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Acupuncture Versus Paroxetine for the Treatment of Premature Ejaculation: A Randomized, Placebo-Controlled Clinical Trial

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Abstract

Background: Acupuncture therapy has been used by many researchers in both male and female sexual dysfunction studies.
Objective: To determine whether acupuncture is effective as a premature ejaculation (PE) treatment compared with paroxetine and placebo.
Design, setting, and participants: The study was conducted with methodologic rigor based on Consolidated Standards of Reporting Trials (CONSORT) criteria. Ninety patients referred to the urology clinic at a tertiary training and research hospital with PE were included in this randomized controlled trial and randomly assigned into paroxetine, acupuncture, and placebo groups. Heterosexual, sexually active men aged between 28 and 50 yr were included. Men with other sexual disorders, including erectile dysfunction; with chronic psychiatric or systemic diseases; with alcohol or substance abuse; or who used any medications were excluded.
Intervention: The medicated group received paroxetine 20 mg/d; the acupuncture or sham-acupuncture (placebo) groups were treated twice a week for 4 wk.
Measurements: Intravaginal ejaculation latency times (IELTs) and the Premature Ejaculation Diagnostic Tool (PEDT) were used to assess PE. IELTs were calculated by using a partner-held stopwatch. Data were analyzed statistically.
Results and limitations: Median PEDT scores of paroxetine, acupuncture, and placebo groups were 17.0, 16.0, and 15.5 before treatment, and 10.5, 11.0, and 16.0 after treatment, respectively ($p = 0.001$, $p = 0.001$, and $p = 0.314$, respectively). Subscores after treatment were significantly lower than subscores before treatment in the paroxetine and acupuncture groups but remained the same in the placebo group. Significant differences were found between mean-rank IELTs of the paroxetine and placebo groups ($p = 0.001$) and the acupuncture and placebo groups ($p = 0.001$) after treatment. Increases of IELTs with paroxetine, acupuncture, and placebo acupuncture were 82.7, 65.7, and 33.1 s, respectively. Extent of ejaculation delay induced by paroxetine was significantly higher than that of acupuncture ($p = 0.001$). The most important limitation of the study was the lack of follow-up.
Conclusions: Although less effective than daily paroxetine, acupuncture had a significant stronger ejaculation-delaying effect than placebo.

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1. Introduction

Premature ejaculation (PE) is the most common male sexual complaint, affecting 20–30% of all men [1]. Clinicians tend to use definitions of PE as described in one of the major guidelines, such as the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV-TR) [2]; the International Consultation on Urological Disease [3]; and the American Urological Association guidelines [4]. All of these definitions include three main qualifications: short time interval between penetration and ejaculation; little or no voluntary control of ejaculation; and negative consequences, such as distress. However, control of ejaculation is not mentioned in the DSM-IV-TR; it is only mentioned in the DSM-III [5].

Daily selective serotonin-reuptake inhibitors (SSRIs) are the first choice of treatment in PE; however, this use is off label. Paroxetine, sertraline, and fluoxetine have all been evaluated in patients with PE. Paroxetine, however, has been found to have substantially greater efficiency [6]. Recently, dapoxetine, a new SSRI with a short half-life, has become available in some countries for on-demand treatment of PE but not in our country, Turkey [7].

Acupuncture is a component of the health care system of China that can be traced back at least 2500 yr. The general theory of acupuncture is based on the premise that there are patterns of energy flow through the body that are essential for health. Disruptions of this flow are believed to be responsible for disease. Acupuncture may correct imbalances of flow at identifiable points close to the skin [8]. In 1997, the US National Institutes of Health Consensus Conference concluded that there was sufficient evidence of acupuncture's value to expand its use into conventional medicine and to encourage further studies of its physiology and clinical value [8]. Since then it has been increasingly adapted to treat a wide range of conditions and numerous related research efforts are also currently being conducted. However, no study has investigated acupuncture for the treatment of PE except one made by Chen [9].

In the present study, we aimed to investigate whether acupuncture has an effect on PE treatment by comparing it with paroxetine, a medication that has a proven therapeutic effect on PE, and with a placebo.

