Older Age Is Associated With Similar Improvements in Semen Parameters and Testosterone After Subinguinal Microsurgical Varicocelectomy

Wayland Hsiao, James S. Rosoff, Joseph R. Pale, Eleni A. Greenwood and Marc Goldstein*

From the Center for Male Reproductive Medicine, Department of Urology (WH, JSR, JRP, EAG, MG), and Institute for Reproductive Medicine (WH, MG), Weill Cornell Medical College and The Population Council Center for Biomedical Research (WH, MG), New York, New York

Abbreviations and Acronyms

TMC = total motile sperm count

Submitted for publication June 25, 2010.

Study received institutional review board approval.

Supported by a grant from The Frederick J. and Theresa Dow Wallace Fund of New York Community Trust (Hsiao).

* Correspondence: 525 E. 68th St., Starr 900, New York, New York 10065.

Purpose: It is generally accepted that men with clinically palpable varicocele are at high risk for a progressive decrease in fertility and testosterone levels with time. Varicocelectomy is thought to improve testicular function or at least halt the accelerated decrease in testicular function associated with varicocele. Substantial controversy exists as to whether varicocelectomy is effective in older men, possibly due to irreversible testicular damage or limited potential for recovery from varicocele induced damage.

Materials and Methods: We retrospectively reviewed the records of men who underwent microsurgical subinguinal varicocelectomy, as done by a single surgeon. Demographics, patient questionnaires, operative notes, charts, testosterone and semen analysis were reviewed. Patients were divided into 3 groups based on age at surgery, including less than 30, 30 to 39 and 40 years or greater.

Results: A total of 272 men met study inclusion criteria. In all 3 age groups we noted similar testosterone and baseline semen analysis parameters. There were significant increases in sperm concentration and total sperm count in all age groups. When analysis was restricted to men with baseline testosterone 400 ng/dl or less, there was a mean 110, 133 and 136 ng/dl increase in 21 men who were 40 years old or older, in 30 who were 30 to 39 years old and in 21 who were younger than 30 years, respectively.

Conclusions: Microsurgical varicocelectomy resulted in significant increases in sperm concentration, total sperm count and testosterone in all age groups studied, including men in the fifth and sixth decades of life. Microsurgical varicocelectomy should be offered to older men for infertility and/or hypogonadism.

Key Words: testis; varicocele; infertility, male; hypogonadism; aging

Varicoceles generally appear during or shortly after puberty and are found in 15% of men with up to 35% with primary infertility and 70% to 81% with secondary infertility presenting with varicocele.[1] It is generally accepted that men with varicocele are at risk for an accelerated, progressive decrease in fertility and testosterone with time if left unrepaired.[1–9] Varicocelectomy is thought to improve testicular function or at least halt the gradual decrease in testicular function associated with varicocele. Many studies show that varicocelectomy improves semen parameters, hormonal profiles and pregnancy rates.[1,5,10–12] Most of these studies were not controlled, randomized or stratified by patient age.

0022-5347/11/1852-0620/0
THE JOURNAL OF UROLOGY®

Vol. 185, 620-625, February 2011
Printed in U.S.A.
DOI:10.1016/j.juro.2010.09.114

Controversy exists as to whether varicocelectomy is as effective in older men due to irreversible testicular damage by the longstanding varicocele or limited potential for recovery from varicocele induced damage in older testes. The clinical implication is that if varicocelectomy is less effective in older men, perhaps it should not be offered with men electing androgen replacement and assisted reproduction instead. There are few studies of the effect of age at surgery on varicocelectomy outcomes. A small study by Ishikawa et al showed no significant difference in the response to varicocelectomy with respect to age.[13] Zini et al found similar improvements in semen analysis parameters in older men after varicocelectomy when a 40-year-old cutoff was used.[14]

We tested the hypothesis that varicocelectomy is less effective in older men for treating infertility and/or male hypogonadism. We retrospectively reviewed the records of patients who underwent subinguinal microsurgical varicocelectomy at a tertiary referral center, and reviewed testosterone and semen analysis results.

