

1 **Machine learning approach to assess the association between anthropometric,**
2 **metabolic and nutritional status and semen parameters**

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21 **Running title:** Modeling, metabolic status and semen parameters.
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24

25 **Abstract:**

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27 Many lifestyle factors, such as nutritional imbalance leading to obesity, metabolic disorders and
28 nutritional deficiency, have been identified as potential risk factors for male infertility. The aim
29 of this study was to evaluate the relationship between semen parameters and both anthropometric,
30 metabolic and nutritional parameters individually and then after the application of a previously
31 constructed and validated machine learning score that allows their combination. Anthropometric,
32 metabolic, antioxidant, micronutrient, and sperm parameters from 75 men suffering from
33 idiopathic infertility recruited from four infertility centers in France (Jean-Verdier ART center
34 Hospital, Bondy ; North Hospital ART center, Saint-Étienne ; Navarre Polyclinic ART center,
35 Pau ; Cochin Hospital ART center, Paris) between September 2009 and December 2013 were
36 collected. After assessing standard correlation analysis, a previously built machine learning
37 model, providing a score ranging from 0 (poorest) to 1 (most favorable) was calculated for each
38 man in the study cohort. This machine learning model, that separates infertile/fertile men with
39 unexplained infertility on the basis of their bioclinical signature, providing a more holistic
40 evaluation of the influence of the considered markers (anthropometric, metabolic and oxidative
41 status). We observed a significant correlation of some anthropometric, metabolic and nutritional
42 disorders with some sperm characteristics. Moreover, unfavorable machine learning score was
43 associated with a high level of sperm DNA fragmentation. Favorable anthropometric, metabolic
44 and oxidative patterns, which may reflect an appropriate lifestyle, appear to positively impact
45 overall health, in particular reproductive function. This study, consistent with previous
46 publications, suggests that beyond semen quality parameters, in an essential assessment of male
47 fertility, other key factors should be taken into account. In this regard, the application of
48 emerging artificial intelligence techniques may provide a unique opportunity to integrate all these
49 parameters and deliver personalized care.

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51

52 **Keywords:** lifestyle ; machine learning ; metabolism ; nutrition ; sperm DNA fragmentation

53 **Introduction**

54 As recently published by Levine *et al.*, fertility has been declining worldwide for the past half
55 century, especially sperm quality ¹. Many lifestyle factors have been identified as potential risk
56 factors for infertility in men. Among them, overweight and obesity have been particularly studied
57 ². A global increase in the prevalence of obesity has been observed over the last three decades
58 and now more than half of men of reproductive age are currently considered to be overweight or
59 obese. It has been well established that overweight and obesity are associated with male infertility
60 ³ and have a negative impact on semen parameters including sperm count ^{2,4} and sperm DNA
61 fragmentation ^{5,6}. In addition, metabolic disorders that are often the consequence of an
62 unbalanced diet and/or insufficient physical activity, also contribute to impaired reproductive
63 function ⁷.

64 Recently our team has highlighted, that metabolic syndrome, but also metabolic disorders
65 (increased fasting blood glucose) and anthropometric disorders (increased body mass index
66 (BMI) and abdominal obesity) may be risk factors for idiopathic infertility ⁸. We had also
67 observed that male partners of infertile couples were less physically active than fertile men ⁹.
68 They also had lower plasma levels of antioxidant vitamins ¹⁰.

69 There are many complex mechanisms involved in these phenomena. Overweight, obesity, and
70 metabolic disorders can lead to impaired functioning of the hypothalamic-pituitary-gonadal
71 (HPG) axis. The process of converting steroids into estrogens in peripheral adipose tissue leads
72 to an elevation in estradiol levels, which exerts a negative feedback loop at the hypothalamic-
73 pituitary level. In these men, secondary hypogonadism is therefore observed, characterized by a
74 decrease in serum concentrations of follicle-stimulating hormone (FSH), luteinizing hormone
75 (LH) and testosterone ^{11,12}. Hyperinsulinemia leads to a decrease in hepatic production of Sex
76 Hormone Binding Globulin (SHBG) ¹³. Consequences are increasing level of free testosterone

