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Principal component analysis for diagnostic-therapeutic variables in competitive sports with post traumatic knee synovitis

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ABSTRACT

Introduction: The pain and inflammation are main characteristics of the post traumatic knee synovitis in competitive athletes. **Objective:** To use the principal component analysis for diagnostic-therapeutic variables in competitive athletes during the first phase of rehabilitation with conventional therapy and extremely low frequency electromagnetic field at 60 Hz. **Methods:** It was carried out a longitudinal, retrospective and controlled pilot study. The principal component analysis was applied to analyze the diagnostic-therapeutic variables at the beginning and the end of applications of these two analgesic and anti-inflammatory therapy types in 39 and 43 competitive athletes with post traumatic knee synovitis, respectively. **Results:** The first (individual response of competitive athletes to external agent) and second (individual physical condition) principal components prevailed in this study. The location of these competitive athletes in each quadrant depended on their functional states and the type of therapy applied to them (conventional therapy or extremely low frequency electromagnetic field at 60 Hz). **Conclusion:** The principal component analysis with the first two principal components is useful for the classification of competitive athletes with post traumatic knee synovitis, according to their functional states, the selection of they for the second phase of rehabilitation, and possible prognostic of these athletes with or without the conventional therapy and extremely low frequency electromagnetic field at 60 Hz.

Keywords: Competitive athletes; post traumatic knee synovitis; principal component analysis, analgesic and anti-inflammatory conventional therapy; extremely low frequency electromagnetic field at 60 Hz

Análisis de componentes principales para variables diagnóstico-terapéuticas en deportistas competitivos con sinovitis de rodilla postraumática

RESUMEN

Introducción: El dolor e inflamación son las características principales de la sinovitis de rodilla postraumática en deportistas competitivos. **Objetivo:** Analizar los componentes principales para variables diagnostico-terapéuticas en deportistas competitivos durante la primera fase de la rehabilitación con la terapia convencional y el campo electromagnético de frecuencia extremadamente baja a 60 Hz. **Métodos:** Un estudio piloto, longitudinal, retrospectivo y controlado fue llevado a cabo. El análisis de componentes principales fue aplicado para analizar variables diagnóstico-terapéuticas al comienzo y final de las aplicaciones de estos 2 tipos de terapias analgésico y antiinflamatoria en 39 y 43 deportistas competitivos con sinovitis de rodilla postraumática, respectivamente. **Resultados:** El primer y segundo componentes principales (respuesta individual de deportistas competitivos al agente externo y condición física individual) prevalecieron en este estudio. La ubicación de estos deportistas competitivos ubicados en cada cuadrante dependió de sus estados funcionales y tipo de terapia aplicada a ellos (terapia convencional o campo electromagnético de frecuencia extremadamente baja a 60 Hz). **Conclusión:** El análisis de componentes principales con los 2 primeros componentes es útil para la clasificación de deportistas competitivos con sinovitis de rodilla postraumática, según sus estados funcionales, la selección de ellos para la segunda fase de la rehabilitación, y posible pronóstico de estos deportistas sin y con la acción de la terapia convencional o campo electromagnético de frecuencia extremadamente baja a 60 Hz.

Palabras clave: deportistas competitivos; sinovitis de rodilla postraumática; análisis de componentes principales, terapia convencional analgésica y antiinflamatoria; campo electromagnético de frecuencia extremadamente baja a 60 Hz

INTRODUCTION

The post traumatic knee synovitis (PKS) is one of the most frequent injuries in competitive athletes (CAs) due to trauma from direct impact on the joint, sprain, contusion, dislocation and repetitive microtrauma. [1] The PKS consists of inflammation of the synovial membrane lining the knee joint and is classified as acute (6 months or less) or chronic (more than 6 months) according to the time of evolution. [2]

Cascaret-Fonseca et al. [1] apply conventional therapy (T_{conv}) and therapy with the extremely low-frequency electromagnetic field (ELF-EMF) to 60 Hz, named $T_{ELF-EMF}$, in CAs with PKS (CAs-PKS) at 0, 5, 10, 15 and 20 days during the first phase of rehabilitation (analgesic and anti-inflammatory). They use different criteria for diagnosis (interrogation, medical history, physical examination, ultrasound, absolute values of the Visual Analogue Scale (VAS) and VAS ranges) and analgesic effectiveness index (I_{VAS}) and response of CAs-PKS to T_{conv}/$T_{ELF-EMF}$ (RCAs-PKS) of PKS in CAs. Subsequently, Cascaret-Fonseca et al. [3] assign numbers to these diagnostic-therapeutic criteria, resulting in diagnostic-therapeutic variables, which are analyzed with the Rho of Spearman and eta coefficients to know linear and nonlinear correlation degrees among these variables two by two, respectively. This constitutes a limitation for the integrated analysis of diagnostic-therapeutic variables in biological systems due to the number of interacting components. The descriptive statistical technique Principal Component Analysis (PCA) is feasible to study multicomponent systems. [4] Nevertheless, we are not aware of its use for the analysis of diagnostic-therapeutic variables in CAs-PKS rehabilitated with analgesic-anti-inflammatory therapies. Therefore, the objective of this study is to use PCA for the integrated analysis of diagnostic-therapeutic variables in CAs-PKS during the first phase of rehabilitation with T_{conv}/$T_{ELF-EMF}$.

