Built Environment and Semen Quality in Korean Men with a History of Infertility: A Cross-Sectional Study

Seung-Ah Choe
Korea University - Anam Campus: Korea University
Seulgi Kim
Seoul National University Graduate School of Public Health
Changmin Im
Department of Geography, Korea University
Sun-Young Kim
Department of cancer control and population health, Graduate School of Cancer Science and Policy, National Cancer Center
Gregory Wellenius
Boston University School of Public Health
You Shin Kim
Seoul Infertility and Genetics Clinic: CHA Fertility Center
Tae Ki Yoon
Seoul Infertility and Genetics Clinic: CHA Fertility Center
Dae Keun Kim (kdg070723@gmail.com)
Seoul Infertility and Genetics Clinic: CHA Fertility Center https://orcid.org/0000-0003-3237-6304

Research

Keywords: Semen, Sperm, Built environment, Greenness, Infertility

Posted Date: October 20th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-93400/v1

Built environment and semen quality in Korean men with a history of infertility: a cross-sectional study

Seung-Ah Choe [a, b], Seulgi Kim [c], Changmin Im [d], Sun-Young Kim [e], Gregory Wellenius [f], You Shin Kim [a], Tae Ki Yoon [a] , Dae Keun Kim [g]

[a] Department of Obstetrics and Gynecology, CHA Fertility Center Seoul Station, CHA University School of Medicine, Seoul, South Korea

[b] Department of Preventive Medicine, Korea University Medical College, Seoul, South Korea

[c] Graduate School of Public Health, Seoul National University, Seoul, South Korea

[d] Department of Geography, Korea University, Seoul, South Korea

[e] Department of Cancer Control and Population Health, Graduate School of Cancer Science and Policy, National Cancer Center, Gyunggi-do, South Korea

[f] Department of Environmental Health, Boston University School of Public Health, Boston, MA, United States

[g] Department of Urology, CHA Fertility Center Seoul Station, CHA University School of Medicine, Seoul, South Korea

Address for Correspondence:

Dae Keun Kim

Department of Urology, CHA Fertility Center Seoul Station,

CHA University School of Medicine, 416,

Hangang-daero, Jung-gu, Seoul 04367, Korea.
Email: kdg070723@gmail.com

Background: There is growing interest in the potential impact of the physical environment on human fertility. This study aimed to explore the association between built environment and semen parameters among men who sought fertility evaluation.

Methods: This is a cross-sectional study involving 5,886 men living in the Seoul Capital Area whose semen was tested at a single fertility center during 2016–2018. Environmental exposures evaluated were distance to fresh water (river and lake), the coast, major roadways, and neighborhood greenness measured by Normalized Difference Vegetation Index (NDVI). Outcome indicators were semen volume, sperm concentration, percentage of progressive motility, vitality, normal morphology, and total motile sperm count. We used linear regression to model standardized values of six semen quality indicators.

Results: Majority of the study population (mean age 39 years) were white-collar workers, clerks, and service workers. None of the mean values of semen quality indicators showed linear trends across quartiles of built environment components. Linear associations between built environment features and semen quality indicators were not evident except for NDVI within 500 m and sperm vitality (β = 0.05 per 0.1-increase; 95% confidence interval (CI): 0.01, 0.09). The 2nd quartile of distance to fresh water was associated with lower progressive motility compared to the 1st quartile (β = −0.10; 95% CI: −0.17, −0.03). Proportion of vitality was higher among men in the 2nd quartile of distance to roadways than those in the 1st quartile (0.08; 95% CI: 0.01, 0.15). Men in the 2nd quartile of NDVI showed higher total motile sperm count than those in the 1st quartile (0.09; 95% CI: 0.01, 0.17). In multi-exposure model, the positive association between NDVI and vitality remained (0.03, 95% CI: 0.00, 0.06).

Conclusions: This study contributes potential evidence regarding the impact of built environment on male fertility; specifically, a positive association between residential greenness and percentage of sperm vitality among Korean men with a history of infertility.

Keywords: Semen, Sperm, Built environment, Greenness, Infertility

Background

Growing evidence suggests potential impacts of the outdoor environment on human health. It has been suggested that components of built and the natural environment may influence levels of psychological stress, physical activity, and social relationships; and thereby, potentially improve or worsen human health and wellbeing [1-3]. For example, neighborhood green space has been associated with many beneficial health effects, including reduced all-cause and cardiovascular mortality and improved mental health, possibly mediated by less air pollution, heat and stress, and increased physical activity and social contacts [4].

Male reproductive function is highly sensitive to various physical agents generated by industrial activities [5, 6]. In addition, semen quality itself reflects general health condition, since it is affected during the early stage of medical disorders [7, 8]. Therefore, assessing the relationship between residential environment and semen quality would expand our understanding of the potential role of environmental factors in human reproductive health. Prior studies found that exposure to ubiquitous chemicals including endocrine disruptive chemicals and air pollutants is associated with reduced semen quality [9-11]. Given the association of physical environment with human fertility, male reproductive potential represented by semen quality may be associated with features of the built environment. In this study, we aimed to assess the association between the residential built environment and six parameters indicative of semen quality among men with a history of infertility.

Methods

Study data

This study was a cross-sectional study conducted among men who undertook semen tests between January 2016 and September 2018 at the CHA fertility center, Seoul Station

— the largest single fertility center in the Republic of Korea. Semen tests were conducted as an initial evaluation in all couples who visited the center for a diagnostic purpose. Eligibility criteria include being aged 20–69 years. We restricted our analysis to those living in the Seoul Capital Area, which consists of the metropolitan area of Seoul, Incheon, and Gyeonggi Provinces where the traveling time to the Seoul clinic is within one hour. Excluding those diagnosed with varicocele, azoospermia, cryptorchidism, and a known chromosomal abnormality, we obtained semen analysis results of a total of 5,886 Korean men. We included only the first examination result of each patient to minimize the possible impact of medical intervention. Information on body mass index (BMI), occupation, and smoking was retrieved from their medical records. These analyses are based on retrospective chart reviews and thus the consent requirement was waived. This study is approved by the institutional review board of Gangnam CHA Hospital (approval No: GCI-18-48).

