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Short Communication

Reflections on Abnormal Uterine Bleeding, Personal Care with Evidence Based Medicine

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As a medical student, uterine bleeding was a conundrum. During my residency, in the 90's, the thick fog of mystery surrounding this topic dissipated a little bit. The debates during our department seminars when an endometrial biopsy should be performed in women with abnormal uterine bleeding were intense. There were the supporters of the 35 years old, while others claimed that 38 years old was better.

In my early years as adjunct professor, I was invited to give a lecture on "when an endometrial biopsy should be performed in women before they were submitted to a hysterectomy". This event was a turning point to change the thinking from a football fan to an epidemiological stance.

It is known that the incidence of endometrial cancer increases as women get older. The incidence starts by 35~39 years old and it peaks by 65 years old (2007 info.cancerresearcherchuk.org). In terms of numbers, the prevalence of endometrial cancer is 28.4 in 100,000 women, it means 0.028%, this is a small number [1]. The debate on age became very peripheral when the 0.028% stepped in.

The presence of risk factors and symptoms were the game changer, and I give credits to Dr. Cindy Farquhar, from New Zealand, with her publication in 1999 [1,2]. The presence of an abnormal uterine bleeding increases the pre-test probability to 1.4%. If this symptom is associated with risk factors, the pre-test probability increases from 1.4% to 7.1%, 27.9% and 44% for those with one, two and three risk factors [1,2]. The risk factors include all the scenarios where unopposed estrogen levels are increased, for instance, infertility, nulliparous and obesity. Obesity is defined as a body mass index equal or higher than 30 [3]. In addition, genetic risk, as the Lynch syndrome, increases the risk of having endometrial cancer. In our history taking, it is appropriate to ask about colorectal cancer, gastric, ovarian, small bowel, pancreatic, kidney, bile duct and brain cancers.

With a pre-test probability in mind, the next step is to use a diagnostic tool. The most used diagnostic tools are endometrial biopsy and transvaginal ultrasound. The latter has been used to measure endometrial thickness. The cut-off for endometrial thickness varies in the literature. However, the most important aspect is not the cut-off itself, but the performance of these diagnostic tools. The best way to measure the performance of a diagnostic tool is by its likelihood ratio (LR). The LR of transvaginal ultrasound, using a 5 mm cut-off, is 0.15, when negative, and 2.17, when positive [4]. Likewise, for endometrial biopsy, a negative result has a LR of 0.14, and 66.48, when is positive for diagnosing of hyperplasia or endometrial cancer [5].

Therefore, the concept of using only one aspect of the investigation is inappropriate and deviates from good medical practice. For instance, it is common to someone to ask what we should do, if a post-menopausal patient has an endometrial thickness of 3 mm. If we follow one of many guidelines, such as the one from the Royal College of Obstetricians and Gynaecologists [6]. In their Green-top guideline No. 67, we will find the following statement: "Systematic reviews have suggested a cut-off of 3 mm or 4 mm for ruling out endometrial cancer and have shown that the probability of cancer is reduced to less than 1% when the endometrial thickness is less than the cut-off".

Now, let's consider a real case that occurred in our gynecologic emergency unit, where a ObGyn consult was ordered. A 65 years old, postmenopausal woman was admitted at the emergency room with a pulmonary embolism. She was using rivaroxaban as an anticoagulant therapy. Few days later, she started to have a light vaginal bleeding. Her transvaginal ultrasound revealed an endometrial thickness of 3 mm. Her past medical history was positive for the treatment of colon cancer 3 years ago without any evidence of recurrence. She never had a pregnancy. Her weight and her height were 76 kg and 158 cm, respectively.

After reading the guideline we face the first problem. Are we going to use the 3 mm or the 4 mm cut-off? Our patient had 3 mm. If someone decides to use the 4 mm, this patient should be reassured and sent home.

Nevertheless, good medical practice starts with history and physical examination. From her history we identified 3 risk factors: 1) post-menopausal bleeding, 2) nulliparity, and 3) past medical history of colon cancer. From her physical examination, we found that her body mass index was 30.4. Therefore, this patient has a pre-test probability of 44% of having an abnormal endometrial finding, either cancer, or hyperplasia [1,2]. Then, we have the transvaginal ultrasound thickness of 3 mm. A diagnostic performance of the endometrial thickness with 3 and 4 mm cut-off can be found in the literature. For the 4 mm cut-off, the positive and negative LR are 1.3 and 0.05, respectively [7].

We can easily find an app, such as DocNomo [8], to apply the Bayesian theory. With the Bayesian theory in mind, we will have a better understanding and perspective of this case. From a 44% pre-test probability, with a negative ultrasound, her probability of having endometrial cancer is 3.8%. This is 3 fold higher than what the RCOG guideline mentioned. We performed an endometrial biopsy, and, unfortunately, endometrial cancer was diagnosed by the pathology report.

If the same case, without any risk factor, just abnormal uterine bleeding was present, the pre-test probability would be 1.4%; after a 3 mm endometrial thickness (negative LR = 0.05), her post-test probability would be 0.1%. Under this scenario, we would reassure this patient and send her home.

In summary, it is important for clinicians to understand that we need to consider individual cases under the perspective of risk factors and symptoms; this will give a pre-test probability of having a disease. Next, what would be the chance of having a condition, after a diagnostic test is performed. For these, we need to know how much risk factors increase the probability and what is the performance of the diagnostic tests.

Only then, we are providing personal care to our patients, using evidence-based medicine.

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