MATERIALS AND METHODS

Patients and Evaluation

After obtaining institutional review board approval we retrospectively reviewed the records of patients who underwent subinguinal microsurgical varicocelectomy, as done by a single surgeon from January 1996 to January 2009. All patients were referred for infertility or male hypogonadism (low testosterone) and all were older than 16 years. In our practice indications for varicocelectomy include clinically palpable varicocele with semen parameter abnormalities, clinically palpable varicoceles associated with pain, clinically palpable varicocele associated with infertility without genetic abnormality, grade 3 varicocele associated with testicular atrophy and total testosterone less than 400 ng/dl on 2 morning laboratory draws. Only men with preoperative and postoperative semen analyses, and/or testosterone results were included in analysis. Patients who underwent concomitant varicocelectomy and vasectomy were excluded from analysis, as were men with a history of orchiectomy or solitary testis. We reviewed the charts of 1,469 patients, of whom 272 (18.5%) met study inclusion criteria and were included in the final analysis.

Demographics, patient questionnaires, operative notes, clinical charts, laboratory reports and semen analyses were reviewed. A full history was obtained and physical examination was done by the primary surgeon in all cases. Physical examination included a full general and urological examination with particular emphasis on testicular volume, and varicocele presence and grade. All testicular volume measurements were made at physical examination by the attending physician using an orchidometer. Varicocele clinical grading was done according to the method of Dubin and Amelar.[11] Our surgical technique of subinguinal microscopic inguinal varicocelectomy with testicular delivery was described previously.[15]

We reviewed all semen analysis data and hormonal profiles available in the clinical record. All testosterone levels were obtained before 10 a.m. To be included in our final analysis postoperative laboratory values had to be obtained at least 2 months after and within 3 years of surgery. In cases in which 2 or more analyses were available after surgery we averaged the results of the first 2 semen analyses and used this value in our final analysis. TMC per ejaculate was calculated by the formula, TMC per ejaculate = ejaculate volume in ml $\times$ concentration per ml in millions per ml $\times$ motile fraction in % motile sperm.[16] All patients who were azoospermic and severely oligospermic (less than 1.0×10^7 spermatozoa) at initial semen analysis were excluded from semen analysis. If multiple postoperative hormone values were available, the test done closest to surgery was used.

Statistical Analysis

Patients were divided into 3 groups based on age at surgery, including less than 30, 30 to 39 and 40 years old or older. All patients were stratified by age at surgery and baseline characteristics were compared. Results are shown as the mean $\pm$ SE. We used 1-way ANOVA to compare continuous variables with the Tukey HSD post hoc test applied when ANOVA revealed statistical significance. The Pearson chi-square test was used to compare binary variables and the Kruskal-Wallis test was used to compare categorical variables across all age categories.

To compare preoperative and postoperative hormonal and semen analysis results we applied the paired 2-sample t test. Analysis was restricted to patients with matched preoperative and postoperative semen analysis, and/or hormonal profile results. Patients on clomiphene citrate or aromatase inhibitors (anastrozole) were excluded from testosterone subanalysis, as were those with azoospermia at baseline. Continuous variables were evaluated for normal distribution with the Kolmogorov-Smirnov test. For semen analysis total sperm count and concentration we applied cube root transformation for paired t test analysis to obtain a normal distribution,[16] which was confirmed by the Kolmogorov-Smirnov test. All results are shown as the mean $\pm$ SE with $p < 0.05$ considered statistically significant. Statistical analysis was done with JMP® and SPSS® 16.0.

RESULTS

Baseline Characteristics

A total of 272 men met study inclusion criteria and were divided into 3 groups based on age at surgery, including 74, 187 and 85 who were younger than 30, 30 to 39 and 40 years old or older, respectively (mean 35.6 $\pm$ 0.4). Average partner age was 32.3 $\pm$ 0.3 years and pregnancy had been attempted for a mean of 23.7 $\pm$ 1.2 months. As expected, stratification by age at surgery showed that older men tended to have older partners and the percent of patients with proven fertility with the current partner increased. In all 3 age groups baseline testosterone and baseline semen analysis parameters were similar (table 1).