Chronobiological analysis of patients admitted with upper limb fractures to hospitals in Castille-Leon between 1999 and 2004*

F. Ardura Aragón[a], J. Andrés de Llano[b], J.R. Garmendia Leiza[c] and J. Ardura Fernández[d]

[a]*Department of Trauma Surgery. FREMAP. Miguel de Cervantes University. Valladolid. Spain.*
[b]*Department of Pediatrics. Río Carrión Healthcare Center. Palencia. Spain.*
[c]*Burgos Healthcare Center. Burgos. Spain.*
[d]*Department of Pediatrics. Valladolid University Hospital. Professor of Pediatrics of the School of Medicine of the University of Valladolid. Valladolid. Spain.*
Members of the Valladolid Chronobiology Recognized Research Group. University of Valladolid. Valladolid. Spain.

Purpose. To assess the relationship between fractures of the upper limb and the time dimension.
Materials and methods. A study was conducted of 16,736 patients admitted to Castile-Leon hospitals with a fracture of their upper limb between 1999 and 2004. The following analyses were performed to investigate the existence of rhythm: an univariate analysis performed together with a logistic regression, a rhythmometric study with spectral analysis (Fourier transform) and cosinor method.
Results. Patients' mean age was 45.1 ± 25.7 years, with 57.9% of males. The fracture was sustained in an urban milieu in 62.8% of cases and as a result of a road accident in 21.7%. Surgery was performed in 63.1% of cases, with a mortality rate of 1.6%. Mean hospitalization time was 7.21 days. Logistic regression showed a lower risk for older females, in the urban setting. Spectral analysis: dominant period of 365 days. Cosinor analysis: significant rhythm (acrophase: 13/8 and batiphase: 31/12). All subgroups except for deceased patients and those over 84 years showed rhythm (acrophases: 19/7 to 8/9).
Conclusions. This group of fractures, as well as the majority of subgroups, shows rhythm with acrophases in the summer. Traffic and non-traffic have similar rhythms. The data from the chronobiological study can be applied to clinical practice by planning resources with time-based criteria.

Key words: *fracture, trauma surgery, orthopedics, hospitalization, chronobiology, biorhythms, variability, circannual, seasonal.*

Análisis cronobiológico de los ingresos de fracturas de la extremidad superior en los hospitales de SCACYL 1999-2004

Objetivo. Valoración de la relación entre las fracturas de la extremidad superior y la dimensión temporal.
Material y método. Se estudiaron 16.736 pacientes ingresados en hospitales del sistema público de salud de Castilla y León con fracturas de la extremidad superior, de 1999 a 2004. Se realizó un análisis univariante y una regresión logística, estudio ritmométrico con análisis espectral (transformada de Fourier) y método cosinor, para indagar la existencia de ritmo.
Resultados. La edad media de los enfermos fue de 45,1 ± 25,7 años, con un 57,9% de varones. La fractura se produjo en el ámbito urbano en un 62,8% y por accidente de tráfico en un 21,7%. Fue tratado con cirugía el 63,1%, con una mortalidad del 1,6%. La estancia media fue de 7,21 días. La regresión logística mostró menor riesgo para mujeres, ámbito urbano y aumento de la edad. Análisis espectral: período dominante de 365 días. Análisis de cosinor: ritmo significativo (acrofase: 13/8 y batifase: 31/12). Todos los subgrupos, excepto *exitus* y mayores de 84 años, mostraron ritmo (acrofases de 19/7 a 8/9).
Conclusiones. Este grupo de fracturas y la mayoría de subgrupos muestran ritmo con acrofases en verano. Tráfico y no tráfico tienen ritmos semejantes. Los datos del estudio cronobiológico se pueden aplicar en la clínica, mediante la planificación de los recursos con sentido temporal.

Palabras clave: *fractura, traumatología, ortopedia, hospitalización, cronobiología, biorritmos, variabilidad, circanual, estacional.*

*2007 SECOT Foundation Award for Clinical Research in Orthopedic and Trauma Surgery.

Corresponding author:
F. Ardura Aragón.
C/ Estudios 2, 1.º B.
47005 Valladolid. España.
E-mail: fardura@ono.com

Received: August 2007.
Accepted: December 2007.

INTRODUCTION

Trauma treatment has increasingly become more and more important in the present day development of healthcare activity in clinical medicine. However, both in research studies that are registered on data bases available to the general public as well as in the great variety of approaches to it, little thought is given to the consideration of the relation between fractures and the time factor[1,2].

