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Seasonality in vascular access thrombosis in hemodialysis

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SUMMARY

Different studies have shown that some clinical events, particularly cardiovascular and thrombotic events, show a regularity in its appearance. The aim of our study was to analyse the possible existence of seasonal periodicity in the incidence of the vascular access thrombosis in patients on chronic haemodialysis. Prospectively, we collected information of 164 patients with 250 episodes of vascular access thrombosis referred to our hospital from january 1995 to december 1999. An ANOVA test for comparison of the means, and a time series analysis were performed.

During the five year study the consecutive number of thrombosis were 43, 57, 55, 59 and 36. When the different seasons were analysed, the cumulative number of events in summer during the study period were 91, a significant increase compared to spring, autumn, and winter (54, 54, and 51, respectively; $p < 0.001$). Time series analysis confirmed that thrombotic events during summer showed an increased incidence over the mean ($p < 0.001$), and it accurred every year. The same results were obtained when the PTFE grafts were analyzed separately (july RR 2.62, $p = 0.002$; august, RR 2.37, $p = 0.04$), but not with the arteriovenous fistulae.

In conclusion, this study showed a seasonal periodicity of vascular access thrombosis, with an increased risk during the summer months, particularly in patients with a PTFE graft. Although the causes were unknown, these data alert us on the convenience of an increased attention to the vascular access during the summer months in order to prevent its thrombosis.

Key words: ***Thrombosis. Vascular access. Haemodialysis. Seasonal periodicity.***

RITMO ESTACIONAL EN LA TROMBOSIS DEL ACCESO VASCULAR PARA HEMODIÁLISIS

RESUMEN

Algunos estudios han detectado periodicidad en la aparición de eventos trombóticos y cardiovasculares. No obstante, este tema es motivo de controversia. El objetivo de nuestro estudio fue analizar la posible existencia de un ritmo estacio-

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nal en la aparición de trombosis de los accesos vasculares en pacientes en hemodiálisis. Para ello hemos recogimos de forma prospectiva los episodios de trombosis del acceso vascular remitidos a nuestro hospital desde el 1 de enero 1995 hasta el 31 de diciembre de 1999, contabilizando un total de 250 casos correspondientes a 164 pacientes. Para determinar si existía periodicidad en las trombosis se realizó comparación de medias (test ANOVA) y análisis de series temporales mediante un modelo de regresión de Poison mostrando riesgo relativo (RR) de trombosis.

Durante el periodo de estudio, el numero de casos por año fue de 43, 57, 55, 59 y 36 correspondientes a los años 1995, 1996, 1997, 1998 y 1999 respectivamente. Cuando se realizó el análisis por estaciones se vio que el número de episodios acumulados en verano durante los años analizados fue de 91, prácticamente el doble que en primavera, otoño e invierno (54, 54 y 51 respectivamente) (p < 0,001). El análisis de series temporales mostró que los episodios de trombosis durante el verano presentaban picos de incidencia por encima de la media (p < 0,001) y que este hecho se repetía en todos los años. Estos hallazgos fueron evidentes en el caso de los pacientes portadores de prótesis de PTFE (julio, RR 2,62, p = 0,002; agosto RR 2,37, p = 0,04) sin existir diferencias en el caso de las fístulas autógenas (p = ns).

En nuestra experiencia, la trombosis del acceso vascular en pacientes en hemodiálisis presenta una periodicidad relacionada con las estaciones del año existiendo un mayor riesgo relativo de presentar estos eventos durante los meses de verano especialmente en los pacientes con prótesis de PTFE. Aunque las causas están por determinar, estos hallazgos nos advierten sobre especiales medidas a tomar en los meses de verano para la prevención de posibles trombosis del acceso vascular durante esta época.

Palabras clave: ***Ritmo estacional. Trombosis. Acceso vascular. Hemodiálisis.***

INTRODUCTION

Vascular access thrombosis is one of the problems with the highest comorbidity indexes in hemodialysis patients and the first hospital admission cause in this group of patients. There are many studies regarding this complication aiming at reducing or preventing its occurrence.[1-3]

Some authors have detected seasonality in the occurrence of thrombotic and cardiovascular events. The second national registry of acute myocardial infarction in the Unite States showed a clear seasonal pattern, with 53% more cases in the winter time.[4] Gallerani *et al*. detected an annual seasonality with a peak in October for cerebral ischemic events.[5] In the same way, a seasonality has been studied in hemodialysis patients and it has been shown that high temperatures and low moisture, which are characteristic of the summer time, have an influence on blood pressure values of hemodialysis patients, hypotensive events being more frequent at this time of the year.[6,7]

It has been suggested that there may be a relationship between the occurrence of vascular access (VA) thrombosis in hemodialysis patients and seasonal changes, although the results obtained in the only two published studies differed. Galonsky *et al*. detected a higher incidence of this type of event during the summer time.[8] However, Diskin *et al*. in a study gathering 947 episodes of VA failure due to thrombosis did not confirm this relationship.[9]

The aim of our study was to analyze the possible existence of a seasonal pattern in the occurrence of vascular access thrombosis in hemodialysis patients.

