

Clinical relevance of inherited thrombophilia in implantation failure: who needs to be screened?

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In women undergoing *in vitro* fertilization (IVF) who have an implantation failure (IF) after repeated embryo transfer, an association with the presence of acquired thrombophilia has been demonstrated,¹ and a thromboprophylaxis seems to be efficacious in improving implantation rate.² More recently a role inherited thrombophilia has been recognised to have a role in recurrent otherwise unexplained fetal losses.^{4,5} The study recently appeared in Haematologica by Martinelli and coworkers⁶ seems to suggest that carriers of common causes of thrombophilia (FV Leiden and FII A20210 gene variants) are not at higher risk of IF, so at present thromboprophylaxis is not warranted in women approaching IVF. It is well established that many other factors in addition to thrombophilia could influence the outcome of a spontaneous pregnancy.⁷ Some of them are known to influence also IVF, as the maternal age at the conception and the number of previous failures. In women at their first or second attempt we did not find a higher prevalence of these gene variants in respect of that found in women conceiving spontaneously.⁸ Moreover, women with ≥ 40 yrs were excluded from our study. In this context, women with ≥ 3 IVF-IF showed a higher prevalence of these gene variants. It is to be underlined that we considered also a low risk group formed by women at their first or second attempt, in which we did not find a prevalence of inherited thrombophilia higher than that of controls, according to findings of Martinelli. Our data demonstrate that carriership of thrombophilia only in women with at least 3 previous IVF-IF can negatively influence implantation starting from the fourth cycle of ovarian induction. We agree that women until their third

cycle of ovarian induction do not need to be investigated for thrombophilia, since after the failure of third embryo transfer we can consider to study this aspect. In conclusion, we strongly believe that the selection of sample is in this settings particularly important and could explain the apparent divergences in the results obtained by different studies.

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