METHODS

Bioethics

A longitudinal, controlled and retrospective pilot study was conducted at the Centro Provincial de Medicina Deportiva de Santiago de Cuba (CEPROMEDE), Cuba, from January to October, 2019. The sports traumatologist evaluated CAs injured by trauma. Then, the traumatologist referred CAs to the orthopedic department of the Juan Bruno Zayas hospital, Santiago de Cuba, Cuba, to confirm the diagnosis of PKS. Subsequently, CAs with PKS, named CAs-PKS, were treated at the rehabilitation service of CEPROMEDE.

This study was approved by the Ethics Committee (date November 06, 2018, code ELFEMF06112018 and registry name ELFEMF-DCs-SRP) and the Scientific Council (November 20, 2018) of CEPROMEDE. This study was governed by the ethical standards of the Declaration of Helsinki; the code of ethics, and good medical and clinical practices established by the Ministry of Health of the Republic of Cuba; and protocols 400-1 (diagnosis and evaluation), 400-2.1 (conventional therapy, T_{conv}) and 400-3.1.2 (extremely low frequency electromagnetic field therapy, $T_{ELF\text{-}EMF}$) implemented at CEPROMEDE. The enrollment date of the first participant in this pilot study was January 7, 2019. (5,6)

Selection criteria

The inclusion criteria were voluntariness of 86 CAs (number of the study universe), diagnosis of PKS of both genders who received care at CEPROMEDE in the period of this study. The exclusion criteria were CAs with tumors diagnosed in any location, psychiatric disorders, decompensated chronic diseases and who had hematological disorders. The dropout criteria were death, voluntary dropout and occurrence of serious adverse events due to the application of $T_{conv}/T_{ELF\text{-}EMF}$. Once CAs-PKS were included in this study, they moved on to the first phase of rehabilitation.

Sample characteristics

They were treated 82 CAs-PKS (52 males and 30 females between 15 and 35 years of age). They were randomly grouped into two groups. The first treatment group, called TG1, was initially formed by 43 CAs-PKS; of these, four only attended the first consultation and therefore were not included in this study. Consequently, TG1 consisted of 39 CAs-PKS who received Tconv for 10 days: cryotherapy (ice pack three times a day for 15 min) combined with ibuprofen 400 mg (INTERMED, India) and metamizole 500 mg (Nanjing Baijingyu Pharmaceutical Co., Ltd., Nanjing, China), both administered orally every 8 h. Of the 39 CAs-PKS in TG1, 23 (nine females and 14 males) and 16 (seven females and nine males) were in the ranges of (15-25) years and (26-35) years of age, respectively.

The second treatment group, called TG2, consisted of 43 CAs-PKS who received TELF-EMF (magnetic induction 11 mT, sine wave type, frequency 60 Hz and exposure time of 20 min). They received 20 sessions of TELF-EMF from Monday to Friday with interruption on weekends. Of 43 CAs-PKS in TG2, 37 (14 females and 23 males) and 6 (all males) were in the ranges of (15-25) years and 26-35 years of age, respectively. TELF-EMF was applied with the magnetic stimulator NaK®-02 (Centro Nacional de Electromagnetismo Aplicado, Universidad de Oriente, Santiago de Cuba, Cuba; Medical Equipment Registration Certificate File No. I0350015041150, Code No. 73BWK).

Variables

Twelve variables were used, such as: *X1* (age), *X2* (gender), *X3* (initial physical examination), *X4* (final physical examination), *X5* (initial ultrasound), *X6* (final ultrasound), *X7* (initial VAS, VAS_i), *X8* (final VAS, VAS_f), *X9* (initial VAS ranges), *X10* (final VAS ranges), *X11* (I_{VAS}), and *X12* (RCAs-PKS). *X3, X5, X7*, and *X9* were referenced to t = 0 days (before application of $T_{conv}/T_{ELF\text{-}EMF}$). *X4, X6, X8, X10, X11* and *X12* were referenced to t = 20 days (end of $T_{conv}/T_{ELF\text{-}EMF}$ application). The VAS_i and VAS_f were VAS values at the beginning and end of the application of T_{conv} and $T_{ELF\text{-}EMP}$, respectively. I_{VAS} and RCAs-PKS were the analgesic effectiveness index and response of CAs-PKS to $T_{conv}/T_{ELF\text{-}EMP}$, respectively.

The values of *X1* were 1 (age group 15-25 years) and 2 (age group 26-35 years); those of *X2*: 1 (female gender) and 2 (male gender); those of *X3* and *X4*: 0 (Grade 0), 1 (Grade I), 2 (Grade II) and 3 (Grade III); and those of *X5* and *X6*: 0 (Grade 0), 1 (Grade I), 2 (Grade II) and 3 (Grade III); those of *X7* and *X8*: 0 (no pain); 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 (excruciating pain); those of *X9* and *X10*: 0 (0, no pain), 1(1-3, mild pain), 2 (4-6, moderate pain), 3 (7-9, moderate pain) and 4 (10, excruciating pain); and those of RCAs-PKS: 0 (CC), 1 (RP), 2 (NC) and 3 (P).