Within the field of Chronobiology, the science of the temporal dimension, there has been an increase both in the contributions to basic research and in the number of clinical studies[3-5]. In spite of this, chronobiological studies in trauma treatment are uncommon as well as limited due to the use of inadequate methodologies, or they are otherwise related to metabolic or hormonal aspects of the bone affected by the fracture[6]. The cases that are related to epidemiologic or clinical aspects are almost exclusively cases of hip fractures and only occasionally of other kinds of fractures[2,7].

It is because of this that the aim of our work is the study of the relation between fractures and the time dimension, particularly upper limb fractures. We examine whether there is a certain regular pattern in the production of these fractures, what type of pattern it is (monthly, yearly, seasonal), and the similarities and differences between patterns according to etiological factors, age, treatment and obtained results. Our purpose is to acquire information that can be used in the healthcare environment, in the preventive organization of resources and in the revision of possible risk factors, as has been done in cases with other kinds of pathologies such as severe heart failure, arterial hypertension, diabetes[5] and diverse physiological and pathological features[4].

We also seek to set up a contrastive and systematized methodology that will be used in future studies by researchers into this interesting and controversial, yet scantily developed, issue.

MATERIALS AND METHODS

The target population consisted of the patients with trauma injuries that were admitted into the public health system hospitals in Castile and Leon (SACYL) between January 1st 1999 and December 31st 2004, and were registered on the Minimum Basic Data Group (CMBD). From the CMBD were selected those patients that showed a code of injuries for trauma treatment in the variable «main diagnosis» (C1) or in any of the sections of the variable «other diagnoses» (C2-C13). Next, we used the presence of codes corresponding only to upper limb fractures as inclusion criterion.

Once the cases had been grouped in the final operative base, the population to be studied consisted of a total number of 16,736 patients.

Information connected with numerous variables was registered on the CMBD base. With the aim of preserving confidential information, we suppressed the relevant data, thus complying with Organic Law 15/1999. We subsequently renewed codification generating diverse variables for definitive analysis. The selection of variables was carried out on the basis of the advantages they provided in the practice and in clinical experience and the frequency of citations in published studies. The definitive variables were: age (years), stratification by age (< 15 years, 15-64, > 64, 65-74, 75-84, > 84), gender, traffic accident (yes/no), day of the week, month and year of admission, hospital stay (long, for an over medium stay, or short, for an under medium stay), surgical treatment (yes/no), home address zip code, place of residence (urban or rural, since our aim was to compare urban with non-urban populations; according to criteria of the National Statistics Institute [INE], non-urban population is the sum of intermediate and rural populations; for the purpose of this work we will refer to non-urban population as rural population), type of discharge (home, transfer, voluntary discharge, death, out-patient consultation) and comorbidity (we have selected the most outstanding pathologies and those that are most frequently cited in the literature and apt for comparison: cardiovascular, digestive, endocrinological, genitourinary, mental, neurologic and respiratory[8]).

Subgroups

Depending on the values the groups may take on for each one of the different variables, each group will give rise to several subgroups. Subgroups will make possible the further study of chronobiology by means of the rhythmometric analysis protocol.

Statistical analysis

The following parameters were obtained in the univariate analysis of continuous variables: mean, standard deviation, median and 25-75 percentile. We carried out a goodness-of-fit test by means of the Kolmogorov-Smirnov normality test. Frequency distribution was obtained for discrete and categorical variables.

We carried out a multivariate analysis by means of the binomial logistic regression method with the purpose of determining the degree of association between upper limb fractures and the rest of the potentially confusing variables. For this analysis, upper limb fracture was taken as the dependent variable. The independent variables were: age, gender, place of residence, traffic accident, month of admission, day of admission and comorbidity. Indicating variables were used for polyatomic variables. The modeling strategy we used was the steps backwards strategy, based on the changes in the verisimilitude quotient. As a result of this analysis, we worked out risks for each variable and their confidence intervals by means of the odds ratio.

Chronobiological study. Rhythmometric analysis

In order to confirm the existence of rhythm we used the rhythmometric methods described by Nelson, Halberg et al[9-13], together with the following conceptual bases: the demonstration of the presence of rhythm or its harmonics can be performed with the cosinor method (cosine-vector). An adapted cosine curve with diverse identifiable parameters is obtained with this method (fig. 1). The terms used in the chronobiological analysis with the cosinor method can be described as:

1) Rhythm: a pattern periodicity that oscillates with time. If the variation pattern is not periodic, it lacks rhythm.

