

Correlations between scleroderma renal crisis and videocapillaroscopic patterns in patients with systemic sclerosis

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ABSTRACT: Introduction - Scleroderma renal crisis is one of the major complications of ScS, being the main cause of mortality in patients with systemic sclerosis. Objectives - to establish the correlations between scleroderma renal crisis, the subsets of the disease, videocapillaroscopic patterns and modified Rodnan skin score in patients with ScS. Methods: a number of 35 patients with ScS have been included in the study, 23 with lcScS and 12 from dcScS. Scleroderma renal crisis has been studied in comparison with the two subsets of the disease, capillary nailfold changes and modified Rodnan skin score. Results - scleroderma renal crisis was more frequent in diffuse cutaneous form (25%) than in the limited one (8,70%), occurring with the same frequency in the first 5 years and after an evolution longer than 10 years (40%). In 60% of the patients with SRC, an "active" type scleroderma-like pattern was observed and in 40% a "late" pattern was described, and mRSS recorded an average value of $35,97 \pm 9,02$. Conclusions - During the last two decades, the outcome of scleroderma renal crisis has improved dramatically with the use of angiotensin-converting enzyme (ACE) inhibitors. Prompt diagnosis and early, aggressive initiation of therapy with ACE inhibitors will result in the most optimal outcome.

KEYWORDS: *scleroderma, renal crisis, videocapillaroscopy*

Introduction

Scleroderma (ScS) is a systemic connective tissue disorder characterized by microvascular injury associating both cutaneous and visceral fibrosis and specific immunological abnormalities. The disease can progress either slowly without visceral damage or very rapidly with severe organic implications. [1]

The one to reflect the earliest the consequences of the vascular spasm and the arterial deterioration of the systemic sclerosis is the kidney. Renal impairment can be clinically silent, but can alternatively progress towards chronic kidney failure.

On a microstructural level a high degree of intimal proliferation has been described, especially in the arcuate and interlobular arteries, apart from that there can be present a reduplication of the elastic lamina and laminal occlusion the commonly called „in onion bulb” lesion to which glomerular and tubular interstitial fibrosis can be associated. Vascular modifications lead to renal ischemia, activation of the renin-angiotensin system and of the myofibroblast, responsible of fibrosis. [2] A recent study confirms the high expression of endoteline I in the glomerulus, arterioles and interlobular arteries in patients with a scleroderma renal crisis. [3]

Scleroderma renal crisis is defined clinically by a sudden, severe increase in blood pressure associated with high plasma levels of creatinine and with the occurrence of haemolytic microangiopathic anaemia. [4]

Once the inhibitors of angiotensin conversion enzyme were introduced in therapy protocols there has observed a decrease in the mortality rate and conversely an increase in the survival rate in patients with scleroderma renal crisis. [4]

The objective of the study consists in proving a correlation between the installation of renal crisis in patients with ScS and the characteristic pattern determined through videocapillaroscopy.

Material and method:

We have performed a prospective longitudinal study, on a number of 35 patients diagnosed with systemic sclerosis and committed in the Rheumatology Clinic of the County Emergency Medical Unit of Craiova. The evaluation of the biological parameters was performed in the Laboratory of the County Emergency Medical Unit of Craiova and the capillaroscopic evaluation was performed in Rheumatology Research Centre of Craiova. The study was performed in agreement with the ethical and deontological principles of the

Helsinki „Declaration of Human Rights” approved by the local Ethics Committee as well as by all patients who signed a consent form in this respect, thus ARA 1980 diagnosis criteria. [5]

In accordance with the classification issued by Cutolo et al., the alterations of the microvascular nailfolds have been classified in scleroderma patterns that show the evolution of microangiopathy ScS: early, active and late. [6-8]

Nailfold capillaroscopy has been performed with the use of Videocap 3.0 videocapillaroscope at the level of the nailfold of the non-dominant hand.

The evaluation of the cutaneous impairment was performed by calculating the modified Rodnan skin score (mRSS) on a scale from 0 to 3, 0 representing normal or atrophied skin, where 1 – slight thickening, 2 – moderate thickening and 3 – severe thickening. The 17 areas are represented by 3 symmetrical surfaces (face, anterior thorax, abdomen) and 7 asymmetrical surfaces (fingers, back of the hand, forearm, arm, thigh, leg, foot); at their level we have tried to make a skin fold by taking the tegument between the thumb and the index finger. The cutaneous score is calculated by adding individual scores, the maximum possible being of 51. [9,10]

For data processing we have used Microsoft Excel (Microsoft Corp., Redmond, WA, USA), together with XLSTAT package for MS Excel (Addinsoft SARL, Paris, France) and IBM SPSS Statistics 20.0 (IBM Corporation, Armonk, NY, USA). The parameters we measured for the subjects included in this study were stored in Excel files.