2. Materials and methods

After obtaining approval of the local ethics committee, 90 men with self-reported PE who were referred to the outpatient urology clinic at Ankara Training and Research Hospital, Ankara, Turkey, between February and July 2010 and who were accepted to participate were included in this randomized, placebo-controlled clinical trial. All participants were informed, and written consents were taken. All men were heterosexual; sexually active; in an ongoing, stable, sexual relationship for at least 6 mo; and had no other sexual disorders, including erectile dysfunction (ED) as determined by the International Index of Erectile Function questionnaire [10]. Patients with chronic psychiatric or systemic diseases, such as diabetes mellitus; with hypertension; with alcohol or substance abuse; or who used any medications were excluded. Urinalysis and urine cultures were performed routinely at the first examination to exclude urinary infections. Because none of the men had chronic prostatitis symptoms, such as urethral discharge and pelvic pain, further analysis was not performed. None of the men had received any treatments for PE previously.

Intravaginal ejaculation latency time (IELT), DSM-IV TR criteria, and the Premature Ejaculation Diagnostic Tool (PEDT) were used to assess PE before and after treatment. Men were recruited with self-reported IELTs of $\leq$2 min in $>$ 70% of coital attempts. IELTs before and after treatment were calculated by using a partner-held stopwatch.

PEDT is a brief, multidimensional, psychometrically validated instrument developed by Symonds et al [11] for the diagnosis of PE. The Turkish

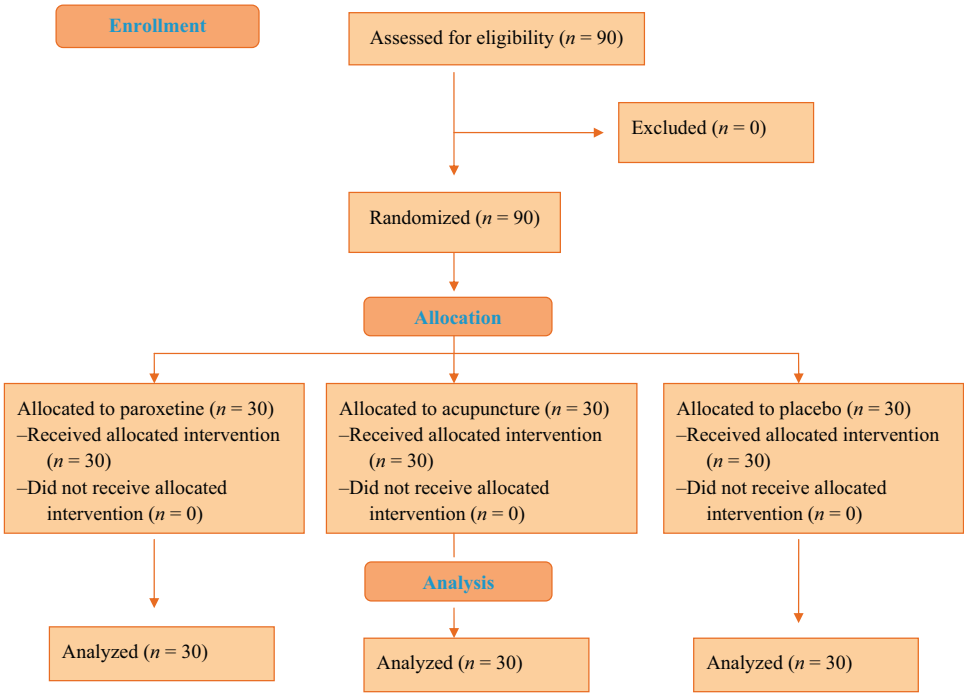

Fig. 1 – CONSORT flow diagram for patients who were brought into trial.