77 available for conversion to estradiol. Chronic systemic inflammation, which plays a critical role
78 in the development of metabolic syndrome, is associated with obesity ¹⁴. Levels of inflammatory
79 cytokines (Interleukin 1-alpha, Interleukin-6, Tumor necrosis factor- α , Activin a, etc.), which are
80 essential for normal spermatogenesis, are disturbed ¹⁵. Systemic oxidative stress is also associated
81 with increased body weight and obesity ¹⁶. Oxidative stress and lipid peroxidation are increased
82 in the testicular microenvironment following the accumulation of adipose tissue ¹⁷. Furthermore,
83 high blood glucose levels have been shown to increase oxidative stress through mitochondrial
84 oxidation of glucose, which releases a substantial amount of free radicals into the cytosol ¹⁸. In
85 addition, oxidative stress leads to the production of nitric oxide (NO) which oxidizes sperm
86 membrane lipids. Oxidative sperm impair spermatogenesis and is detrimental to sperm motility
87 ¹⁹. Germ cells are thought to be more sensitive to free radical oxidation than somatic cells,
88 because their plasma membranes contain a greater quantity of polyunsaturated fatty acids leading
89 to lipid peroxidation ²⁰. Oxidative stress increases sperm damage and results in increased sperm
90 DNA fragmentation, which affects early embryo development, future child health, and increases
91 the risk of miscarriage ^{21,22}.

92
93 Thus, finally, the mechanisms involved in the impact of obesity and metabolic disorders on male
94 reproductive functions are numerous, but strongly interlinked. Until recently, most of the studies
95 have independently investigated the relationship between infertility and anthropometric,
96 metabolic and dietary elements. Therefore, identifying the parameter(s) involved in male or
97 female infertility is challenging. Artificial intelligence, especially machine learning, has been
98 adopted in scientific and medical research in the last few years, providing access to innovative
99 and more powerful tools. We previously built and evaluated a Machine Learning (ML) model to
100 identify and stratify fertile couples as well as those with idiopathic infertility. This score was

101 based on a panel of lifestyle-influenced parameters, including the anthropometric, metabolic and
102 antioxidant status of both partners. This tool combines several easily measurable parameters and
103 generates a score to assess the impact of anthropometric, metabolic and antioxidant factors on the
104 couple's risk of infertility. Although less efficient, we have also shown that this score, in its
105 version built on male parameters alone, could identify almost 70% of men who were at risk of
106 infertility¹⁰.

107 However, a score combining different elements influenced by lifestyle has never been used to
108 identify the risk of impaired sperm parameters.

109 The objective of this study was to evaluate the relationship between semen parameters and
110 anthropometric, metabolic, and nutritional parameters. First, we analyzed each parameter
111 individually, and then we applied a previously constructed and validated machine learning score
112 to combine them.

113

114 **Material and methods**

115

116 Subjects:

117 “*Alimentation et FERTilité*” (ALIFERT) is a cross-sectional case-control study enrolling
118 infertile men between September 2009 and December 2013 (National biomedical research ID no.
119 P071224; ethics committee approval (‘Comité de Protection des Personnes’) ID no. AOM 2009-
120 A00256–51; NEudra CT ID no. 08180; clinicaltrials.gov ID no. NCT01093378). The design of
121 ALIFERT was multicenter. The study cohort included 75 infertile men recruited from four
122 infertility centers in France (Jean-Verdier ART center Hospital, Bondy (JV); North Hospital ART
123 center, Saint-Étienne (SE); Navarre Polyclinic ART center, Pau (PAU); Cochin Hospital ART
124 center, Paris (CCH)).

125 Men were between 18 to 45 and exhibiting idiopathic infertility for over 12 months. Eligibility
126 criteria have been described previously and include the provision of written informed consent ¹⁰.
127 Eligibility criteria for subjects were as follows: (i) primary idiopathic infertility >12 months, (ii)
128 age between 18 and 45 years, (iii) absence of severe oligozoospermia (<5 million/ml), (iv)
129 absence of male reproductive tract abnormalities such as undescended testis, varicocele or
130 infection, (v) written informed consent. Subjects with any current known or previous metabolic
131 or digestive disease and smokers were excluded.

132 Assessments:

133 Anthropometric, metabolic, antioxidant, and micronutrient parameters were assessed as described
134 below:

135 Height, weight, visceral fat (Tanita BC-420MA analyzer, TANITA USA, Issaquah, WA,
136 USA), and waist circumference measured at the narrowest point between the lower edge of the
137 ribs and the iliac crest were measured by the investigator. The measurements were carried out by
138 a trained investigator in the morning under fasting conditions.

139
140 Blood samples were obtained after 12 hours of fasting for measurement of total
141 cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL)
142 cholesterol, triglycerides, and glucose in fresh plasma. Both serum and plasma were frozen at -
143 80°C until further analysis.

144
145 After 5 minutes of rest, systolic and diastolic blood pressures were assessed with a
146 sphygmomanometer cuff around the patient's forearm while lying down. The values for systolic
147 and diastolic pressures were calculated as the mean of the right and left measurements.

