The incidence of varicocele is high in infertile men—in 19 to 41 percent who present for an infertility exam and in an estimated 60 to 80 percent of those diagnosed with secondary infertility. Research has documented that varicoceles adversely affect sperm function, but the exact mechanism of this negative effect has not yet been elucidated. The Cleveland Clinic evaluated the role of oxidative stress (OS) on sperm function and found that men with varicoceles have sperm with high levels of nuclear DNA damage.

High levels of seminal OS have been correlated with sperm dysfunction through different mechanisms that include lipid peroxidation of sperm plasma membrane and impairment of sperm metabolism, motility and fertilizing capacity. In addition, OS has been shown to affect the integrity of the sperm chromatin and to cause high frequencies of single and double DNA strand breaks. Recent data indicate that increased sperm nuclear DNA damage negatively impacts natural and assisted reproduction. Also, sperm chromatin/DNA is an independent measure of sperm quality that may have better diagnostic and prognostic capabilities than the standard sperm parameters. Researchers here hypothesized that spermatozoal dysfunction associated with varicoceles may be related, in part, to increased levels of sperm DNA damage caused by high levels of OS. A study was designed to examine and compare levels of sperm nuclear DNA damage using the sperm chromatin structure assay (SCSA) and OS among a group of infertile men clinically diagnosed with varicocele, a group of infertile men with normal genital examination, and fertile donors.

Sperm parameters and infertility status. Also, levels of reactive oxygen species were positively correlated with DNA damage \((P = .02; r = .57)\) in men with varicoceles (see table below).

The median (interquartile range) DNA fragmentation index (percent DFI) was significantly higher in the patients with varicoceles as compared to the fertile controls [25 (20, 35) versus 15 (10, 22); \(P = .002\)]. In addition, infertile patients with varicoceles had higher DFI values than infertile patients with a normal genital examination. The difference between these 2 groups, however, was not statistically significant. The presence of a varicocele was significantly correlated with DFI \((P = .04)\) after adjusting for standard sperm parameters and infertility status.

Results of the study indicate that infertile men with varicoceles have sperm with significantly high levels of nuclear DNA damage. The association of varicoceles with evidence suggesting that high levels of OS mediate the DNA fragmentation in spermatozoa of infertile men, we speculate that increased DNA damage in spermatozoa from varicocele patients is related, at least in part, to OS.

Further research in this area is needed to understand the exact mechanism(s) by which DNA damage increases in spermatozoa from infertile men with varicoceles and to determine whether correction of the varicocele can reduce such damage. Men with varicoceles should be counseled about the potential negative effects of increased sperm DNA damage on their fertility potential.