Ordering Tests, Delaying Treatment

Timothy Rowe, MB BS, FRCSC
Editor-in-Chief

It's a reflex action that we all take from time to time. A patient presents with a problem that is truly puzzling, and a run through our mental bank of clinical vignettes identifies nothing similar. Our history-taking elicits no clues. A physical examination provides no reasonable explanation for the patient's symptoms. The symptoms are a genuine cause for concern, but finding an explanation (and a path to treatment) eludes you. You don't want to seem baffled—although this is neither more nor less than the truth—so you start ordering tests. The patient is relieved because the diagnostic wheels are turning and the answer will naturally soon appear. But you're not so sure, because the tests you order may be quite irrelevant. The patient feels better, but you certainly don't.

The testing you order is, from the patient's perspective, intended to identify a cause for her symptoms. From your perspective, however, it is equally (or perhaps more) intended to rule out serious causes, particularly a neoplastic cause. This can be considered practising "defensive" medicine. Usually your instinct is that nothing abnormal will be found. As Rachel Kupets and colleagues note in the current issue of the journal, one in five patient–physician encounters results in a request for some form of imaging.[1] Such requests for imaging are targeted at either finding an anatomical abnormality or demonstrating that all is normal. But this can backfire, when imaging that is ordered ostensibly to reassure a patient finds something unusual but unrelated (an incidentaloma[2]).

The field of obstetrics and gynaecology is replete with examples of this scenario: "routine" fetal ultrasound examinations will not infrequently identify abnormalities that require specific and sometimes vital follow-up. Pelvic ultrasound examinations in non-pregnant women commonly identify "ovarian cysts," but are these physiological or pathological? Clinicians who are performing their own ultrasound examinations can use clinical data to resolve this question at the time of the procedure, but when the ultrasound examination is performed by a technician in isolation, subsequent interpretation of the images by a radiologist may be nuanced. Thus a radiologist may be required to use terms such as "consistent with" or "clinical correlation required," leaving the patient in a state of suspended anxiety until a firm diagnosis is made. A radiologist who is uncertain about the significance of a cyst will commonly recommend additional forms of imaging to resolve uncertainty, adding to cost and potentially delaying a definitive diagnosis.

If a Canadian clinician identifies an adnexal mass in a non-pregnant woman and believes it is not physiological, what does he or she do? The SOGC Clinical Practice Guideline "Initial Evaluation and Referral Guidelines for Management of Pelvic/Ovarian Masses" recommends transvaginal or transabdominal ultrasound assessment and also recommends that "CA 125 measurement should be considered."[3] Specific features to be recorded in the ultrasound report, to permit calculation of the risk of malignancy score, are cited. Do we know whether these recommendations are followed consistently? Unfortunately we do not, although charitably we should assume that in most cases they are.

If that same clinician is faced with a patient with pelvic or abdominal symptoms but who on examination has no detectable pelvic abnormality, what does he or she do? We can't be sure, but it is likely that a proportion, at least, of Canadian clinicians would order at least some screening for ovarian cancer (serum CA 125 measurement and transvaginal ultrasound). A study in the United States of a cohort of physicians (roughly one third family physicians, one third general internists, and one third obstetrician-gynaecologists) found that 28% offered this screening to women at low risk for ovarian cancer, and 65% to women at medium risk, despite the lack of recommendation to do so.[4] This is no small matter, because the British Health Technology Association has determined that if women

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aged 50 to 64 were routinely screened for ovarian cancer with serum CA 125 assays annually and transvaginal ultrasound every two years, this would detect at most an additional four cases of ovarian cancer per 10 000 women screened per year. [5] The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, which used serum CA 125 measurements and transvaginal ultrasound for screening for ovarian cancer, has reported an 8.4% false-positive rate; of the women who had a false-positive result, one third had subsequent surgery, and 15% of them had significant complications.[6] With this degree of morbidity, we are obliged to be selective in applying these screening techniques, and cautious in interpreting them.

