Men's meat intake and treatment outcomes among couples undergoing assisted reproduction

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Objective: To study the relationship between men's meat intake and clinical outcomes in couples undergoing infertility treatment with the use of assisted reproductive technology (ART).
Design: Prospective cohort study.
Setting: Fertility center.
Patient(s): A total of 141 men whose female partners underwent 246 ART cycles from 2007 to 2014.
Intervention(s): None. Total and specific types of meat intake were estimated from dietary questionnaires.
Main Outcome Measure(s): Fertilization, implantation, clinical pregnancy, and live-birth rates per initiated cycle. Mixed-effects models account for multiple IVF cycles per woman.
Result(s): There was a positive association between poultry intake and fertilization rate, with a 13% higher fertilization rate among men in the highest quartile of poultry intake compared with those in the lowest quartile (78% vs. 65%). Processed meat intake was inversely related to fertilization rate in conventional IVF cycles but not in IVF cycles using intracytoplasmic sperm injection. The adjusted fertilization rates for men in increasing quartiles of processed meat intake were 82%, 67%, 70%, and 54% in conventional IVF cycles. Men's total meat intake, including intake of specific types of meat, was not associated with implantation, clinical pregnancy, or live-birth rates.
Conclusion(s): Poultry intake was positively associated with fertilization rates, whereas processed meat intake was negatively associated with fertilization rates among couples undergoing conventional IVF. This, however, did not translate into associations with clinical pregnancy or live-birth rates. (Fertil Steril® 2015;104:972–9. ©2015 by American Society for Reproductive Medicine.)
Key Words: Cohort studies, men, meat intake, infertility, assisted reproductive technology

Infertility is a common problem for couples in the United States, with an estimated prevalence of 15% (1). Male factors, including azoospermia, oligospermia, and other semen analysis abnormalities, contribute to roughly half of infertility cases (2). However, the impact that potentially modifiable risk factors may have on male factor infertility remains relatively unexplored. Increasing evidence suggests that diet may influence male reproductive function as evidenced by multiple reports of associations between dietary factors and conventional semen quality parameters (3–6).

One dietary factor that has received significant attention as a potential risk factor for male factor infertility is meat intake (7–10). Meats are a major source of saturated fat, which is related to lower sperm counts among men from a fertility clinic (6) and among young men from the general population (11). Furthermore, meats could serve as

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vehicles for environmental chemicals that may negatively impact spermatogenesis (12). We have previously reported that processed meat intake was associated with lower total sperm count among healthy young men (13) and with a lower percentage of morphologically normal sperm among men from subfertile couples presenting to a fertility clinic (7). However, given the poor ability of conventional semen parameters to predict fertility potential in natural and assisted conception (14, 15), it is not clear whether these associations necessarily translate into diminished fertility. To address this question, we evaluated the association of men's meat intake with treatment outcomes of subfertile couples undergoing treatment using assisted reproductive technologies (ART).

MATERIALS AND METHODS

Study Population

Subfertile couples seeking evaluation and treatment at the Massachusetts General Hospital (MGH) Fertility Center were invited to participate in the Environment and Reproductive Health (EARTH) Study, an ongoing prospective cohort study focused on identifying how environmental factors impact human fertility (16). Men (ages 18–55) and women (ages 18–45) planning to use their own gametes during infertility treatment were eligible for the study. A food frequency questionnaire (FFQ) was introduced in 2007 and was completed by 241 of the 392 men (61%) recruited through June 2014. Of these 241 men, 107 were excluded: the female partners of 54 did not join the study, the female partners of 44 had not yet undergone any ART cycles, and the female partner of nine men had already started an ART cycle before diet assessment. After these exclusions, there were 141 men whose female partners underwent at least one ART cycle (IVF with conventional insemination or intracytoplasmic sperm injection [ICSI]) and for whom pretreatment diet data were collected during the study period. At the time of enrollment, trained research nurses measured the height and weight of each subject and completed a general health questionnaire including lifestyles, demographics, and reproductive history. This study was approved by the Human Subject Committees at the Harvard T.H. Chan School of Public Health and MGH. In addition, informed consent was obtained from all participants.

Dietary Assessment

Participants were asked to complete a previously validated FFQ and report how often, on average, they had consumed 131 foods and beverages during the past year (17). In a separately published validation study, the deattenuated correlation coefficient ranged from 0.56 for chicken and turkey to 0.83 for processed red meats for meat intake assessed by FFQ and the 1-year average of prospectively collected diet records (18). The FFQ had nine categories for intake frequency, from never to two or more servings/day. The nutritional content of each food and the specified portion size were obtained from a database of the United States Department of Agriculture (19). Total meat intake was defined as the sum of unprocessed red meat, processed red meat, poultry, fish, and organ meat intake. The definitions and serving size of each meat have been described elsewhere (7). Two dietary patterns were identified using principal components analysis: the Prudent pattern and the Western pattern, as described elsewhere (20). A summary score for each pattern was calculated to reflect how closely each participant adhered to them (20). A higher score indicates higher adherence to the respective dietary pattern.

Clinical Procedures and Assessment of Outcomes

Female partners underwent one of three stimulation protocols: [1] luteal phase GnRH-agonist protocol, [2] GnRH-antagonist protocol, or [3] follicular phase GnRH-agonist/flare protocol. Briefly, on day 3 of induced menses, treatment with gonadotropins was initiated, and the GnRH agonist or antagonist was continued or started after the usual ovarian stimulation protocols (21). HCG was administered 36 hours before oocyte retrieval to trigger maturation. Oocyte retrieval was performed when transvaginal ultrasound showed at least three dominant follicles ($\geq$16 mm) and serum E_2 had reached at least 500 pg/mL. Couples underwent IVF with conventional insemination or with ICSI, as clinically indicated. At our center, ICSI is typically recommended in cases of severe teratospermia ($\leq$2% normal morphology), low total motile count ($<$1 M) after swim-up or gradient separation, or prior failed fertilization with conventional insemination. Oocytes were classified by embryologists as germinal vesicle, metaphase I (MI), metaphase II (MII), or degenerated. Fertilized oocytes were classified as normally fertilized if they had two pronuclei. After an embryo was transferred, clinical outcomes were assessed. Successful implantation was defined as an elevation in plasma β-hCG levels above 6 IU/L measured 2 weeks after ET. Clinical pregnancy was defined as the presence of an intrauterine pregnancy confirmed by ultrasound at 6 weeks. Live birth was defined as the birth of a neonate on or after 24 weeks' gestation.

Statistical Analysis

Men were categorized into quartiles according to total meat intake. To test for differences in demographic, reproductive, and dietary characteristics across quartiles, we used a Kruskal-Wallis test for continuous variables and an extended Fisher's exact test for categorical variables. Multivariable generalized linear mixed models with random intercepts, binominal distribution, and logit link function were used to examine the association of meat intake with fertilization, implantation, clinical pregnancy, and live-birth rates, while accounting for multiple treatment cycles per couple and adjusting for other covariates. Tests for linear trend were performed by modeling intake as a continuous variable where each man was assigned the median intake of his corresponding quartile category. Population marginal means were calculated (22) to allow presentation of results as probabilities adjusted for the covariates in the model. Four sets of models were used to account for potential confounding factors. The first model included terms for men's