Results

The study group included 35 patients with ScS, 5 men and 30 women, 65.71% patients (23) with lcScS and 34.29% (12) with dcScS, the proportion between the limited and diffuse type being of approximately 2:1 (1,916:1). The average age of the study group was of $50,77 \pm 9,13$ years, in women the average being of $49,60 \pm 9,25$ years and in men of $57,80 \pm 4,09$ years. We have identified a significant difference ($p = 0,0064$) between the average age of women and men with scleroderma, the female patients being of lower ages. No significant differences were recorded regarding the average age on disease subsets ($p=0,992$) between dcScS (the average

age being of $50,75 \pm 9,78$ years) and lcScS (the average age being $50,78 \pm 9,01$ years).

Depending on the disease clinical subtype 75% (9) out of the patients with a diffuse cutaneous disease diagnose are represented by women and 25% (3) by men and of the 23 patients with a limited cutaneous form, the majority - 91,30% - are of female gender (21) and only 8,70 % are men (2).

The sclerodermic renal crisis affected 3 patients with a diffuse type of the disease and 2 of those with a limited type. The occurrence of the sclerodermic renal crisis is not significantly more frequent ($p = 0,312$) in dcScS (25%) as compared to lcScS (8,70%). (Fig.1)

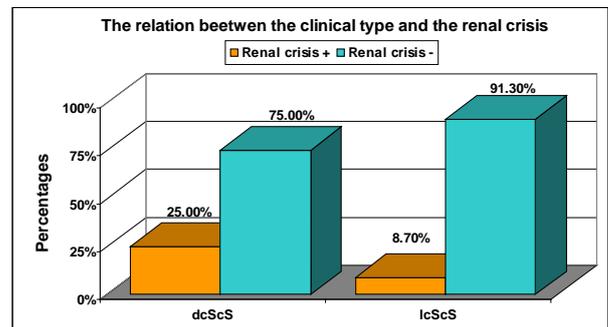


Fig. 1. The distribution of the lot in relation to the occurrence of the sclerodermic renal crisis

In terms of disease duration (1-5 years, 6-10 years and >10 years), we haven't identified a statistically significant difference ($p = 0,830$) between the percentage of the patients affected by the scleroderma renal crisis in the first 5 years (40%), in 6-10 years (20%) and those with an evolution longer than 10 years (40%). (Fig.2)

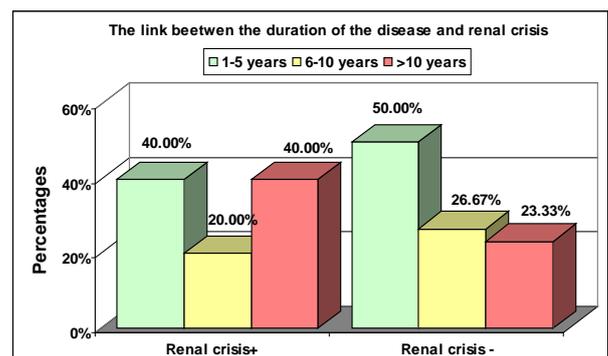


Fig.2. The relation between the duration of the disease and sclerodermic renal crisis

After the examination performed with the help of the videocapillaroscope we have noticed that from the total of 14,29% patients (5) affected by a scleroderma renal crisis, 60% (3) had an „active” capillaroscopic pattern, 40% (2) a „late” pattern, the „early” pattern of the

disease not manifesting at any of the subjects. We have thus noticed a statistically significant difference ($p = 0.018$) between the patients with different capillaroscopic patterns and a scleroderma renal crisis (Fig. 3)

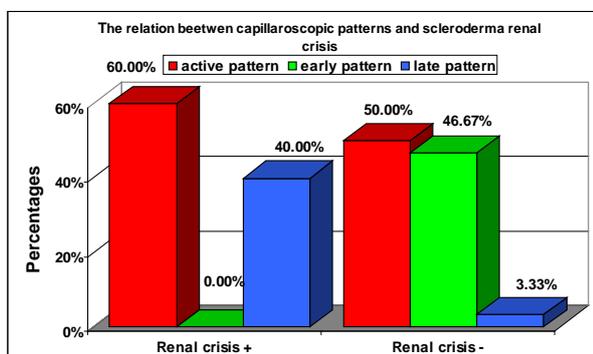


Fig.3. Distribution of the patients according to the renal crisis and capillaroscopic pattern

