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# Density of tubal ring vascularization: A new marker for prediction of success of medical treatment in tubal ectopic pregnancy



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#### ABSTRACT

Objectives: The diagnosis of ectopic pregnancy has been facilitated especially by the use of Doppler ultrasonography. In previous studies the presence of peri-trophoblastic blood flow by Doppler ultrasound and the detection of a low-resistance, high-velocity flow pattern were defined as specific signs for trophoblastic tissue. The aim of this study was to evaluate the efficacy of Doppler ultrasonography in the prediction of treatment success in tubal pregnancies being treated with single dose conservative methotrexate.

Study design: A total of 104 patients with non-ruptured ectopic pregnancy who were hemodynamically stable and eligible for methotrexate treatment were included in the study. The spectral wave form of the mass was classified according to the vascularization density by Power Doppler. It was defined as Grade 1, 2 and 3, respectively. All patients received a single  $50 \text{ mg/m}^2$  dose of systemic methotrexate. Serum  $\beta$ -hCG levels were measured on the 4th and 7th days of treatment. The treatment was considered unsuccessful in patients without a decrease of 15% or more in the serum  $\beta$ -hCG levels between days 0 and 7

Results: Twenty-four patients with grade I vascularity, 11 patients with grade II vascularity and 13 patients with grade III vascularity were referred as Group I, II and III, respectively, according to the degree of adnexal vascularity assessed by Doppler ultrasonography. Overall success rate of MTX treatment was found to be 72.9%. The response rates to systemic MTX treatment in cases with Grade I, II and III ectopic pregnancy mass vascularization were found to be 58.3%, 81.8% and 92.3%, respectively. Comparison of the groups' treatment responses revealed a linear-by-linear correlation with the Chi-square test. Increased vascularization grade of ectopic pregnancy was associated with a higher likelihood of responding to MTX treatment.

Conclusions: Detection of the vascularization grade with Doppler ultrasound could be considered a remarkable parameter in predicting treatment success considering its ease of utilization and low cost.

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### Introduction

Ectopic pregnancy rates have been increasing recently and despite the advances in diagnostic techniques it is still among the life-threatening conditions. Ectopic pregnancy accounts for 6–10% of pregnancy related mortality [1]. Tubal rupture is seen in 22–34% of all tubal pregnancies [2]. Transvaginal ultrasonographic findings, the most commonly used method for diagnosing tubal ectopic pregnancy, have been described in the late 1980s [3,4]. The main sonographic finding of tubal pregnancy is the presence of an

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extraovarian mass in the adnexal region. The diagnosis of ectopic pregnancy has been facilitated especially by the use of Doppler ultrasonography (US). Presence of peri-trophoblastic blood flow defined as "ring of fire" and detection of a low-resistance, high-velocity flow pattern specific to trophoblastic tissue by color and power Doppler ultrasonography have been used in identification and differentiation of tubal pregnancy from corpus luteum. The sensitivity and specificity of Doppler ultrasonography has been reported to be 85% and 96%, respectively [5–7].

Single dose methotrexate (MTX) use in the treatment of ectopic pregnancy has first been defined by Stovall et al. [8]. It is the most commonly used method in conservative treatment of unruptured ectopic pregnancy due to its non-invasiveness, cheapness and outpatient applicability combined with high success rates [9,10]. Various studies have reported success rates around 74–95% with

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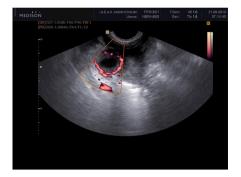


Image 1. Grade I vascularization.

methotrexate treatment protocol [11,12]. However, necessity of a second MTX dose, unresponsiveness to treatment and risk of tubal rupture cannot be ignored. Tubal rupture has been reported in 7–14% of cases during MTX treatment [13]. Barnhard et al. reported a 0.5–1% rate of adverse effects with single dose regimen [14]. Although rare in the single regimen preferred in ectopic pregnancy treatment, bone marrow suppression, dermatitis and stomatitis are possible side effects [12]. Various markers such as serum  $\beta$ -hCG, progesterone and folic acid levels, endometrial thickness, ectopic pregnancy mass dimensions, visualization of yolk sac or embryo in the gestational sac and presence of free fluid in the abdominal cavity have been evaluated to predict the response to



Image 2. Grade III vascularization.

medical treatment [9,15–20]. Nonetheless, no consensus on the predictability of the markers evaluated has yet been reached. The only parameter with an approved consensus on its predictive value in the success of MTX treatment is pre-treatment level of  $\beta\text{-hCG}$ . Although several cutoff values between 1300 and 10,000 IU have been reported by various investigators for the predictive value of serum  $\beta\text{-hCG}$ , no consensus on pre-treatment cutoff value yet exists [21–23]. Moreover, serum  $\beta\text{-hCG}$  rising rate during 48-h pre-treatment follow-up and serum  $\beta\text{-hCG}$  level alterations on days 1, 4 and 7 of treatment are among the parameters assessed for predicting treatment success. Combined use of clinical and

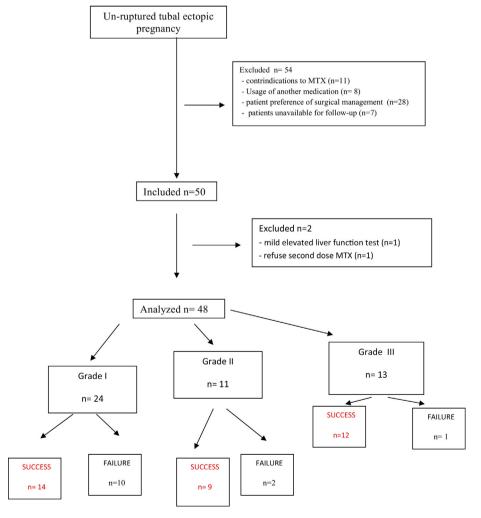


Fig. 1. Flowchart.

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