questionnaires. A total of 550 cases and 1,971 controls were studied.

In univariate analysis, the only significant flight-associated risk factor for short-term VTE was total flight time longer than 12 hours (OR, 1.91; 95% confidence interval, 1.08-3.39). In multivariate analysis adjusted for BMI, surgery, and past history of VTE, the only significant risk factors for VTE within 4 weeks of flying were any flight leg longer than 4 hours (OR, 2.20; 95% CI, 1.29-3.73) and total flying time greater than 12 hours (OR, 2.75; 95% CI, 1.44-5.28). By week 12, however, neither flight leg duration nor total flight time was significantly associated with increased risk for VTE.

The funding source for the study was not disclosed. Dr. MacCallum said that he had no relevant conflict-of-interest disclosures. ■