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Use of Ultrasound Criteria May Help Reduce Unnecessary Thyroid Biopsies

BY KURT SAMSON

Using an ultrasound diagnostic strategy that focuses on three characteristics of thyroid nodules could eliminate the need for an estimated 90 percent of biopsies in patients who do not have cancer, according to a retrospective case-control study of 8,806 patients who underwent 11,618 thyroid ultrasound examinations.

The study, published in *JAMA Internal Medicine* (2013;173:1788-1795), included 105 patients who were subsequently diagnosed with cancer and listed in the California Cancer Registry.

Three ultrasound nodule characteristics—micronodules, size greater than 2 cm, and entirely solid nodules—were found to be able to differentiate cancerous growths from benign nodules. And while these were common in 96 percent of those screened patients who did have cancer, more than half of those who also had them did not have cancer.

The researchers, led by Rebecca Smith-Bindman, MD, Professor in Residence in the Department of Radiology and Biomedical Imaging at the University of California, San Francisco, determined that if one of these features was used as an indication for biopsy, 88 percent of thyroid cancers would be detected with a high false-positive rate (0.44) and a low positive-likelihood ratio of 2.0. Using this, 56 biopsies would be performed for each positive cancer diagnosis.

If two characteristics were required for biopsy, the sensitivity and false-positive rates would be lower (sensitivity of 0.52), with a false-positive rate of just 0.07, and the positive likelihood of cancer ratio would be significantly greater (7.1), with only 16 biopsies performed for each cancer diagnosis.

As opposed to routinely performing a biopsy of all nodules larger than 5 mm, these features were used as an indication for biopsy, 88 percent of thyroid cancers would be detected with a high false-positive rate (0.44) and a low positive-likelihood ratio of 2.0. Using this, 56 biopsies would be performed for each positive cancer diagnosis.

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requiring two of these abnormal nodule characteristics would reduce unnecessary biopsies by 90 percent and just five out of 1,000 patients with cancer would not be detected.

“Ours is the first study, to our knowledge, that permits estimating thyroid cancer risk based on nodule characteristics, although these findings should be validated in a large prospective cohort,” Smith-Bindman said in an interview. “Ultrasound can help identify patients at low risk and those at high risk to help guide management, but it cannot perfectly separate those who will and will not develop cancer—no medical test can.

“This uncertainty is something that patients and their physicians must understand, but we hope to do a good job of ensuring that patients in whom we defer biopsy have a truly low risk. Using the criteria we suggest, the risk of cancer is less than one half of one percent for patients for whom we believe biopsy can be deferred. If a nodule has any of the three features we identified as abnormal, the risk is sufficiently elevated that biopsy should be considered, but if the nodule did not have these features, the risk was sufficiently reduced that we believe biopsy could be avoided.”

When used in combination, these three characteristics could be used to help determine which nodules should be sampled, she noted.

“We are suggesting a simpler way to interpret this test to ensure a balance between finding cancer cases and avoiding unnecessary biopsies in patients who are unlikely to have cancer.”

“I am suggesting a simpler way to interpret this test to ensure a balance between finding cancer cases and avoiding unnecessary biopsies in patients who are unlikely to have cancer. Doing unnecessary procedures—be it an imaging test, biopsy, or even open surgical biopsy because the initial biopsy was questionable, which is often the case in the thyroid—is not only costly, and time consuming, but also unpleasant and painful for patients. It can also lead to over-diagnosis and over-treatment, as well as the labeling of patients as having cancer who would never have known or been harmed by their disease.”

In the study, which was funded by the National Cancer Institute and the University of California, the researchers followed patients for three to 10 years, and found that the technique continued to prove effective in the prediction of thyroid cancer for many years after the initial ultrasound. “If a patient does not have any suspicious findings, and no clinical changes, then no surveillance is necessary,” she said.

Biggest Obstacle?

“I believe the biggest obstacle that might prevent physicians from using these guidelines is that many feel it is not that difficult to do a biopsy, even if the risk is low, so why not just go ahead and do one? But this minimizes the very real impact of biopsies on patients, including the cost,” she said.

David S. Cooper, MD: “Although this study points us in the right direction with regard to adopting more of a triage approach toward nodule evaluation, no test is 100 percent accurate. Even if this strategy detects almost all cancers, there is still a risk, however small. You can never rule out that a patient does not have cancer without a biopsy, and most people in the U.S. just will not accept this.”

The coauthor of an accompanying invited commentary (JAMA Intern Med 2013;173:1796-1797), David S. Cooper, MD, Professor of Medicine and Radiology at Johns Hopkins University School of Medicine and Director of the Thyroid Clinic at Johns Hopkins Hospital, said that although thyroid nodes are extremely common, especially as people age, as many as 75 percent are benign. Many smaller studies have suggested specific ultrasound features of thyroid nodules as a potential way of determining which ones require biopsy.

