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Semen quality and risk factors for mortality

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To the Editor:

A short series of recent studies have shown that men with lower quality semen – as indexed by concentration, count, motility – have a raised risk of subsequent mortality,¹ chronic disease,² and health service use.³ With data in this area being drawn from fertility clinic samples where potentially important covariates have, with few exceptions,³ typically not been collected, the possibility that the reported semen quality–health relationships are biased by unmeasured confounding remains. While there seems to be a consensus that selected risk factors for mortality – cigarette smoking,⁴ higher alcohol intake,⁵ and obesity or overweight⁶ – are correlated with poorer semen quality, there is a paucity of evidence for many other characteristics, particularly biomarkers.

Described in detail elsewhere,^{7;8} the Vietnam Experience Study was devised as a cohort study to examine the post-theatre health experience of Vietnam war-era male army personnel who had entered the service in the 1960s and 70s. The protocol was approved by the US Office for Technology Assessment, the Department of Health and Human Sciences Advisory Committee, the Agent Orange Working Group Science Panel, and a panel from the US Centers for Disease Control. Following an orientation session, potential participants also provided written consent.

Data in the present study are cross-sectional. During a telephone survey in 1985, study members reported their health, health behaviors, marital status, and socioeconomic characteristics, largely in response to standard enquiries. In a medical examination the following year, after an overnight fast, participants provided a blood sample from which triglycerides, cholesterol fractions, and serum glucose level were measured. With the participant in a seated position, blood pressure, resting heart rate, and pulmonary function were assessed.

Study members without self-reported vasectomy were asked to abstain from ejaculation for at least 48 hours prior to semen collection and were provided with a plastic receptacle with insulating cups to maintain sample temperature.⁷ Following masturbation in their hotel rooms without the use of lubricants or condoms, the men noted the number of days since their most recent ejaculation and delivered samples to a processing room within 30 minutes. We used the following three markers of semen quality: sperm concentration

(millions of sperm per ml of semen), sperm count (millions of sperm in the total ejaculate), and sperm motility (percentage of motile sperm).

A total of 571 men provided a semen sample, and after excluding participants whose samples were not viable owing to spillage, complete results were available on all three measures for 463 (our analytic sample). The mean age of this group was 38.9 yr (standard deviation 2.5) and it was predominantly ethnically white (83%). The mean sperm concentration was 105 (SD=83) millions of sperm per ml of semen, the mean sperm count was 272 (standard deviation 262) million in the total ejaculate, and the mean percent motility was 59 (standard deviation 24). For analysis, sperm concentration and sperm count were log transformed and all three measures were standardized (Mean=0, SD=1).

In the Table (categorical risk factors) and eTable, <http://links.lww.com/EDE/B459> (continuous) we show the relationships between the standardized values of these three markers of semen quality and an array of risk factors for mortality. In general, men with higher levels of mortality risk factors had the least favorable semen quality profile, and relationships were most commonly seen for sperm concentration. As depicted in the Table, lower sperm concentrations were evident in black men and cigarette smokers. All markers of socio-economic status were linked to semen quality such that men with more basic educational attainment, a modest income, and lower occupational prestige had a lower sperm concentration. Of the more novel relationships examined, associations with mortality risk factors were again typically strongest for sperm concentration, followed by sperm count, and sperm motility.

The present study, though hampered by a small sample size, provides some empirical support for selected variables being candidate confounders and mediators in studies of sperm concentration and disease risk.