From the perspective of making screening for ovarian cancer effective—as opposed to averting harm in doing so—Angela Chan and colleagues from the BC Cancer Agency propose that screening strategies used to date have failed because of the assumption that all ovarian cancer is the same.[7] They argue that assays of serum CA 125 and transvaginal ultrasound each have significant shortcomings when it comes to identifying early-stage disease. The perceived shortcomings of CA 125 are that it is not a reliable biomarker for nonserous cancers and that serum levels are elevated in only 50% of women with stage I tumours.[8] The perceived shortcoming of ultrasound as a screening tool arises from the hypothesis that high-grade serous carcinoma (the most lethal form) arises in most cases in the distal fallopian tube and spreads transcelomically, involving the ovary secondarily[7]; although there is evidence, nonetheless, to support the hypothesis that fimbrial and ovarian surface epithelium are likely to contribute equally to the development of ovarian epithelial cancer.[9] Regardless, neither an assay of serum CA 125 nor a transvaginal ultrasound examination would necessarily detect an early ovarian cancer. Therefore, even if clinicians bend the rules to offer these screening methods to women, negative results do not exclude the possible presence of cancer.

The study reported by Rachel Kupets and colleagues in this issue of the Journal shows that, even after detection of a suspicious adnexal mass, a patient may be managed suboptimally.[1] They found that almost 60% of women with an adnexal mass subsequently shown to be malignant had either a CT scan or an MRI before referral, serving only to delay referral and surgical management; further, these women were mostly referred to a gynaecologist rather than a gynaecologic oncologist, reducing survival benefit.[10] These deviations in management are reminiscent of "false passages" in endoscopy: they are misdirections that result in potential for harm.

We serve our patients better if we stop and think before ordering testing by rote, and in multiple areas of our specialty we need better and more productive forms of screening and testing. We also must ensure that management after detection of an abnormality is streamlined. Using ovarian cancer as an example, it's not surprising that our oncology colleagues want to target means of prevention rather than means of detection.[11] The tests we order should be relevant and reliable, and should lead directly to appropriate management. Imagine yourself as the patient.

REFERENCES

1. Kuperts R, Fernandes K, Miroshnichenko G, Paszat L. Are too many imaging tests being performed in women with an adnexal mass? J Obstet Gynaecol Can 2013;35(3):246–51.
2. Stone JH. Incidentalomas—clinical correlation and translational science required. N Engl J Med 2006;354:2748–9.
3. Le T, Giede C, Salem S, Lefebvre G, Rosen B, Bentley J, et al.; SOGC/GOC/SCC Policy and Practice Guidelines Committee; SOGC Diagnostic Imaging Committee. Initial evaluation and referral guidelines for management of pelvic/ovarian masses. Joint SOGC/GOC/SCC Clinical Practice Guideline, No. 230, July 2009. J Obstet Gynaecol Can 2009;31:668–73.
4. Baldwin L-M, Trivers KF, Matthews B, Andrilla CHA, Miller JW, Berry DL, et al. Vignette-based study of ovarian cancer screening: do US physicians report adhering to evidence-based recommendations? Ann Int Med 2012;156:182–94.
5. Bell R, Petticrew M, Luengo S, Sheldon TA. Screening for ovarian cancer: a systematic review. Health Technol Assess 1998;2(i-iv):1–84.
6. Buys SS, Partridge E, Black A, Johnson CC, Lamerato L, Isaacs C, et al. Effect of screening on ovarian cancer mortality: the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Randomized Controlled Trial. JAMA 2011;305:2295–303.
7. Chan A, Gilks B, Kwon J, Tinker AV. New insights into the pathogenesis of ovarian carcinoma: time to rethink ovarian cancer screening. Obstet Gynecol 2012;120:935–40.
8. Gupta D, Lis CG. Role of CA125 in predicting ovarian cancer survival—a review of the epidemiological literature. J Ovarian Res 2009;2:13.
9. Auersperg N. The origin of ovarian carcinomas: a unifying hypothesis. Int J Gynecol Pathol 2011;30:12–21.
10. Mayer AR, Chambers SK, Graves E, Holm C, Tseng PC, Nelson BE, et al. Ovarian cancer staging: does it require a gynecologic oncologist? Gynecol Oncol 1992;47:223–7.
11. Tone A, McAlpine J, Finlayson S, Gilks CB, Heywood M, Huntsman D, et al. It sounded like a good idea at the time. J Obstet Gynaecol Can 2012;34;1127–30.