2) Period: the time that is necessary to complete the cycle of a rhythmic phenomenon. It is inverse to frequency.

3) Circannual: a rhythm on an approximate basis of 365 days.

4) Frequency: the number of cycles that are completed in a definite time unit.

5) MESOR (Midline Estimating Statistic of Rhythm): the mean value between the maximum and minimum values of the sinusoidal curve around which all the measurements of the experimental phenomenon oscillate.

6) Amplitude: the measurement of the peak value of a rhythm over the median threshold estimated by a mathematical function. It measures the difference between the highest and lowest values in the cosine curve.

7) Acrophase: the time at which the maximum variable value in the adapted cosine curve occurs.

8) Bathyphase: the time at which the minimum variable value in the adapted cosine curve occurs.

9) Cosine analysis: the adaptation of a cosine curve to a rhythm by means of the least squares regression method.

The cosinor method enables the confirmation of the existence of rhythm by means of the null amplitude test, and the comparison of different rhythms by means of the amplitude-acrophase test.

In this study we carried out an inferential statistical analysis with the use of rhythmometry taking into account the patients' date of admission into hospital and observing the following steps: the search for periodicity in temporal series, with the day of the year variable, by means of spectral analysis with the fast Fourier transform; the search for rhythm by means of the multiple component cosinor test, with dominant periods found in the spectral analysis by means of the null amplitude test; analyses rendering an error probability under 5% were considered statistically significant; when rhythm was found in a group, a subgroup analysis of specific variables and their clinical interest was implemented; and finally a comparative analysis between the different subgroups was carried out using the amplitude-acrophase test.

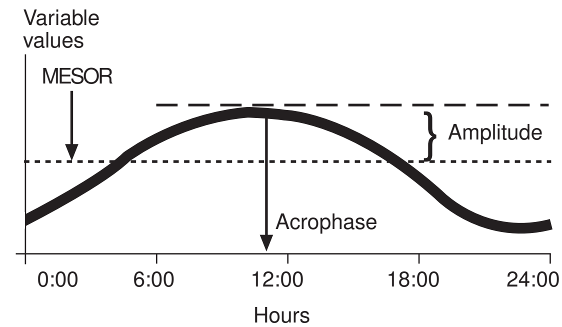

Figure 1. Graphic representation of cosinusoidal curve and its three basic parameters: MESOR, amplitude and acrophase. If amplitude is statistically different from zero, the rhythm represented by the cosine function is considered to be significant.

The statistical analysis was carried out with the SPSS.V14/Win amos 6 program, and for the management of CMBD, the elaboration of tables and the writing of texts, Windows XP, Excel, Access and Word were used, all these with software licenses from Valladolid University.

Before planning the design, we searched for relevant bibliography using MEDLINE®, the Spanish Medical Index, and the TESEO doctoral theses data base, apart from the internet searchers Tripdatabase®, SUMSearch® and the Cochrane Plus® Library. On MEDLINE®, the search was initiated using the following descriptors: chronobiology, biorhythms, rhythm, variability, circannual, seasonal, fracture, trauma, orthopedics.

The research Project was accepted by the research commission of the Valladolid Clinical University Hospital.

RESULTS

The total number of fractures was 16,736. Mean age was 25.7 ± 45.1 years. 57.9% were male patients and 42.1% were women; 62.8% lived in urban areas. 21.7% of fractures were produced in traffic accidents. 63.1% of the patients were treated surgically and the hospital death rate was 1.6%. 92% of the patients went back to their homes following discharge from hospital. The mean stay period in days was 7.21 and the median was 4, with a 25 and 75 percentile for 2 and 9 days respectively. Patients with upper limb fractures were admitted at a higher frequency in the summertime (July and August) and at a lower one in winter (January and February). Yearly, monthly and daily admission distribution is shown on tables 1 to 3.

In the logistic regression analysis (table 4) the age variable was stratified into three groups: under 15 years of age, between 15 and 64, and over 64 years, and the risk of upper limb fracture was worked out for the oldest age group with respect to the youngest one. The risk of lower limb fractures is lower in women than in men, in the urban area than in the

Table 1. Upper limb fracture distribution in relation to year of admission.

