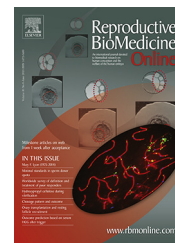




www.sciencedirect.com
www.rbmonline.com



ARTICLE

How to define, diagnose and treat poor responders? Responses from a worldwide survey of IVF clinics




Pasquale Patrizio ^{a,*}, Alberto Vaiarelli ^b, Paolo E Levi Setti ^c, Kyle J Tobler ^d,
Gon Shoham ^e, Milton Leong ^f, Zeev Shoham ^{g,h}

^a Yale University Fertility Center, New Haven, Connecticut, USA; ^b Centre for Reproductive Medicine, Vrije University Brussels, Belgium; ^c Department of Gynecology, Division of Gynecology and Reproductive Medicine, Humanitas Research Hospital Fertility Center, Rozzano, Milan 20084, Italy; ^d Department of Gynecology and Obstetrics, Division of Reproductive Endocrinology and Infertility, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; ^e Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel; ^f The Women's Clinic, Hong Kong; ^g Department of Obstetrics and Gynaecology, Kaplan Medical Center, Rehovot, Israel; ^h Hadassah Medical School, Jerusalem, Israel
* Corresponding author. E-mail address: pasquale.patrizio@yale.edu (P Patrizio).



Dr Pasquale Patrizio is a board certified specialist in Obstetrics and Gynecology and Reproductive Endocrinology and Infertility. He is Professor of Obstetrics and Gynecology, and Director of the Yale Fertility and Preservation program. He received his MD from the University of Napoli, Italy, and completed residencies in Obstetrics and Gynaecology and Andrology in Italy and the USA. In 2003, he became a certified High Complexity Laboratory Director and completed a Master of Bioethics at the University of Pennsylvania. Dr Patrizio has published extensively in IVF, male infertility and ICSI. Research includes cumulus cells gene expression and oocyte aging and embryo competence.

Abstract Poor responders represent a significant percentage of couples treated in IVF units (10–24%), but the standard definition of poor responders remains uncertain and consequently optimal treatment options remain subjective and not evidence-based. In an attempt to provide uniformity on the definition, diagnosis and treatment of poor responders, a worldwide survey was conducted asking IVF professionals a set of questions on this complex topic. The survey was posted on www.IVF-worldwide.com, the largest and most comprehensive IVF-focused website for physicians and embryologists. A total of 196 centres replied, forming a panel of IVF units with a median of 400 cycles per year. The present study shows that the definition of poor responders is still subjective, and many practices do not use evidence-based treatment for this category of patients. Our hope is that by leveraging the great potential of the internet, future studies may provide immediate large-scale sampling to standardize both poor responder definition and treatment options. 

© 2015 Reproductive Healthcare Ltd. Published by Elsevier Ltd. All rights reserved.

KEYWORDS: decreased ovarian function, IVF, management, ovarian stimulation, poor responder, survey

<http://dx.doi.org/10.1016/j.rbmo.2015.03.002>

1472-6483/© 2015 Reproductive Healthcare Ltd. Published by Elsevier Ltd. All rights reserved.

Introduction

Physiologically, after the period of optimal fertility (at age 18–31 years), oocyte quality decreases in parallel with the progressive reduction in number of follicles, and this deterioration accelerates after 37–38 years of age (Faddy, 2000; Faddy et al., 1992; Gougeon, 1996). It has been estimated that, in the general population, about 10% of women younger than 40 years have a premature reduction in the number of ovarian follicles (Nikolaou and Templeton, 2003; van Noord et al., 1997).

Several possible causes for diminished ovarian reserve have been identified, and include inherited chromosomal (De Vos et al., 2010; Gleicher et al., 2009) and genetic disorders (e.g. Fragile-X and galactosaemia) (te Velde and Pearson, 2002) and iatrogenic causes (Treloar, 1981; Ferraretti et al., 2011); however, most cases of premature ovarian insufficiency are still unexplained (Nikolaou and Templeton, 2003).

Additionally, in recent years, there has been an increased tendency to delay pregnancy, for social, economic reasons, or both, resulting in an increasing number of women seeking infertility treatment at an advanced age, when their chances of optimal ovarian response and live birth are severely compromised (Wyndham et al., 2012). Assisted reproduction technology data available through the Society for Assisted Reproductive Technologies show that, between 1999 and 2008, the number of women aged 40 years or older seeking fertility treatment increased by more than 80%, whereas, for women younger than 35 years, the increase was about 45%.