References

- (1) Jensen TK, Jacobsen R, Christensen K, Nielsen NC, Bostofte E. Good semen quality and life expectancy: a cohort study of 43,277 men. *Am J Epidemiol* 2009; 170(5):559-565.
- (2) Latif T, Kold JT, Mehlsen J, Holmboe SA, Brinth L, Pors K et al. Semen Quality as a Predictor of Subsequent Morbidity: A Danish Cohort Study of 4,712 Men With Long-Term Follow-up. *Am J Epidemiol* 2017; 186(8):910-917.
- (3) Latif T, Lindahl-Jacobsen R, Mehlsen J, Eisenberg ML, Holmboe SA, Pors K et al. Semen quality associated with subsequent hospitalizations - Can the effect be explained by socio-economic status and lifestyle factors? *Andrology* 2018; 6(3):428-435.
- (4) Sharma R, Harlev A, Agarwal A, Esteves SC. Cigarette Smoking and Semen Quality: A New Meta-analysis Examining the Effect of the 2010 World Health Organization Laboratory Methods for the Examination of Human Semen. *Eur Urol* 2016; 70(4):635-645.
- (5) Ricci E, Al BS, Cipriani S, Candiani M, Chiaffarino F, Vigano P et al. Semen quality and alcohol intake: a systematic review and meta-analysis. *Reprod Biomed Online* 2017; 34(1):38-47.
- (6) Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. *Hum Reprod Update* 2013; 19(3):221-231.
- (7) The Centers for Disease Control Vietnam Experience Study. Health status of Vietnam veterans. II. Physical Health. *JAMA* 1988; 259(18):2708-2714.
- (8) Batty GD, Shipley MJ, Mortensen LH, Boyle SH, Barefoot J, Gronbaek M et al. IQ in late adolescence/early adulthood, risk factors in middle age and later all-cause mortality in men: the Vietnam Experience Study. *J Epidemiol Community Health* 2008; 62(6):522-531.

Table. Age-adjusted association between semen quality and categorically scored risk factors for mortality in the Vietnam Experience Study (N=463)

	N	Differences in standardized values (95% CI) from reference group		
		Sperm concentration	Sperm count	Sperm motility
Age at medical examination (yrs)				
≤ 37	165	Ref	Ref	Ref
38 – 39	159	-0.01 (-0.23, 0.21)	-0.03 (-0.25, 0.19)	-0.10 (-0.32, 0.12)
40 – 47	139	0.00 (-0.22, 0.23)	0.15 (-0.08, 0.37)	0.00 (-0.23, 0.23)
Ethnic group				
White	385	Ref	Ref	Ref
Black	78	-0.37 (-0.67, -0.08)	-0.15 (-0.44, 0.15)	-0.18 (-0.47, 0.12)
Other	42	0.04 (-0.34, 0.42)	0.22 (-0.16, 0.61)	0.12 (-0.26, 0.51)
Marital status				
Married	343	Ref	Ref	Ref
Divorced/widowed/separated	78	-0.22 (-0.47, 0.02)	0.09 (-0.15, 0.34)	0.14 (-0.11, 0.39)
Never married	42	0.05 (-0.27, 0.38)	0.12 (-0.20, 0.44)	0.26 (-0.06, 0.58)
Smoking Habit				
Never smoker	127	Ref	Ref	Ref
Ex-smoker	119	-0.04 (-0.29, 0.20)	-0.06 (-0.31, 0.19)	-0.06 (-0.31, 0.19)
Current smoker	204	-0.26 (-0.48, -0.04)	-0.14 (-0.36, 0.08)	-0.06 (-0.28, 0.17)
Alcohol consumption				
Non/never drinker	177	Ref	Ref	Ref
≤7 drinks/week	179	0.09 (-0.12, 0.30)	0.07 (-0.14, 0.28)	0.18 (-0.02, 0.39)
≥8 drinks/week	106	0.06 (-0.19, 0.30)	0.11 (-0.13, 0.35)	0.14 (-0.10, 0.38)
Educational attainment				
≤ Grade 11	49	Ref	Ref	Ref
Grade 12	172	0.34 (0.03, 0.66)	0.22 (-0.10, 0.53)	0.11 (-0.21, 0.43)
≥ Grade 13	241	0.34 (0.04, 0.65)	0.21 (-0.09, 0.52)	0.14 (-0.17, 0.45)
Family income (\$/y)				
≤ 20,000	121	Ref	Ref	Ref
20,001 - 40,000	231	0.08 (-0.14, 0.30)	0.07 (-0.15, 0.29)	-0.08 (-0.31, 0.14)
> 40,000	96	0.43 (0.17, 0.70)	0.21 (-0.06, 0.48)	0.14 (-0.13, 0.418)