PATIENTS AND METHODS

We have consecutively collected all episodes of vascular access thrombosis referred to our hospital from January 1st of 1995 to December 31st of 1999. A protocol studying the vascular access incidences and the following variables were assessed: thrombosis date, patient's age and gender, and type of vascular access (native fistula or PTFE prosthesis).

Because of the characteristics of our Hospital as a reference center for Vascular Surgery and Vascular Radiology during the study period, most episodes of vascular access thrombosis occurring during that period at our reference area were referred to our Center.

During that period, 250 VA thromboses were referred, corresponding to 164 patients from 25 hemodialysis centers. Fifty-one percent were male, and 48% female. Mean age was 63.4 ± 14 years (19-89). 66.8% of thrombosed VA were PTFE prostheses (167 cases) and only 33.8% were autologous fistulae (82 cases). In 146 cases (58.4%) percutaneous thrombectomy was tried. Sixty-eight (41.4 %) patients were on anti-aggregant or anti-coagulant therapy. Sixty (36.5 %) patients received anti-aggregants and eight (4.8 %) were taking dicoumarin agents.

In order to determine whether there were seasonal differences in thrombosis occurrence, we carried out a comparison of the means (ANOVA test). To analyze seasonality, the temporal series was assessed by means of a Poisson regression model in which the response variable is the number of cases on a logarithmic scale and explanative variables are month, quarter, year, and type of VA. The result is expressed as a relative risk (RR) for thrombosis, taking the month of January as a reference. In the case of the vascular access, the thrombosis RR for autologous fistula was considered = 1. We used the statistical software packages EGRET and SPSS. SPSS was used for diagrams.

RESULTS

During the 5 follow-up years, a total of 250 cases of VA thrombosis were gathered. The greatest number of cases was observed in 1998, with 59 cases, followed by 57 cases in 1996, 55 cases in 1997, 43 in 1995, and 36 episodes in 1999, with no significant differences between years (ANOVA test p = 0.08) (Figure 1).

When analyzing the different months of the year, August was the one accumulating the highest number of thrombosis episodes (32), followed by July (31). There were 28 in September and 25 in October. In the remaining months, the number of episodes ranged 11-18. The ANOVA test showed significant differences (p = 0.017) (Figure 2). The number of thrombosis events per month ranged between 3.5 ± 1.9 and 5.1 ± 2.8 (p = 0.15). The number of cases during the summer months was almost twice that of the rest of the year. Ninety-one events occurred during the summer, 54 in spring, 54 in fall, and 51 in winter time (p = 0.003) (Figure 3). The temporal series analysis showed that the thrombosis episodes during the summer had incidence peaks above the other seasons (p = 0.014) and this pattern was repeated each year (see the arrows in Figures 4 and 5). Figure 5 shows how peaks of thrombosis episodes during the summer are above the mean all the years.

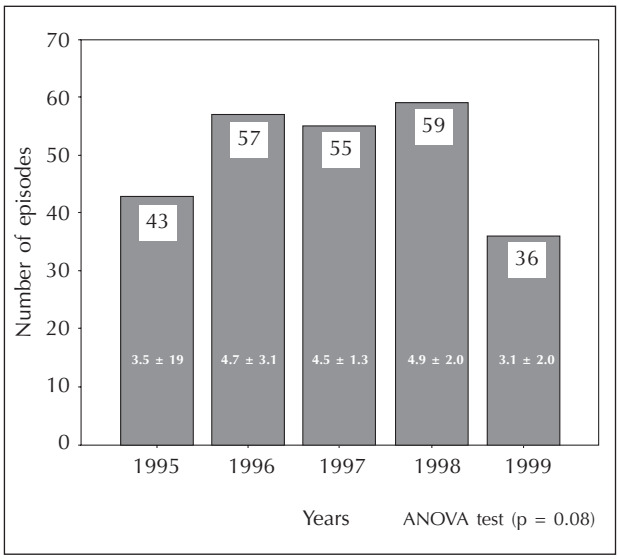

Fig. 1.—Número de thromobosis episods by years of the study period. The mean of thrombosis episodes/month is shown for each year.