Year of admission	N	%
1999	2,733	16.3
2000	2,661	15.9
2001	2,831	16.9
2002	2,759	16.5
2003	2,875	17.2
2004	2,877	17.2
Total	16,736	100.0

rural area and as age increases (table 4). The risk is higher in the summer months and shows a low probability of the concurrence of digestive, genitourinary, mental neurologic or cardiovascular comorbidity (table 4).

The spectral analysis showed a dominating period of 365 days (fig. 2). The cosinor analysis for this period presented a significant rhythm with acrophase in the summer (August 13th) and bathyphase in the winter (December 31st) (table 5 and fig. 3). As for the subgroups deriving from the gender variable, both male and female patients showed rhythm and these rhythms were different. Nevertheless they presented similar acrophases and bathyphases, and their curves were also similar (table 5 and fig. 4). The subgroups resulting from the age sections, < 15, 15-64 y > 64, had rhythm on admission and were all different from one another. In the over-64 years subgroup, the 65-74 and 75-84 subgroups presented rhythm, while those in the over-84 group did not. When the age subgroups were compared, the same rhythm was found in the under 15 and the 15-64 subgroups, and in the 15-64 and the over 64 subgroups. The totality of the acrophases was in the summertime (table 5 and fig. 5). In the subgroups deriving from the place of residence variable, both the patients living in urban and rural areas showed significant rhythms, but they were different from each other. The acrophases and bathyphases, however, were similar (table 5 and fig. 4). The subgroups deriving from the hospital stay variable, both long and short, showed rhythm, and it was different in each one. The subgroups related to the death variable revealed that the patients that died during hospital stay did not present rhythm on admission, whereas those that were discharged from hospital showed a significant rhythm. As regards the subgroups related to the traffic accident variable, both the patients that experienced a traffic accident and those that did not showed rhythm, but it was different in the two groups; however, their acrophases and bathyphases were similar and their curves highly analogous (table 5 and fig. 6).

Table 2. Upper limb fracture distribution in relation to month of admission

Month of admission	N	%
January	1,174	.0
February	1,065	6.4
March	1,253	7.5
Apri	1,262	.5
May	1,386	8.3
June	1,506	9.0
July	1,764	10.5
August	1,938	1.6
September	1,673	10.0
October	1,428	8.5
Novembe	1,161	6.9
December	1,126	6.7
Total	6,736	100.0

DISCUSSION

This kind of fracture is common in young patients. The logistic regression analysis shows that the risk of fracture is lower in older patients (table 4). Since the upper limb bones do not normally bear weight, the effect of osteoporosis is not so prevalent and fractures require a higher energy trauma or a fall on the upper limb itself.

Sports traumas and work accidents are the main causes of these fractures, a fact that is widespread in the literature[14-20]. These causal mechanisms are more usual in young people[18,19] and since this region is quite unprotected it is liable to suffer a fracture. Hospital stay is low, probably due to the fact that these patients can walk and that these fractures have a low association with important complications, these two circumstances leading to a healthier general state of the patient.

The death rate of these fractures is also low, probably due to the same reasons expressed above. These fractures do not require staying in bed, do not affect walking and the associated morbidity is not high.

Upper limb fractures are more common in the summertime. The probable causes of this are a higher rate of activity in the open air and an increase in leisure activities and sports.

In the logistic regression analysis we observe that the risk in women is lower than in men. Also, patients residing

Table 3. Upper limb fracture distribution in relation to day of the week of admission

Day of the week	N	%
Monday	2,591	15.5
Tuesday	2,372	14.2
Wednesday	2,203	13.2
Thursday	2,343	14.0
Friday	2,246	13.4
Saturday	2,424	14.5
Sunday	2,557	15.3
Total	16,736	100.0

Table 4. Logistic regression analysis of upper limb fractures. Variables presenting statistically significant values are shown.

		p	*Odds ratio*	95% Confidence Interval
	< 15 (Ref. Cat.)	0.000	1	
	5-64	0.000	0.294	0.273-0.317
	> 64	0.000	0.139	0.129-0.151
Gender				
	Male (Ref. Cat.)	1		
	Female	0.000	0.916	0.878-0.955
Place of residence				
	Rural (Ref. Cat.)	0.000	1	
	Urban	0.000	0.854	0.821-0.889
Month of admission				
	January (Ref. Cat.)	1		
	July	0.002	1.159	1.057-1.270
	August	0.009	1.127	1.030-1.233
	September	0.000	1.198	1.092-1.315
Comorbidity				
	Digestive	0.000	0.764	0.702-0.830
	Genitourinary	0.000	0.757	0.686-0.835
	Mental	0.000	0.775	0.731-0.823
	Neurologic	0.000	0.855	0.795-0.921
	Cardiovascular	0.000	0.811	0.768-0.855

Ref. Cat.: reference category; p: statistic significance value

in urban areas have a lower risk factor. On the other hand, the risk of this fracture being produced in the summer months (July-September) is higher. Additionally, the risk of an associated pathology is low (table 4).

