hypersignal in T1 of the posterior pituitary, suggesting no secretion of antidiuretic hormone (ADH) and, therefore, central DI.

The desmopressin requirement decreased after delivery (cesarean section at week 38), and the drug was withdrawn on day 5. Urine output remained stable at 2 L/d, and urine osmolality remained above 350 mOsm/kg. Another MRI scan was performed 6 weeks after delivery and revealed a slight reappearance of the hyperintense signal. Finally, a third MRI scan performed 6 months later showed complete recovery of the neurohypophyseal signal (Fig. 1).

In physiological terms, clearance of ADH increases during pregnancy, due to the presence of placenta-derived vasopressinase and increased hepatic and renal blood circulation. Vasopressinase levels rise in relation to placental size. Under certain circumstances, the increase in vasopressinase levels may lead to transient DI, usually during the third trimester. Ten to twelve weeks after delivery, clearance of ADH returns to normal and vasopressinase is undetectable in plasma [1].

DI in pregnancy can be the result of a deficit in ADH production (congenital or acquired), renal tubular insensitivity, or the presence of vasopressinase [1]. The absence of a hyperintense signal in T1 as a characteristic finding of central DI was first reported by Fujisawa et al. [2]. However, this signal may be absent in 10% of the healthy population [3]. Yamamoto et al. [4] reported the absence of the physiological signal in a case of a gestational DI, a finding that was similar to ours. The explanation for the disappearance of the signal remains unclear. We suggest that it is related to peripituitarial ADH depletion because this is the theoretical first site of contact between vasopressinase and ADH.

In conclusion, severe polyuria in pregnancy means that gestational DI should be ruled out. Follow-up with MRI provides intriguing new information about the site of action of vasopressinase and the nature of the hyperintense neurohypophyseal signal.

References

[1] Aleksandrov N, Audibert F, Bedard MJ, Mahone M, Goffinet F, Kadoch IJ. Gestational diabetes insipidus: a review of an underdiagnosed condition. J Obstet Gynaecol Can 2010;32(3):225–31.
[2] Fujisawa I, Nishimura K, Asato R, et al. Posterior lobe of the pituitary in diabetes insipidus: MR findings. J Comput Assist Tomogr 1987;11(2):221–5.
[3] Colombo N, Berry I, Kucharczyk J, et al. Posterior pituitary gland appearance on MR images in normal and pathologic states. Radiology 1987;165(2):481–5.
[4] Yamamoto T, Ishii T, Yoshioka K, et al. Transient central diabetes insipidus in pregnancy with a peculiar change in signal intensity on T1-weighted magnetic resonance images. Intern Med 2003;42(6):513–6.

Borja Quiroga[1,*]
Nephrology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

María Carmen Viñuela[1]
Obstetrics Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Patrocinio Rodríguez Benítez
Nephrology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Ana Pereda
Teresa Navarro
Ángel Aguarón
Obstetrics Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Alberto Tejedor
Nephrology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

*Corresponding author at: C/ Doctor Esquerdo, 46, 28007 Madrid, Spain
E-mail address: borjaqg@gmail.com (B. Quiroga)

[1]These authors contributed equally.

16 December 2011

doi:10.1016/j.ejogrb.2012.02.022

The independent effect of tumor size in predicting ovarian malignancy

Dear Editor,

In a recent issue of this journal, it was stated that 'the additional value of tumor size in predicting ovarian malignancy is debatable' [1]. The authors further mentioned that tumor size is not considered as an independent predictor of malignancy in the literature. We believe that this is not correct. The prediction model for malignancy LR1, developed by the International Ovarian Tumor Analysis (IOTA) consortium, included tumor size (defined as maximum diameter of three measurements of the largest diameters of the lesion in two perpendicular planes and expressed in millimeters) as an independent predictor [2]. This model was also covered in a review paper on ovarian cancer [3]. However, given the result that a Risk of Malignancy Index (RMI) variant that includes tumor size (albeit dichotomized) does not perform better than the standard RMI or its adaptations RMI2 and RMI3 [1,4], we decided to further assess the independent effect of tumor size on a large set of data from phase 2 of the IOTA study [2].

We used data containing information from 1938 patients with at least one persistent adnexal (i.e. ovarian, para-ovarian, or tubal) mass that was selected for surgery [5]. Patients were recruited between November 2005 and November 2007 in 19 clinical centers. In this dataset, 1396 patients (72%) had a benign tumor, 111 (6%) a borderline tumor, and 431 (22%) an invasive tumor. As possible predictors of malignancy (defined as a borderline or invasive tumor) we selected tumor size and other variables included in the RMI and/or the IOTA prediction model [2]. This resulted in a list of 15 variables (Table 1). Some variables of the original models are ignored as they are dichotomized variables covered by continuous variables: menopausal status (covered by patient age), and entirely solid tumor and presence of solid parts, which are covered by the maximum diameter of the largest solid component. We divided the solid component diameter by tumor size. This ratio of diameters, labeled 'standardized solid component diameter', is a percentage with values between 0 and 100 that has a very high correlation with the ratio of the volumes of the largest solid component and the lesion. Missing values for CA-125 (22%) were imputed using predictive mean matching, missing values for the presence of metastases (23%) were imputed with 0 (see [4] for more information). We assessed the independent effects of these variables using multivariable logistic regression with a random intercept to account for the multicenter nature of the data. We assessed whether variables had to be transformed because of a nonlinear effect on malignancy.