148 Finally, concentrations of serum vitamin D (ng/mL), vitamin B9 (folic acid-erythro)
149 (nmol), vitamin B9 (nmol/L), vitamin B12 (pmol/L), alpha-tocopherol (vitamin E) ($\mu\text{mol/L}$), zinc
150 (mmol/L), selenium (mmol/L), vitamin C (mg/mL), alpha-carotene ($\mu\text{mol/L}$), beta-carotene
151 ($\mu\text{mol/L}$), Lycopene ($\mu\text{mol/L}$), lutein ($\mu\text{mol/L}$), beta-kryptoxanthin ($\mu\text{mol/L}$), and retinol
152 ($\mu\text{mol/L}$) (vitamin A) levels were determined at the Department of Integrated Biology -
153 Nutritional Biology and Oxidative Stress (Grenoble Hospital, Grenoble, France). Ascorbic acid
154 (vitamin C) in serum was assessed by an automated continuous-flow method. The concentrations
155 of retinol, tocopherol, and carotenoids (lutein, β -cryptoxanthin, lycopene, α -carotene, and β -
156 carotene) in serum were obtained by HPLC (Biotek-Kontron, Montigny-le-Bretonneux, France).
157 Concentrations of serum zinc were measured by flame atomic absorption spectrometry (model
158 3110; Perkin Elmer, Norwalk, CT, USA) and selenium by atomic absorption spectrometry (4100
159 ZL; Perkin Elmer).

160

161 Semen quality parameters:

162 The semen specimens were collected in the laboratory by masturbation into a sterile plastic cup
163 after an abstinence period of 2 to 5 days. The samples were liquefied at room temperature for 30
164 minutes and conventional semen quality (semen volume, sperm concentration, vitality and
165 motility) was assessed according to the 2010 WHO guidelines ²³. David's criteria were used to
166 evaluate sperm morphology ^{24,25}.

167

168 Sperm DNA fragmentation: The TUNEL (terminal deoxynucleotidyl transferase dUTP nick end
169 labeling) technique with an In Situ Cell Death Detection Kit (Fluorescein, Roche Applied
170 Science, Meylan, France) was used to determine sperm DNA fragmentation.

171

172 Machine learning model:

173 In previous work, our team developed and evaluated three machine learning models, capable of
174 separating infertile/fertile (1) couples, (2) men and (3) women through their bioclinical signature,
175 in order to facilitate the management of couples with unexplained infertility¹⁰. This signature
176 was the result of a precise selection of biomarkers among hundreds of parameters investigated
177 and is based on the findings of a large-scale clinical study evaluating the impact of lifestyle and
178 nutrition on couples' infertility. A major contribution of lifestyle parameters to the discriminatory
179 power of the model had been demonstrated. The result generated and calculated by the model
180 produces a score ranging from 0 (the highest risk of infertility with involvement of nutritional and
181 metabolic factors) to 1 (the lowest risk, therefore rather healthy nutritional and metabolic profile).
182 We therefore calculated the model score for each man in the study cohort, using the formula
183 obtained previously¹⁰. A score between 0 and 1 was therefore calculated for each man in the
184 cohort, with the aim of assessing more globally the nutritional and metabolic status on fertility
185 (Figure 1) and comparing its results with sperm parameters.

186

187 Statistical analysis

188 Python 3.9.12 was used to carry out the statistical analysis, and the SciPy package version 1.9.3
189 was used. Data are shown as means and standard deviation . Correlation analysis of metabolic
190 and sperm parameters was investigated by parametric Pearson test. P-value < 0.05 was
191 considered statistically significant.

192

193 **Results:**

194 Data are summarized as mean and standard deviation and shown in Table 1.

195
196
197 Association between anthropometric, metabolic, and dietary parameters and semen parameters is
198 presented in Table 2.

199
200 In this population of idiopathic infertile men, we observed a correlation between some
201 anthropometric characteristics and semen parameters. A decrease in sperm motility was observed
202 with high BMI ($r = -0.233$, $p < 0.05$). In addition, high visceral fat was associated with a decrease
203 in sperm vitality and motility ($r = -0.285$, $p < 0.01$ and $r = -0.27$, $p < 0.05$).

204
205 Regarding the correlation between metabolic characteristic and sperm parameters, high levels of
206 total cholesterol and serum LDL were associated with lower sperm count ($r = -0.272$ and $r = -$
207 0.249 , $p < 0.05$). In addition, lower sperm vitality was observed in patients with high total
208 cholesterol and serum LDL ($r = -0.311$ and $r = -0.326$ $p < 0.01$). Finally, sperm DNA
209 fragmentation was negatively correlated with serum HDL concentration ($r = -0.364$, $p < 0.01$).

