



Review Article

Improvement in Sperm Capacitation Measured by Cap-Score™ Demonstrated after Varicocele Repair

Samuel Aly¹ and Eric K Seaman^{2*}

¹Urology Resident Physician, Rutgers New Jersey Medical School, Newark, New Jersey, USA

²Male Reproductive Medicine and Surgery, New Jersey Urology, Millburn, New Jersey, USA

Abstract

Approximately 30% of infertile men have a significant varicocele, which may affect testicular function. Semen analysis remains an essential part of initial male fertility evaluation. However, its predictive ability is limited and therefore its use to assess fertility before and after varicocelectomy can be problematic. Cap-Score™ is a validated test using Monosialotetrahexosylganglioside (GM1) localization patterns to measure sperm capacitation and has been shown to prospectively predict male fertility. In this case report, Cap-Score™ and semen analysis were used to evaluate improvement in fertility after varicocelectomy. A 37-year-old Asian male presented with secondary infertility. Evaluation included scrotal ultrasound, serum testosterone, the Cap-Score™ male fertility assay and standard semen analysis before and after surgery. Following varicocele correction, there was improvement in Cap-Score™ from abnormal to normal, as well as in semen parameters of motility and Kruger morphology. Addition of Cap-Score™ to semen analysis may offer urologists a complementary tool to better evaluate the effectiveness of treatment of causes of male infertility, including varicocele.

***Corresponding author:** Eric K Seaman, Male Reproductive Medicine and Surgery, New Jersey Urology, Millburn, NJ 07041, New Jersey, USA, Tel: +1 9732189400; Fax: +1 9732189420; Email: eseaman@njurology.com

Citation: Aly S, Seaman EK (2018) Improvement in Sperm Capacitation Measured by Cap-Score™ Demonstrated after Varicocele Repair. J Reprod Med Gynecol Obstet 3: 013.

Received: August 27, 2018; **Accepted:** September 27, 2018; **Published:** October 11, 2018

Copyright: © 2018 Aly S and Seaman EK. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Introduction

Semen analysis remains a fundamental part of the male infertility evaluation. The test is an assessment of gross physical and observable microscopic characteristics of semen including a measurement of semen volume, pH, viscosity as well as measurements applicable to sperm such as the sperm density, percent motility, quality of motility and morphology. Despite the pervasiveness of its use, there is recognition of limitations of semen analysis with respect to accuracy, reliability and its ability to predict male fertility. This is likely due in part to the fact that standard semen analysis does not measure sperm function. Recently, Androvia Life Sciences introduced the Cap-Score™ male fertility assay, a sperm function test that measures sperm capacitation and the ability to undergo acrosome exocytosis, both of which are necessary events for a sperm to fertilize an egg.

Varicoceles are the most common surgically correctible cause of male infertility [1]. A large number of reports show improvement in semen parameters after correction of varicocele [2-4]. Using Cap-Score™ as an adjunct to the semen analysis may serve to provide a more reliable method of evaluating infertility caused by varicoceles and a better measurement of change in fertility after repair. In this case report, we evaluated a patient with bilateral varicoceles, abnormal preoperative semen analysis and Cap-Score™ with subsequent improvement in semen analysis and correction of Cap-Score™ from “abnormal” to “normal” post-varicocelectomy. This is the first such case report in the literature where the Cap-Score™ has been used in a clinical setting for assessing improvement after intervention.

Case Presentation

A 37 year old Asian male presented for evaluation of secondary infertility after 12 months of trying to conceive. The patient denied any interval changes in medical history since his prior live birth. He denies any significant past medical or surgical history. On physical exam, genital exam was significant for Grade 3 left varicocele. Pre-operative laboratory values demonstrate a total serum testosterone of 326 (normal 264-916) ng/dl, serum FSH 4.4 (normal 1.5-12.4) IU/mL and serum estradiol 28 (normal <39) pg/mL. Scrotal sonography shows 11 and 10 cc for left and right testicular volumes, a large left varicocele of 0.32 cm and moderate right varicocele of 0.23 cm. Post-operative serum and semen specimens were collected approximately four months after varicocelectomy.