The degree of inflammation was classified as grade 0 (no patellar elevation), grade I (slight patellar elevation), grade II (patella compresses against the trochlear groove) and grade III (inability to compress the patella against the groove). Knee ultrasound allowed assessment of synovial fluid increase which was classified as grade 0 (no effusion), grade I (slight effusion), grade II (moderate effusion) and grade III (severe effusion). (1)

The I_{VAS} was calculated to evaluate the analgesic effectiveness of CAs-PKS receiving $T_{conv}/T_{ELF\text{-}EMP}$, according to the following equation . (1)

$$I_{VAS} = [(VAS_i - VAS_f)/VAS_i]100\ \%.$$

RCAs-PKS was classified into progression (P: $I_{VAS} < 0\%$ and grade III on physical examination and ultrasound), no change (NC: $0 \le I_{VAS} < 33\%$ and grades II and III on physical examination and ultrasound), partial response (PR: 33 ≤ I_{VAS} < 100% and grades I and II on physical examination and ultrasound) and complete cure (CC: I_{VAS} = 100% and grade 0 on physical examination and ultrasound) of the pathology. As RCAs-PKS were ordered from worst to best, CAs-PKS were placed in the previous response if they did not simultaneously meet these three conditions. As the first phase of rehabilitation was analgesic-anti-inflammatory, RCAs-PKS was referred to pain relief and absence of inflammation. [1]

Principal Component Analysis

The PCA was applied to 12 original variables at *t* = 0 and 20 days for TG1 and TG2. The Kaisser criterion (eigenvalues greater than 1) was used to select the number of principal components (PCs). The original variables with the highest weight/contribution to PCs were those with absolute values of loadings equal to or bigger than 40.0g%, which was named threshold of the loading vector, as suggested in Columbie-Regüeiferos et al. [4] Three scenarios were analyzed for both groups. First, PCA considered *X1, X2, X5, X7*, and *X9* at *t* = 0 days (scenery 1). Second, PCA included *X1, X2, X6, X8, X10, X11* and *X12* at *t* = 20 days (scenery 2). The scenery 3 was similar to the scenery 2 without the inclusion of *X11* and *X12* at *t* = 20 days.

In PCA, highly correlated variables (*r* = 1), such as *X3-X5* and *X4-X6*, were not simultaneously used because they complemented each other and provided the same information on PKS in CAs. [7,3,1] This and the greater relevance of ultrasound (diagnostic-confirmative) in the assessment of PKS with respect to physical examination (diagnostic-presumptive) were why we used *X5* and *X6* in this study, and not *X3* and *X4*. [1] Outlier, sedimentation, score (CAs-PKS positioning), influence (variable placement) and double projection plots were obtained for each of the three scenarios of TG1 and TG2. The score and influence plots were shown only in this study with their four quadrants: quadrant I (upper right region), quadrant II (upper left region), quadrant III (lower left region) and quadrant IV (lower right region).

Data processing

All original datasets used in this study were reported by Cascaret-Fonseca et al. Furthermore, PCA was implemented in the statistical program Minitab® 14 (Minitab Inc for Windows, 2003, free software, National Institute of Standards and Technology, Pennsylvania State University, USA, https://www.minitab.com/en-x/products/minitabs). [1] This program was run on a computer (Department of Mathematics, Universidad de Oriente) with Windows 8 operating system with RAM 2.6 GB; 64 bits, 64 processor, Inter R cor etm. The duration of the statistical processing of the data was approximately 2 s.

RESULTS

Conventional therapy

The eigenvalues, proportion of variance explained, proportion of variance explained and weights of each original variable in each of the PCs corresponding to TG1 were showed in table 1. All figures were showed only for the PCs that had eigenvalues greater than 1 in TG1 (figure 1). The influence plots for Scenery 1 (figure 1 A), scenery 2 (figure 1 C) and Scenery 3 (figure 1 E) were showed in figure 1. Furthermore, the score plots for scenery 1 (figure 1 B), Scenery 2 (figure 1 D) and scenery 3 (figure 1 F) were showed in this figure too. Scenery 1: PC1, PC2 and PC3 were the dominant components. *X5, X7* and *X9* had the highest weights and were positively related to PC1. *X1* and *X2* had the highest weights for PC2 and PC3. PC2 was negatively related to *X1* and *X2*. PC3 was positively related to *X1* and negatively related to *X2*. As PC2 and PC3 provided the same information, PC2 was chosen for PCA (table 1). The score plot (figure 1b) showed that CAs-PKS were distributed on different well-defined straight lines PC1 = ± C (C > 0): PC1 = -3.4, PC1 = -3.0, PC1 = -0.5, PC1 = 0.0, PC1 = 0.5 and PC1 = 1.7 corresponding to absolute values 5, 6, 7, 8, 9 and 10 of VAS, respectively. Most of them were distributed between PC1 = -0.5 and PC1 = 0.5.