210
211 A high concentration of certain antioxidants in the serum is associated with better sperm
212 parameters. Correlation between sperm count and plasma Glutathione peroxidase activity ($r =$
213 0.23 , $p < 0.05$), as well as between sperm motility and vitamin B12 (cobalamin) concentration
214 was observed ($r = 0.275$, $p < 0.05$).

215
216 Unfavorable machine learning score, based on a combination of anthropometric, metabolic and
217 oxidative status, was associated with a high level of sperm DNA fragmentation ($r = -0.263$, p -
218 value < 0.05).

219

220 **Discussion**

221 The aim of this study was to explore the impact of factors such as anthropometric and
222 metabolic status along with the nutritional environment on semen parameters in a population of
223 patients with unexplained infertility. This study explore the relationship between a circulating
224 metabolic and nutritional signature and sperm DNA fragmentation, a qualitative marker of
225 spermatogenesis.

226 We observed a significant correlation of some anthropometric, metabolic and nutritional
227 disorders with some sperm characteristics. These associations were not as pronounced as those
228 described in other publications ^{2,4-6}. This difference may be related to the fact that men in our
229 study did not have major alterations in conventional semen parameters. Moreover, traditional
230 sperm parameters are known to be highly variable between ejaculates, meaning intra-individual
231 variability. DNA fragmentation, on the other hand, appears to be more stable across ejaculates.
232 Traditional univariate analyses, particularly simple pairwise correlations, may have limitations in
233 this work, given this particular population, and may lack the power to capture more complex
234 associations. The contribution and integration of new methods from artificial intelligence may
235 provide an interesting way to better process available clinical and biological data.

236

237 The fertility score previously developed and published by our team was built on
238 anthropometric, metabolic, and antioxidative factors, parameters close to those studied in this
239 work. As shown in figure 1, the result of the score was put into perspective with sperm
240 parameters. Interestingly, this score is the only feature, along with HDL level, that correlates
241 significantly with DNA fragmentation level. Notwithstanding controversial findings in the

242 literature, DNA fragmentation level is widely recognized as a marker of intrinsic semen quality.
243 Its levels seem to affect embryo quality, implantation and miscarriage risk ²⁶. Many factors can
244 increase the level of sperm DNA fragmentation, including obesity, high local temperature, drug
245 treatment, exposure to environmental pollutants, and smoking.

246 Using the strength of multivariate statistical modelling, the score may reveal underlying
247 phenomena that are difficult to identify using conventional univariate methods alone. By
248 correlating significantly with DNA fragmentation, the score may provide a more comprehensive
249 way of assessing male semen quality, particularly in patients with normal or subnormal semen.
250 This assumption must be demonstrated by further studies. Furthermore, from an analytical and
251 technical point of view, DNA fragmentation is a more challenging and less standardized
252 biomarker than other semen analysis parameters.

253 Although only men with no severe sperm alteration were recruited, a negative correlation
254 between BMI, visceral fat and sperm motility was observed. Obesity in males has been found to
255 be a risk factor for infertility and increased time to conception ³. In men, many studies, supported
256 by a meta-analysis ²⁷, have reported an alteration of sperm parameters in case of overweight and
257 obesity, more specifically a decrease in sperm concentration and sperm count ²⁸⁻³⁰. Sperm
258 motility also appears to be affected by overweight or obesity ³¹.

259 Dyslipidemia has been reported to negatively affect testicular and epididymal function,
260 sperm maturation and quality, and ejaculatory function ³². Consistent with these findings, in this
261 population of patients with unexplained infertility, we observed an association between lipid
262 levels and some semen parameters. Indeed, despite the absence of patients with dyslipidemia,
263 unfavorable lipid composition (high total and LDL cholesterol, and/or low HDL) may be
264 negatively associated with semen parameters. However, while blood glucose was a strongly

265 discriminating factor between fertile vs infertile couples (as studied previously ¹⁰), it does not
266 appear to be correlated with sperm parameters in this population of infertile men. The molecular
267 mechanisms involved in this phenomenon are unclear, but hypotheses have been proposed.
268 Impairment of steroidogenesis has been reported. Cholesterol may modulate the renin-
269 angiotensin system in the testes, leading to inhibition of steroidogenesis. This in turn leads to a
270 decrease in testosterone production ³³. Post-testicular sperm maturation may also be affected:
271 hypercholesterolemia would induce changes in the epididymal epithelium such as an
272 accumulation of cholesterol ester lipid droplets in the smooth muscle of the epididymal tract.
273 Epididymal peristalsis contractions would be impaired, compromising sperm progression inside
274 the epididymal lumen, and thus the maturation process ³⁴. Eventually, an increase of oxidative
275 stress and an excess of free radical production could also be the consequence of dyslipidemia ³⁵.
276 This last hypothesis is consistent with our findings. Indeed, in our cohort, the HDL level and thus
277 the “good” cholesterol level was correlated with the DNA fragmentation level, directly related to
278 oxidative stress.

