Ultrasound May Cut Thyroid Biopsy Rate

Certain characteristics of thyroid nodules identified on ultrasound can help predict the likelihood of cancer, and may also help determine if fine-needle aspiration biopsy can be deferred, a large, single-center study suggested.

Features that were associated with an increased risk of cancer on multiple-predictor modeling were the presence of microcalcifications (odds ratio 8.1, 95% CI 3.8-17.3, $P<0.001$), solid composition (OR 4, 95% CI 1.7-9.2, P=0.001), and size larger than 2 cm (OR 3.6, 95% CI 1.7-7.6, P=0.001), according to Rebecca Smith-Bindman, MD, of the University of California San Francisco, and colleagues.

In a patient with two of these characteristics seen on ultrasound, the sensitivity would be 0.52 (95% CI 0.42-0.62), the false-positive rate would be 0.07 (95% CI 0.07-0.08), and the positive predictive value (PPV) would be 6.2% (95% CI 4.7-8.7), the researchers reported online in JAMA Internal Medicine

Thyroid nodules are very common, being present in up to half of adults, but thyroid cancer is rare, developing in fewer than 1% of individuals.

"Uncertainty about which nodules may harbor cancer and lack of evidence-based management guidelines have resulted in a myriad of conflicting recommendations regarding which nodules warrant biopsy, frequent thyroid biopsies, and the overdiagnosis of thyroid cancers that would otherwise likely have remained asymptomatic in the absence of detection," Smith-Bindman and colleagues wrote.

To see if specific features on ultrasound could help narrow down the number of nodules needing biopsy, the researchers conducted a retrospective case-control study that included 8,806 patients who had 11,618 ultrasound examinations from January 2000 to March 2005.

The 96 cases of cancer they identified were matched with 369 controls in a population-based registry who had ultrasound examinations but were not diagnosed with cancer.

In those 96 cases, there were 102 nodules considered malignant and 87 classified as benign, and the number of nodules increased with age. Among controls, there were 428 benign nodules, and the number remained constant across ages.

On single-predictor modeling, the strongest predictor of cancer was the presence of microcalcifications, which was associated with a seven times higher risk, with a likelihood positive ratio of 7 (95% CI 6.0-8.2) and a likelihood negative ratio of 0.65 (95% CI 0.56-0.76).

When the researchers analyzed the accuracy of the three features confirmed on multiple-predictor modeling as being associated with cancer, they determined that if a single positive

characteristic were considered as warranting biopsy, the sensitivity would be 0.88 (95% CI 0.80-0.94), but the false-positive rate would be high, at 0.44 (95% CI 0.43-0.45).

In addition, the PPV would be low, at 1.8% (95% CI 1.5-2.2), and 56 biopsies would be needed to diagnose one case of cancer.

In contrast, for two positive features, 16 biopsies would be needed for a single cancer diagnosis.

"Compared with existing guidelines that recommend biopsy of all thyroid nodules greater than 5 mm, adoption of this more stringent rule requiring 2 abnormal characteristics to prompt biopsy would reduce unnecessary biopsies by 90% while maintaining a low risk of cancer in patients in whom biopsy is deferred," the researchers observed.

In this study, only 1.6% of patients whose nodules were 5 mm or more were found to have cancer, and 98.4% of the nodules were benign, "highlighting the importance of being prudent in deciding which nodules should be sampled to reduce unnecessary biopsies," Smith-Bindman and colleagues stated.

However, these findings differed from previous work, according to Erik K. Alexander, MD, of Harvard University and David Cooper, MD, of Johns Hopkins University.

For instance, most studies have found a cancer prevalence of 8% to 15% in thyroid nodules, rather than the 1.6% seen in this analysis. In addition, among cases of cancer, the number of nodules rose with age, which was not seen among controls.

"These facts suggest a nonrepresentative study population and an increased potential for sampling bias," Alexander and Cooper wrote in an invited commentary.

Alexander and Cooper agreed with the study authors that "sonographic features are, and should remain, the principal tool to guide thyroid cancer risk assessment."

They also agreed that nodules that are exclusively cystic can usually be monitored conservatively.

"I think this study does a very nice job of supporting the current standard and the current use of technology, which is trying to utilize ultrasound in the optimal way possible," Alexander told *MedPage Today.*

Limitations of the study included a lack of information about tumor histology and the reasons cases and controls had been referred for ultrasound examinations.