Scenery 1: PC1, PC2 and PC3 were the dominant components. *X5, X7* and *X9* had the highest weights and were positively related to PC1. *X1* and *X2* had the highest weights for PC2 and PC3. PC2 was negatively related to *X1* and *X2*. PC3 was positively related to *X1* and negatively related to *X2*. As PC2 and PC3 provided the same information, PC2 was chosen for PCA (table 1). The score plot (figure 1b) showed that CAs-PKS were distributed on different well-defined straight lines PC1 = ± C (C > 0): PC1 = -3.4, PC1 = -3.0, PC1 = -0.5, PC1 = 0.0, PC1 = 0.5 and PC1 = 1.7 corresponding to absolute values 5, 6, 7, 8, 9 and 10 of VAS, respectively. Most of them were distributed between PC1 = -0.5 and PC1 = 0.5.

Scenery 2: PC1 and PC2 prevailed. *X6, X8, X10, X11* and *X12* had the highest weights in PC1 (positively related to *X6, X8*, and *X10*, and negatively related to *X11* and *X12*). *X1* and *X2* had the highest weights and were negatively related to PC2. (table 1). The score plot (figure 1 D) showed that CAs-PKSs were not located in straight lines PC1 = ± C (C > 0), but in two well-defined zones. The first (between PC1=-1.0 and PC1 = 4.0) concentrated the majority of CAs-PKS who reported pain relief (absolute VAS values 1-7, and mild and moderate degrees of synovial fluid effusion)1. The second zone (between PC1 = -4.5 and PC1 = -4.0) concentrated all healed DCs (VAS absolute value 0, and no edema or synovial fluid effusion), who were not distributed on a single line, as expected, but on two lines very close to each other. [1]

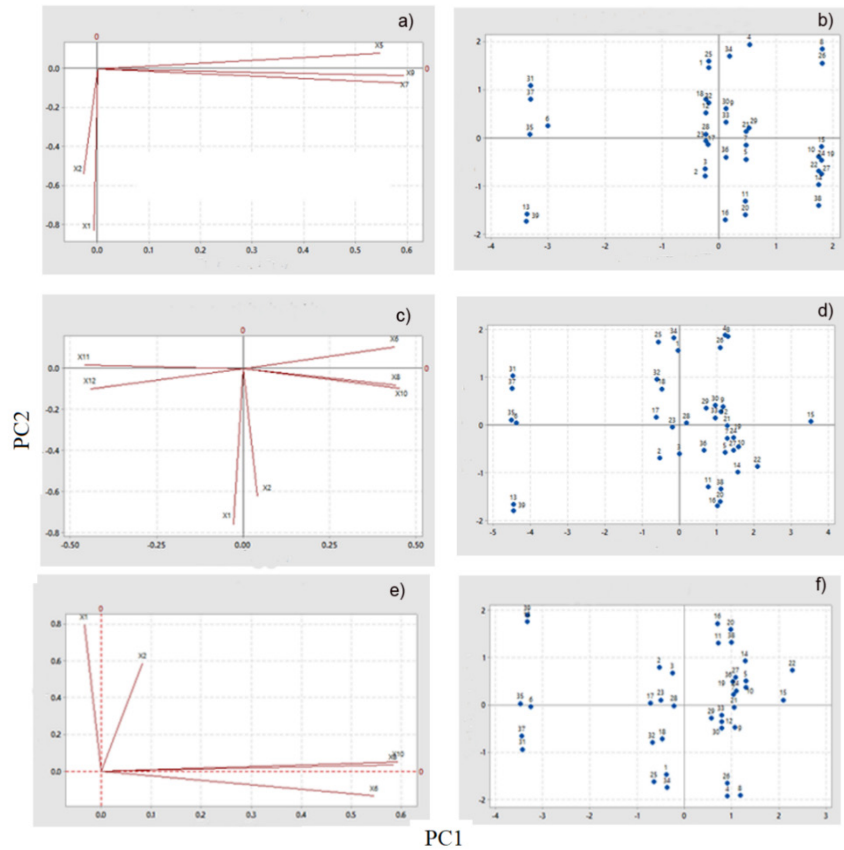

Fig. 1. Plots of PC2 (second principal component) versus PC1 (first principal component) corresponding to TG1: influence (A) and score (B) for Scenario 1; influence (C) and score (D) for Scenario 2; influence (E) and score (F) for Scenario 3

Table 1. Result of the principal component analysis of Scenarios 1-3 corresponding to treatment group 1 t = 0 and 20 days

	***t* = 0 days**			***t* = 20 days**			
	Scenery 1			**Scenery 2**		**Scenery 3**	
Eigenvalues	2.5952	1.0560	1.0108	4.4098	1.0767	2.6696	1.0650
Proportion	0.519	0.211	0.202	0.630	0.154	0.534	0.213
Cumulative proportion	0.519	0.730	0.932	0.630	0.784	0.534	0.747
Eigenvectors							
Variables	PC1	PC2	PC3	PC1	PC2	PC1	PC2
X1	-0.007	-0.833	0.500	-	-0.760	-	0.797
X2	-0.027	-0.541	-0.821	-	-0.622	-	0.586
X5	0.547	0.081	-0.235	-	-	-	-
X7	0.590	-0.075	0.057	-	-	-	-
X9	0.593	-0.033	0.129	-	-	-	-
X6	-	-	-	0.437	-	0.545	-
X8	-	-	-	0.443	-	0.584	-
X10	-	-	-	0.452	-	0.594	-
X11	-	-	-	-0.459	-	-	-
X12	-	-	-	-0.442	-	-	-