Measurement of built environment

The Korean peninsula is mainly mountainous along its east coast, most of its river water flows west, and highly populated towns are located mostly in the north-west region. Four built environment components commonly used in prior studies were measured: distance to fresh water, distance to the coast, distance to major roadways, and Normalized Difference Vegetation Index (NDVI) [12-15]. We used distance to the nearest major roadway since it is often used as a proxy for long-term residential levels of air and/or noise pollution due to traffic [16]. Distance to the nearest fresh water body, coast, and the average NDVI within a 500 m circular buffer were assessed as indicators of neighborhood restorative environment (Supplementary Fig. 1), as in previous studies [15, 17]. The distance from the geocoded address to the environmental variables was calculated using Arcmap's Spatial Join analytical tool, which analyzes the spatial relationship between two geographical features. We defined the distance between any two features as the shortest separation between them, such that the two features are closest to each other. Euclidean distance to environmental features was calculated up to the boundary of a polygon, not to the center or centroid. For geospatial analyses, we used ArcGIS Desktop v. 10.5 (ESRI, Redlands, CA).

River and lake data were integrated into data on fresh water. Both data sets were retrieved from the National Spatial Data Infrastructure (http://www.nsdi.go.kr). River data was retrieved on January 21, 2016, and lake data on July 5, 2019. Integrated data is a nationwide polygonal data set consisting of 209,216 inland water bodies. We used coastline data provided by the National Geographic Information Institute and retrieved via the National Spatial Data Infrastructure portal (www.nsdi.go.kr). The nationwide polyline dataset was compiled on July 5, 2019. We calculated the distance perpendicular to the closest coastline from a geocoded point.

Data on major roads were obtained from national standard node links provided by the Korean Transport Database (KTDB) of the Korea Transport Institute (http://www.ktdb.go.kr). The original road data set was compiled on September 20, 2019, and was classified into nine categories: national highways, metropolitan city highways, general national roads, metropolitan city roads, government-financed provincial roads, provincial roads, district roads, highway link lamps, and other roads. In this study, we defined major roads as national highways, metropolitan city highways, metropolitan city roads, highway link lamps, and roads more than six lanes wide in other classes.

For data on NDVI, we used Landsat 7 satellite data provided by the United States Geological Survey (USGS) (https://earthexplorer.usgs.gov/). We assessed NDVI over the entire satellite image of the Korean peninsula from a combination of 13 Landsat satellite images taken over June, September, and October 2017 for cloud-free observation. The reasons for combining satellite image data for the above three months are as follows: 1) Since the revisit time of Landsat 7 is 16 days, it takes at least three visits and a month and a half to cover the entire Korean peninsula; and 2) In order to improve the accuracy of the

NDVI value, only satellite images with less than 10% of the area obscured by clouds during this period were extracted.

Semen collection and assessment

Semen analysis was done as described in a previous study [18]. In brief, patients were asked to produce semen samples in the andrology laboratory by masturbating into a sterile plastic cup after 3 to 5 days of sexual abstinence. The semen specimen was left for 30 minutes at room temperature (22°C–24°C) for liquefaction. General semen quality parameters were assessed based on the 2010 World Health Organization (WHO) criteria [19]. Sperm morphology was analyzed after centrifugation of semen with a resuspended pellet dyed with Diff-Quik fixative solution. The fixed specimen was then immersed in oil dropped on a microscope slide and observed using x1000 polarized microscopy. We assessed six continuous indicators (volume, sperm concentration, percentage (%) of progressive motility, vitality, normal morphology, and total motile sperm count) obtained via semen analysis. Total motile sperm count is defined as the number of moving sperm in the entire ejaculate, and is calculated by multiplying the volume by the concentration (million/mL) by the motility (%).

Statistical analyses

Descriptive analyses involved calculation of mean and standard deviations or frequencies and percentages (%) for demographic characteristics and semen quality parameters. We conducted multiple imputation by chained equations (MICE) for the missing covariate data [20], assuming data were missing at random and were conditioned upon the variables included in the imputation model. This study conducted three main analyses: First, we explored the pairwise correlation structure between three built environment components and sperm quality indicators, normalized using z-scores. Second, we tested for heterogeneity and linear trends in the mean values of sperm quality indicators across quartiles of environmental exposures using the Kruskal-Wallis rank sum test and Kendall's rank correlation test, respectively. Third, after examining the shape of relationships using a generalized additive model with a spline function and adjustment for potential covariates (R software ver. 3.6.2), we used linear regression models to estimate the change in mean values of sperm quality indicators per inter-quartile range (IQR)-increase and for each quartile of exposure to the built environment (denoted as Q1, Q2, Q3, and Q4). We included individual characteristics such as age (categorized as 20s, 30s, 40s and 50s), BMI (< 23, 23-24.99, 25-29.99, and ≥30 kg/m^2) based on the criteria for Asian populations [21], occupation (2 groups), current smoking (yes or no), season (Mar-May, Jun-Aug, Sep-Nov, Dec-Feb), and clustering effect of district (‘*Shigungu*’, n=68) in a generalized estimating equation to adjust for potential confounding effects. We additionally explored linear associations between built environment and six semen quality indicators with a multi-exposure model. A two-sided p-value of < 0.05 was considered statistically significant.

Results

The mean age of the study population was 39 years (Table 1). The vast majority (96%) were white-collar workers, clerks, or service workers. Half of the men (49.3%) were obese (BMI ≥ 25 kg/m^2) and were smokers at the time of examination. Regarding environmental exposures, the median distance to fresh water, the coast, and a major roadway was 382.8, 24869.5 and 486.7 m, respectively. The median NDVI was −0.2. The mean semen volume and concentration were 3.1 mL and 104.3 million/mL, respectively. The proportion of progressive motility and vitality were 45.6% and 62.6%, on average. The mean percentage of normal morphology was 3.7%. The mean value of the calculated total motile sperm count was 142.5 million per ejaculate. The pairwise correlation coefficients between four components of built environment and six sperm quality indicators were mostly low (Supplementary Fig. 2). There was a positive correlation between the proportion of progressive motility and the proportion of vitality (ρ = 0.74). There were weak correlations among the four built environment components.

