Medical treatment of comorbidities among infertile men: a step toward improving semen quality and general health status of infertile men?

From a historical perspective, the main clinical and research focuses have been on the long-term health outcomes of infertile women, including the effects of ovarian stimulation on the risk of mortality and cancer. However, in recent years, it has become more evident that a man's reproductive and somatic health also are closely related.

Male infertility is common and is estimated to contribute to up to 40% of infertility cases (1). In addition to the well-established link between male infertility and testicular cancer, cohort studies from Europe and the United States have shown that male factor infertility is associated with an increased risk of chronic non-malignant diseases and overall mortality (2). The causal relationship remains unclear, but it has been hypothesized that common underlying etiologies such as in utero exposures, genetics, or lifestyle factors may explain the association.

Despite these inherent associations and in the era of assisted reproductive techniques, a thorough investigation of the male partner may be bypassed as pregnancy can be achieved without an evaluation. This is of concern for several reasons. Men are generally younger when they present for an infertility evaluation, so this contact with the health care provider may serve as a window of opportunity for initiating proper preventive action. The initial evaluation of the infertile man is aimed at identifying reversible causes and should, at a minimum, include a reproductive history and semen sample. Treatment of medical comorbidities may ultimately improve semen quality, so it seems plausible that fertility treatment may prove unnecessary if the semen quality can be significantly improved via medical treatment. This could be of inestimable benefit to the infertile couple because undergoing fertility treatment often is costly, is time consuming, and places an unfair burden on the female partner.

In this current issue of *Fertility and Sterility*, Shiraishi et al. (3) investigated the prevalence of medical comorbidities among men evaluated for infertility and assessed whether treatment of medical comorbidities improved spermatogenesis. In this case control study of 3,780 Japanese men, the prevalence of comorbidities was higher among infertile men with hypertension and hyperlipidemia, representing the most prevalent types. Both age and body mass index (BMI) were similarly distributed between the two groups. Treatment of medical comorbidities statistically significantly improved the patients' semen quality compared with their baseline values. The authors argued that medical treatment may be beneficial not only for restoring spermatogenesis but also for improving the general health of men.

As the first study to investigate the association between male reproductive and somatic health in an Asian population, these findings from Shiraishi et al. (3) support the importance of further investigations of infertile men. Previous studies have suggested a possible link between male infertility and the metabolic syndrome, which is a cluster of symptoms including visceral obesity, hypertension, and hyperglycemia, and a known risk factor for cardiovascular disease. The impact of BMI on semen quality has been thoroughly investigated, but the association between male infertility and hypertension has received less attention thus far. A recent study found the use of antihypertensive medication to be associated with impaired semen parameters, but whether the findings were related to the medical treatment or the underlying hypertension were difficult to discern (4). In the study by Shiraishi et al. (3), semen quality improved with antihypertensive treatment, which supports that hypertension rather than treatment leads to poor semen quality.

Given the findings of this present study, further monitoring of infertile men after reproductive efforts may be warranted. More research is needed to understand the pathophysiology of the observed associations in view of developing methods for preventive strategies. For example, diet and lifestyle interventions may be beneficial to both fertility and health, so they should be further explored. Finally, it is evident that men become more prone to chronic disease as they age. As more and more couples delay their childbearing, the mean paternal age has increased in the United States (5), which may have potential clinical implications and should be further investigated.

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https://doi.org/10.1016/j.fertnstert.2018.08.023

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REFERENCES

1. Thonneau P, Marchand S, Tallec A, Ferial ML, Ducot B, Lansac J, et al. Incidence and main causes of infertility in a resident population (1,850,000) of three French regions (1988–1989). Hum Reprod 1991;6:811–6.
2. Glazer CH, Bonde JP, Eisenberg ML, Giwercman A, Haervig KK, Rimborg S, et al. Male infertility and risk of nonmalignant chronic diseases: a systematic review of the epidemiological evidence. Semin Reprod Med 2017;35:282–90.
3. Shiraishi K, Matsuyama H. Effects of medical comorbidity on male infertility and comorbidity treatment on spermatogenesis. Fertil Steril 2018;110:1006–11.
4. Guo D, Li S, Behr B, Eisenberg ML. Hypertension and male fertility. World J Mens Health 2017;35:59–64.
5. Khandwala YS, Zhang CA, Lu Y, Eisenberg ML. The age of fathers in the USA is rising: an analysis of 168 867 480 births from 1972 to 2015. Hum Reprod 2017;32:2110–6.