279
280
281 Besides overweight and lipid and carbohydrate profile, some microelements and vitamins
282 were positively correlated with sperm count and motility. Vitamin B12 levels and glutathione
283 peroxidase activity (GPX) were correlated with sperm motility and total sperm count,
284 respectively, in this cohort. A meta-analysis by Banihani ³⁶ highlighted the importance of
285 vitamin B12 in sperm physiology and quality, particularly on total sperm count ³⁷. Indeed, lower
286 vitamin B12 levels have been reported in infertile men ³⁸. Several beneficial mechanisms of
287 vitamin B12 have been described, including its link to homocysteine metabolism and its
288 antioxidant properties ³⁹.

289 Numerous studies have demonstrated the importance of the GPX during spermatogenesis and its
290 relationship with male fertility^{40,41}. Similarly, previous studies have reported higher GPX activity
291 in seminal plasma in patients with better sperm quality^{42,43}. GPX plays a key function as reactive
292 oxygen species (ROS) scavengers for spermatozoa, to maintain the balance between ROS
293 production and recycling⁴⁴.

294 A limitation of this study was the lack of measurement of antioxidant status in seminal
295 plasma for the entire cohort of patients. In addition, and in accordance with international
296 recommendations⁴⁵⁻⁴⁷, exploratory andrological assessments (hormone tests, ultrasound, etc.)
297 were not carried out in our patients.

298
299 This study focused on a particular population of men from couples with unexplained
300 infertility, and a limited population size of 75 patients. However, measurement of sperm
301 parameters alone, which were normal or subnormal in this population, does not appear to be
302 sufficient to evaluate and stratify these patients. These findings suggest that despite a normal or
303 subnormal semen parameters, the metabolic and oxidative status factors considered in this study,
304 which are probably in part linked to the lifestyle and behavior of these patients, should be
305 integrated into a holistic and comprehensive diagnostic and therapeutic strategy. Unlike other
306 factors or causes of infertility (genetic or hormonal abnormalities, chemotherapy, etc.), in this
307 case patients can be involved in the management of their health, especially given the reversible
308 character of these indicators. Indeed, an improvement in metabolic and oxidative status could be
309 associated with a reduced risk of infertility, and even a better chance of success when in vitro
310 fertilization (IVF) treatment is still required.

311

312 Improving lifestyle for these patients therefore appears to be essential, and even beyond
313 reproductive health alone, for overall physical and mental well-being. Such improvement should
314 be advised by healthcare professionals, using dietary and physical activity coaching or guidance
315 properly designed and validated by international guidelines. Interventional studies are needed to
316 confirm the positive impact of lifestyle improvement ⁴⁸.

317

318 **Conclusion**

319 Favorable anthropometric, metabolic and oxidative patterns, which may reflect an
320 appropriate lifestyle, appear to positively impact overall health, in particular reproductive
321 function. Despite normal or subnormal semen parameters, findings reported in this work using
322 patients from a cohort of idiopathic infertile couples show that altered body composition, as well
323 as unfavorable lipid balance and vitamin and microelement deficiency were associated with
324 lower semen parameters.

325 This study, consistent with previous publications in this area, suggests that beyond semen
326 quality parameters, in an essential assessment of male fertility, other key factors should be taken
327 into account. A more comprehensive evaluation of the patients' health, affecting their nutritional,
328 metabolic and oxidative status, seems to be an indispensable element to consider for a more
329 holistic care. In this regard, the application of emerging artificial intelligence techniques may
330 provide a unique opportunity to integrate all these parameters and deliver personalized care.

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332

333 **Author contributions:**

334 GB participated in the study's conception and design, performed statistical analysis, and drafted the manuscript. RL
335 supervised the study, participated in patient recruitment, interpreted the data, and critically revised the manuscript for
336 intellectual content. CF was involved in study conception and design, patient recruitment, interpretation of data,
337 critical revision of the manuscript for intellectual content. SC and AL both worked on the study conception and
338 design and critically revised the manuscript for intellectual content. CD contributed to study conception and design,
339 patient recruitment, interpretation of data, and drafting of the manuscript.