Scenery 3: the proportion of the cumulative explained variance decreased by 4.7% of PC1 and PC2 (table 1) and all the original variables (figure 1E) and points (figure 1F) rotated around the PC1 axis, with respect to those of Scenario 2. *X6, X8* and *X10* had the highest weights and were positively related to PC1. *X1* and *X2* showed the highest weights and positively related to PC2. The score plot revealed that CAs-PKS relieved (most) and cured of pain were concentrated between PC1 = -1.0 and PC1 = 2.5, and PC1 = -3.5 and PC1 = -3.0, respectively.

TG1 was the group of CAs-PKS treated with the conventional therapy (cryotherapy+ibuprofen+metamizole). *X1* (age), *X2* (gender), *X3* (initial physical examination), *X4* (final physical examination), *X5* (initial ultrasound), *X6* (final ultrasound), *X7* (initial visual Analogue Scale), *X8* (final visual analogue scale), *X9* (ranges of initial visual analogue scale), *X10* (ranges of final visual analogue scale), *X11* (analgesic effectiveness index), and *X12* (response of CAs-PKS to conventional therapy). The PC1, PC2 and PC3 were the first, second and third principal components, respectively.

Extremely low-frequency electromagnetic field at 60 Hz

The eigenvalues, proportion of variance explained and weights of each original variable in each of the PCs corresponding to TG2 were showed in table 2. All figures were showed only for the PCs that had eigenvalues greater than 1 in TG2 (figure 2). The influence plots for Scenery 1 (figure 2 A), scenery 2 (figure 2 C) and Scenery 3 (figure 2 E) were showed in figure 2. Furthermore, the score plots for scenery 1 (figure 2 B), Scenery 2 (figure 2 D) and scenery 3 (figure 2 F) were showed in this figure too. Scenery 1: PC1 and PC2 prevailed. *X5, X7* and *X9* had the highest weights and positively related to PC1. PC2 was positively related to *X1* and *X2* (table 2). The score plot (figure 2 B) showed that CAs-PKS were distributed at PC1 = -5.3, PC1 = -2.7, PC1 = -0.5, PC1 = 0.0, PC1 = 0.5 and PC1 = 2.5 corresponding to absolute values 5, 6, 7, 8, 9 and 10 of VAS, respectively. Most of them were distributed between PC1 = -0.5 and PC1 = 0.5.

Scenery 2: similar results to those of Scenery 2 in TG1, except that *X1* and *X2* had the highest weights and positively related to PC2 (table 2); and CAs-PKS that essentially relieved and cured (most of) their pains were located between PC1 = 6 and PC1 = 7.0 (absolute values 3, 2 and 1 of the VAS), and PC1 = -1.0 and PC1 = 0.0, respectively (figure 2 D). Surprisingly, the healed CAs were not arranged in a single straight line, but in three closely spaced lines.

Scenery 3: similar results to Scenery 2, except that the proportion of the cumulative explained variance decreased by 5.6% of PC1 and PC2 (Table 2); all original (figure 2 E) and point (figure 2 F) variables rotated around the PC1 axis; *X1* and *X2* had the highest weights and negatively related to

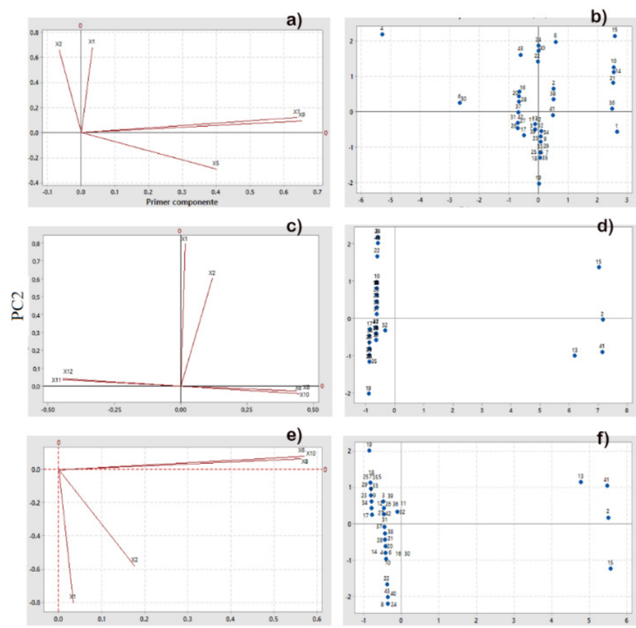

Fig. 2. Plots of PC2 (second principal component) versus PC1 (first principal component) corresponding to TG2: influence (A) and score (B) for Scenario 1; influence (C) and score (D) for Scenario 2; influence (E) and score (F) for Scenario 3

