CORRESPONDENCE

The sFlt-1:PlGF Ratio in Women with Suspected Preeclampsia

TO THE EDITOR: The article by Zeisler and colleagues (Jan. 7 issue)[1] showed that a ratio of soluble fms-like tyrosine kinase 1 (sFlt-1) to placental growth factor (PlGF) of 38 or lower ruled out preeclampsia with a negative predictive value of 99.3% within 1 week in women with clinical suspicion of it. Critical in this study are the inclusion criteria used to define "impending" preeclampsia. In medicine, a definition of suspected preeclampsia is lacking, and the inclusion of patients at low risk may artificially increase the negative predictive value of a test by diluting the weight of false negative events. Only 41.5% of the women in the validation cohort had new-onset hypertension or an exacerbation of preexisting hypertension. Other clinical symptoms considered as inclusion criteria are often described in women with overt preeclampsia and used to define its severity, but in the absence of an elevated blood pressure, they lose their clinical importance. We wonder whether the simple inclusion of blood pressure instead of the angiogenic ratio in the evaluation of symptomatic patients would have yielded the same figure for the negative predictive value.

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No potential conflict of interest relevant to this letter was reported.

1. Zeisler H, Llurba E, Chantraine F, et al. Predictive value of the sFlt-1:PlGF ratio in women with suspected preeclampsia. N Engl J Med 2016;374:13-22.

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THE AUTHORS REPLY: In PROGNOSIS (Prediction of Short-Term Outcome in Pregnant Women with Suspected Preeclampsia Study), pregnant women were enrolled on the basis of signs and symptoms of preeclampsia or the HELLP syndrome (characterized by hemolysis, elevated liver-enzyme levels, and low platelet counts), including high blood pressure, as described in clinical guidelines.[1,2] The prevalence of preeclampsia in our cohort was 19.0%, as compared with 2 to 5% among all pregnant women (indicating that women with a high risk of preeclampsia were included in the study). Blood pressure is limited in predicting adverse pregnancy outcomes (e.g., the HELLP syndrome and eclampsia).[3] Importantly, up to 20% of cases of the HELLP syndrome develop in women without previous onset of hypertension.[4]

The area under the curve in the receiver-operating-characteristic analysis for prediction of preeclampsia or the HELLP syndrome within 1 week was 0.884 (95% confidence interval [CI], 0.837 to 0.932) for the sFlt-1:PlGF ratio, as compared with 0.715 (95% CI, 0.650 to 0.780) for systolic and diastolic blood pressure in the full PROGNOSIS

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data set. As we noted in the article, a post hoc analysis suggested that the addition of the sFlt-1:PlGF ratio to blood-pressure and proteinuria assessments improved the prediction of preeclampsia over these other measures alone.

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Since publication of their article, the authors report no further potential conflict of interest.

1. American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Hypertension in pregnancy: report of the American College of Obstetricians and Gynecologists Obstet Gynecol 2013;122:1122-31.
2. Tranquilli AL, Dekker G, Magee L, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: a revised statement from the ISSHP. Pregnancy Hypertens 2014;4:97-104.
3. Sibai BM, Stella CL. Diagnosis and management of atypical preeclampsia-eclampsia. Am J Obstet Gynecol 2009;200(5):481.e1-7.
4. Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynecol 2004;103:981-91.

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Azithromycin versus Doxycycline for Chlamydia

TO THE EDITOR: Within the community of providers who treat sexually transmitted infections, there has been concern that azithromycin may be less effective than doxycycline in treating *Chlamydia trachomatis* infection. Geisler et al. (Dec. 24 issue)[1] report on their trial comparing these two drugs, and in an accompanying editorial, Quinn and Gaydos[2] discuss the problem of treatment for these genital tract infections. Yet, neither the article nor the editorial mentions the treatment of extragenital infections. Such infections are not rare. Testing men who have sex with men for rectal and oropharyngeal *C. trachomatis* infection, as compared with testing for urethral infection alone, doubles the number of men who are found to have *C. trachomatis* infection.[3] Such infections are also common in women, although with additional testing for rectal and oropharyngeal infection, the increment is less.[4]

Many anecdotal reports have indicated that azithromycin is less effective than doxycycline for the treatment of rectal, oropharyngeal, or genital infection. For example, in a retrospective cohort study, 23 of 136 men (17%) tested positive for chlamydia infection 14 to 60 days after treatment with azithromycin, and 0 of 36 men tested positive 14 to 60 days after treatment with doxycycline.[5] These studies were suggestive, not conclusive. The biologic features of *C. trachomatis* infection and antibiotic levels may vary according to the anatomical site of infection. Data from trials of treatment of extragenital *C. trachomatis* infection as well as from trials of treatment of genital *C. trachomatis* infection are lacking.

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1. Geisler WM, Uniyal A, Lee JY, et al. Azithromycin versus doxycycline for urogenital *Chlamydia trachomatis* infection. N Engl J Med 2015;373:2512-21.
2. Quinn TC, Gaydos CA. Treatment for chlamydia infection — doxycycline versus azithromycin. N Engl J Med 2015;373:2573-5.
3. Schachter J, Philip SS. Testing men who have sex with men for urethral infection with Chlamydia trachomatis and Neisseria gonorrhoeae is only half the job, and we need the right tools. Sex Transm Dis 2011;38:925-7.
4. Dukers-Muijrers NH, Schachter J, van Liere GA, Wolffs PF, Hoebe CJ. What is needed to guide testing for anorectal and pharyngeal Chlamydia trachomatis and Neisseria gonorrhoeae in women and men? Evidence and opinion. BMC Infect Dis 2015;15:533.
5. Khosropour CM, Dombrowski JC, Barbee LA, Manhart LE, Golden MR. Comparing azithromycin and doxycycline for the treatment of rectal chlamydial infection: a retrospective cohort study. Sex Transm Dis 2014;41:79-85.

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TO THE EDITOR: Geisler et al. do not establish the noninferiority of azithromycin to doxycycline for the treatment of urogenital *C. trachomatis* infection. Both drugs are currently recommended as first-line options for *C. trachomatis* infections (genotypes D through K).[1,2]

In the trial reported by Geisler and colleagues, 4 of the 5 patients with treatment failure in the