Table 1 presents the results of the logistic regression analysis. It clearly shows that the odds of ovarian malignancy increase with 10% for each centimeter increase in tumor size (95% CI, 7–14%), demonstrating the independent effect of tumor size even after controlling for a large set of important variables. When fixing the other variables at their respective averages, the predicted risk of malignancy increases from around 12% for tumor sizes of 1–2 cm

Table 1
Results of the multivariable logistic regression analysis.

Variable	Unit	Odds ratio	95% CI	*P*
Tumor size (maximum lesion diameter)	mm	1.10 per cm	1.07–1.14	<0.001
Patient age	Years	1.44 per 10 years	1.27–1.64	<0.001
Standardized solid component diameter	%	1.32 per 10%	1.24–1.41	<0.001
Serum CA-125 level	U/ml	1.39 per doubling[b]	1.25–1.56	<0.001
Irregular internal cyst walls	Yes/no	2.61	1.68–4.04	<0.001
Color Doppler score of intratumoral flow[a]	Ordinal	2.67	2.06–3.46	<0.001
Personal history of ovarian malignancy	Yes/no	20.98	6.76–65.11	<0.001
Acoustic shadows	Yes/no	0.28	0.14–0.55	<0.001
Papillations with detectable flow	Yes/no	6.06	3.14–11.71	0.001
Ascites	Yes/no	4.10	1.75–9.64	0.001
Metastases	Yes/no	12.63	2.58–61.7	0.002
Pelvic pain during examination	Yes/no	0.47	0.25–0.87	0.02
Multilocularity	Yes/no	1.67	1.03–2.69	0.04
Bilateral masses	Yes/no	1.43	0.83–2.48	0.20
Current use of hormonal therapy	Yes/no	1.20	0.60–2.39	0.61

[a] Color Doppler score of intratumoral flow has 4 ordinal levels: no blood flow, minimal flow, moderate flow, and very strong flow.
[b] CA-125 was log-transformed, therefore the odds ratio is expressed as the change in odds per doubling of the CA-125 level.

to around 68% for tumor sizes of 30 cm. Admittedly, this does not imply that it is essential to include this variable in prediction models for ovarian malignancy. The additional effect on overall model performance may be (too) small despite a clear independent effect. For example, LR2 is a simpler six-predictor alternative to the 12-predictor LR1 that does not include tumor size [2]. This model demonstrated similar performance on external validation [5]. When including a continuous variable such as tumor size, however, dichotomization as in the RMI variant should be avoided since this incurs a substantial loss of information.

Conflict of interest

The authors have no conflict of interest to disclose.

Acknowledgments

Research supported by the Research Foundation – Flanders (FWO Vlaanderen) (postdoctoral fellowship to Ben Van Calster, 1251609N, 1251612N; research project grant G049312N) and Agency for Innovation by Science and Technology (grant IWT-TBM070706-IOTA3). The funding sources had no involvement in design, data collection, analysis, interpretation, or manuscript writing.

References

[1] Van den Akker PA, Zusterzeel PL, Aalders AL, et al. External validation of the adapted Risk of Malignancy Index incorporating tumor size in the preoperative evaluation of adnexal masses. Eur J Obstet Gynecol Reprod Biol 2011;159:422–5.
[2] Timmerman D, Testa AC, Bourne T, et al. Logistic regression model to distinguish between the benign and malignant adnexal mass before surgery: a multicenter study by the International Ovarian Tumor Analysis Group. J Clin Oncol 2005;23:8794–801.
[3] Hennessy BT, Coleman RL, Markman M. Ovarian cancer. Lancet 2009;374:1371–82.
[4] Van Holsbeke C, Van Calster B, Bourne T, et al. External validation of diagnostic models to estimate the risk of malignancy in adnexal masses. Clin Cancer Res [Epub 2011 November 23].
[5] Timmerman D, Van Calster B, Testa AC, et al. Ovarian cancer prediction in adnexal masses using ultrasound-based logistic regression models: a temporal and external validation study by the IOTA group. Ultrasound Obstet Gynecol 2010;36:226–34.

Ben Van Calster*
Department of Obstetrics and Gynecology, University Hospitals KU Leuven, Leuven, Belgium

Laure Wynants[a,b]
[a]*Department of Electrical Engineering (ESAT-SCD), KU Leuven – University of Leuven, Leuven, Belgium*
[b]*IBBT Future Health Department, KU Leuven – University of Leuven, Leuven, Belgium*

Jeroen Kaijser
Department of Obstetrics and Gynecology, University Hospitals KU Leuven, Leuven, Belgium

Sabine Van Huffel[c,d]
[c]*Department of Electrical Engineering (ESAT-SCD), KU Leuven – University of Leuven, Leuven, Belgium*
[d]*IBBT Future Health Department, KU Leuven – University of Leuven, Leuven, Belgium*

Dirk Timmerman
Department of Obstetrics and Gynecology, University Hospitals KU Leuven, Leuven, Belgium

*Corresponding author at: Department of Obstetrics and Gynecology, University Hospitals KU Leuven, Herestraat 49 Box 7003, 3000 Leuven, Belgium.
Tel.: +32 16 346258
E-mail address: ben.vancalster@med.kuleuven.be
(B. Van Calster)

26 January 2012

doi:10.1016/j.ejogrb.2012.02.023