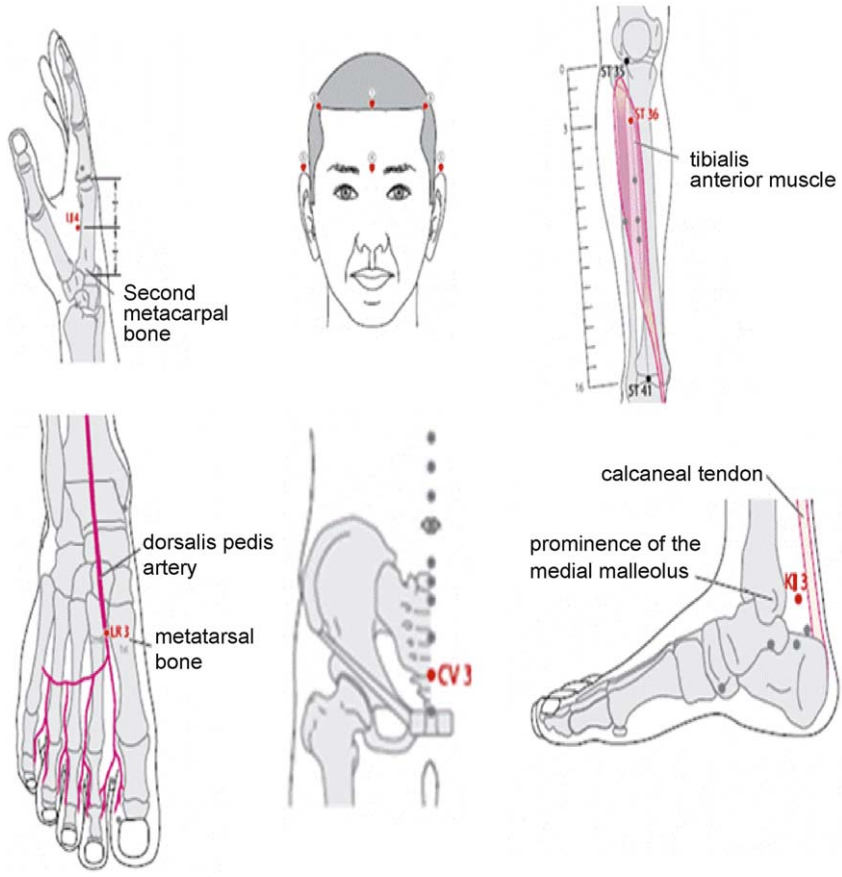

Fig. 2 – Acupuncture points.

version of PEDT developed by Serefoglu et al [12] was used. The tool consisted of five items that capture the essence of DSM-III and DSM-IV-TR: control, frequency, minimal stimulation, distress, and interpersonal difficulty. Sensitivity and specificity analyses suggested a score ≤ 8 indicated no PE, 9 and 10 indicated probable PE, and ≥ 11 indicated PE.

Participants were randomly assigned, by using random sampling numbers, into three treatment groups of 30 men each: paroxetine, acupuncture, and placebo (Fig. 1). The acupuncture group received acupuncture twice a week for a total of eight sessions by a licensed and experienced acupuncturist. Sterile, disposable, 0.25×25 mm, silver needles were used. The needles were inserted bilaterally in four acupuncture points (ST36 Zusanli, LI4 Hegu, KI3 Taixi, and LR3 Taichong) and in EX-HN3 Yintang and CV3 Zhongji points and were left for 20 min after *de qi*, a sensation of heaviness or soreness around the needle experienced by the subject, was obtained without manual or electrical stimulation (Fig. 2). The points were selected by the acupuncturist according to the publication *World Health Organization Standard Acupuncture Point Locations in the Western Pacific Region* [13].

Establishing an effective and realistic placebo is a continuing challenge for acupuncture research. Whereas a pill placebo in drug trials is assumed to be inert and can be administered in a double-blind fashion, this is not possible with acupuncture. Placebos for acupuncture take three forms: nonspecific acupuncture, sham acupuncture, and use of placebo needles [14]. Sham acupuncture was used for the placebo control in this study. It is a type of acupuncture in which needles of the same size as used in the treatment group are prevented from actually being inserted into the body, whether at traditional or nontraditional points. Same-size needles are retracted into the needle handle instead of penetrating the skin at the same points as the treatment group and the subject experiences a non-skin-penetrating pricking sensation instead of *de qi*. Thus the placebo group received sham acupuncture twice a week for a total of eight sessions by the same acupuncturist.

The paroxetine group received 20 mg paroxetine in a daily, early morning dose for 4 wk. All participants were asked to use a partner-held stopwatch to time IELT over a 4-wk duration and were asked not to use condoms or topical penile anesthetic creams or sprays.