340 The ALIFERT collaborative group members contributed to the study design and were involved in patient recruitment
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345

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505 **Table 1** : Baseline characteristics: clinical, biological and sperm analysis. Data reported as mean
506 \pm standard deviation. BMI : Body mass index ; LDL : Low-density lipoprotein ; HDL : High-
507 density lipoprotein
508 § : 4 patients with unknown systolic blood pressure (mmHg) and diastolic blood pressure (mmHg), 6 patients with
509 unknown ascorbic acid
510

Parameters	n = 75
Baseline, metabolic and biological parameters	
Age (years)	33.6 \pm 5.3
BMI (kg/m ²)	26.1 \pm 4.3
Waist measurement (cm)	92.6 \pm 11.3
Visceral fat (%)	7.0 \pm 4.2
Systolic Blood pressure (mmHg) §	126.8 \pm 12.2
Diastolic Blood pressure (mmHg) §	80.8 \pm 10.0
Glycemia (mmol/L)	5.0 \pm 0.7
Cholesterol (mmol/L)	5.2 \pm 1.0
LDL (mmol/L)	3.3 \pm 1.0
HDL (mmol/L)	1.3 \pm 0.4
Triglyceride (mmol/L)	1.4 \pm 0.9
Micronutrients and vitamins	
Vitamin D (ng/mL)	23.2 \pm 11.3
Folate (nmol/L)	12.7 \pm 7.2
Cobalamin (pmol/L)	300.0 \pm 111.0
Retinol (μ mol/L)	2.1 \pm 0.5
Alpha-Tocopherol (μ mol/L)	25.0 \pm 6.1
Zinc (μ mol/L)	12.8 \pm 1.9
Selenium (mmol/L)	1.2 \pm 0.2
Glutathione peroxidase (mUI/mL)	391.6 \pm 61.0
Ascorbic acid (mg/mL) §	42.3 \pm 18.8
Alpha-Carotene (μ mol/L)	0.1 \pm 0.1
Lycopene (μ mol/L)	0.6 \pm 0.3
Lutein (μ mol/L)	0.3 \pm 0.2
β -Cryptoxanthin (μ mol/L)	0.2 \pm 0.2
Glutathione (μ mol/L)	829.6 \pm 200.0
Beta-Carotene (μ mol/L)	0.4 \pm 0.3
Machine learning model score	0.5 \pm 0.1
Semen quality parameters	

Semen volume (ml)	3.4 ± 1.6
Sperm concentration (10 ⁶ /ml)	44.2 ± 29.8
Total sperm count (TSC) (10 ⁶)	143.7 ± 109.4
Progressive Motility a+b (%)	37.5 ± 11.6
Vitality (%)	63.4 ± 15.4
Normal morphology (%)	20.7 ± 9.9
DNA fragmentation rate (%)	28.6 ± 18.4

