Clinical Digest

Blood Disorders

An Ethnic Disproportion in Fatal Pulmonary Embolism

In-hospital studies have shown distinct ethnic differences in the epidemiology of deep venous thrombosis and pulmonary embolism (PE), but fewer studies have been done on the role of ethnicity in out-of-hospital, fatal PE. Researchers from Albert Einstein College in New York, New York, analyzed 578 consecutive, out-of-hospital, fatal PE cases between June 2005 and December 2009, in the first demographic and baseline comparison of out-of-hospital fatal PE for 3 major ethnic groups in a major metropolitan area.

The study was conducted in New York City, where all sudden, out-of-hospital deaths are investigated by the Office of Chief Medical Examiner. Unlike the in-hospital process for PE-related deaths, which may not be confirmed by autopsy, the standard investigation includes a complete autopsy. Fatal PE was considered an immediate cause of death for all cases. This study focused on cases where PE lesions were fresh, recent, and fatal, and were determined to be the immediate cause of death.

Although the Asian population is included in this study, the researchers focused primarily on blacks, whites, and Hispanics. Blacks represented 58% of the deaths, followed by whites (25%), Hispanics (16%), and Asians (1%). This ethnic breakdown, the researchers say, contrasts with the general population of New York City, in which non-Hispanic whites represent 35% of the population, followed by Hispanics (28%), blacks (25%), and Asians (12%).

When standardized to the New York City population, the overall incidence of out-of-hospital, fatal PEs per 100,000 people per year was 1.6. Adjusted for race, the data revealed that blacks were more than 3 times as likely to die of PE, compared with whites and Hispanics.

A commonly identified risk factor was immobility. Nearly half of all the decedents had acute or chronic immobility. However, 10% of blacks had atherosclerotic and hypertensive cardiovascular disease, compared with 6% of whites and Hispanics. Blacks also were much more likely to have idiopathic PE (18% vs 10% of whites and 8% of Hispanics).

Obesity, defined as body mass index ≥ 30 kg/m^2, was as much as 3 times more prevalent in fatal PE cases than in the general New York City population. The majority of all ethnic groups were obese: 51% of whites, 57% of blacks, and 62% of Hispanics. Again, those rates contrasted with general obesity rates in New York City: 17% of whites, 29% of blacks, and 26% of Hispanics. More than 10% of the decedents were morbidly obese.

A unique finding in the study was the younger age at death of Hispanics and blacks compared with whites. In other studies, rates of in-hospital, fatal PE increased with age for both blacks and whites. However, the researchers in this study say the reasons for the earlier deaths were not clear. They suggest interactions among multiple risk factors, such as obesity, immobility, and socioeconomic and health care issues, may play a part. The study also revealed significant information about the genetic component of out-of-hospital PE. The researchers performed genetic analyses for factor V (FV) Leiden, prothrombin (FII) G20210A, and methylenetetrahydrofolate reductase (MTHFR) C677T on all 578 cases. In addition to non-white ethnicity, heterozygous carriers for FV Leiden and obesity were significantly associated with younger age at death.

This study, according to the researchers, had several limitations. There were no matched, health control subjects from the same geographical area to compare genotypes. Also, the ethnic information for the people in this study was derived from family reports, which can be culturally or socially influenced and, therefore, may be inaccurate.

The researchers note that, when found in conjunction with other risk factors for PE, such as pregnancy or the FII variant, FV Leiden is associated with earlier onset of thrombosis. Although the significance of their finding is as yet unclear, the researchers say, "it will be interesting to see whether our results are confirmed in future studies," identifying genetic and other risk factors that lead to PE.

Source: *Circulation.* 2011;123(5);2219-2225. doi:10.1161/CIRCULATIONAHA.110.976134.

Women's Health

Reassessing Risk Factors for Ovarian Cancer

When your patient doesn't have a family history of certain cancers, or a known BRCA1 or BRCA2 genetic mutation, how do you assess her risk for ovarian cancer? A tool developed by researchers from Brigham and Women's Hospital in Boston, and Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire, may help.

Using data from 3 phases of a case-control study from 1992 to 2008 in New England, the researchers selected

1,098 women with invasive ovarian cancer, and 1,363 who were older than 40, had not had a hysterectomy, and did not have a personal or family history of breast or ovarian cancer. Statewide cancer registries and hospital tumor boards were used to identify ovarian cancer cases in eastern Massachusetts and the entire state of New Hampshire.

The researchers used 2 approaches to identify women who might be at greater risk for ovarian cancer after hysterectomy and more likely to benefit from elective bilateral salpingo-oophorectomy. In the first approach, they constructed a risk-factor score that might be useful to the "average risk" woman. All women with prior hysterectomy or who had an above-average risk because of personal or family history of cancer, were excluded from this portion. In the second approach, they examined women in both groups, still excluding women with a prior hysterectomy or above-average risk, to determine whether risk profiles or reasons for the surgery could have distinguished those who developed ovarian cancer.

Then, using logistic regression, the researchers distinguished significant risk factors between the 2 groups. To make their model more relevant to women considering oophorectomy at the time of hysterectomy, researchers excluded women younger than 40 years of age who might be inappropriate candidates for elective oophorectomy without known ovarian pathology. The resulting list contained 8 conditions: Jewish ethnicity, less than 1 year of oral contraceptive use, nulliparity, no breastfeeding, no tubal ligation, painful periods or endometriosis, polycystic ovary syndrome or obesity, and long-term genital talc use. The researchers next created a 5-level score that correlated with increasing relative risks for ovarian cancer. They assessed the score in 126 women in the case group and 136 in the control group to determine whether women who developed ovarian cancer could be distinguished.

Emerging evidence suggests that many high-grade invasive ovarian cancers originate in the fallopian tubes rather than in the ovaries.

They assigned "average risk" to women with a score of 2. A 40-year-old woman, with 0 to 1 risk factors, would have an absolute risk of 1.2% of developing ovarian cancer by age 85. A woman with 5 or more risk factors would have a risk of 6.6%.

Their risk score doesn't provide a "precise formula" for when to recommend elective oophorectomy, the researchers say, because they did not do a cost-benefit analysis that allowed for other factors, such as long-term complications of bilateral salpingo-oophorectomy (for example, bone fracture). They add that, based on the relative rarity of ovarian cancer, it's possible that, even if all cases were predicted and eliminated, overall benefits might not be shifted toward selective bilateral salpingo-oophorectomy.

Researchers point out that a limitation to the study was that most of the women enrolled in the study were non-Hispanic whites. Case-control data were used to create the study's scoring system, another factor that the researchers say provided limitations. However, they feel as though the risk factors observed agree with other published data.

Nonetheless, say the researchers, it is important for physicians and their patients to discuss and weigh individual risk for ovarian cancer when considering elective oophorectomy. Emerging evidence, they point out, suggests that many high-grade invasive ovarian cancers originate in the fallopian tubes rather than in the ovaries; thus, salpingectomy, without oophorectomy, might be a better choice for women coming in for hysterectomy—and the risk score might help identify those women.

Although the researchers believe their scoring system is an improvement to existing methods for assessing risk for ovarian cancer, they confirm that it should be viewed as a prototype until it can be validated in other data sets. They specify that the method should be used in studies that include more non-white women, a group that was underrepresented in this study.

Source: *Obstet Gynecol.* 2011;117(5):1042-1050. doi:10.10197/AOG.0b013e318212fcb7.

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