Table 2. Result of the principal component analysis of Scenarios 1-3 corresponding to treatment group 2 at *t* = 0 and 20 days

	***t* = 0 days**		***t* = 20 days**			
	Scenery 1		**Scenery 2**		**Scenery 1**	
Eigenvalues	2.0654	1.1554	5.005	1.081	3.0253	1.0742
Proportion	0.413	0.231	0.715	0.154	0.605	0.215
Cumulative proportion	0.413	0.644	0.715	0.869	0.605	0.820
Eigenvectors						
Variables	PC1	PC2	PC1	PC2	PC1	PC2
X1	0.033	0.677	-	0.794	-	-0.804
X2	-0.066	0.657	-	0.602	-	-0.580
X5	0.400	-0.294	-	-	-	-
X7	0.639	0.120	-	-	-	-
X9	0.653	0.095	-	-	-	-
X6	-	-	0.446	-	0.571	-
X8	-	-	0.438	-	0.563	-
X10	-	-	0.446	-	0.571	-
X11	-	-	-0.445	-	-	-
X12	-	-	0.446	-	-	-

PC2; the CAs-PKS that significantly relieved and cured their pain were distributed between PC1 = 4.5 and PC1 = 5.5, and PC1 = -1.0 and PC1 = 0.0, respectively.

TG2 was the group of CAs-PKS treated with the extremely low-frequency electromagnetic field (ELF-EMF) to 60 Hz. *X1* (age), *X2* (gender), *X3* (initial physical examination), *X4* (final physical examination), *X5* (initial ultrasound), *X6* (final ultrasound), *X7* (initial Visual Analogue Scale), *X8* (final Visual Analogue Scale), *X9* (ranges of initial Visual Analogue Scale), *X10* (ranges of final Visual Analogue Scale), *X11* (analgesic effectiveness index), and *X12* (response of CAs-PKS to ELF-EMF therapy). PC1 and PC2 were the first and second principal components, respectively.

DISCUSSION

The PCA reduces the original 12 variables to two (PC1 and PC2). Although the presumptive and confirmatory diagnostic methods of PKS provide the same information, the differences between these two diagnostic methods are also verified in PCA. This may be argued because absolute value and range of VAS are arranged in the same quadrant whereas ultrasound in another quadrant adjacent to the PC1 axis. Furthermore, the good concordance between presumptive-confirmative variables verified in clinics and excellent correlation (linear and curvilinear) studies at *t* = 0 and 20 days may be established in PCA by mean of the angle formed between these variables with center at the origin of coordinates. [1,3] The greater concordance between presumptive-confirmative variables corresponds to the smaller angle formed between them. Most of the CAs-PKS curated in TG2 (Scenarios 2 and 3) explain why all the presumptive-confirmative variables are located in the same quadrant and the angle between them is close to zero (see influence graphs).

PC1 and PC2 can be interpreted as the individual response and the individual physical condition of the CAs-PKS to the external stimulus, respectively. The external stimulus is the direct trauma (contusion) leading to acute PKS in CAs (*t* = 0 days) or the application of $T_{conv}/T_{ELF\text{-}EMF}$ during the first phase of rehabilitation ($0 < t \leq 20$ days). At *t* = 0 days, the individual response of each of CAs-PKS depends on the cause and intensity of the direct trauma; the severity of the acute PKS; and pain perception (threshold and degree of tolerance). These three aspects, type of therapy ($T_{conv}/T_{ELF\text{-}EMF}$) and timing of CAs-PKS assessment may influence their responses at $0 < t \leq 20$ days.

The individual response of RCAs-PKS to the external stimulus can be favorable (negative values of PC1) or unfavorable (positive values of PC1) at *t* = 0 and 20 days. This may be justified because the variables ultrasound, absolute value and range of VAS are positively related to PC1, while I_{VAS} and RCAs-PKS are negatively related to PC1 in TG1 and TG2.

The lower and higher individual physical fitness of RCAs-PKS (comprehensive bodily, mental and social well-being to perform their physical activities at the indicated time) correspond with the positive and negative values of PC2, respectively. [8] This may be argued because age and gender variables have the highest weights and are negatively related to PC2. This confirms that higher physical condition of RCAs-PKS corresponds to the male gender and age group (26-35) years since they have longer time in sport practice; higher total body density, testosterone level, muscle mass, lean body mass and cardiorespiratory capacity; better strength level; lower flexibility; and less anxiety. These aspects can have a negative impact on rapid recovery of CAs and in the fulfillment of their training programs and/or participation in competitions, in agreement with Roberts et al. [9]

The results presented in the previous paragraph are also explained by the fact that female CAs-PKS have a higher percentage of fat due to estrogens and low levels of testosterone, as reported in; and the high level of competition, the lesser mastery of technique, and the greater number of competitive practitioners occur in the (15-25) years age group, mainly in the male gender. [10] The latter and the immature osteomyoarticular system in CAs under 20 years of age increase the likelihood of them to suffer trauma and thus PKS. Consequently, CAs-PKS in the age group (15-25) years respond unfavorably to direct trauma at t = 0 days. Nevertheless, all CAs-PKS respond satisfactorily to T_{conv} (most relieve pain) and $T_{ELF\text{-}EMF}$ (most cure pain) in both age groups, but the responses of female CAs to T_{conv} and $T_{ELF\text{-}EMF}$ are more unfavorable than those of male CAs because of differences in their physical conditions and types of hormones (estrogen and testosterone), in agreement with Roberts et al and Crewther et al. [9,10]