Table 1. Characteristics of 5,886 Korean infertile men

Variables	Study population
Age (years)	39.0 ± 4.6
Body mass index (kg/m^2)	
< 23	1454 (24.7%)
23-24.9	1530 (26.0%)
25-29.9	2379 (40.4%)
≥30	523 (8.9%)
Occupation	
White-collar workers, Clerks, Service workers	5667 (96.3%)
Others	219 (3.7%)
Current smoking	3012 (51.2%)
Season	
Mar-May	1652 (28.1%)
Jun-Aug	1550 (26.3%)
Sep-Nov	1169 (19.9%)
Dec-Feb	1515 (25.7%)
Environmental exposures	
Distance to fresh water (m)	453.2 ± 304.0 (Median: 382.8, IQR: 405.1)
Distance to coast (m)	24869.5 ± 8210.3 (Median: 24609.6, IQR: 8948.2)
Distance to major road (m)	1053.9 ± 1946.8 (Median: 486.7, IQR: 810.1)
NDVI	-0.1 ± 0.1 (Median: -0.2, IQR: 0.1)
Sperm parameters	
Volume (mL)	3.1 ± 1.8
Count (million/mL)	104.3 ± 68.6
Progressive motility (%)	45.6 ± 13.2
Vitality (%)	62.6 ± 12.5
Morphology (%)	3.7 ± 1.8
Total motile sperm count (million)	142.5 ± 111.0

NDVI, Normalized Difference Vegetation Index; IQR, interquartile range. Continuous variables are presented as mean ± standard deviation. Others in occupation includes those unemployed.

The mean value of progressive sperm motility was different across quartiles of distance to fresh water and a major roadway (Supplementary Table 1). Proportion of progressive motility was highest in those with 1st quartile of distance to fresh water. For distance to a major roadway, progressive motility was highest in the 2nd quartile and lowest in the 4th quartile. None of the semen quality parameters showed a linear trend across quartiles of built environment components.

Linear associations between built environment features and semen quality indicators were not evident except for NDVI within 500 m (Table 2). An IQR-increase in NDVI (0.1) was associated with 0.05-increase in z-score of vitality (95% confidence interval (CI): 0.01, 0.09). In the analyses using quartiles of exposures, living at the maximum distance to fresh water (i.e., in the 4th quartile) was generally associated with lower semen quality, but this did not reach statistical significance. The 2nd quartile of distance to fresh water (209.9–382.8m) was associated with lower percentage of progressive motility compared with the 1st quartile (β = −0.10, 95% CI: −0.17, −0.03). The proportion of vitality was higher in men in the 2nd quartile of distance to a major roadway compared with those in the 1st quartile (0.08; 95% CI: 0.01, 0.15). The association between NDVI and sperm vitality was positive when comparing the 4th (−0.08–0.35) versus 1st quartile (−0.34 – −0.20). Men in the 2nd quartile of NDVI had a higher total motile sperm count than those in the 1st quartile (0.09; 95% CI: 0.01, 0.17). The association between NDVI and the z-score for sperm vitality had the form of a cubic (S-shaped) pattern (Supplementary Fig. 3). None of the semen quality indicators was associated with distance to the coast. In the multi-exposure model, linear associations between built environment features and semen quality indicators were not evident except for that between NDVI and vitality (0.03; 95% CI: 0.00, 0.06; Figure 1).

Table 2. Association between six semen quality parameters and four built environment components in single exposure models among 5,886 Korean infertile men

	Semen volume	Sperm concentration	% of progressive motility	% of vitality	% of morphology	Total motile sperm count
Distance to fresh water						
Per IQR increase	-0.01 (-0.04, 0.03)	0.00 (-0.04, 0.03)	0.01 (-0.03, 0.04)	0.02 (-0.01, 0.06)	0.00 (-0.04, 0.03)	0.00 (-0.04, 0.03)
Quartiles of distance						
Q1	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)
Q2	-0.01 (-0.09, 0.06)	-0.03 (-0.10, 0.04)	**-0.10 (-0.17, -0.03)**	-0.02 (-0.09, 0.05)	-0.02 (-0.09, 0.05)	-0.06 (-0.13, 0.02)
Q3	-0.03 (-0.11, 0.04)	0.01 (-0.06, 0.08)	-0.07 (-0.14, 0.00)	0.00 (-0.07, 0.07)	0.00 (-0.07, 0.07)	-0.04 (-0.11, 0.03)
Q4	-0.01 (-0.09, 0.06)	-0.03 (-0.10, 0.04)	-0.03 (-0.10, 0.04)	0.02 (-0.06, 0.09)	-0.03 (-0.10, 0.04)	-0.03 (-0.11, 0.04)
Distance to coast						
Per IQR increase	0.01 (-0.02, 0.04)	0.00 (-0.03, 0.03)	-0.01 (-0.04, 0.02)	-0.02 (-0.04, 0.01)	0.00 (-0.03, 0.03)	0.00 (-0.03, 0.03)
Quartiles of distance						
Q1	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)
Q2	-0.04 (-0.12, 0.03)	0.03 (-0.05, 0.10)	-0.05 (-0.12, 0.03)	-0.02 (-0.10, 0.05)	0.01 (-0.06, 0.09)	-0.02 (-0.09, 0.06)
Q3	-0.02 (-0.10, 0.06)	0.04 (-0.04, 0.11)	0.00 (-0.08, 0.07)	-0.02 (-0.09, 0.06)	0.03 (-0.05, 0.10)	0.01 (-0.06, 0.09)
Q4	0.01 (-0.07, 0.09)	0.04 (-0.04, 0.11)	-0.01 (-0.09, 0.06)	-0.04 (-0.11, 0.04)	0.01 (-0.06, 0.09)	0.04 (-0.04, 0.11)
Distance to major road						
Per IQR increase	-0.01 (-0.03, 0.01)	0.01 (-0.01, 0.03)	0.00 (-0.02, 0.02)	0.00 (-0.02, 0.02)	0.00 (-0.02, 0.02)	0.00 (-0.02, 0.02)
Quartiles of distance						
Q1	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)

