Reply: Biochemical markers for endometriosis: a long way to go

Sir,

There is definitely a long way to go regarding biochemical markers for endometriosis. We completely agree with that and appreciate the comments and suggestions raised by Galazis *et al.* in their recent Letter to the Editor.

They have pointed out and suggested a very interesting proposal for further analysis and validation studies, such as the mathematical modeling already used in ovarian cancer—the risk of malignant index (RMI). This is something very important and should be considered and discussed in our field. During the past years we developed a very accurate transvaginal ultrasound (TUS) examination for endometriosis (Abrão *et al.*, 2007; Gonçalves *et al.*, 2009) with bowel preparation before the procedure in Brazil, which seems to have high sensitivity and specificity for the diagnosis of endometriosis, especially in deep endometriosis (including different affected sites like the rectum and retrocervical area) or endometriomas. This examination could be helpful in such a model.

We also agree that the possibility of validation of a mathematical model as they have suggested, gathering clinical parameters (chronic pelvic pain, dysmenorrhea, dyspareunia, cyclic dyschezia or dysuria, and infertility), a panel of biochemical markers, which could include the chemokines that we showed to be more relevant as well as other markers known to be raised in endometriosis, such as annexin V, VEGF, CA125 and sICAM-I (Vodolazkaia *et al.*, 2012), and finally adding radiological findings from TUS and/or magnetic resonance imaging could really improve the accuracy of a noninvasive test for endometriosis—the 'endometriosis clinical test'. This may improve screening, diagnosis and even staging of the disease. Hence, we believe that our systematic review (Borrelli *et al.*, 2014) and the points raised by Galazis *et al.* should stimulate further collaborative multi-center research in this matter.

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doi:10.1093/humrep/deu193
Advanced Access publication on July 31, 2014

Quality control of training and performance in embryo transfer: time to broadcast LC CUSUM and CUSUM tests

Sir,

We would like to make a few comments about the very good paper by Jesus Lopez *et al.* (2014).

In this study, the acquisition of performance in embryo transfer (ET) of five first year trainees was monitored by the learning curve cumulative summation test (LC CUSUM); CUSUM curves were used thereafter to test that competence was maintained.

This is, in our opinion, the right approach in quality control (Biau *et al.*, 2011). LC-CUSUM was developed to help decide when the LC for a procedure is complete by indicating when it has reached a predefined level of performance (Biau and Porcher, 2010). Conversely, CUSUM detects when a process deviates from adequate to inadequate performance. CUSUM techniques have simple formulations, intuitive graphical representations and are capable of detecting small persistent changes (Biau *et al.*, 2008a).

In the study of Jesus Lopez, there were shorter LC and less inter-trainee variability than reported previously (Dessolle *et al.*, 2010). However this study confirms that time to proficiency varies between individuals and the take home message is that individualized training with continuous monitoring of the LC of ET is necessary and useful. Comparable observations have been published in surgery (Biau *et al.*, 2008b), obstetrics (Papanna *et al.*, 2011), ultrasound diagnosis (Bazot *et al.*, 2011; Rodriguez *et al.*, 2014) and assisted reproductive technology (Dessolle *et al.*, 2009, 2010, 2014).

The authors added important new information on the learning process. After acquisition of competence, the performance of the trainees was impacted by the interval between two successive sessions and one of the trainees showed a loss of proficiency. We have also observed that some trainees, especially those with the shortest LC, showed CUSUM scores around the limit shortly after becoming proficient (Dessolle *et al.*, 2010). This was also the case of Trainee A and Trainee B in Jesus Lopez *et al.* as shown in Fig. 1 of their article. Therefore, it is important to test that competence is maintained over time after the learning phase. A CUSUM curve with few peaks, close to the horizontal, reflects a stable performance.

This study confirms the exportability of CUSUM methodology and the reproducibility of the methods that we first described to monitor performance in ET (Dessolle *et al.*, 2010). Patients and protocols were very different in the two settings and the distribution of the LC differed. However, using very close LC-CUSUM parameters, personalized training and tailored monitoring of the learning curve were feasible in both departments.

There has been a growing number of studies using LC CUSUM and CUSUM over the past 3 years and we recommend their use for quality control in ET. CUSUM might also help practitioners in monitoring their results, optimizing their technique and reducing time to decision in the event of decreased performance. CUSUM might be used to evaluate the impact of new strategies that are developed to improve the quality of care.

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