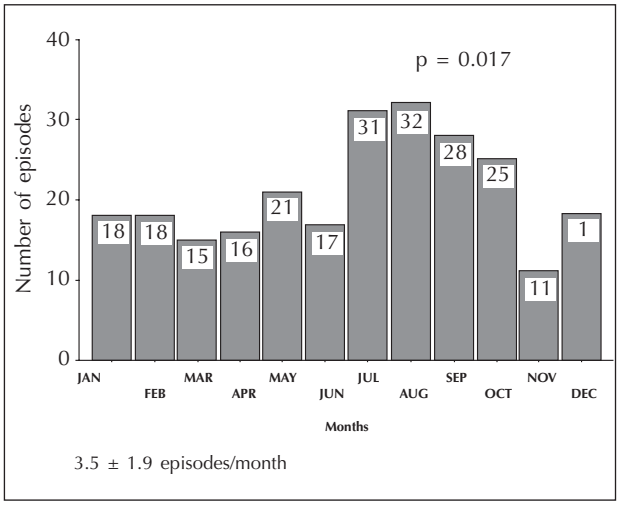

Fig. 2.—Number of cumulated thrombosis episodes by months of the year during the study period.

The analysis by seasons showed that the summertime, especially the months of July and August were risk factors for VA thrombosis (RR: 1.78, 1.72, and 1.77, respectively).

When stratifying by vascular access, the analysis showed that the incidence of these events was significantly higher for PTFE prostheses during the summer moths (RR 2.07), especially July, August and September (RR: 2.62, 2.37, and 2.27, respectively) as com-

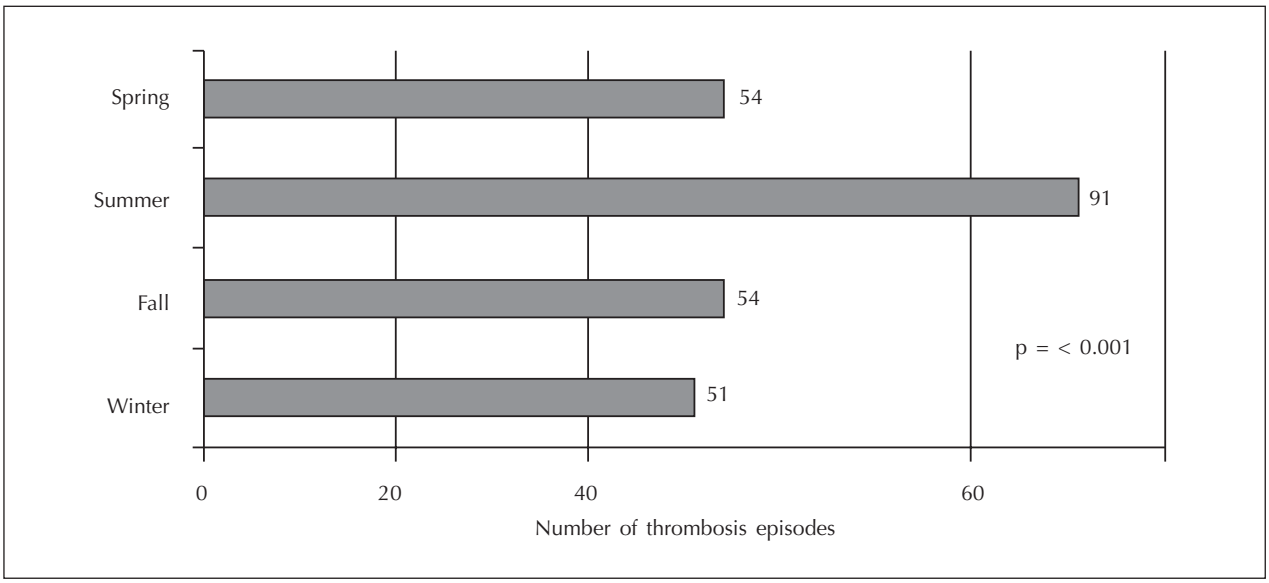

Fig. 3.—Number of cumulated thrombosis episodes by seasons of the year during the study period.