Q2	-0.04 (-0.11, 0.04)	-0.03 (0.04, -0.1)	0.04 (-0.03, 0.11)	**0.08 (0.01, 0.15)**	0.06 (-0.02, 0.13)	-0.03 (-0.11, 0.04)
Q3	-0.02 (-0.1, 0.05)	-0.04 (0.03, -0.12)	0.00 (-0.07, 0.07)	0.02 (-0.05, 0.09)	0.04 (-0.03, 0.11)	-0.04 (-0.12, 0.03)
Q4	-0.01 (-0.11, 0.1)	-0.03 (0.07, -0.13)	-0.08 (-0.18, 0.02)	-0.01 (-0.11, 0.09)	0.05 (-0.05, 0.15)	-0.07 (-0.18, 0.03)
NDVI within 500m						
Per IQR increase	0.00 (-0.04, 0.04)	0.01 (-0.03, 0.05)	0.02 (-0.02, 0.06)	**0.05 (0.01, 0.09)**	-0.02 (-0.06, 0.02)	0.00 (-0.04, 0.04)
Quartiles of NDVI						
Q1	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)	0.00 (reference)
Q2	0.03 (-0.05, 0.10)	0.04 (-0.03, 0.11)	0.06 (-0.01, 0.13)	0.06 (-0.01, 0.13)	-0.04 (-0.11, 0.03)	**0.10 (0.03, 0.17)**
Q3	0.00 (-0.08, 0.07)	0.00 (-0.07, 0.07)	0.03 (-0.04, 0.10)	0.05 (-0.02, 0.12)	-0.01 (-0.08, 0.06)	0.05 (-0.02, 0.13)
Q4	0.03 (-0.06, 0.12)	-0.04 (-0.12, 0.04)	0.05 (-0.03, 0.14)	**0.09 (0.01, 0.17)**	-0.03 (-0.11, 0.05)	0.05 (-0.03, 0.14)

IQR, interquartile range; NDVI, Normalized Difference Vegetation Index. Coefficients are calculated for standardized semen parameters (z-scores). Single exposure linear regression models included age, body mass index, occupation, smoking, season of semen test, and administrative district of home address. Results with P value <0.05 were bolded.

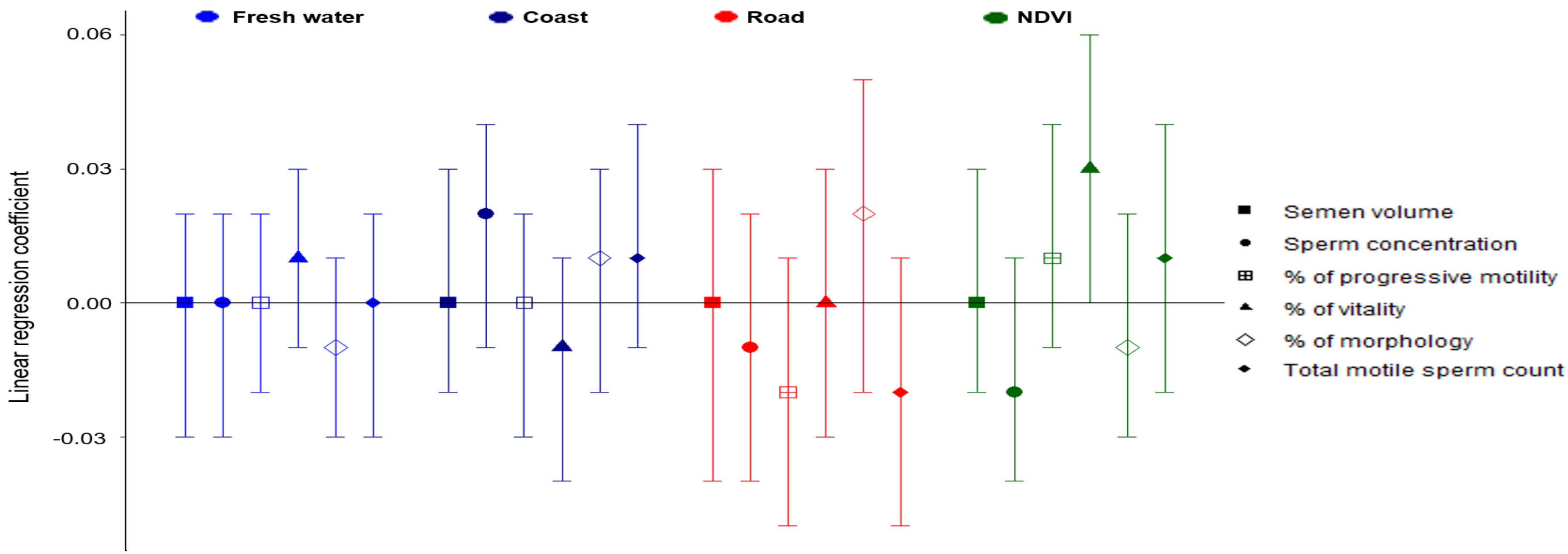


Figure 1. Association between six standardized semen parameters (z-scores) and built environment components in a multi-exposure model among 5,886 Korean infertile men.

NDVI, Normalized Difference Vegetation Index. All coefficients are per interquartile range-increase of built environment components. Coefficients are calculated using a multivariable linear regression model including four built environmental components, age, body mass index, occupation, smoking, season of semen test, and administrative district of home address.

Discussion

We did not find a consistent association between built environment and semen quality among men with a history of infertility. In single- and multi-exposure model, we observed that a higher value for NDVI within 500 m was positively associated with percentage of sperm vitality. The observed associations between environmental components and semen quality indicators were generally non-linear. For example, distance to fresh water was associated with lower percentage of progressive motility upon comparison of the first two quartiles. The 2^{nd} quartile of NDVI was associated with higher total motile sperm count compared to the 1^{st} quartile. To the best of our knowledge, this is the first report to assess the association between land use and semen quality using large hospital-based data.

Several components of physical environment have been known to be associated with male infertility. Heat exposure and extreme ambient temperature is associated with lower semen quality [12, 22]. Exposure to environmental noise is expected to be high when living close to a major road, and is associated with higher risk of subfecundity [23] or male infertility [24]. Air pollution is also reported to be related to semen abnormality [10, 25]. Although the strength of association with exposures is heterogenous across different semen indicators, the results of this study suggest a potential impact of the neighborhood's physical environment.

Our study found a heterogenous association between the built environment and semen quality across different exposures and semen indicators. There is limited knowledge regarding how each component of semen quality indicators is affected by different environmental exposures. Several studies have demonstrated increased sperm motility in physically active men [26, 27]. Although our study did not detect a dose-response relationship, some of our results suggest the existence of a negative association of proximity to fresh water with sperm motility and a positive association of remoteness to roadway and NDVI with vitality.

The results of this study need to be interpreted with caution. First, as a single fertility center study, our study population was mostly restricted to white collar workers living in an urban area. Second, misclassification of exposure may have potentially occurred due to the use of residential address for exposure assessment, or due to the distance between the home address and the workplace, where patients may have spent a substantial amount of time. However, assuming that the misclassification was non-differential, it may have biased our results towards the null [28]. We believe our study may still have important implications due to the use of hospital data belonging to a large infertile population who is expected to be particularly vulnerable to environmental exposure.