The positioning of each point on the scoring graph can represent the individual functional status of CAs-PKS, which depends on their physical condition and response to external stimulus of each of them. In addition, the quality of the functional status of CAs-PKS may be better/worse by the higher/lower functional capacity (lower/lower functional limitation, FL) of their knees to perform sports activities and thus lower/greater recovery time (Tr), depending on whether CAs-PKS are rehabilitated or not, as schematically shown in figure 3 for TG1 and TG2 at t = 0 days (figure 3 A) and t = 20 days (figure 3 B). The intervals for FL (in %) and Tr (in days) suggested in each quadrant of figure 3 are in accordance with the interpretation of PC1 and PC2, the PCA results for Scenarios 1-3 of TG1 and TG2, and the experience in rehabilitation of CAs for more than 20 years at CEPROMED.

The figure 3 may suggests that CAs-PKS located to the left (quadrants II and III) and right (Quadrants I and IV) of the PC2 axis have their best and worst functional state qualities, respectively. These qualities do not change with the rotation of all points and variables around the PC1 axis because the same is an invariant transformation. This also explains why the positive relationships and higher weights of the ultrasound, absolute value and VAS range variables do not change when the I_{VAS} and RCAs-PKS variables are not included in PCA. The latter confirms that the first three variables can be used interchangeably for the diagnosis and prognosis of PKS in DCs, as suggested previously. [1,3]

The CAs-PKS that respond favorably to direct trauma (figure 3a) and $T_{conv}/T_{ELF\text{-}EMF}$ (figure 3 B) and have higher and lower fitness are distributed in quadrants III and II, respectively. In quadrants IV and I are located those who respond unfavorably to these external stimuli with higher and lower physical conditions, respectively. The quality of the functional state of each of CAs-PKS are modified with the application of $T_{conv}/T_{ELF\text{-}EMP}$ fundamentally in those that are concentrated further away (no pain) and closer (significant pain relief) to the PC2 axis in quadrants II and III (figure 3B, and scenarios 2 and 3 of figures 1 and 2) for TG1 and TG2, an aspect that is marked for CAs-PKS in TG2.

Figure 3 A corresponds to non-rehabilitated CAs-PKS due to their good adaptations (long sports practice times and good physical condition) and pain tolerance (high pain threshold), aspects that may lead to acute PKS in them evolving physiologically (in days or months) towards chronic (Tr ≥ 60 days). Nevertheless, for ethical reasons of pain management in CAs-PKS and the need to quickly reincorporate them into their training and competition programs, each of them is included in the three phases of rehabilitation. [11,1] Therefore, the physiological evolution of PKS does not occur in our medical practice in DCs. In addition, $0 \leq FL < 10$ and $70 \leq FL < 100$ at t = 0 days, and $50 \leq FL < 100$ at t = 20 days are not referenced because none of CAs-PKS have synovial fluid effusion without pain, functional impotence from severe trauma, and symptomatic with moderate/major functional limitation, respectively.

At t = 0 days, the distribution of CAs-PKS in different PC1 = ± C (C > 0) lines depends only on the absolute value of VAS because the cause, type and severity of PKS are similar in them, regardless of gender, age and physical condition. This confirms the diversity in their individual perceptions (threshold, tolerance and adaptation) to pain, a distinctive feature that prevails in PRRS and the main reason why they attend CEPROMEDE, in agreement with other studies. [2] In addition, the distribution of CAs-PKS along the same straight line PC1 = ± C (C > 0) means that they with different gender, age and physical condition (positive and negative PC2 values) may have the same pain perception. The response to pain differs between genders because hormonal and biological mechanisms for coping with pain in men and women are different, in agreement with Christopher et al. [12]

The differences between T_{conv} and $T_{ELF\text{-}EMP}$ in terms of their modes of application, possible analgesic-anti-inflammatory

