Anticoagulant May Control Localized Prostate Ca

BY PATRICE WENDLING

CHICAGO — Along with its known cardiovascular benefits, anticoagulation therapy may improve biochemical control of localized prostate cancer treated with radiotherapy.

In a retrospective study of 662 patients, the biochemical control rate at 48 months was significantly better (at 91%) in men taking warfarin, clopidogrel, and/or aspirin, compared with 78% in men not taking blood-thinning therapy. Distant metastases were also significantly reduced in the anticoagulant group, compared with the nonanticoagulant group (1% vs. 5%).

The overall survival rates were 92% and 90%, respectively, which did not reach statistical significance, Dr. Kevin S. Choe and his colleagues reported in a poster at the annual meeting of the American Society for Radiation Oncology.

Previous clinical trials have produced limited and inconsistent data in metastatic prostate disease, although epidemiologic studies have shown that men on anticoagulants develop prostate cancer less frequently. There is also substantial evidence from preclinical models suggesting that anticoagulants may influence multiple tumor processes including tumor growth, angiogenesis, and the metastatic pathway, Dr. Choe of the University of Chicago said at a press briefing.

"According to our data, we think that the most plausible path [by which an anticoagulant influences prostate cancer patients] … is by limiting metastases, because we see the biggest effect among patients who have very aggressive types of prostate cancer that tend to spread," he said.

In subgroup analysis, the improvement in biochemical control was statistically significant only for patients with high-risk disease as defined by National Comprehensive Cancer Network criteria.

The 4-year, freedom-from-biochemical-failure rate using the Phoenix definition (prostate-specific antigen greater than nadir plus 2 ng/mL) was 82.4% in high-risk men on anticoagulants vs. 57.6% in high-risk controls. The biochemical failure rate for patients both on and off anticoagulants was 92.5% vs. 83% in intermediate-risk men and 95% vs. 90.5% in low-risk men.

In multivariate analysis, anticoagulant use was independently associated with improved biochemical control, lowering the risk of biochemical failure by almost half (hazard ratio, 0.54). The type of anticoagulant did not significantly influence biochemical failure rates, nor was the combination of two agents better than a single agent.

The current study grew out of another study in the same cohort by Dr. Choe and his colleagues showing that warfarin and clopidogrel use during external-beam radiotherapy substantially increased the risk of grade 3 or higher rectal bleeding (Int. J. Radiat. Oncol. Biol. Phys. 2009 May 20 [doi:10.1016/j.ijrobp.2009.02.026]).

Although aspirin and other less potent blood-thinning agents such as enoxaparin may lessen the risk of this bleeding toxicity, Dr. Choe balked at recommending anticoagulation for all prostate cancer patients.

"In patients already taking anticoagulants for cardiovascular risks, there may be additional benefits in prostate cancer," he said, adding that if an anticoagulant were ever to be recommended, "it would need to be planned out very carefully" and will require larger prospective studies to determine whether the benefit is worth the risk.

The median dosage used by patients at consult or during follow-up was warfarin 5 mg/day and clopidogrel 75 mg/day. Aspirin dosage was not recorded. All patients were treated with external-beam radiotherapy, permanent seed implant, or both. No patients underwent surgery. Their median age was 69 years, and median initial PSA was 8.4 ng/mL.

Dr. Choe plans to conduct a prospective database analysis of prostate cancer patients who had surgery instead of radiotherapy to test the hypothesis that the benefit results from an effect on the cancer itself and not an interaction between the anticoagulants and radiotherapy.

The investigators reported no study sponsorship or conflicts of interest. ■