Conclusions

We did not find a consistent association between the built environment and different measures of semen quality among men with a history of infertility, although some features of neighborhood land use may be associated with semen quality, highlighting the potential impact of the built environment on human fertility. Further studies in different populations are required to add to the evidence on the impact of built environment on human reproduction and health.

List of Abbreviations: IQR, interquartile range; NDVI, Normalized Difference Vegetation Index

Declarations

Ethics approval and consent to participate

The study design was approved by the institutional review board of Gangnam CHA hospital (GCI-18-48). As a research involving the retrospective review, this study qualified a waiver of informed consent.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available due to the nature of information that could compromise the privacy of research participants but are available from the first (seungah@korea.ac.kr) or corresponding author (kdg070723@gmail.com) on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research was supported by the National Research Foundation of Korea grant (NRF-2016R1D1A1B03933410 and 2018R1D1A1B07048821), which is funded by the Korean Government. This funding source had no role in study design, in the collection, analysis and interpretation of data, in the writing of the report, and in the decision to submit the article for publication. The contents of this report are solely the responsibility of the authors and do not necessarily represent the official views of the sponsoring organizations.

Authors' contributions

DKK and SAC conceptualized and designed the study. SAC conducted primary statistical analysis and wrote the draft. GW and SYK reviewed and revised the draft. SK and CI conducted data curation and geospatial data production. YSK and TKY Yoon supervised the process of study and provided the study data.

Acknowledgements

We thank Sun-Wha Shim and Shi-Ha Jung for their technical support.

References

1. Dadvand P, Bartoll X, Basagaña X, Dalmau-Bueno A, Martinez D, Ambros A, Cirach M, Triguero-Mas M, Gascon M, Borrell C, Nieuwenhuijsen MJ: Green spaces and General Health: Roles of mental health status, social support, and physical activity. Environ Int. 2016, 91:161-167.
2. de Vries S, Verheij RA, Groenewegen PP, Spreeuwenberg P: Natural Environments—Healthy Environments? An Exploratory Analysis of the Relationship between Greenspace and Health. Environment and Planning A: Economy and Space. 2003, 35:1717-1731.
3. Gascon M, Zijlema W, Vert C, White MP, Nieuwenhuijsen MJ: Outdoor blue spaces, human health and well-being: A systematic review of quantitative studies. Int J Hyg Environ Health. 2017, 220:1207-1221.
4. Nieuwenhuijsen MJ, Khreis H, Triguero-Mas M, Gascon M, Dadvand P: Fifty Shades of Green: Pathway to Healthy Urban Living. Epidemiology. 2017, 28:63-71.
5. Oliva A, Spira A, Multigner L: Contribution of environmental factors to the risk of male infertility. Human Reproduction. 2001, 16:1768-1776.
6. Hamerezaee M, Dehghan SF, Golbabaei F, Fathi A, Barzegar L, Heidarnejad N: Assessment of Semen Quality among Workers Exposed to Heat Stress: A Cross-Sectional Study in a Steel Industry. Safety and Health at Work. 2018, 9:232-235.
7. Omu AE: Sperm parameters: paradigmatic index of good health and longevity. Med Princ Pract. 2013, 22 Suppl 1:30-42.

8. Wdowiak A, Bień A, Iwanowicz-Palus G, Makara-Studzińska M, Bojar I: Impact of emotional disorders on semen quality in men treated for infertility. Neuro Endocrinol Lett. 2017, 38:50-58.

9. Spira A, Multigner L: The effect of industrial and agricultural pollution on human spermatogenesis. Human Reproduction. 1998, 13:2041-2042.

10. Nobles CJ, Schisterman EF, Ha S, Kim K, Mumford SL, Buck Louis GM, Chen Z, Liu D, Sherman S, Mendola P: Ambient air pollution and semen quality. Environmental research. 2018, 163:228-236.

11. Jurewicz J, Hanke W, Radwan M, Bonde JP: Environmental factors and semen quality. Int J Occup Med Environ Health. 2009, 22:305-329.

12. Al-Otaibi ST: Male infertility among bakers associated with exposure to high environmental temperature at the workplace. Journal of Taibah University Medical Sciences. 2018, 13:103-107.

13. Dadvand P, de Nazelle A, Figueras F, Basagaña X, Su J, Amoly E, Jerrett M, Vrijheid M, Sunyer J, Nieuwenhuijsen MJ: Green space, health inequality and pregnancy. Environ Int. 2012, 40:110-115.

14. Dadvand P, Ostro B, Figueras F, Foraster M, Basagaña X, Valentín A, Martinez D, Beelen R, Cirach M, Hoek G, et al: Residential proximity to major roads and term low birth weight: the roles of air pollution, heat, noise, and road-adjacent trees. Epidemiology. 2014, 25:518-525.

15. Choe SA, Kauderer S, Eliot MN, Glazer KB, Kingsley SL, Carlson L, Awad YA, Schwartz JD, Savitz DA, Wellenius GA: Air pollution, land use, and complications of pregnancy. Sci Total Environ. 2018, 645:1057-1064.

16. Kingsley SL, Eliot MN, Whitsel EA, Wang Y, Coull BA, Hou L, Margolis HG, Margolis KL, Mu L, Wu W-CC, et al: Residential proximity to major roadways and incident hypertension in post-menopausal women. Environmental research. 2015, 142:522-528.

17. Glazer KB, Eliot MN, Danilack VA, Carlson L, Phipps MG, Dadvand P, Savitz DA, Wellenius GA: Residential green space and birth outcomes in a coastal setting. Environ Res. 2018, 163:97-107.

18. Yoon YE, Kim TY, Shin TE, Lee E, Choi KH, Lee SR, Hong YK, Park DS, Kim DK: Validation of SwimCount™, a Novel Home-Based Device That Detects Progressively Motile Spermatozoa: Correlation with World Health Organization 5th Semen Analysis. The world journal of men's health. 2020, 38:191-197.

19. World Health Organization: **WHO laboratory manual for the examination and processing of human semen.** 5th ed edition. Geneva: World Health Organization; 2010.

20. van Buuren S, Groothuis-Oudshoorn K: mice: Multivariate Imputation by Chained Equations in R. 2011. 2011, 45:67.