All parameters of each groups were assessed at the end of the fourth week. Data were analyzed using SPSS v.15 software (SPSS Inc, Chicago, IL, USA). Definitive statistics were expressed as mean rank, difference, and median for continuously measured variables (PEDT scores and IELT values) and as frequency and percentage for nominal variables. The Shapiro-Wilk test was used to assess the group-variance distributions of total PEDT scores and IELTs before and after treatment. According to this assessment, the distributions of PEDT scores and IELT values were not normally distributed ($p < 0.05$). Therefore, the Mann-Whitney *U* test and the Kruskal-Wallis test were used to assess the presence of a statistical difference between two groups and among three groups, respectively. The Wilcoxon signed-rank test was used for within-group comparisons. Results were considered significant at $p < 0.05$.

3. Results

The mean ages of the groups were similar: 37.5 yr (range: 28–47), 40.4 yr (range: 30–50), and 38.3 yr (range: 28–48) in the paroxetine, acupuncture, and placebo groups, respectively. The majority of the participants (91.1% [82 of 90]) were married.

Table 1 – The frequency of sexual intercourse and the characteristics of premature ejaculation

	Paroxetine group, No. (%)	Acupuncture group, No. (%)	Placebo group, No. (%)	Total, No. (%)
Frequency of intercourse				
Daily	0 (0.0)	1 (3.3)	0 (0.0)	1 (1.2)
2–3 times per week	23 (76.7)	24 (80.0)	23 (76.7)	70 (77.8)
1 time per week	6 (20.0)	3 (10.0)	5 (16.7)	14 (15.5)
1–2 times per month	1 (3.3)	2 (6.7)	2 (6.6)	5 (5.5)
Classification of premature ejaculation				
Lifelong (primary)	21 (70.0)	19 (63.3)	19 (63.3)	59 (65.5)
Acquired (secondary)	9 (30.0)	11 (36.7)	11 (30.0)	31 (34.5)
Ejaculation time				
With very little stimulation	2 (6.7)	2 (6.7)	2 (6.7)	6 (6.7)
Before penetration	1 (3.3)	0 (0.0)	1 (1.3)	2 (2.2)
At penetration	7 (23.3)	9 (30.0)	8 (26.7)	24 (26.7)
Shortly after penetration	20 (66.7)	19 (63.3)	19 (65.3)	58 (64.4)

The frequency of sexual intercourse and the characteristics of PE are shown in Table 1. The majority of the subjects (65.5% [59 of 90]) had lifelong PE. Although in 64.4% of the men ejaculation time was determined as shortly after penetration (26.7%), ejaculation times of the others were at penetration with very little stimulation and before penetration (6.7% and 2.2%, respectively).

The comparisons of median PEDT values of groups before and after treatment are shown in Table 2. The median values of PEDT scores before treatment were 17.0, 16.0, and 15.5 in the paroxetine, acupuncture, and placebo groups, respectively. After treatment, values decreased to 10.5 in the paroxetine group, 11.0 in the acupuncture group, and 16.0 in the placebo group. The decreases in median values of

Table 2 – Comparison of study groups' self-reported Premature Ejaculation Diagnostic Tool scores

		Median	Mean rank	*p*
Question 1 Before treatment	Paroxetine	4.0	64.30	0.388
	Acupuncture	3.0	55.00	
	Placebo	3.5	62.20	
After treatment	Paroxetine	2.0	46.15	0.001
	Acupuncture	2.0	50.05	
	Placebo	3.5	85.30	
Question 2 Before treatment	Paroxetine	4.0	62.50	0.552
	Acupuncture	4.0	62.50	
	Placebo	4.0	56.50	
After treatment	Paroxetine	2.5	50.50	0.001
	Acupuncture	3.0	54.00	
	Placebo	3.5	77.00	
Question 3 Before treatment	Paroxetine	3.0	56.40	0.589
	Acupuncture	4.0	62.55	
	Placebo	4.0	62.55	
After treatment	Paroxetine	1.5	44.50	0.001
	Acupuncture	2.5	57.35	
	Placebo	4.0	79.65	
Question 4 Before treatment	Paroxetine	3.0	61.00	0.973
	Acupuncture	3.0	59.50	
	Placebo	3.0	61.00	
After treatment	Paroxetine	1.0	47.60	0.005
	Acupuncture	2.0	61.85	
	Placebo	3.0	72.05	
Question 5 Before treatment	Paroxetine	3.0	63.50	0.781
	Acupuncture	3.0	59.00	
	Placebo	3.0	59.00	
After treatment	Paroxetine	1.5	54.95	0.064
	Acupuncture	1.0	55.90	
	Placebo	3.0	70.65	
Total scores Before treatment	Paroxetine	17.0	64.10	0.712
	Acupuncture	16.0	58.10	
	Placebo	15.5	59.30	
After treatment	Paroxetine	10.5	46.95	0.001
	Acupuncture	11.0	55.60	
	Placebo	16.0	78.95	
Total score differences	Paroxetine	5.0	76.80	0.001
	Acupuncture	4.0	66.90	
	Placebo	0.0	37.80	