The patients in this group show rhythm on admission, with an acrophase in the summer and a bathyphase in the winter. This rhythm is the same within the variables for gender, place of residence, surgical treatment, hospital stay and traffic accident (table 5). In the gender variable there are differences that are statistically significant but are not considered clinically relevant, since the cosine curves are similar and the acrophases are close (table 5 and figs. 4-6).

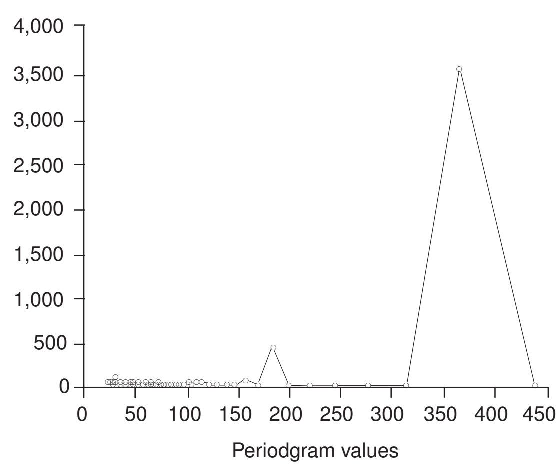

Figure 2. Upper limb fractures. Spectral analysis with fast Fourier transform. Circannual periodicity is observed with a predominant 365-day harmonic.
Number of cases: 2,190. From 5 to 100.

As regards age, the < 15 and 15-64 subgroups have similar acrophases and bathyphases and their cosine curves are analogous, due to which the differences between their rhythms, though significant, are not considered clinically relevant. The over-64 group, however, differs more markedly from these two groups (table 5).

Despite the fact that the rhythms of patients that underwent surgery are different from those of the patients that did not, the acrophases are analogous, and thus the differences are not clinically relevant (fig. 4). As regards hospital stay, there is a discrepancy in the acrophases (27 days) and the bathyphases (11 days) between the long-stay group and the short-stay group, and although the latter group's amplitude is greater, the tendencies of the curves are similar and the differences are clinically irrelevant (table 5 and fig. 6). No rhythm was found in the patients that died, but this is probably due to the small number of cases in this subgroup. In the traffic variable, the differences are statistically significant but are deemed clinically irrelevant, since the acrophases and bathyphases are almost identical and their curves are similar (table 5 and fig. 6).

Independently from the preceding issues and considering the applicability of results, the information provided by the acrophases could be construed as pointing out the concrete periods in the year in which there is an increase in the demand for healthcare in the field of the pathologies that concern us. The need of resources to respond to this demand could in turn be interpreted as the need to plan an increase in staff number, an increase in the availability of beds and operating theaters, the organization of programmed surgery, etc. Considering that acrophases concen-

Table 5. Results of the analysis of rhythm for upper limb fractures

	Acrophase	Bathypase	p	Comparative p
UL Group	13 aug (5 aug-22 aug)	31 dec (22 aug-10n)	0.000000	
Male	10 aug (2 aug-21 aug)	21 dec (9 dec-5 jan)	0.000000	0.000001
Female	17 aug (1 aug-31 aug)	6 jan*	0.000000	
Alive	15 aug (6 aug-23 aug)	31 dec (23 aug-11 jan)	0.000000	0.000000
Dead	5 jul*	26 mar (26 feb-20 apr)	0.316140	
Urban	8 aug (5 aug-21 aug)	16 dec (5 dec-19 jan)	0.000000	0.000000
Rural	19 aug (3 aug-31 aug)	3 jan (31 aug-19 jan)	0.000000	
Traffic Yes	18 aug (2 aug-2 sept)	31 dec (2 sept-19 may)	0.000000	0.002772
Traffic No	12 aug (3 aug-22 aug)	31 dec (22 aug-17 may)	0.000000	
Surgery Yes	16 aug (5 aug-25 aug)	5 jan (25 aug-30 jan)	0.000000	0.001901
Surgery No	8 aug (4 aug-23 aug)	9 dec (26 nov-11 apr)	0.000000	
Short stay	12 aug (5 aug-18 aug)	20 dec (10 dec-31 dec)	0.000000	0.000000
Long stay	8 sept (4 aug-24 aug)	31 dec (22 aug-3 en)	0.000000	
< 15 years	17 aug (12 aug-22 aug)	31 dec (22 aug-3 en)	0.000000	
15-64 years	10 aug*	19 dec (7 dec-5 jan)	0.000000	
> 64 years	20 jul (29 jun-22 sept)	28 apr (25 jan-8 may)	0.000000	
65-74 years	19 jul (28 jun-21 sept)	24 feb (23 jan-9 may)	0.000000	
75-84 years	25 jul (30 jun-12 feb)	14 mar (12 feb-25 may)	0,016562	
> 84 years	6 sept (23 aug-16 sept)	5 may (10 abr-23 jul)	0.113711	
< 15/15-64			0.000007	
< 15/> 64			0.000000	
15-64/> 64			0.000001	