21. WHO Expert Consultation: Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004, 363:157-163.

22. Zhou Y, Meng T, Wu L, Duan Y, Li G, Shi C, Zhang H, Peng Z, Fan C, Ma J, et al: Association between ambient temperature and semen quality: A longitudinal study of 10 802 men in China. Environment International. 2020, 135:105364.

23. Christensen JS, Raaschou-Nielsen O, Ketzel M, Ramlau-Hansen CH, Bech BH, Olsen J, Sørensen M: Exposure to residential road traffic noise prior to conception and time to pregnancy. Environment International. 2017, 106:48-52.

24. Min K-B, Min J-Y: Exposure to environmental noise and risk for male infertility: A population-based cohort study. Environmental

Pollution. 2017, 226:118-124.

25. Huang G, Zhang Q, Wu H, Wang Q, Chen Y, Guo P, Zhao Q: Sperm quality and ambient air pollution exposure: A retrospective, cohort study in a Southern province of China. Environ Res. 2020, 188:109756.

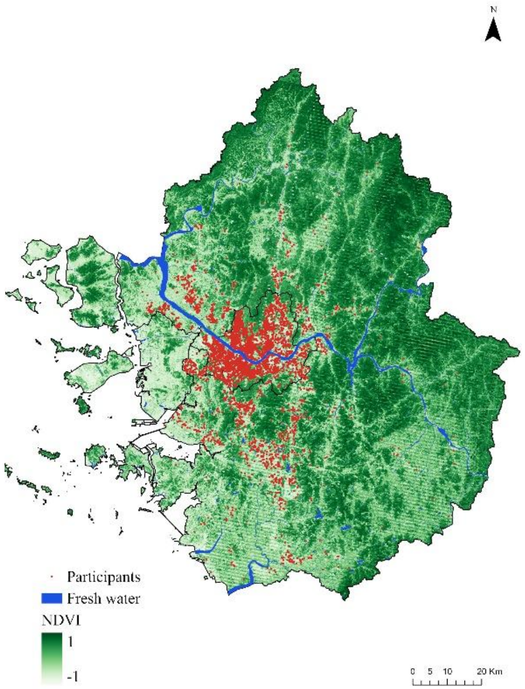
26. Lalinde-Acevedo PC, Mayorga-Torres BJM, Agarwal A, du Plessis SS, Ahmad G, Cadavid ÁP, Cardona Maya WD: Physically Active Men Show Better Semen Parameters than Their Sedentary Counterparts. International journal of fertility & sterility. 2017, 11:156-165.

27. Vaamonde D, Da Silva-Grigoletto ME, García-Manso JM, Barrera N, Vaamonde-Lemos R: Physically active men show better semen parameters and hormone values than sedentary men. Eur J Appl Physiol. 2012, 112:3267-3273.

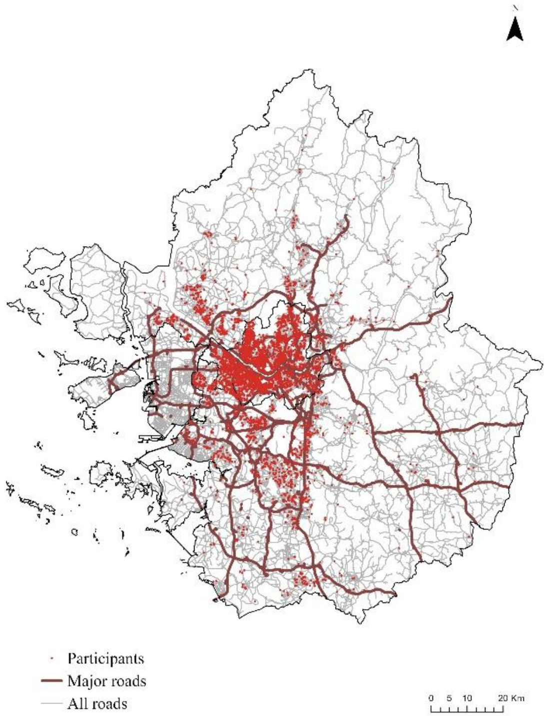
28. Pekkanen J, Sunyer J, Chinn S: Nondifferential disease misclassification may bias incidence risk ratios away from the null. J Clin Epidemiol. 2006, 59:281-289.

Supplementary Fig. 1. Distribution of residential address of male participants, (A) with inland fresh water and NDVI and (B) with major roadway in Seoul Capital Area