The new findings add additional support to these studies but, more significantly, establish a system that might help to guide such decisions, he said in an interview. “I think this study points us in the right direction with regard to adopting more of a triage approach toward nodule evaluation.”

In the commentary, he and Erik K. Alexander, MD, an endocrine cancer specialist at Harvard Medical School, said that the study confirmed the importance of module size, analyzing solid or cystic parenchymal tissue, and identifying...
Thyroid Cancer Survival Rates High After Chernobyl Disaster Despite Lag in Care

BY RABIYA S. TUMA, PHD

A
fter the Chernobyl nuclear acci-
dent in 1986, public health of-
icians feared there would be a
high incidence of and mortality
from thyroid cancer in radiation-exposed
children and adolescents. However, with
a median follow-up of just over 11 years,
researchers now report a very high rate
of survival among 234 children and ad-
olescents from the Republic of Belarus
who underwent radioiodine therapy in
Germany for the treatment of very high-
risk thyroid cancer.

“Even though some patients did not
receive optimal treatment initially, the
vast majority went into remission after
receiving state-of-the-art radioiodine
treatment and follow-up care,” the lead
author of the study, Christoph Reiners,
MD, of the University of Würzburg,
Germany, said in a news release from
the Endocrine Society about the study,
published in the organization’s Journal
of Clinical Endocrinology & Metabolism

“Many patients recovered from ad-
vanced cancers. Of this group, 97 percent
had cancer spread to the lymph nodes,
and 43 percent had cancer metastasize in
the lungs.”

During their treatment in Germany,
134 children and adolescents without
distant metastases received a median of
two courses of radioiodine therapy (range
of one to five), for a median cumulative
dose of 6.6 GBq (141 MBq/kg). The
100 patients with distant metastases
received a median of four (range of 2-12)
courses of radioiodine therapy, for a median cumulative
dose of 16.9 GBq (268 MBq/kg).

The median lag between the patients’
last surgery and their first radioiodine
treatment was 0.7 years, with a maximum
of 5.5 years.

Of those patients treated, 229 com-
pleted their recommended course of
therapy and were available for follow-
up. One hundred forty-seven (64%) had
a complete response, 69 (30%) had a
“nearly complete remission,” and 11 (5%) had a partial response.

As expected, patients with localized
disease were more likely to have a com-
plete response than those with dis-
tant metastases (77% vs. 47%).

Median follow-up is now 11.2 years for
patients with a complete response
and 14.9 years for those with a partial response. At 10 years, the
progression-free survival rate was 100 per-
cent for patients with a complete response and 92 percent for those with a partial response.

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ULTRASOUND CRITERIA

features, on ultrasound including mi-
icrocalcifications, irregular margins, and
increased vascular flow.

Still, the editorial noted, while the
findings validate the results from less
rigorous retrospective analyses, all of
the data about suspicious nodules were
based on characteristics of just 96 malig-
nant tumors. And unlike the 1.6 percent
prevalence among patients in the study,
most research on thyroid cancer nod-
ules place that rate at between eight and
15 percent, Cooper and Alexander wrote.

“These facts suggest a nonrepresentative
study population and an increased poten-
tial for sampling bias.”

‘Major Epidemiological Debate’

Whether or not to conduct biopsies on
all nodules has become “a major epide-
miological debate,” Cooper noted. “If we
could find a foolproof way of validating
whether the characteristics can detect all
cancers, maybe we would not have to per-
form so many biopsies. But no test is 100
percent accurate. Even if this strategy de-
tects almost all cancers, there is still a risk,
however small. You can never rule out that
a patient does not have cancer without a
biopsy, and most people in the United
States just will not accept this.”

The concept is correct, but support
from patients is the real issue, he said. In
addition, there is a degree of subjectivity
in sonogram interpretation, and not all ra-
diologists always provide a description of
nodule characteristics.

“Things are getting better, but there is
often a paucity of data on which to make a
decision to biopsy or not,” Cooper con-
cluded. “I do about 15 biopsies every
week and have found that about half of the
patients did not need one. There is patient
anxiety to consider as they await biopsy
results, and biopsies are expensive. One in
100 [malignancies] look benign on physical
examination, but patients want them.”

“Doing unnecessary procedures—be it an
imaging test, biopsy, or even open surgical
biopsy because the initial biopsy was questionable,
which is often the case in the thyroid—is not
only costly, and time consuming, but also
unpleasant and painful for patients.”