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515 **Table 2:** Correlations (Pearson's parametric test) between the studied parameters and sperm
516 quality. BMI : Body mass index ; LDL : Low-density lipoprotein ; HDL : High-density
517 lipoprotein
518 **: P < 0.01 ; * : P < 0.05 ; n.s., not significant.
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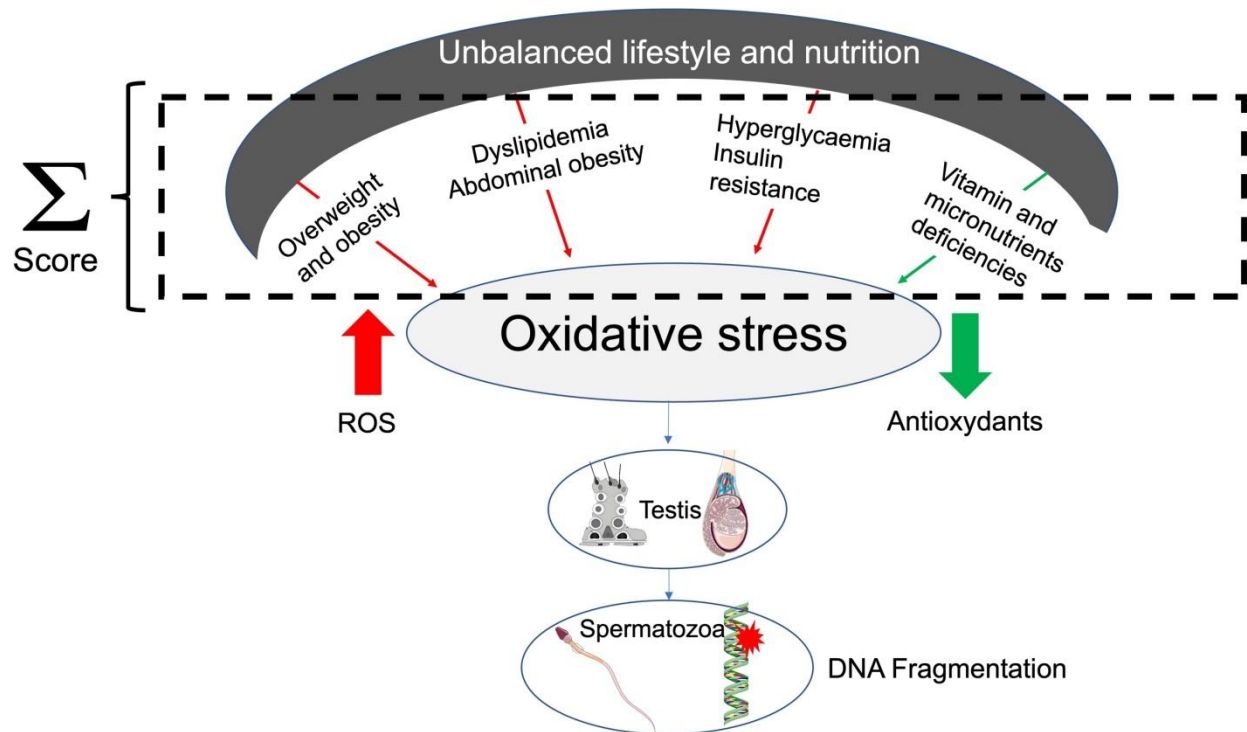
Parameters	Semen volume (ml)	Sperm concentration (10 ⁶ /ml)	Total sperm count (TSC) (10 ⁶)	Progressive Motility a+b (%)	Vitality (%)	Normal morphology (%)	DNA fragmentation rate (%)
	r (P value)	r (P value)	r (P value)	r (P value)	r (P value)	r (P value)	r (P value)
baseline, metabolic and biological parameters							
Age (years)	-0.142 (n.s.)	0.243 (n.s.)	0.199 (n.s.)	-0.066 (n.s.)	-0.119 (n.s.)	0.045 (n.s.)	0.107 (n.s.)
BMI (kg/m ²)	-0.307 (*)	-0.08 (n.s.)	-0.136 (n.s.)	-0.233 (*)	-0.217 (n.s.)	-0.068 (n.s.)	0.078 (n.s.)
Waist measurement (cm)	-0.286 (*)	-0.102 (n.s.)	-0.157 (n.s.)	-0.191 (n.s.)	-0.169 (n.s.)	0.015 (n.s.)	0.152 (n.s.)
Visceral fat (%)	-0.221 (n.s.)	-0.06 (n.s.)	-0.062 (n.s.)	-0.27 (*)	-0.285 (**)	-0.067 (n.s.)	0.152 (n.s.)
Blood pressure Systolic(mmHg)	-0.194 (n.s.)	0.129 (n.s.)	0.053 (n.s.)	0.087 (n.s.)	-0.045 (n.s.)	0.073 (n.s.)	-0.12 (n.s.)
Blood pressure Diastolic(mmHg)	-0.23 (n.s.)	0.187 (n.s.)	0.078 (n.s.)	-0.011 (n.s.)	-0.107 (n.s.)	0 (n.s.)	-0.088 (n.s.)
Glycemia (mmol/L)	0.059 (n.s.)	0.127 (n.s.)	0.132 (n.s.)	-0.147 (n.s.)	-0.166 (n.s.)	0.018 (n.s.)	-0.064 (n.s.)
Cholesterol (mmol/L)	-0.189 (n.s.)	-0.155 (n.s.)	-0.272 (*)	-0.211 (n.s.)	-0.311 (**)	-0.117 (n.s.)	-0.034 (n.s.)
LDL (mmol/L)	-0.13 (n.s.)	-0.201 (n.s.)	-0.249 (*)	-0.208 (n.s.)	-0.326 (**)	-0.022 (n.s.)	0.053 (n.s.)
HDL (mmol/L)	0.031 (n.s.)	-0.045 (n.s.)	-0.054 (n.s.)	-0.003 (n.s.)	0.011 (n.s.)	-0.186 (n.s.)	-0.364 (**)
Triglycerides (mmol/L)	-0.152 (n.s.)	0.088 (n.s.)	-0.04 (n.s.)	-0.016 (n.s.)	-0.041 (n.s.)	-0.066 (n.s.)	0.1 (n.s.)
Micronutrients and vitamins							
Vitamin D (ng/mL)	0.208 (n.s.)	-0.028 (n.s.)	0.095 (n.s.)	-0.077 (n.s.)	0.002 (n.s.)	0.12 (n.s.)	0.149 (n.s.)
Folate (nmol/L)	0.09 (n.s.)	-0.121 (n.s.)	0 (n.s.)	0.197 (n.s.)	0.027 (n.s.)	0.155 (n.s.)	0.161 (n.s.)
Cobalamin (pmol/L)	-0.173 (n.s.)	0.057 (n.s.)	-0.08 (n.s.)	0.275 (*)	-0.063 (n.s.)	0.106 (n.s.)	0.074 (n.s.)
Retinol (µmol/L)	-0.049 (n.s.)	-0.046 (n.s.)	-0.076 (n.s.)	0.025 (n.s.)	0.159 (n.s.)	-0.037 (n.s.)	0.126 (n.s.)
Alpha-Tocopherol (µmol/L)	-0.042 (n.s.)	-0.194 (n.s.)	-0.226 (n.s.)	0.05 (n.s.)	-0.035 (n.s.)	-0.105 (n.s.)	-0.043 (n.s.)
Zinc (µmol/L)	-0.039 (n.s.)	-0.001 (n.s.)	0.008 (n.s.)	-0.122 (n.s.)	0.124 (n.s.)	0.043 (n.s.)	0.027 (n.s.)
Selenium (mmol/L)	-0.031 (n.s.)	0.022 (n.s.)	0.015 (n.s.)	0.051 (n.s.)	-0.105 (n.s.)	0.03 (n.s.)	0.07 (n.s.)
Glutathione peroxidase (mUI/mL)	0.055 (n.s.)	0.204 (n.s.)	0.23 (*)	0.017 (n.s.)	-0.182 (n.s.)	-0.053 (n.s.)	0.002 (n.s.)
Ascorbic acid (mg/mL)	-0.114 (n.s.)	-0.077 (n.s.)	-0.145 (n.s.)	0.141 (n.s.)	0.067 (n.s.)	0.091 (n.s.)	0.129 (n.s.)
Alpha-Carotene (µmol/L)	-0.082 (n.s.)	-0.003 (n.s.)	-0.05 (n.s.)	-0.042 (n.s.)	0.041 (n.s.)	-0.05 (n.s.)	-0.041 (n.s.)
Lycopene (µmol/L)	0.13 (n.s.)	-0.111 (n.s.)	-0.074 (n.s.)	-0.032 (n.s.)	-0.221 (n.s.)	-0.117 (n.s.)	-0.077 (n.s.)
Lutein (µmol/L)	-0.086 (n.s.)	-0.148 (n.s.)	-0.872 (n.s.)	0.149 (n.s.)	-0.05 (n.s.)	0.009 (n.s.)	0.073 (n.s.)
β-Cryptoxanthin	-0.146 (n.s.)	-0.028 (n.s.)	-0.112 (n.s.)	0.069 (n.s.)	-0.018 (n.s.)	0.045 (n.s.)	-0.086 (n.s.)