With respect to performing the Cap-Score™ male fertility assay, a kit is provided by Androvia Life Sciences (Mountainside, NJ) that includes all necessary media, reagents and consumables. Following standard semen collection, the sperm are washed through a density gradient to remove seminal plasma. The sperm concentration is determined and modified human tubal fluid (Irvine Scientific, Santa Ana, CA) is added to each of two tubes. One tube is void and one contains 2-hydroxypropyl-β-cyclodextrin, which serves to capacitate the sperm [5]. After 3hr incubation, a fixative is added to the cells, which are then shipped overnight to Androvia’s laboratory, where the assay is performed. Androvia assesses over 150 sperm having different patterns of GM1 localization using fluorescence microscopy and

the percentage of sperm having patterns consistent with capacitation is defined as the Cap-Score™ [6].

Pre- and post-operative results shown below, demonstrate overall improvement in semen analysis parameters (Table 1), serum testosterone (Table 2) and correction of Cap-Score™ from “abnormal” to “normal” (Table 3).

	Volume	Sperm Density	Percent Motile	Kruger Morphology
*WHO 5 th percentile [7]	≥1.5 mL	≥15 M/mL	≥40%	≥4%
Pre-Operative	2.4 mL	49 M/mL	33%	3%
Post-Operative	2.0 mL	51 M/mL	65%	6%

Table 1: Semen analysis parameters, pre- and post varicocelectomy.
*World Health Organization (WHO) [7].

	Testosterone
Pre-Operative	326 ng/dl (normal range 264-916 ng/dl)
Post-Operative	426 ng/dl

Table 2: Total testosterone values pre- and post-varicocelectomy.

	Cap-Score™
Pre-Operative	19.1% (normal range >27.6%, mean 35.3; SD = 7.7%)
Post-Operative	35%

Table 3: Cap-Score™ values pre- and post-varicocelectomy.

Discussion

Cap-Score™ provides urologists with another diagnostic assay to assist in the evaluation and treatment of male infertility. Selvaraj et al., demonstrated that during sperm capacitation, a series of molecular mechanisms result in focal enrichment of GM1 on the plasma membrane of mature sperm [8]. They were also able to demonstrate that sperm with this specific GM1 localization pattern on the plasma membrane could undergo the acrosome reaction and induce fertilization. While there have been other assays developed to determine sperm capacitation, they are technically demanding and have not been incorporated into clinical practice [9]. Unlike the previous assays, the Cap-Score™ is technically feasible with a quantitative result and has been shown prospectively to predict male fertility [6,10]. In addition, the assay results are reproducible, whereas semen analysis results can have significant variability. Moody et al., was able to present the accuracy, repeatability and precision of Cap-Score™ [5].

As suggested by the results in this case study, Cap-Score™ could also be used to determine the effects of interventions designed to improve male fertility, such as surgical repair of varicocele. The functional changes that result from varicocele, which impede a man’s fertility, are poorly defined and remain somewhat contentious [11-13]. Nonetheless, increased Reactive Oxygen Species (ROS) and decreased antioxidant capacity have been observed in spermatozoa and semen samples obtained from individuals with varicocele [14].

While ROS play an important role in capacitation and maintenance of fertilizing ability, an over production may lead to the oxidation and dysfunction of lipids and proteins necessary for proper sperm function [15-17]. In fact, multiple studies have shown that patients presenting with varicocele produce sperm with modified membrane permeability, decreased protein tyrosine phosphorylation a hindered ability to undergo acrosome exocytosis and reduced zona pellucida and oolemma binding [18-21]. Interestingly, the surgical correction of varicocele can reduce the levels of ROS and increase antioxidants within seminal plasma, potentially improving the ability of sperm to respond to capacitation stimuli [22].

In this report, we found that although sperm density did not change appreciably from pre- to post-operative assessments, serum testosterone, the Cap-Score™, and sperm motility and morphology improved. Traditional semen analysis parameters do not always correlate with male fertility, suggesting that improvements in Cap-Score™ might more reliably reflect possible improvements in male fertility observed in response to varicocelectomy [23,24].

Conclusion

This is the first documentation in the literature about the clinical application of using Cap-Score™ to assess the effect of varicocelectomy on male fertility. Cap-Score™ may offer urologists a complementary tool for the evaluation of male infertility when used in conjunction with a semen analysis in the setting of varicocele or other male fertility related disorders.