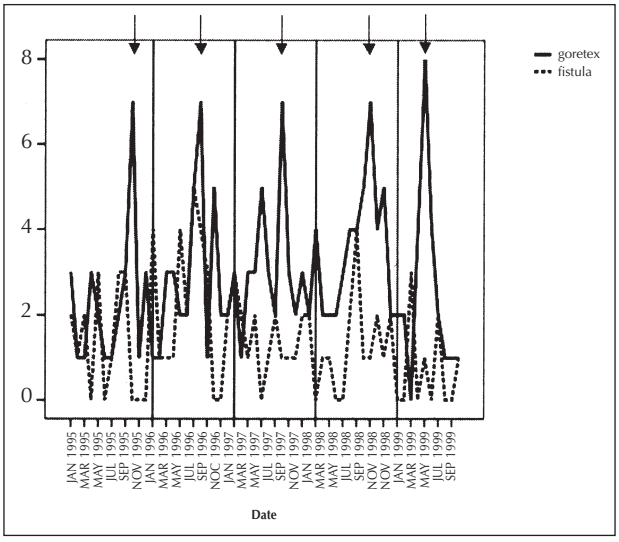

Fig. 4.—Temporal series analysis: number of thrombosis episodes in PTFE grafts and autologous grafts.

pared to January, which was taken as the reference) (Table I).

DISCUSSION

Seasonality in the occurrence of vascular access thrombosis has not been sufficiently studied, the two only published studies showing conflicting results.[8,9] However, there have no been published prospective randomized studies analyzing factors related with its occurrence. In our experience, thrombosis of the vascular access in hemodialysis patients show a periodicity related with the year seasons, with a greater relative risk for having these events during the summer months.

Some studies have shown an increase of hypotension episodes during hemodialysis in the summer months.[6,7] The different weather conditions vary according to the geographical setting, and this may have an influence on the contradictory results obtained in other studies.[10,11]

The causes for a higher incidence of VA thrombosis found in the summer time, especially in July and August, are still unclear, but there may be several. On the one hand, high temperatures may facilitate a relative volume contraction, and thus, the occurrence of hypotension episodes, this being one of the main factors favoring VA thrombosis, as our study shows.

On the other hand, it may be speculated on treatment and manipulation of vascular accesses by the health care and ancillary personnel, sometimes being less experienced in hemodialysis during the summer months.

When separately analyzing thrombosis episodes in native fistulae and in PTFE prostheses, we found that the latter had a seasonal pattern that was not detected in autologous VA. It is likely that the higher thrombosis risk in PTFE prostheses as compared to autologous fistulae, evident in any series, may be worsen during the summer months because of the mentioned reasons.

