

B4.2 Novel measures of sperm DNA damage increase its usefulness to diagnose male infertility and predict live births following both IVF and ICSI

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Aims and Objectives: Sperm DNA fragmentation is a biomarker of male infertility resulting in poorer IVF outcomes. In addition to using conventional average Comet Score (ACS), we aim to quantify the proportion of sperm with low (LCS) or high (HCS) DNA damage to assess their effectiveness.

Content: Conventional ACS (mean of all comets scored) and two novel parameters LCS and HCS (% sperm with a statistically designated low or high score respectively) were assessed in 76 fertile sperm donors and 166 men with couples with idiopathic subfertility with Receiver Operator curve (ROC) analysis to determine their potential to diagnose male infertility. ROC analysis was further performed on samples from 381 male partners of subfertile couples undergoing IVF (101) or ICSI (280) to determine thresholds for each parameter and assess the livebirth rates (LBR) following ART using these ACS, LCS and HCS thresholds.

Relevance/Impact: The proportion of sperm with low or high levels of DNA damage provides discriminatory information for male infertility diagnosis and choice of ART pathway.

Outcomes: ACS >26%, HCS >4% and LCS <74% were all highly predictive of male infertility (ROC>0.9, p<0.0001). IVF LBR declined sharply once sperm DNA damage exceeded all ROC threshold levels identified with HCS >6% the most predictive of IVF failure (38% vs 13%; p<0.05). A trend for worsening ICSI LBR was also demonstrated using all parameter ROC thresholds but not achieving statistical significance. Trends in IVF and ICSI differed in that IVF LBRs decreased as damage increased whereas in ICSI, LBRs decreased but then remained stable.

Discussion: Unlike other assays, the Comet assay measures DNA damage in individual sperm enabling the degree of heterogeneity of the whole sperm population to be assessed.

This increases its accuracy to both diagnose male infertility and predict ART outcome.