Acknowledgement

Androvia Life Sciences for providing Cap-Score™ testing.

References

1. Belker AM (1981) The varicocele and male infertility. Urol Clin North Am 8: 41-51.
2. Agarwal A, Deepinder F, Cocuzza M, Agarwal R, Short RA, et al. (2007) Efficacy of varicocelectomy in improving semen parameters: New meta-analytical approach. Urology 70: 532-538.
3. Nork JJ, Berger JH, Crain DS, Christman MS (2014) Youth varicocele and varicocele treatment: A meta-analysis of semen outcomes. Fertil Steril 102: 381-387.
4. Kruger T (2016) Critical appraisal of conventional semen analysis in the context of varicocele. Asian J Androl 18: 202-204.
5. Moody MA, Cardona C, Simpson AJ, Smith TT, Travis AJ, et al. (2017) Validation of a laboratory-developed test of human sperm capacitation. Mol Reprod Dev 84: 408-422.
6. Cardona C, Neri QV, Simpson AJ, Moody MA, Ostermeier GC, et al. (2017) Localization patterns of the ganglioside G_{M1} in human sperm are indicative of male fertility and independent of traditional semen measures. Mol Reprod Dev 84: 423-435.
7. WHO (2010) WHO laboratory manual for the examination and processing of human semen (5th edn). WHO, Geneva, Switzerland.
8. Selvaraj V, Buttke DE, Asano A, McElwee JL, Wolff CA, et al. (2007) GM1 dynamics as a marker for membrane changes associated with the process of capacitation in murine and bovine spermatozoa. J Androl 28: 588-599.
9. Visconti PE, Bailey JL, Moore GD, Pan D, Olds-Clarke P, et al. (1995) Capacitation of mouse spermatozoa. I. Correlation between the capacitation state and protein tyrosine phosphorylation. Development 121: 1129-1137.

10. Schinfeld J, Sharara F, Morris R, Palermo GD, Rosenwaks Z, et al. (2018) Cap-Score™ prospectively predicts probability of pregnancy. *Mol Reprod Dev*.
11. Skoog SJ, Roberts KP, Goldstein M, Pryor JL (1997) The adolescent varicocele: What's new with an old problem in young patients? *Pediatrics* 100: 112-121.
12. Hauser R, Paz G, Botchan A, Yogev L, Yavetz H (2001) Varicocele: Effect on sperm functions. *Hum Reprod Update* 7: 482-485.
13. Naughton CK, Nangia AK, Agarwal A (2001) Pathophysiology of varicoceles in male infertility. *Hum Reprod Update* 7: 473-481.
14. Hendin BN, Kolettis PN, Sharma RK, Thomas AJ Jr, Agarwal A (1999) Varicocele is associated with elevated spermatozoal reactive oxygen species production and diminished seminal plasma antioxidant capacity. *J Urol* 161: 1831-1834.
15. Kodama H, Kuribayashi Y, Gagnon C (1996) Effect of sperm lipid peroxidation on fertilization. *J Androl* 17: 151-157.
16. Agarwal A, Makker K, Sharma R (2008) Clinical relevance of oxidative stress in male factor infertility: An update. *Am J Reprod Immunol* 59: 2-11.
17. Gonçalves FS, Barretto LS, Arruda RP, Perri SH, Mingoti GZ (2010) Effect of antioxidants during bovine *in vitro* fertilization procedures on spermatozoa and embryo development. *Reprod Domest Anim* 45: 129-135.
18. Fuse H, Kazama T, Katayama T (1991) Hypoosmotic swelling test in patients with varicocele. *Arch Androl* 27: 149-154.
19. Buffone MG, Brugo-Olmedo S, Calamera JC, Verstraeten SV, Urrutia F, et al. (2006) Decreased protein tyrosine phosphorylation and membrane fluidity in spermatozoa from infertile men with varicocele. *Mol Reprod Dev* 73: 1591-1599.
20. Vigil P, Wöhler C, Bustos-Obregón E, Comhaire F, Morales P (1994) Assessment of sperm function in fertile and infertile men. *Andrologia* 26: 55-60.
21. Benoff S (1998) Modelling human sperm-egg interactions *in vitro*: Signal transduction pathways regulating the acrosome reaction. *Mol Hum Reprod* 4: 453-471.
22. Mostafa T, Anis TH, El-Nashar A, Imam H, Othman IA (2001) Varicocelectomy reduces reactive oxygen species levels and increases antioxidant activity of seminal plasma from infertile men with varicocele. *Int J Androl* 24: 261-265.
23. Guzick DS, Overstreet JW, Factor-Litvak P, Brazil CK, Nakajima ST, et al. (2001) Sperm morphology, motility, and concentration in fertile and infertile men. *N Engl J Med* 345: 1388-1393.
24. van der Steeg JW, Steures P, Eijkemans MJ, F Habbema JD, Hompes PG, et al. (2011) Role of semen analysis in subfertile couples. *Fertil Steril* 95: 1013-1019.