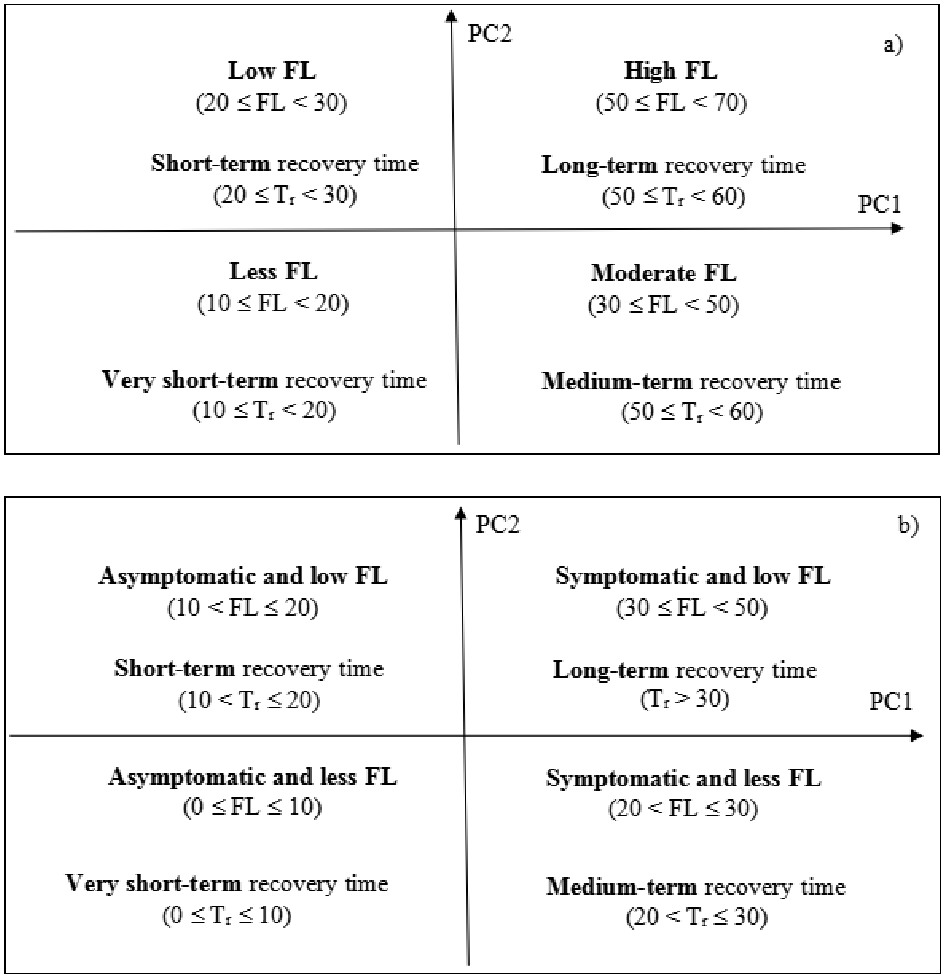

Fig. 3. Schematic representation of PC2 (second principal component) versus PC1 (first principal component) for two treatment groups that received conventional and extremely low-frequency electromagnetic field therapies. A) t = 0 days. B) t = 20 days. The percentage range for functional limitation (FL, in %) and recovery time (Tr, in days) of posttraumatic knee synovitis in competitive athletes are specified in each quadrant

mechanisms of action [1, 13-15] and therapeutic scheme, explain why Scenarios 2 and 3 of TG1 differ from those of TG2. (1)

The discussed above confirms that CAs-PKS have differences in their individual perceptions of pain and respond to the same external stimulus depending on the antecedent, belief, sociocultural environment, the time of the direct trauma injury, the application time of $T_{conv}/T_{ELF\text{-}EMP}$ and the individual physical condition of each of them, in agreement with other authors. (12) From clinical point of view, healed CAs move on to the second phase of rehabilitation (allows restoration of joint mobility arcs, soft tissue extensibility, muscle strength and endurance, including unloading). (1) Nevertheless, PCA suggests that all CAs-PKS located in and to the left of the PC2 axis (Quadrants II and III) may move to the second phase of rehabilitation, not so for those distributed in Quadrants I and IV (PKS active and persists at the macroscopic level at the end of $T_{conv}/T_{ELF\text{-}EMF}$ application). This means that CAs-PKS who pass to this second phase do not necessarily have to be completely cured of pain because they have better functional capacity of their knees and good functional status.

In principle, all CAs-PKS cured with $T_{conv}/T_{ELF\text{-}EMF}$ should be concentrated on a single line PC1 = C (most negative value of C). Nevertheless, PCA reveals that they are distributed on two (figures 1 D, F) or three (figures 2 D, F) closely spaced perpendicular lines to PC1 that correspond to the smallest negative values of PC1. This may suggest that the functional states of these healed CAs-PKS are degenerate. This may be argued because the same functional self-state corresponds to different degrees of pathological alterations at the microscopic level (cellular, molecular and/or electronic) that persist in the knee at the end of $T_{conv}/T_{ELF-EMF}$ application. These pathological micro-alterations may lead *posteriori* to degenerative processes, due to microtraumas/repeated traumas, that may lead to a low quality of life of CAs and interruptions of their training programs and competitions. These possible pathological micro-alterations are not discriminated from the absolute value and range of VAS, ultrasound and physical examination reported in clinics. (1) Other methods may be used to detect them, such as: analysis of biomarkers in the synovial fluid;(16) microscopies of atomic force, scanning electron, immunofluorescence and biomedical; automated and deep learning; and electromagnetic and photo-acoustic microscopy imaging. (17,18,19,20,21,22,23)

Conclusions

Principal component analysis with the first two principal components is useful for the classification of competitive athletes with post-traumatic knee synovitis according to their functional states; the selection of them for the second phase of rehabilitation; and the possible prognosis of these athletes with or without the action of conventional therapy and the extremely low frequency electromagnetic field at 60 Hz.

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Conflicts of Interest

Authors declare that they have no conflicts of interest.

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