*Confidence interval cannot be worked out..
apr:April; aug: August; dec: December; jan: Jauary; UL: upper limb; feb: February; jul: July; jun: June; mar: March; nov: November; sept: September.

trate in the summer (table 5 and figs. 4-6), usually a holiday time, it seems apparent that if there has previously been no planning, not even one based on an empirical observation of the phenomenon, then there should be one triggered off by the scientific basis we provide in this work.

On the positive side of the study we might mention that it consists of an extensive analysis of a multicenter series. It informs about novel facts concerning bone fractures, these facts being obtained working with a descriptive rhythmometric analysis and on justified hypotheses. No series as extensive as this and associating numbers of cases with bio-

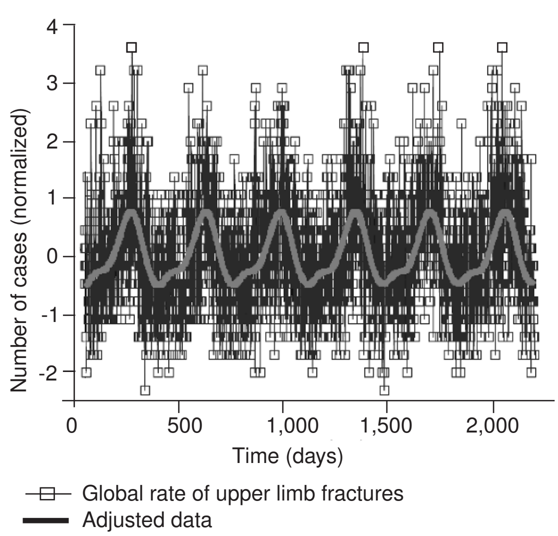

Figure 3. *Analysis of admission rhythm of upper limb fractures throughout the study. Adjusted data show cosine curve uniformity in 6 consecutive years with significant amplitude (p = 0.000) and acrophase on August 13th.*

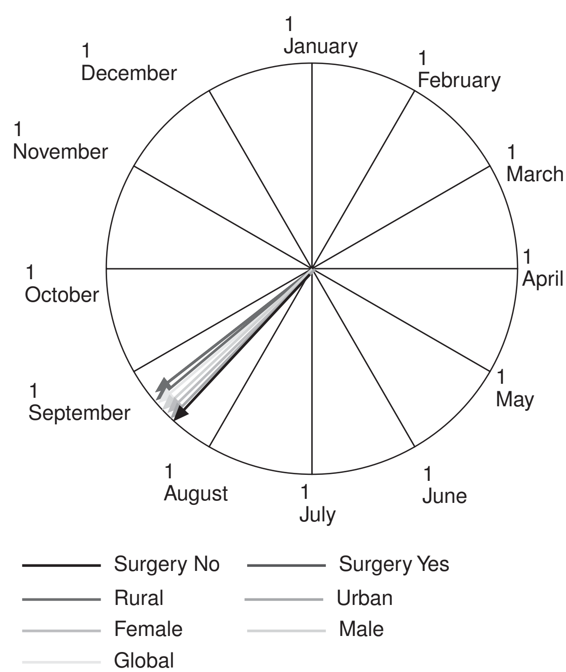

Figure 4. *Representation of the acrophases corresponding to indicated subgroups, by means of polar cosinor method. The circumference corresponds to the twelve-month scale. Vector tips show acrophase positions.*