Journal of Anesthesia & Clinical Care
Journal of Addiction & Addictive Disorders
Advances in Microbiology Research
Advances in Industrial Biotechnology
Journal of Agronomy & Agricultural Science
Journal of AIDS Clinical Research & STDs
Journal of Alcoholism, Drug Abuse & Substance Dependence
Journal of Allergy Disorders & Therapy
Journal of Alternative, Complementary & Integrative Medicine
Journal of Alzheimer's & Neurodegenerative Diseases
Journal of Angiology & Vascular Surgery
Journal of Animal Research & Veterinary Science
Archives of Zoological Studies
Archives of Urology
Journal of Atmospheric & Earth-Sciences
Journal of Aquaculture & Fisheries
Journal of Biotech Research & Biochemistry
Journal of Brain & Neuroscience Research
Journal of Cancer Biology & Treatment
Journal of Cardiology & Neurocardiovascular Diseases
Journal of Cell Biology & Cell Metabolism
Journal of Clinical Dermatology & Therapy
Journal of Clinical Immunology & Immunotherapy
Journal of Clinical Studies & Medical Case Reports
Journal of Community Medicine & Public Health Care
Current Trends: Medical & Biological Engineering
Journal of Cytology & Tissue Biology
Journal of Dentistry: Oral Health & Cosmesis
Journal of Diabetes & Metabolic Disorders
Journal of Dairy Research & Technology
Journal of Emergency Medicine Trauma & Surgical Care
Journal of Environmental Science: Current Research
Journal of Food Science & Nutrition
Journal of Forensic, Legal & Investigative Sciences
Journal of Gastroenterology & Hepatology Research
Journal of Gerontology & Geriatric Medicine
Journal of Genetics & Genomic Sciences
Journal of Hematology, Blood Transfusion & Disorders
Journal of Human Endocrinology
Journal of Hospice & Palliative Medical Care
Journal of Internal Medicine & Primary Healthcare
Journal of Infectious & Non Infectious Diseases
Journal of Light & Laser: Current Trends
Journal of Modern Chemical Sciences
Journal of Medicine: Study & Research
Journal of Nanotechnology: Nanomedicine & Nanobiotechnology
Journal of Neonatology & Clinical Pediatrics
Journal of Nephrology & Renal Therapy
Journal of Non Invasive Vascular Investigation
Journal of Nuclear Medicine, Radiology & Radiation Therapy
Journal of Obesity & Weight Loss
Journal of Orthopedic Research & Physiotherapy
Journal of Otolaryngology, Head & Neck Surgery
Journal of Protein Research & Bioinformatics
Journal of Pathology Clinical & Medical Research
Journal of Pharmacology, Pharmaceutics & Pharmacovigilance
Journal of Physical Medicine, Rehabilitation & Disabilities
Journal of Plant Science: Current Research
Journal of Psychiatry, Depression & Anxiety
Journal of Pulmonary Medicine & Respiratory Research
Journal of Practical & Professional Nursing
Journal of Reproductive Medicine, Gynaecology & Obstetrics
Journal of Stem Cells Research, Development & Therapy
Journal of Surgery: Current Trends & Innovations
Journal of Toxicology: Current Research
Journal of Translational Science and Research
Trends in Anatomy & Physiology
Journal of Vaccines Research & Vaccination
Journal of Virology & Antivirals

Submit Your Manuscript: <http://www.heraldopenaccess.us/Online-Submission.php>