As for the cutaneous involvement the evaluation of the Rodnan modified skin score showed an average value of $35 \pm 14,76$ in patients with a scleroderma renal crisis, the difference being statistically relevant ($p = 0.027$) as compared with patients not suffering from scleroderma renal crisis ($23,97 \pm 9,02$). (Fig. 4)

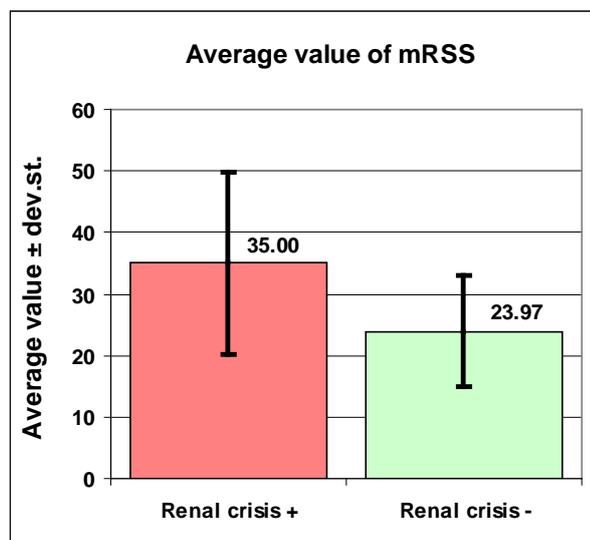


Fig.4. Average value of mRSS in patients with renal crisis

Discussions

Therapeutic insertion of angiotensin conversion enzyme inhibitors (ACE) has significantly reduced the occurrence of renal diseases – especially that of the renal crisis – in patients with systemic sclerosis. However, in the absence of an early diagnosis and excessive

temporisation of the proper therapy, irreversible renal injuries can occur, as well as even death.

Sclerodermic renal crisis is frequently associated with a diffuse type, in 10-15% of the patients with dcScS, but may occur in limited type as well (1-2%) [11]. The rapid progression of the cutaneous impairment, the presence of anti-ARN-polymerase III and anti-topoisomerase I antibodies as well as the treatment with corticoids in high doses (>15 mg/day) and HLA alleles DRB1*0407 and *1304 are frequently associated with scleroderma renal crises. Anti-centromere antibodies seem to have a protective effect. [11,12] In 20% of the cases the renal crisis precedes the scleroderma diagnosis. [12,13]

Our study confirms the presence of the renal crisis, especially in patients with dcScS (25%), diffused form and anti SCL-70 antibodies, having a higher risk of developing a renal impairment that would need a careful monitoring of the systemic arterial tension in these patients. Also, the association of the renal crisis with anti-ARN polymerase III antibodies occurs in a percentage of 25-33% of patients. [14,15]

Steen and al. have proved that in over 75% of the cases, scleroderma renal crises occur at the debut of ScS [16,17], especially in diffuse type, data which has also been confirmed by our study in which we have shown that the renal crisis occurred both during the first 5 years as well as after a longer evolution of over 10 years (40%).

From the total of 14, 29% of the patients included in the lot that manifested a renal crisis, we have identified an “active” capillaroscopic pattern in 60% of patients, a “late” pattern in 40% of them (2), while an „early” pattern didn’t manifest in the renal crisis, a statistically significant difference ($p = 0.018$).

Our data has also shown a high value of the modified Rodnan skin score (>20) with an average of $35 \pm 14,76$ in patients with a renal crisis, as compared with an average of $23,97 \pm 9,02$ in those without a renal crisis, thus showing a statistically significant difference – $p = 0,027$, which is in agreement with specialized studies, Steen and col. proving that severe tegumentary damage is a predicting factor for the occurrence of the renal crisis. [16,17]

Conclusions

Scleroderma renal crisis remains the major complication of systemic sclerosis, its early

diagnosis and immediate treatment being able to prevent irreversible renal injuries.

Periodical evaluation of the capillaroscopic pattern could bring crucial support for the identification of patients at risk for developing a scleroderma renal crisis and subsequently for properly treating these patients.

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