Serendipitous Breast Lesions on Magnetic Resonance Imaging: Why Is This Lesion Different From All Other Lesions?

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Dr. Gamliel,1 the local mammographer, refers a patient with a suspicious lesion that he doesn’t think is cancer to the local magnetic resonance imaging (MRI) machine for a further test. The result confirms his suspicion: the lesion he had seen on mammography appears benign and there is no apparent worry. However, unexpected news arrived in the report: there is another lesion in the same breast that had not been detected by the initial mammography. Dr. Gamliel is about to recommend surgical biopsy when his expert colleague says she has just read an article in the Journal of the National Cancer Institute about these lesions and the patient need not be sent for any invasive procedures. Astonished, Dr. Gamliel asks his colleague, ‘‘Why is this lesion different from all other lesions’’? When his colleague has no satisfactory answer, he returns home to ponder the problem.

Dr. Gamliel sat down at dinner faced with the intriguing challenge of the question at hand and immediately recognized that he had four children who could help him formulate an answer. He gave them a copy of the paper by Lawrence et al. (1), published in this issue of the Journal, and decided to pose to each of them a single question that would, in part, address the initial question and help develop a more complete answer.

He asked his first-born son, the official at the country’s most powerful regulatory agency: ‘‘What do the label and promotional claims of the MRI manufacturer say regarding incidental lesions’’? (He did not like the label ‘‘serendipitous’’—it just seemed to have the wrong connotation.)

The statistician responds: This study has numerous strengths, but some important weaknesses that must be acknowledged in order that we understand its implications. First, there are quite a few assumptions that underlie the composition of the model and its analysis. For example, the assumptions contained in the formula for post-test odds have a dramatic negative effect on the positive predictive value of MRI, and it is this low value that heavily influences the decision model. Other key assumptions include: the sensitivity and specificity of MRI for detection of breast cancer is the same for incidental as for index lesions and that diagnostic accuracy of clinical breast examination (CBE) and mammography is conditionally independent of MRI. The most important strength of this analysis lies in the direction it provides for future research and the identification of key parameters that must be measured in just such a study.

His other daughter is a skilled lawyer, and he poses the very difficult question, ‘‘What are my legal and ethical responsibilities in this particular case and in other similar cases’’?

The lawyer ponders the problem and reminds her father of how Disraeli dismissed the usefulness of statistics. How can you not follow to completion the detection of an enhanced MRI lesion, however incidental it may be, she asks? It’s one thing not to know something is there. But, once you have discovered clear evidence of some irregularity, once you tell the patient as you must ethically and legally, and once the possibility of cancer, even a remote one, has been raised with no other means of surveillance except biopsy or repeat MRI, you must take a serious look at that lesion. With no longitudinal studies to show the feasibility or benefit of ‘‘benign neglect,’’ your statistics are not yet strong enough to defeat my claim of negligence based on the risk factors of my particular client. Unless my client is under a clinical protocol with the aim of following these apparently low-risk lesions...
and she is aware of the potential risks and benefits, the legal imperative here suggests that once you have made the referral to MRI you must deal with all the findings, positive or otherwise.

Finally, he turns to his youngest son, an exceptional clinician (a surgeon and radiologist) and asks, ‘‘Doesn’t this lesion require the identical clinical attention that any other lesion found on MRI would dictate; do I have different clinical or ethical responsibilities in this particular case’’?

The doctor appears conflicted about the situation, especially after hearing his siblings. He wants to entrust his patient’s care to these statistics, after all he has a degree in public health, but it doesn’t appear so simple, especially when he knows that delay in diagnosis of breast cancer is one of the most litigated claims in America. Look, he says, some of these ‘‘lesions’’ are dependent on menstrual cycles, so many represent benign proliferative disease. Yet, a few (admittedly a very few) are cancer, and if it’s ‘‘my’’ cancer, it’s my problem. The mammographic examination and CBE didn’t show it the first time, just like some of those cancers metastatic to lymph nodes that are shown only on MRI. I’m not sure I can follow it with these more conventional tools the second time. Close follow-up, like my stock portfolio, may sound better than it really is. Therefore, the recommendation of the authors, that these lesions need not be subject to immediate biopsy, while likely a reasonable scenario in the future, requires additional clinical study for validation.

Dr. Gamliel reclines in his chair, finishes his fourth cup of wine, and tries to summarize:

Thank you my children, your collective wisdom has persuaded me that we are at a starting point, not an end point. Truly, it is too early to decide the appropriate management of these incidental findings. The protocols have not been standardized, the information not much better than anecdotal, and no longitudinal studies of these lesions are available to establish a reasonable approach from a clinical perspective. Perhaps you will help me write a multicenter grant for the study of these incidental lesions, with a focus on a well-standardized protocol for longitudinal study. May we hope that future serendipity will not throw us such a difficult curve ball.

REFERENCE


NOTE

1Dr. Gamliel is a fictitious character used to convey the editorial message.

Lest We Abandon Digital Rectal Examination as a Screening Test for Prostate Cancer

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Until the mid-1980s, early detection for prostate cancer had only one tool—digital rectal examination (DRE). The tool is subjective with high interobserver variability (1,2), upward of 10% of prostate cancers are considered abnormal, but only about 1%–2% of men examined are found to have disease. Even then, two thirds or more of the cancers discovered are found to be pathologically advanced (3). Perhaps more worrisome is the fact that, in one study, many men who ultimately died of prostate cancer had a normal DRE at the time of diagnosis (4).

Enter prostate-specific antigen (PSA) testing. There is no question that PSA testing has improved our ability to detect prostate cancer at an earlier clinical stage. PSA testing has 1) dramatically increased the number of tumors detected, 2) detected a population of tumors [stage T1c (5) that are by most measures clinically important, and 3) streamlined our metastatic evaluation of prostate cancer (e.g., identifying a class of patients for whom bone scans and even lymph node dissections may be unnecessary). By using PSA derivatives such as lower PSA thresholds for biopsy (e.g., 2.5 ng/mL for all men), age- and race-adjusted cutoffs, free/total PSA ratio (<25%), PSA/transition zone volume density, etc., the majority of prostate cancers can probably be detected serologically.

So what do we do with our clinical relic of times past? Do we discard DRE and perform our early diagnosis en absentia: merely ask the patient to have a blood test and never examine the patient? Reporting in this issue of the Journal, Schröder et al. (6) would have us believe so. They screened 10,523 men aged 54–76 years with three tests—DRE, measurement of PSA levels, and transrectal ultrasonography (TRUS). Using estimated disease prevalence, they determined the performance characteristics of DRE and PSA. Across the board, the performance of PSA was superior to DRE. However, we are not yet ready to dismiss DRE because of concerns with the study of Schröder et al. and a body of evidence supporting the value of DRE.

We have several criticisms of the methodology used by Schröder et al. (6) that directly affect the stated conclusions. 1)