Table 3 – Comparisons of intravaginal ejaculation latency times of the groups before and after treatment

IELT		Median	Mean rank	*p*
Before treatment	Paroxetine	20	59.80	0.617
	Acupuncture	25	64.55	
	Placebo	20	57.15	
After treatment	Paroxetine	70	77.70	0.001
	Acupuncture	70	63.50	
	Placebo	25	40.30	
Difference	Paroxetine	60	82.70	0.001
	Acupuncture	20	65.70	
	Placebo	0	33.10	

IELT = intravaginal ejaculation latency time.

PEDT scores were 5, 4, and 0, and negative mean ranks were 18.4, 18.2, and 20.1 in the paroxetine, acupuncture, and placebo groups, respectively. Total scores after treatment were significantly lower than scores before treatment in the paroxetine and acupuncture groups, but no difference was found in the placebo group ($p = 0.001$, 0.001, and 0.314, respectively). No significant differences were found between the total scores of the paroxetine and acupuncture groups before and after treatment, but significant differences were determined between the paroxetine and placebo groups ($p = 0.001$) and between the acupuncture and placebo groups ($p = 0.001$) after treatment. Similarly, no significant differences were found between subscores of the paroxetine and acupuncture groups before and after treatment, but significant differences were determined between the paroxetine and placebo groups and between the acupuncture and placebo groups after treatment.

In the present study, each man had an IELT value calculated before and after treatment. Therefore, it was not appropriate to assess geometric mean IELT, and we used mean rank and difference of IELT for statistical analysis. Hence no differences were found among groups before treatment according to mean-rank IELTs ($p = 0.617$). However, significant differences were determined between mean-rank IELTs of the paroxetine and placebo groups ($p = 0.001$) and the acupuncture and placebo groups ($p = 0.001$) after treatment. The increases of IELTs with paroxetine, acupuncture, and placebo acupuncture were 82.7 s, 65.7 s, and 33.1 s, respectively. When the extent of ejaculation delay was compared, it was found that ejaculation delay induced by paroxetine was significantly higher than that induced by acupuncture after treatment ($p = 0.001$) (Table 3).

No questionnaire was used to evaluate the side effects; however, no side effects were observed in any of the patients.

4. Discussion

PE is the most frequent male sexual complaint, and it has a serious impact on quality of life for both the patient and his partner. Therefore, one of the goals for treatment of PE should be improvement in patient and partner satisfaction in relation to sexual intercourse and quality of life [15]. In our study, before treatment, patients felt moderately or very frustrated due to PE and were concerned about their partners feeling unfulfilled. The main elements of DSM-IV-TR—frequency, minimal stimulation, distress, and interpersonal difficulty—were significantly improved and IELTs were increased with paroxetine and with acupuncture therapies, compared to placebo.

Significant advances have been made in recent years in the management of PE. Currently, daily SSRI treatments are the first choice in treatment of PE [7]. Based on a systematic review, SSRIs were observed to increase the mean IELT value 2.6- to 13.2-fold [6]. Among SSRIs, paroxetine has been found to have greater efficacy and 20-mg paroxetine daily demonstrated an approximately 8-fold increase in IELT versus placebo [1,16–19]. We also found that paroxetine was effective in PE treatment versus placebo and was significantly more effective than acupuncture in delaying ejaculation. However, although less effective than daily paroxetine, acupuncture had a significantly stronger ejaculation-delaying effect than placebo.