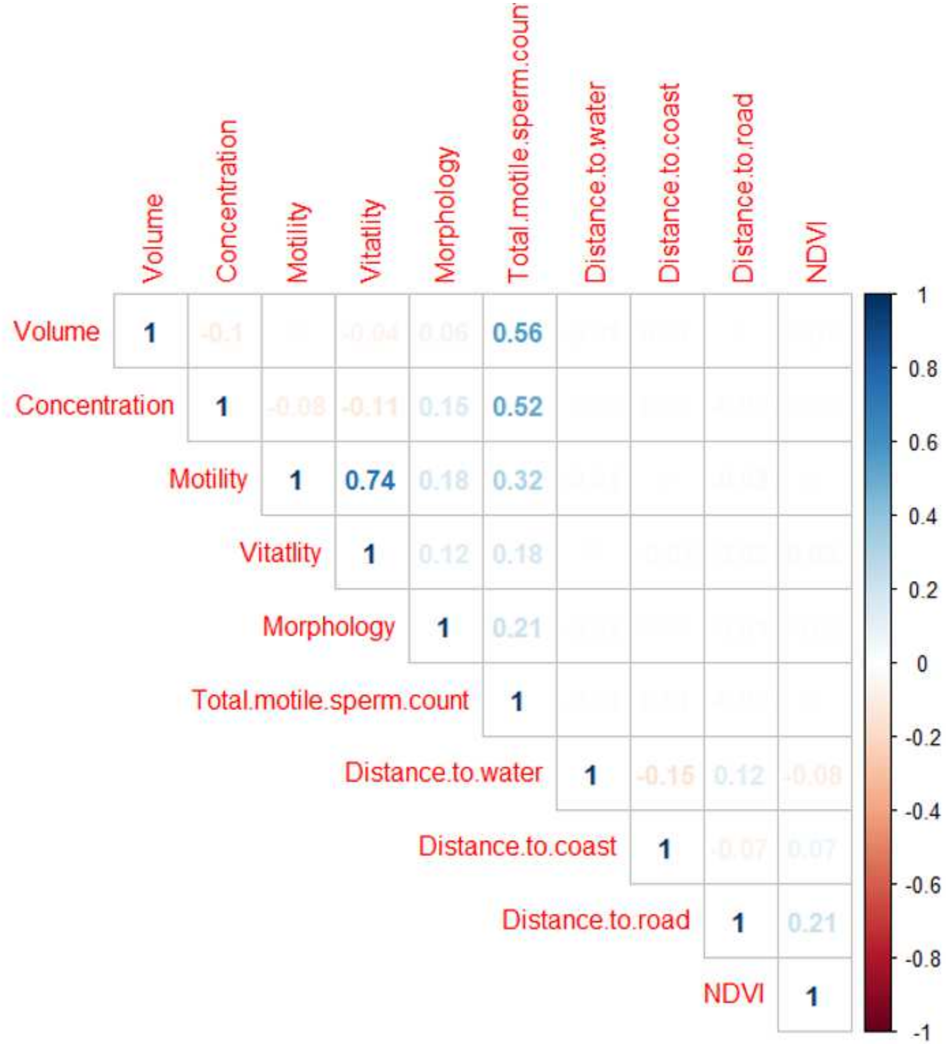
A. Inland fresh water and NDVI



B. Network of major roadway



Supplementary Fig. 2. Pairwise correlation structure between four components of built environment and six sperm quality indicators



Supplementary Table 1. Mean value of semen quality indicators in each quartile of distance to fresh water, coast, and road with NDVI among 5,886 Korean infertile men

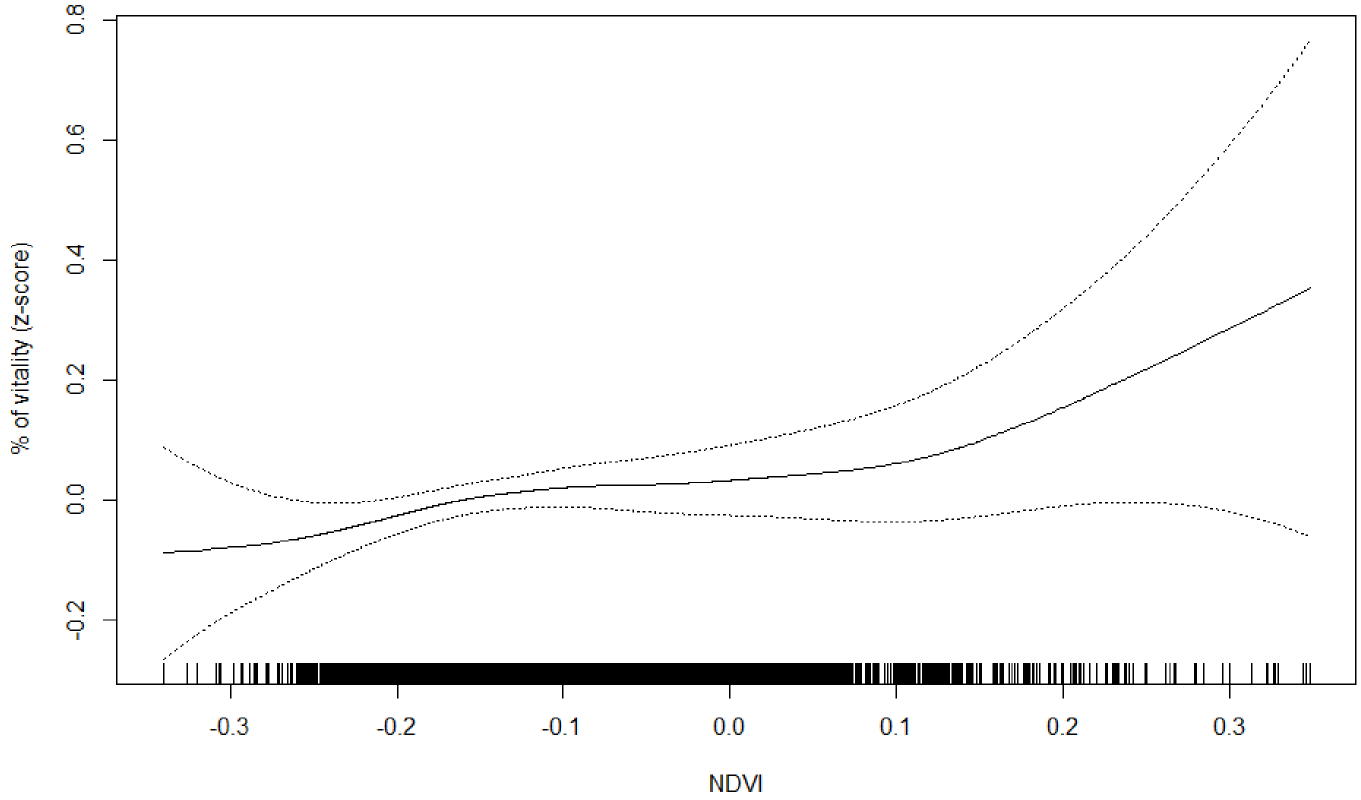
Semen indicators	Distance to fresh water					
	Q1 (0—209.9m)	Q2 (209.9—382.8m)	Q3 (382.8—615.0m)	Q4 (615.0—1984.1m)	P^h	P^t
Volume (mL)	3.1 ± 2.1	3.1 ± 1.8	3.0 ± 1.9	3.1 ± 1.6	0.828	0.698
Count (million/mL)	104.2 ± 71.2	102.9 ± 64.9	106.1 ± 72.1	103.9 ± 65.9	0.717	0.632
Progressive motility (%)	**46.1 ± 12.9**	**44.8 ± 13.3**	**45.5 ± 13.4**	**45.9 ± 13.1**	**0.025**	0.880
Vitality (%)	62.5 ± 12.7	62.3 ± 12.8	62.5 ± 12.4	63.0 ± 12.3	0.63	0.355
Morphology (%)	3.7 ± 1.8	3.7 ± 1.9	3.7 ± 1.8	3.7 ± 1.8	0.907	0.947
Total motile sperm count (million)	144.9 ± 120.8	139.7 ± 107.2	141.6 ± 106.4	143.9 ± 109.2	0.682	0.733
	Distance to coast					
	Q1 (63.0-19837.4m)	Q2 (19837.4-24609.6m)	Q3 (24609.6-28785.6m)	Q4 (28785.6-79100.3m)	P^h	P^t
Volume (mL)	3.1 ± 2	3 ± 2.4	3.1 ± 1.5	3.1 ± 1.5	0.099	0.280
Count (million/mL)	102.3 ± 65.9	104.1 ± 65.9	105.3 ± 67.3	105.7 ± 71.8	0.664	0.301