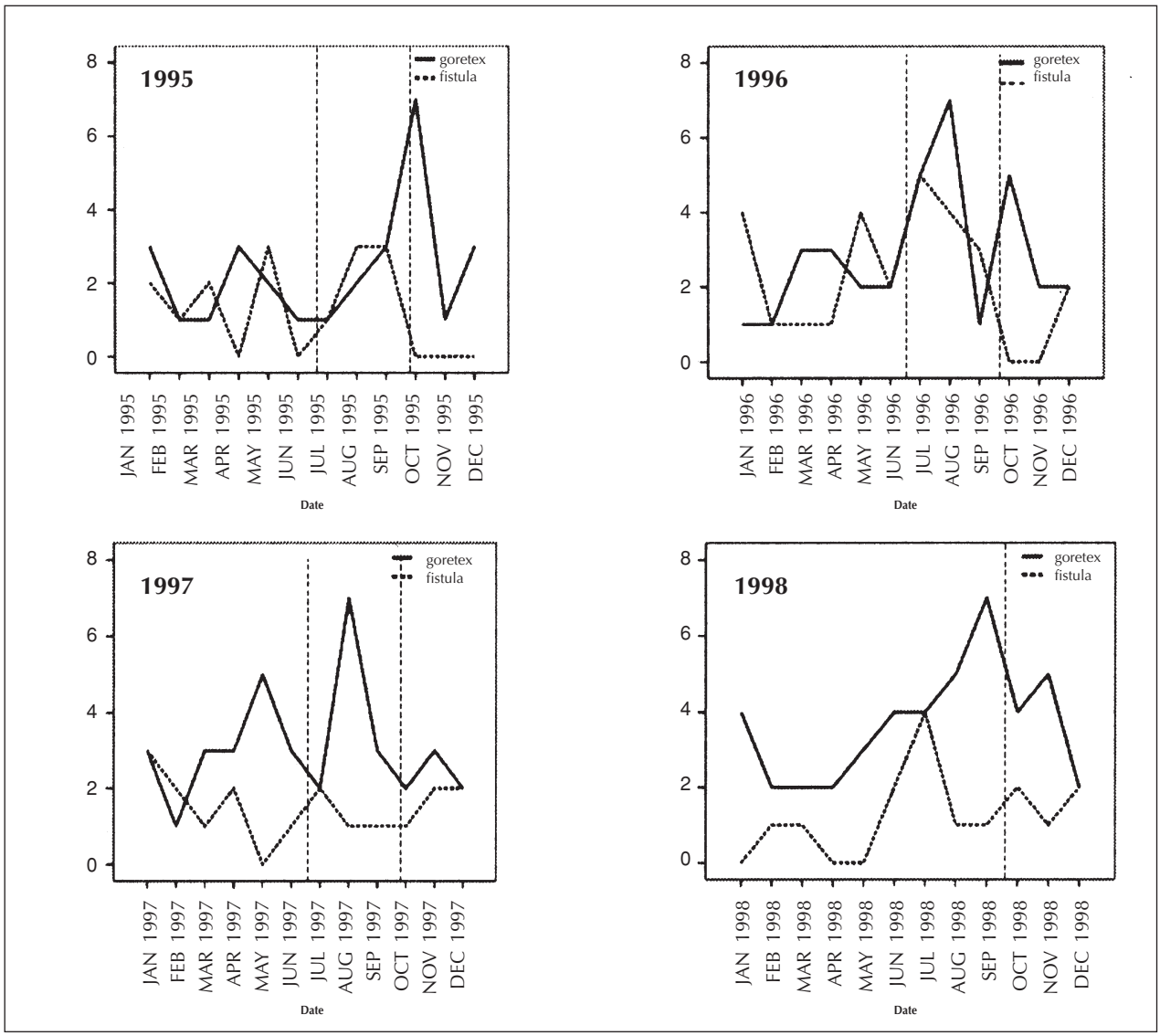

Fig. 5.—Temporal series analysis: number of thrombosis episodes in PTFE grafts and autologous grafts in different graphs by years. Note the peaks of thrombosis episodes during the summer time above the mean all the years. The summer time is comprised between dotted vertical lines.

Table I. Risk factors for vascular access thrombosis: PTFE *vs* autologous AV fistula

		PTFE GRAFT		AV FISTULA	
		p	**RR (95% CI)**	**p**	**RR**
Year		ns	–	ns	–
Month	July	0.020	2.62 (1.16-5.92)		
	August	0.040	2.37 (1.04-5.42)		
	September	0.056	2.25 (0.98-5.18)		
	October	0.010	2.87 (1.29-6.42)	ns	–
Season	Summer	0.002	2.07 (1.32-3.25)	ns	–

For the periods not shown, the difference was not statistically significant ($p > 0.05$).

Since PTFE prostheses represent, by themselves, a risk for VA thrombosis, by contrast with autologous fistulae, the addition of the above-mentioned factors to other undetected ones during the summer months might condition the increase in the number of thromboses detected.

Our study has several limitations. One of them is that we cannot assure that we gathered all the VA thrombosis episodes occurred at the reference area throughout the analyzed period, although the characteristics of being a reference center for Vascular Surgery and Vascular Radiology during the study period, and the need for an immediate access and preventing the use of catheters as much as possible for treating these patients, may predict that the potential number of cases not included in the study is low.

The creation of new interventional radiology units since the year 2000 made us limit the analysis period to 1999, since the number of cases referred to our center significantly decreased, very likely because of that cause. Similarly, the financial reimbursement policies in subsequent periods for dialysis centers to self manage VA thrombosis would make our analysis difficult any further.

Another limitation is the low number of patients with thrombosis of the autologous arterial-venous fistula, since two thirds of the sample were prostheses and only one third were autologous fistulae, making the sample size too small to obtain statistically significant outcomes. Finally, the main limitation comes from the study design. Ours is an observational study with its advantages and drawbacks. This type of study shows the result derived from an observation and analyses the patterns of the daily clinical practice. However, in order to obtain conclusions with the highest level of evidence, a randomized study minimizing confounding and biasing factors, that are many in this type of patients, should be designed. It is likely that the reason for the lack of reporting of this type of studies in the literature is the difficulty in putting into practice such a study design and the existence of multiple confounding factors. Our study just gives an insight into the problem based on an observational and descriptive analysis.

To conclude, in our study the episodes of VA thrombosis presented a seasonal peak during the summer months, which was significantly significant for PTFE prostheses and not with autologous arterial-venous fistulae. This might be related with higher weather temperatures and the likely repercussion on patients' hemodynamics, as well as in the changes in the hemodialysis units' personnel due to summer vacations.

A larger collaborative study would be necessary to confirm our observation and verify whether this fact also occurs in native fistulae. The reasons for this finding are not known, although they warn us about the need for taking special precautions during this time of the year and open new research ways for preventing vascular access thrombosis.

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