Acupuncture therapy has been used by many researchers both in male and female sexual dysfunction; however, the results are conflicting. Kho et al [20] investigated the use of acupuncture in ED and found that acupuncture did not influence the profile of the stress and sex hormones but did improve the quality of erection and restored the sexual activity with an overall effect of 39%. Aydin et al [21] examined the effects of acupuncture in the treatment of male sexual dysfunction and concluded that although the improvement was not statistically significant, treatment with acupuncture could be used as an adjuvant therapy in nonorganic male sexual dysfunction. Yaman et al [22] evaluated the curative effects of acupuncture therapy in men with purely psychogenic impotence and found that 69% of the patients demonstrated successful erections. In a review by Lee et al [23] of four studies of acupuncture therapy for ED, one randomized controlled trial showed beneficial effects of acupuncture compared with sham acupuncture in terms of response rate, while another found no effects of acupuncture. The authors concluded that the evidence was insufficient to suggest that acupuncture is an effective intervention for treating ED.

As stated above, most of the researchers who studied the effect of acupuncture therapy on male sexual dysfunction were focused on ED, and the field lacks studies of PE. The only study that we found in the literature regarding acupuncture therapy in PE was conducted by Chen [9]. He compared therapeutic effects of acupuncture and medication (oral Sailete 20 mg/d) on primary, simple PE and found the total effective rates were 82.1% in the acupuncture group and

63.6% in the medication group. In our study, acupuncture had a significant effect on ejaculation delay compared to placebo; however, it was less effective than daily paroxetine.

Many studies in animals and humans have demonstrated that acupuncture can cause multiple biologic responses [24,25]. These responses can occur at or close to the site of application or at a distance, mediated mainly by sensory neurons to many structures within the central nervous system. This can lead to activation of pathways affecting various physiologic systems in the brain as well as in the periphery. A focus of attention has been the role of endogenous opioids in acupuncture analgesia. Stimulation by acupuncture may also activate the hypothalamus and the pituitary gland, resulting in a broad spectrum of systemic effects. Alteration in the secretion of neurotransmitters and neurohormones and changes in the regulation of blood flow, both centrally and peripherally, have been documented [8]. The results of the present study, albeit speculative, may support the hypothesis that acupuncture, as mentioned before, alters the secretion of neurotransmitters like SSRIs.

Some commentators have suggested that alternative therapies might have pronounced and clinically significant placebo effects. Generally, across the various trials, outcomes did not differ between real and sham-acupuncture groups; however, subjects in both of these groups had substantially greater symptom improvement than did those in no-treatment and usual clinical-care groups. These results, therefore, accord with the hypothesis that acupuncture works by means of a placebo effect. Placebo mechanisms can interact with drug treatments, even if no placebo is given, since every treatment has the potential to activate and modulate placebo mechanisms, many of which can act on similar biochemical pathways as the actual drug does [26]. The result of the present study showed that real acupuncture was more effective than placebo acupuncture. This result seems to refute the hypothesis that it has a placebo effect. It can be speculated that acupuncture might have an effect through some mechanisms that we could not explain. It is certain that further studies are needed for definitive results.

Despite the importance of the current findings, several limitations must be mentioned. First, acupuncture therapies were performed in an outpatient clinic with other patients and the environment was not suitable. Next, only two IELT measurements, one at baseline and one after treatment, were made; thus, these IELT values were an unreliable tool to measure treatment effects. In addition, as no follow-up was conducted, we could not know if treatment effects continued.

5. Conclusions

Although acupuncture is less effective than daily paroxetine, it had a significantly stronger ejaculation-delaying effect than placebo and seems to be an alternative to other treatment models in the treatment of PE. However, further investigations in large cohorts with longer follow-up are needed to obtain more reliable results.

Author contributions: Melih Sunay had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: D. Sunay, M. Sunay, Arslan.
Acquisition of data: M. Sunay, Aydoğmuş, Bağbancı, Arslan.
Analysis and interpretation of data: D. Sunay, M. Sunay, Aydoğmuş.
Drafting of the manuscript: D. Sunay, M. Sunay, Aydoğmuş.
Critical revision of the manuscript for important intellectual content: D. Sunay, M. Sunay, Karabulut, Emir.
Statistical analysis: D. Sunay, Aydoğmuş.
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