Progressive motility (%)	45.8 ± 13.4	45.2 ± 12.8	46.0 ± 12.7	45.5 ± 13.4	0.344	0.937
Vitality (%)	62.9 ± 12.5	62.6 ± 12.5	62.7 ± 12	62.2 ± 12.9	0.746	0.272
Morphology (%)	3.6 ± 1.8	3.7 ± 1.8	3.7 ± 1.8	3.7 ± 1.8	0.637	0.383
Total motile sperm count (million)	143.3 ± 111.2	141.3 ± 123.2	145.2 ± 109	146.4 ± 110.2	0.268	0.214
	Distance to major roadway					
	Q1 (5.1—184.8m)	Q2 (184.8—495.7m)	Q3 (495.7—1295.9m)	Q4 (1295.9—58607.8m)	P^h	P^t
Volume (mL)	3.1 ± 2.1	3.1 ± 1.9	3.1 ± 1.5	3.1 ± 1.8	0.907	0.537
Count (million/mL)	104.9 ± 68.2	104.7 ± 67.1	103.7 ± 68.9	103.8 ± 70.1	0.677	0.334
Progressive motility (%)	**45.4 ± 13.5**	**46.2 ± 12.7**	**45.8 ± 13.2**	**44.9 ± 13.3**	**0.033**	0.510
Vitality (%)	62.2 ± 12.8	63.1 ± 12.4	62.6 ± 12.4	62.5 ± 12.5	0.263	0.298
Morphology (%)	3.7 ± 1.8	3.7 ± 1.9	3.7 ± 1.8	3.6 ± 1.9	0.374	0.767
Total motile sperm count (million)	142.9 ± 119.8	144.9 ± 109.3	143.0 ± 109.7	139.3 ± 104.7	0.420	0.602
	NDVI within 500m					

	Q1 (-0.34— -0.20)	Q2 (-0.20— -0.15)	Q3 (-0.15— -0.08)	Q4 (-0.08—0.35)	P^h	P^t
Volume (mL)	3.06 ± 1.88	3.11 ± 2.28	3.07 ± 1.51	3.05 ± 1.54	0.955	0.974
Count (million/mL)	104.26 ± 66.35	106.35 ± 69.78	104.15 ± 70.1	102.28 ± 68.04	0.233	0.113
Progressive motility (%)	45.35 ± 13.04	45.91 ± 13.08	45.4 ± 13.41	45.61 ± 13.21	0.458	0.722
Vitality (%)	62.13 ± 12.42	62.81 ± 12.43	62.54 ± 12.77	62.81 ± 12.5	0.165	0.118
Morphology (%)	3.74 ± 1.82	3.64 ± 1.8	3.73 ± 1.87	3.6 ± 1.83	0.070	0.094
Total motile sperm count (million)	138.86 ± 102.73	148.12 ± 120.87	143.07 ± 113.01	139.93 ± 106.43	0.153	0.595

Q1, lowest quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile; NDVI, Normalized Difference Vegetation Index; P^h, P value for heterogeneity; P^t, P value for linear trend. Heterogeneity across quartiles was tested using Kruskal-Wallis rank sum test. Trend test was done with Kendall's rank correlation test. Results with P value < 0.05 were bolded.

Supplementary Fig 3. Association between NDVI within 500 m and % of sperm vitality in generalized additive model



Figures

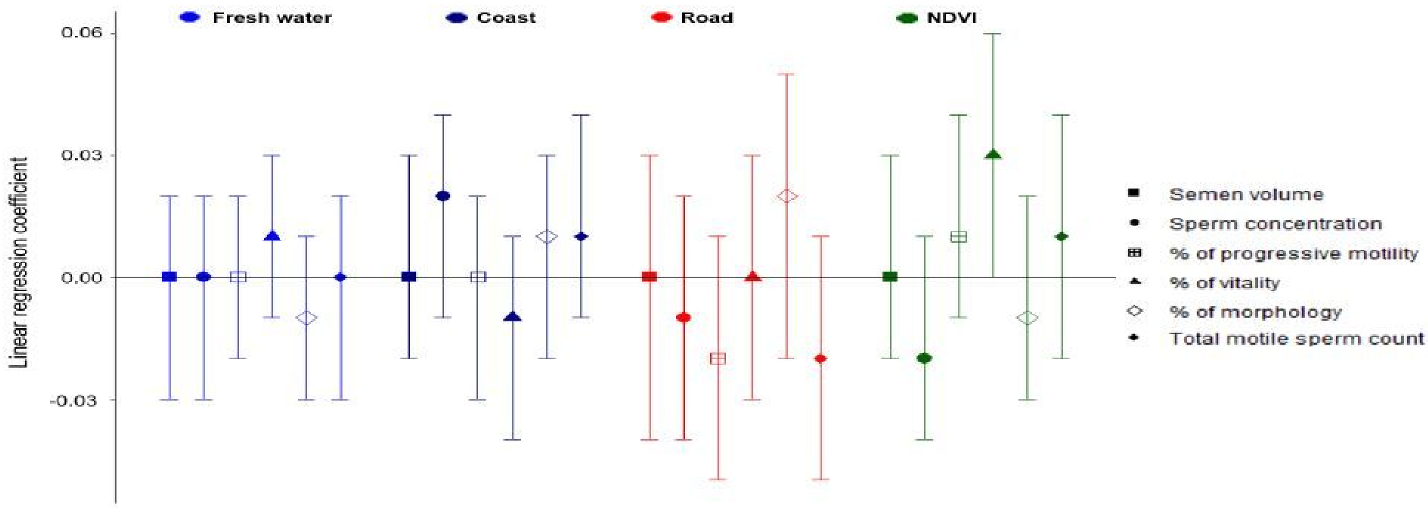


Figure 1

Association between six standardized semen parameters (z-scores) and built environment components in a multi-exposure model among 5,886 Korean infertile men. NDVI, Normalized Difference Vegetation Index. All coefficients are per interquartile range-increase of built environment components. Coefficients are calculated using a multivariable linear regression model including four built environmental components, age, body mass index, occupation, smoking, season of semen test, and administrative district of home address.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- FigS1.JPG
- FigS2.JPG
- FigS3.JPG