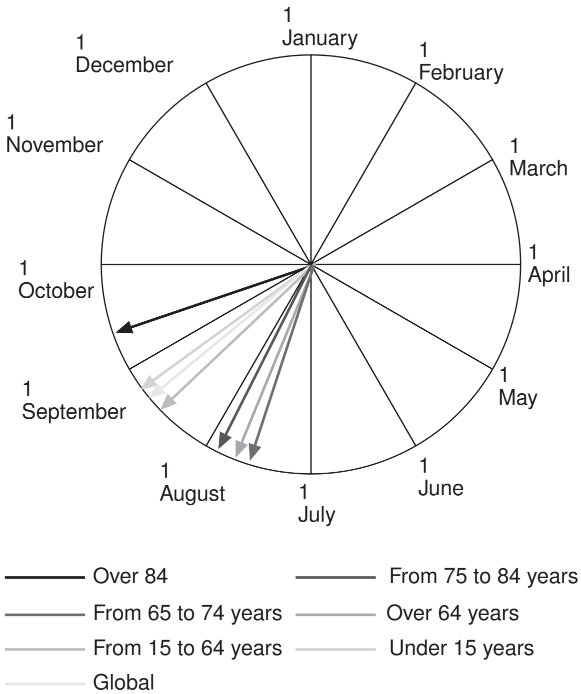

Figure 5. Representation of the acrophases corresponding to the indicated subgroups, by means of the polar cosine method. The circumference corresponds to the twelve-month scale. Vector tips show acrophase positions.

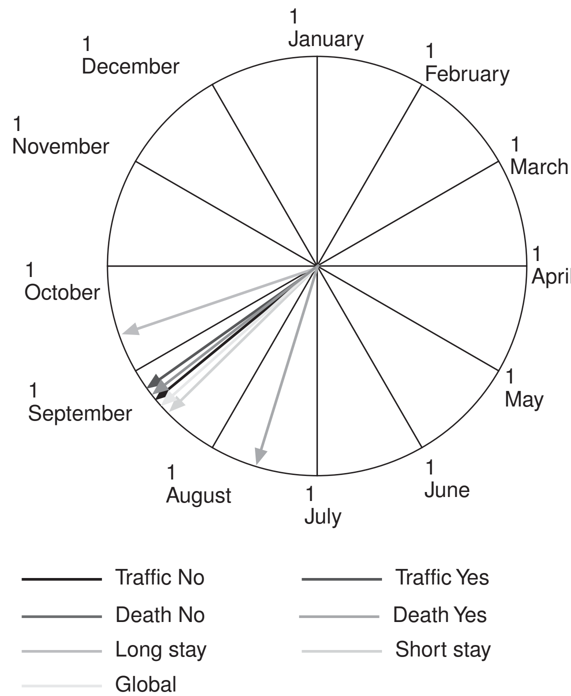

Figure 6. Representation of the acrophases corresponding to the indicated subgroups, by means of the polar cosine method. The circumference corresponds to the twelve-month scale. Vector tips show acrophase positions.

logical rhythm models of analysis has been found in the bibliography. Additionally, the information we provide could be used to improve the programming of health services, since resources could be conducted towards the periods of higher demand thus reducing surgery waiting time. In response to a need arising out of the results of the analysis, we provide a protocol for the study of biological rhythms based on specific scientific methods and attested in various studies. The results obtained with this protocol have agreed with the hypothesis and objectives, which enables its use by other research groups interested in biological rhythms.

Although the study has been found to be highly positive, we are also aware of its limitations. One possible drawback could be the survival factor. There will always be cases of patients that die at the moment when the fracture is produced, especially in traffic accidents, and the fact that they are not admitted into hospital produces a bias in the values. Another possible limitation might be the fact that we have used the mathematical models we consider valid, but other models could have been taken into account too. Further drawbacks might be mentioned, but they would lie outside the field of work and objectives that we set at the beginning of our study.

In conclusion, upper limb fractures show rhythms that are related to the moment of admission into hospital, and the acrophase or peak period of admissions takes place in the summer (August 13th). Subgroups that derive from the chosen variables also present rhythm (with the exception of the deceased and over.84 subgroups) and all their acrophases are situated in the summer (from July 19th to September 8th). Traffic accidents show acrophases that are similar to non-traffic mechanisms and their rhythms are similar. Unexpectedly enough, this factor did not prove to be such a discriminating or relevant factor as we thought it would be when we chose it. The chronobiological study carried out with rhythmometric analysis provides information about the incidence of acrophases in certain periods of the year. This scientific information can be translated into the concrete clinical practice through the programming of resources including a temporal discernment for periods when the healthcare demand increases.

