Moving the science forward on dietary patterns and male fertility

Evidence linking a healthy diet to improved semen quality parameters continues to grow (1, 2). In this issue of *Fertility and Sterility*, Efrat and colleagues (3) add additional insight into this research area by investigating the association between four a priori defined dietary patterns: the alternate Mediterranean Diet (aMED), the Dietary Approaches to Stop Hypertension (DASH), the Healthy Eating Index 2010 (HEI-2010), and the Alternative Healthy Eating Index 2010 (aHEI-2010) scores, in relation to semen quality parameters in a large cross-sectional study from Israel (3). While the authors found positive associations between each of the four dietary patterns with at least one measure of sperm quality, the most consistent and strong results were found with the aHEI-2010 score. The novelty of this paper is the use of pre-defined as opposed to data-defined dietary patterns. This is an important step forward as pre-defined dietary patterns tend to be easier to compare across studies and more easily translatable into dietary advice because of their set scoring criteria. However, as we look to make recommendations based off these patterns, there are a couple points worth remembering.

First, two of the dietary patterns that were investigated in this paper, the aMED and the DASH diet, rely on relative rankings to score the dietary pattern. Thus, a high score on either the aMED or DASH should be interpreted as a high adherence to that score relative to others in that specific population. Scores that rely on relative rankings can sometimes be problematic as often they end up reflecting the distribution of the selected food groups in the examined population but not adherence to a universal Mediterranean diet (4). Because of this, it is critical that information on the dietary components which make up the score be reported in the paper so others can understand what it means to have a high aMED or DASH score in that population. A distinct advantage of the HEI-2010 and aHEI-2010 patterns is that scoring is standardized to set cutoffs, which allows it to be directly comparable across study populations. Yet care needs to be taken when implementing these scores to make sure they are calculated correctly. In the study by Efrat and colleagues (3), for example, standard deviations of 0 are reported for men in the second and third quartile of the aHEI-2010 score suggesting errors in the calculation of the score in this study. While these scores can be more statistically challenging to calculate, many times freely accessible code is available. For example, the National Cancer Institute has sample SAS code on their website for researchers to use in deriving the HEI-2010 score (5).

As the studies on diet and semen quality become larger, researchers need to be careful not to over interpret statistically significant findings as clinically significant findings. In this study, the differences in semen quality parameters detected between the extreme quartiles of aMED, HEI-2010, and DASH were all very small: 3-6 millions/mL for sperm concentration, 3-5% for % motile sperm, and 0.5% for % morphologically normal sperm. When effect sizes are small, not only is the clinical relevance questioned, but the likelihood that residual confounding is completely explaining the association is high. Moreover, while quite a large difference was detected in sperm concentrations, counts, and % normal morphology comparing men in the highest versus lowest quartile of the aHEI-2010, the association was not linear across quartiles. This suggests that either there is a threshold effect (e.g. the benefits of a healthy diet on semen quality are only observed with strong adherence), which could be plausible given the overall low aHEI-2010 scores observed in this population, or there is something else about these men in the fourth quartile (other than their strong adherence to the aHEI-2010 diet) that is driving this trend.

Finally, as a broader point, while the semen analysis is an important component of the clinical evaluation of men's fertility potential, it is a poor predictor of fertility. Thus, before we can begin to make strong advice regarding diet's effects on male fertility, studies are needed that focus on better markers of couple fertility such as time to pregnancy among couples trying to conceive on their own or probability of live birth among couples undergoing assisted reproduction. Given the growing number of observational studies showing a consistent association between healthy diets and improved fertility in both men and women, it is also time to consider randomized controlled trials involving food-based interventions. In summary, while the article by Efrat and colleagues (3) is a step forward in the right direction to moving the literature on dietary patterns and semen quality forward, we still have a long way to go before solid recommendations can be made. Hopefully some of the considerations laid out here will help inform future researchers as they design, plan, and implement future studies on dietary patterns and male fertility.

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