As a consequence, fertility clinics worldwide need to address the reproductive desires of women who are labelled as poor responders. Various methods have been proposed to assess ovarian reserve before starting a cycle of ovarian stimulation, such as basal hormone assessment (cycle day 3 FSH and oestradiol), anti-Müllerian hormone (AMH) and antral follicle count (AFC) (Penzias, 2004). Age, however, remains the single most important factor in predicting ovarian reserve.

At present, it is increasingly difficult to compare treatment protocols owing to the absence of a uniform method for defining poor responders; a disparity that in turn leads to a lack of standardization in treatment modes. In previous studies, the definition of a poor responder has represented a broad range of metrics and categories from the number of follicles produced, number of oocytes retrieved, use of a variety of laboratory values and ultrasound findings as well as gonadotrophin doses. Some define poor responders as patients who produce no more than five follicles after ovarian stimulation; others, no more than three or four. Some define poor responders as patients with oestradiol levels lower than 650 pg/mL (Surrey and Schoolcraft, 2000), after stimulation with high doses of gonadotrophins, whereas others use a combination of factors (Ferraretti et al., 2011). Further criteria have also been used to define poor responders, including at least one cancelled IVF cycle (Manzi et al., 1994), increased total dose of FSH (Shaker et al., 1992), increased daily (>300 IU/day) gonadotrophin dose used (Faber et al., 1998) and prolonged duration of gonadotrophin stimulation (Toth et al., 1996).

In essence, ovarian stimulation can be viewed as a dynamic test for the resting ovarian follicular pool (Beckers et al., 2002). In fact, the size of the cohort of recruitable follicles

may be a reflection of the actual resting follicle pool (Gougeon, 1996). To this extent, a review conducted in 1999 identified more than 35 different definitions (Surrey and Schoolcraft, 2000). Because of the high number of varying definitions, The European Society of Human Reproduction and Embryology produced a committee consensus to define poor ovarian responders as patients having at least two of the following criteria: a previous episode of poor ovarian response (three oocytes or less) with standard dosing of medications; an abnormal ovarian reserve with AFC less than five to seven follicles or AMH less than 0.5–1.1 ng/mL; or women above 40 years of age or presenting other risk factors for poor response (Ferraretti et al., 2011). It is sufficient, however, to categorize women above the age of 40 years as poor responders or reduced ovarian reserve based on their age alone in the absence of ovarian stimulation or other defining metrics.

Despite attempts to more uniformly classify patients with poor ovarian response (POR), these definitions have not yet proved helpful in identifying optimal treatment protocols for assisted reproduction (Oudendijk et al., 2012). Various strategies have been proposed to improve outcomes in patients with low ovarian response. No overarching agreement has been reached, however, on the most optimal management strategy for patients with POR caused by the heterogeneous and varying parameters used to define POR. In both prospective (van Hooff et al., 1993) and retrospective studies (Karande and Gleicher, 1999; Land et al., 1996), increasing the daily dose of gonadotrophins to 450 IU proved ineffective in enhancing ovarian response, increasing pregnancy rates, or both.

With the aim of providing greater clarity on the definition, diagnosis and treatment of patients with reduced ovarian reserve, an online worldwide survey of IVF practices was conducted, taking advantage of new and innovative web-based technologies. In particular, our survey leveraged the IVF-Worldwide network (www.IVF-Worldwide.com), a comprehensive IVF-focused website for doctors, embryologists, nurses and social workers, providing its members with the ability to locate IVF units anywhere in the world and communicate directly with them.

Materials and methods

A web-based questionnaire entitled 'Poor responders: how to define, diagnose and treat?' was posted on the IVF-Worldwide website on 25 June 2010, and was open for data entry until 25 July, 2010. The survey collected the following demographic information: the name of the IVF clinic and medical director, email address, country and number of IVF cycles completed by the unit in the most recent year. The survey was divided into three parts: the first focused on the various modes of defining poor responders, the second on screening methods to facilitate the diagnosis and the third on treatment strategies. The respondent's practice patterns and opinions were evaluated through 'Yes', 'No', and multiple choice questions. The survey question stems are listed in [Appendix I](#).

Quality-assurance methods

To minimize duplicates and inaccurate reports from responding units, computerized software compared four demographic

Download English Version:

<https://daneshyari.com/en/article/3970061>

Download Persian Version:

<https://daneshyari.com/article/3970061>

[Daneshyari.com](https://daneshyari.com)