Glutathione ($\mu\text{mol/L}$)	0.137 (n.s.)	-0.041 (n.s.)	0.067 (n.s.)	-0.003 (n.s.)	-0.078 (n.s.)	-0.035 (n.s.)	0.135 (n.s.)
Beta-Carotene ($\mu\text{mol/L}$)	0.022 (n.s.)	-0.078 (n.s.)	-0.111 (n.s.)	-0.104 (n.s.)	-0.14 (n.s.)	0.044 (n.s.)	-0.059 (n.s.)
Machine learning model score	0.091 (n.s.)	0.008 (n.s.)	-0.008 (n.s.)	0.132 (n.s.)	0.167 (n.s.)	-0.06 (n.s.)	-0.263 (*)

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525 **Figure 1: A complex relationship between lifestyle, diet, antioxidants and sperm DNA**
 526 **fragmentation.**

527 An unbalanced lifestyle and diet lead to anthropometric, metabolic and nutritional changes,
 528 which can lead to an imbalance in oxidative stress. These consequences are multiple and
 529 interrelated, and the use of artificial intelligence represents a unique opportunity to provide a
 530 more holistic evaluation of the influence of the considered marker.

531 This oxidative stress could be one of the main drivers leading to a decline in male reproductive
 532 functions and consequently in sperm parameters, in particular sperm DNA fragmentation.

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