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# Predictive value of sperm morphology and progressively motile sperm count for pregnancy outcomes in intrauterine insemination

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**Objective:** To investigate the value of sperm parameters to predict an ongoing pregnancy outcome in couples treated with intrauterine insemination (IUI), during a methodologically stable period of time.
**Design:** Retrospective, observational study with logistic regression analyses.
**Setting:** University hospital.
**Patient(s):** A total of 1,166 couples visiting the fertility laboratory for their first IUI episode, including 4,251 IUI cycles.
**Intervention(s):** None.
**Main Outcome Measure(s):** Sperm morphology, total progressively motile sperm count (TPMSC), and number of inseminated progressively motile spermatozoa (NIPMS); odds ratios (ORs) of the sperm parameters after the first IUI cycle and the first finished IUI episode; discriminatory accuracy of the multivariable model.
**Result(s):** None of the sperm parameters was of predictive value for pregnancy after the first IUI cycle. In the first finished IUI episode, a positive relationship was found for ≤4% of morphologically normal spermatozoa (OR 1.39) and a moderate NIPMS (5–10 million; OR 1.73). Low NIPMS showed a negative relation (≤1 million; OR 0.42). The TPMSC had no predictive value. The multivariable model (i.e., sperm morphology, NIPMS, female age, male age, and the number of cycles in the episode) had a moderate discriminatory accuracy (area under the curve 0.73).
**Conclusion(s):** Intrauterine insemination is especially relevant for couples with moderate male factor infertility (sperm morphology ≤4%, NIPMS 5–10 million). In the multivariable model, however, the predictive power of these sperm parameters is rather low. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)
**Key Words:** Intrauterine insemination, IUI, prognostic value, semen analysis

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In a previous study, we evaluated the prognostic value of sperm morphology to predict pregnancy outcomes in couples treated with in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) (1). Our research filled a gap in the literature on the subject, which dated from the period before the introduction of ICSI in the 1990s and thus needed an update. Over the past decades, the reported percentages of morphologically normal spermatozoa has decreased with the introduction of stricter criteria and the tendency toward lower reference values (2). This is a disturbing factor in the use of sperm morphology as a prognostic factor for the probability of achieving a pregnancy. The strength of our study (1) was the selection of a stable period of time (i.e., 2004 to 2011) with respect to the methodology of sperm morphology assessment. In contrast to older studies, as reviewed by Coetzee et al. (3), we concluded that sperm morphology has no prognostic value in individual in vitro fertilization (IVF) and ICSI patients.

However, we can hypothesize that the role of sperm factors in intrauterine insemination (IUI) is different from their role in IVF and ICSI. Literature reviews reveal an ongoing debate on the value of sperm parameters as predictors of IUI outcome (4–6). More specifically, conflicting results have been reported for the influence of sperm morphology assessment using strict criteria on pregnancy outcomes with IUI (7–16). These studies are characterized by a lack of standardization, so repeating our previous study with couples treated with IUI is valuable.

Besides sperm morphology, there is disagreement about the predictive value of the total progressively motile sperm count (TPMSC) to predict IUI outcomes (6). In their review, Ombelet et al. (4) stated that the TPMSC has a substantial discriminative value. Others, however, have concluded that the TPMSC has poor sensitivity for selecting the couples most likely to conceive with IUI, but high specificity for identifying the couples unlikely to conceive with IUI (6, 17, 18). The required number of inseminated progressively motile spermatozoa (NIPMS) is under discussion as well, although in general a minimum of 5 million spermatozoa is stated as accurate (2).

We investigated the value of sperm parameters to predict ongoing pregnancy outcomes in couples treated with IUI during a methodologically stable period of time. The sperm parameters studied were sperm morphology and TPMSC, both assessed during fertility workup, and NIPMS assessed at the time of IUI. Additionally, the predictive power of these parameters for the probability of achieving a pregnancy is examined in conjunction with other known predictors.

## MATERIALS AND METHODS

### Study Population

In this retrospective, observational study, anonymized data sets were included of all couples who visited the fertility laboratory of the Radboud University Medical Centre Nijmegen for confirmed, finished IUI episode between January 1, 2004, and June 30, 2013. A finished episode is defined as a sequence of treatment cycles that ends when a cycle results in a pregnancy or when IUI treatment is stopped. Records were excluded when data on pregnancy outcome or sperm parameters were missing. In cases where multiple assessments of morphology and/or TPMSC were performed, the data from the most recent fertility workup were used. The ethics review board of the Radboud University Medical Center Nijmegen provided approval for this study.

### Study Period

The study period was based on the stability of methods for semen analysis and semen preparation. In our previous study (1), we established this period between the years 2004 and 2011. Our methods did not change since 2011; the period for the present study was extended to June 30, 2013.

### Semen Analysis

Sperm samples were collected preferably after 2 to 3 days of ejaculatory abstinence and were delivered to the laboratory within 1 hour. Semen analysis was performed as described in our previous study (1). Briefly, the volume was determined by aspirating the ejaculate with a scaled pipette, the sperm concentration was determined by counting in a Makler chamber, and the fraction of progressively motile spermatozoa was determined in a 20-$\mu$m deep wet preparation. For the sperm morphology assessment, a small drop of semen was mixed with an equal amount of aniline blue/eosin solution, which consisted of 2 g of eosin yellow and 25 g of aniline blue (VWR) in 100 mL of phosphate-buffered saline (Gibco-Invitrogen) and 1 mL of ethanol. The mix was spread on a microscopic slide and flame fixed. A total of 200 spermatozoa per slide were evaluated according to the current World Health Organization (WHO) criteria at an original magnification of $\times$1,000 (19, 20). From this sperm assessment during the fertility workup, the percentage of morphologically normal spermatozoa and the TPMSC were calculated.

### Intrauterine Insemination

We performed IUI in natural cycles or in cycles with mild ovarian stimulation. The semen preparation was performed using a one step (80%) PureSperm (Nidacon) gradient after dilution of the semen with 5-mL of wash medium (human tubal fluid medium; Gynotec) supplemented with 10% albumin (GPO; Sanquin). After centrifugation (500 $\times$ $g$), the semen was washed with wash medium, and the NIPMS was assessed in the samples used for insemination. The sperm variables were determined as described earlier, and the NIPMS was calculated by multiplying the volume by sperm concentration and the fraction of progressively motile sperm of the prepared semen. Approximately 2 weeks after insemination, a pregnancy test was performed; 8 to 10 weeks later, an ultrasound examination was used to confirm an ongoing pregnancy.

### Assessment of Variables

The main variables of interest in the predictive model were the percentage morphologically normal spermatozoa and the TPMSC. Both diagnostic sperm parameters were assessed