

Pulmonary Embolism Rises With BMI in Women

‘There is a strong, independent, positive, linear association between BMI and incident PE.’

BY NEIL OSTERWEIL

BOSTON — The more women weigh, the greater their risk for incident pulmonary embolism, according to an analysis of prospective data from more than 85,000 women enrolled in the Nurses’ Health Study.

The investigators found a relative risk for pulmonary embolism (PE) of 1.08 for every 1 kg/m² increase in body mass index (BMI), said Dr. Christopher Kabrhel at a meeting of the International Society on Thrombosis and Haemostasis.

“We found that there is a strong, independent, positive, linear association between BMI and incident PE, and that this effect seems to impact not only obese subjects, but [also] subjects with relatively modest increases in their BMI,” reported Dr. Kabrhel, of Harvard Medical School and Massachusetts General Hospital in Boston, and his colleagues.

Cross-sectional and case-control studies have shown that patients who experience deep vein thrombosis and pulmonary embolism tend to have higher BMIs, and prospective studies have shown an association between severe

overweight or obesity and pulmonary embolism, he noted.

The investigators examined the association between weight and thromboembolic events using data from 87,226 women enrolled in the prospective, longitudinal Nurses’ Health Study, which has collected data on PE since its inception in 1976 and on diet, physical activity, and other risk factors for PE since 1984.

Participants enrolled in the Nurses’ Health Study during 1984-2002, and were excluded from the current analysis if they had a PE diagnosis before 1984 or if their records were missing data necessary to calculate BMI.

The investigators divided participants into six BMI categories: less than 22.5 kg/m², 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, and 35.0 or greater.

The primary outcome was idiopathic PE, defined as cases of PE that were confirmed in the medical record and not associated with prior surgery, trauma, or malignancy. The authors also performed a secondary analysis of nonidiopathic PE. They used a multivariate Cox proportional hazards model to control for

age, physical activity, caloric intake, smoking and pack-years, race, spouse’s educational attainment, parity, menopausal status, NSAID use, warfarin use, multivitamin supplement use, hypertension, coronary heart disease, and rheumatologic disease.

During the period studied, there were 157 incident cases of idiopathic PE and 338 cases of nonidiopathic PE, and these correlated strongly with BMI. For both idiopathic and nonidiopathic PE, the relative risk for every 1 kg/m² increase in BMI was 1.08. In multivariate analysis, the relative risk for idiopathic PE, compared with patients in the lowest BMI category (under 22.5), ranged from 1.37 among patients with BMIs of 22.5-24.9 (not significant) to 5.79 among patients with BMIs of 35 or higher (*P* less than .001).

Associations between BMI and nonidiopathic PE were similar, ranging from a relative risk of 1.48 for patients in the 22.5-24.9 range compared with those in the lowest BMI category, to a relative risk of 5.42 for patients in the highest vs. lowest BMI categories.

“There is a significant increase with the combined idiopathic PE and nonidiopathic PE. In other words, for our total PE, there is a significant increase in the risk of PE even with relatively mod-

est increases in BMI—that is to say, subjects that would not be considered either overweight or obese, but within the normal range,” Dr. Kabrhel said.

In secondary analyses adjusted for all of the variables, neither waist-to-hip ratio nor weight change since age 18 were significantly associated with risk for PE.

A potential mechanism for the association between BMI and PE is the regulatory hormone leptin, which has been shown to induce tissue-factor activity in vitro and to be elevated in obese individuals, he said.

Alternatively, estrogen and progesterone, which have been linked to obesity and the risk of PE in women, may play a role, although there was no evidence of a hormone-PE interaction in their study, he said.

Dr. Kabrhel acknowledged that the study was limited by its inclusion of only women, and by the racial and ethnic imbalance of the Nurses’ Health Study cohort, which represents a demographic sample of nurses in the United States. The study may also be subject to measurement bias because it relied on subject-reported weights.

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High HDL Linked to Thromboembolism Risk in Women

BY NEIL OSTERWEIL

BOSTON — High-density lipoprotein cholesterol may not be as beneficial as once believed, according to the results of a large data analysis.

Among women, high levels of HDL cholesterol were associated with a near 40% increased risk for unprovoked venous thromboembolic events (VTE), compared with women with lower levels of the so-called “good cholesterol,” according to Dr. Knut H. Borch from the Center for Atherothrombotic Research, University of Tromsø in Norway.

“We found no association between HDL cholesterol levels and risk of provoked VTE in men or in women. However, high HDL cholesterol was associated with increased risk of unprovoked VTE in women, but not in men,” Dr. Borch explained at a meeting of the International Society on Thrombosis and Haemostasis.

The investigators looked for a potential protective effect of HDL on VTE by examining data from a prospective population-based study on all men and women age 25 and older in the town of Tromsø.

A total of 26,676 adult men and women were included in the study, after exclusion of some participants for missing HDL data, or for other reasons. The investigators looked for all first lifetime events of VTE during follow-up from the date of enrollment (1994-1995) through Sept. 1, 2007.

Cases were identified by a computerized index of discharge diagnoses, autopsy registry, and radiology procedure registry. VTE was confirmed either by diagnostic procedure or autopsy, and the data collected included diagnosis of deep vein thromboembolism or pulmonary embolism, signs and symptoms consistent with VTE and VTE treatment.

The investigators further classified VTE as being provoked or unprovoked. Provoked VTEs were those as-

sociated with major surgery or an acute medical condition within 8 weeks of the event, cancer at the time of the event, prolonged immobilization, or other known risk factors. Unprovoked VTEs were those occurring in the absence of any of the known provoking factors.

The median follow-up was 12.5 years, and a total of 288,572 person-years.

During that time, there were 458 VTEs in the cohort, 191 (42%) of which were identified as provoked, and of this group, 64% were DVT. This translated into an incidence of 1.6 VTEs per 1,000 person-years. There were no between-gender differences in provoking factors or type of VTE.

In a multivariate analysis, the researchers found no significant differences between the lowest and highest HDL quartiles for either women (hazard ratio .90, .73-1.11) or men (HR 1.06, .83-1.35).

In terms of unprovoked VTE events, however, there was a significantly increased risk for VTE among women with the highest versus the lowest HDL quartiles (HR 1.39, 1.10-1.75). There was no significant difference in unprovoked VTE events among men in the highest versus lowest HDL quartiles (HR 1.15, .87-1.53).

Dr. Borch said that the strengths of the study include its prospective design, large number of participants, high compliance rate (77%), and exclusive hospital care by the University Hospital of Northern Norway. Limitations included HDL blood draws performed at dif-

ferent times of day with patients in a nonfasting state.

“However, HDL is not known to have a substantial diurnal variation or to be severely affected by meals,” Dr. Borch said.

He also noted that a common problem of cohort studies is that risk factors for individual patients may change over time, especially when there is a long follow-up period. Additionally, the researchers had no information about treatment during follow-up, and, therefore, could not control for it.

The findings are consistent with those of two previous cohort studies examining a possible link between HDL cholesterol levels and VTE, and raise doubts about potential antithrombotic properties of HDL particles (Blood 2008;112:2675-80; J. Thromb. Haemost. 2009;7:588-96).

Dr. Borch said that further studies are needed to determine whether the increased risk of unprovoked VTE in women is a direct result of HDL particles or of some unrecognized confounder.

Dr. Borch reported that neither he nor his colleagues had any financial disclosures relevant to the study. ■

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