REFERENCES

1. Brulajic M. Seasonal variations in incidence of fractures among elderly people. Inj Prev. 2000;6:1-2.
2. Jacobsen SJ, Goldberg J, Miles TP, Brody JA, Stiers W, Rimm AA. Seasonal variation in the incidence of hip fracture among white persons aged 65 years and older in the United States, 1984-1987. Am J Epidemiol. 1991;133:996-1004.
3. Halberg F, Cornelissen G. Introduction to Chronobiology. Medtronic Chronobiology Seminar, 47. Library of Congress (USA); 1994.
4. Moore-Ede MC, Czeisler CA, Richardson GS. Circadian time-

keeping in health and disease. Part 2. Clinical implications of circadian rhythmicity. N Engl J Med. 1983;309:530-6.
5. Muller JE, Stone PH, Turi ZG, Rutherford JD, Czeisler CA, Parker C, et al. Circadian variation in the frequency of onset of acute myocardial infarction. N Engl J Med. 1985;313:1315-22.
6. Swinson DR, Tam CS, Reed R, Hoffman D, Little AH, Cruickshank B. Bone growth kinetics IV: a preliminary investigation on a biorhythm in human osteogenesis. J Pathol. 1975;116:13-6.
7. Pedrazzoni M, Alfano FS, Malvi C, Ostanello F, Passeri M. Seasonal variation in the incidence of hip fractures in Emilia-Romagna and Parma. Bone. 1993;14 Suppl 1:S57-63.
8. Olsson C, Petersson CJ. Clinical importance of comorbidity in patients with a proximal humerus fracture. Clin Orthop Relat Res. 2006;442:93-9.
9. Nelson W, Tong YL, Lee JK, Halberg F. Methods for cosinor-rhythmometry. Chronobiologia. 1979;6:305-23.
10. Díez-Noguera A, Cambras T. Determinación de las características del ritmo en variables biológicas. Método de cosinor. Inf Med Bio. 1989;1:25-30.
11. Fernández JR, Hermida RC. Inferential statistical method for analysis of nonsinusoidal hybrid time series with unequidistant observations. Chronobiol Int. 1998;15:191-204.
12. Bingham C, Arbogast B, Guillaume GC, Lee JK, Halberg F. Inferential statistical methods for estimating and comparing cosinor parameters. Chronobiologia. 1982;9:397-439.
13. Alberola-López C, Martín-Fernández M. A simple test of equality of time series. Signal Processing. 2003;83:1343-8.
14. Marcireau D, Oberlin Ch. Fracturas de la epífisis distal del húmero. En: Enciclopedia Médico Quirúrgica. Aparato Locomotor. 5. Paris: Ed. Elsevier (ed. esp.); 2000. p. 14-678.
15. Cuenca J, Martínez AA, Herrera A, Domingo J. The incidente of distal forearm fractures in Zaragoza (Spain). Chir Main. 2003;22:211-5.
16. Gustilo RB, Bechtold JE. Revisión histórica del tratamiento de las fracturas y luxaciones. En: Gustilo RB, Kyle RD, Templeman DC, editores. Fracturas y luxaciones. I. Madrid: Mosby/ Doyma; 1995. p. 3-9.
17. Vandenbussche E, Huten D. Fracturas del extremo superior del húmero. En: Enciclopedia Médico Quirúrgica. Aparato Locomotor. 5. Paris: Ed. Elsevier (ed. esp.); 2000. p. 14-672.
18. Jouve JL, Guillaume JM, Jacquemier M, Bollini G, Petit P. Fracturas del antebrazo en el niño. En: Enciclopedia Médico Quirúrgica. Aparato Locomotor. 5. Paris: Ed. Elsevier (ed. esp.); 2000. p. 14-702.
19. Coudane H, Hardy Ph, Huttin P, Benoît J. Fracturas de la diáfisis humeral. En: Enciclopedia Médico Quirúrgica. Aparato Locomotor. 5. Paris: Ed. Elsevier (ed. esp.); 2000. p. 14-675.
20. Lenoble E, Dumontier C. Fractura de la extremidad distal de los dos huesos del antebrazo en el adulto. En: Enciclopedia Médico Quirúrgica. Aparato Locomotor. 5. Paris: Ed. Elsevier (ed. esp.); 2000. p. 14-699.

Conflict of interests

The authors have declared that they have no conflict of interests.