Underrecognized Peripheral Arterial Disease in Patients With Acute Coronary Syndrome: Prevalence of Traditional and Emergent Cardiovascular Risk Factors

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Introduction and objectives. Peripheral arterial disease (PAD) frequently coexists with coronary artery disease. Our objective was to determine the prevalence of traditional and emergent cardiovascular risk factors in patients with acute coronary syndrome (ACS), with or without PAD.

Patients and method. A prospective study of 141 consecutive patients (<70 years old) admitted to our hospital with ACS was performed. PAD was diagnosed when the ankle-brachial index (ABI) was ≤0.9. Traditional cardiovascular risk factors were evaluated. C-reactive protein, homocysteine, amyloid A, lipoprotein (a), fibrinogen, apolipoprotein A1, and apolipoprotein B100 serum levels, and microalbuminuria were measured. Specific genotypes were also determined.

Results. Patients were divided into two groups according to whether PAD was present (37 patients, 26% of total, ACS-PAD group) or absent (104 patients, ACS group). In the ACS-PAD group, patients were older, and diabetes and hypertension were significantly more common. Moreover, levels of C-reactive protein (3.1 mg/L vs 2.18 mg/L; *P*<.05), homocysteine (11.45 mmol/L vs 9.4 mmol/L; *P*<.01), amyloid A (5.2 mg/mL vs 3.7 mg/mL; *P*<.05), and microalbuminuria (4.89 mg/L vs 3.1 mg/L; *P*<.05) were significantly higher in this group. Logistic regression analysis showed that poorly controlled diabetes (OR=6.3; 95% CI, 1.1-36.7), time-dependent tobacco exposure (OR=1.5 per decade; 95% CI, 1.2-2.0), and high pulse pressure (OR=1.9 per 10 mm Hg; 95% CI, 1.3-2.7) were independent predictors of the presence of PAD.

Conclusions. Several traditional and emergent cardiovascular risk factors were more prevalent in patients with acute coronary syndrome and peripheral arterial disease. Moreover, some factors were independent predictors of peripheral arterial disease.

Key words: *Peripheral arterial disease. Coronary disease. Cardiovascular risk factors.*

Enfermedad arterial periférica desconocida en pacientes con síndrome coronario agudo: prevalencia y patrón diferencial de los factores de riesgo cardiovascular tradicionales y emergentes

Introducción y objetivos. La enfermedad arterial/vascular periférica frecuentemente se asocia con enfermedad coronaria. El objetivo es evaluar la prevalencia de factores de riesgo cardiovascular tradicionales y emergentes entre pacientes con síndrome coronario agudo (SCA) con o sin enfermedad vascular periférica.

Pacientes y método. Realizamos un estudio prospectivo en 141 pacientes (< 70 años) que ingresaron consecutivamente por síndrome coronario agudo. El diagnóstico de enfermedad arterial periférica (EVP) se basó en un índice tobillo-brazo ≤ 0,9. Se evaluaron los factores de riesgo cardiovascular tradicionales y se midieron las concentraciones séricas de proteína C reactiva, homocisteína, amiloide A, lipoproteína (a), fibrinógeno, apolipoproteína A1 y B100, y microalbuminuria. Además, se determinaron varios genotipos.

Resultados. Los pacientes fueron estratificados en 2 grupos de acuerdo con la presencia (n = 37, el 26% del total, grupo SCA-EVP) o ausencia (n = 104, grupo SCA) de enfermedad arterial periférica. Los pacientes del grupo SCA-EVP eran más viejos y tenían una significativa mayor prevalencia de diabetes e hipertensión. Las concentraciones de proteína C reactiva, homocisteína, amiloide A y microalbuminuria fueron significativamente mayores en el grupo SCA-EVP (3,1 frente a 2,18 mg/l [p < 0,05]; 11,45 frente a 9,4 mmol/l [p < 0,01]; 5,2 frente a 3,7

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ABBREVIATIONS

CAD: coronary artery disease.
PAD: peripheral artery disease.
CRF: cardiovascular risk factors.
ABI: ankle-brachial index.
ACS: acute coronary syndrome.

mg/ml [p < 0,05], y 4,89 frente a 3,1 mg/l [p < 0,05], respectivamente). El análisis de regresión logística mostró que la diabetes mal controlada, la exposición al tabaco tiempo-dependiente y la presión de pulso fueron predictores independientes de la presencia de EVP.

Conclusiones. Varios factores de riesgo cardiovascular tradicionales y emergentes son más prevalentes en pacientes con SCA y enfermedad arterial periférica, y algunos de ellos son predictores independientes de ésta.

Palabras clave: *Enfermedad arterial periférica. Enfermedad coronaria. Factores de riesgo cardiovascular.*

INTRODUCTION

Atherosclerosis is a systemic disease involving the entire arterial tree. Patients with symptomatic lesions in one vascular territory have additional atherosclerotic lesions, which are often asymptomatic, in other vascular regions.[1] Likewise, patients with atherosclerosis in multiple vascular regions also have a worse prognosis than patients with atherosclerosis in just one vascular territory. Thus, in patients with known coronary artery disease (CAD), the additional presence of peripheral arterial disease (PAD) considerably worsens prognosis considerably.[2,3] On the other hand, some studies have shown the varying involvement of cardiovascular risk factors (CRF) in the development of atherosclerosis in different vascular regions.[4] The search for undiagnosed atherosclerotic lesions in peripheral vascular territories is not a systematic practice in patients admitted with a coronary event. Moreover, not only certain traditional CRF, but also some newer factors as well, may play a role in the development of peripheral lesions associated with coronary lesions.

Accordingly, the aims of this study were:

1. To detect the presence of atherosclerosis coexisting in various different vascular regions in patients admitted with an acute coronary syndrome (ACS), following a systematic study strategy based on non-invasive diagnostic techniques.

2. To assess the prevalence of traditional CRF, as well as the so-called emergent factors, in these patients, according to whether they had or did not have accompanying PAD.

PATIENTS AND METHOD

Patients

This prospective study enrolled 141 patients, aged from 35 to 70 years old, who were admitted consecutively with a diagnosis of ACS. These patients were diagnosed and treated in accordance with the recommendations of the Spanish Society of Cardiology and the European Society of Cardiology.[5,6]

The patients in this study formed part of the group of cardiology patients included in a larger cohort, known as the AIRVAG study. The AIRVAG (Atención Integral al Riesgo Vascular Global) study is a prospective study started at our hospital in the year 2000 and which involving the follow-up and observation of a cohort of patients admitted with an ischemic event in different vascular territories. This article focuses on the group of patients who were admitted with an acute coronary event.

Exclusion criteria included chronic, advanced renal insufficiency with a serum creatinine >4 mg/dL or patients on dialysis and the coexistence of non-vascular diseases known to reduce short- to medium-term survival (neoplasia, severe chronic obstructive pulmonary disease).

Method

Study Design

Following the prospective inclusion of patients during their admission, they were requested to return one month after the coronary event in order to undergo examinations and have laboratory tests, as mentioned below. Later, for data analysis and in accordance with the aims of this study, the patients were divided into two groups, depending on whether they had or did not have PAD according to the ankle-brachial index (ABI).

Procedures Undertaken

All the studies and laboratory measurements were done one month after admission for the coronary event.

Methods to evaluate atherosclerosis in different coronary vascular territories. The following clinical variables and diagnostic methods were included:

1. Clinical variables: presence of intermittent claudication, a prior history of carotid surgery and peripheral vessel surgery.

2. Diagnostic methods:

– Arterial blood flow study in the arms and legs using Doppler ultrasound. The systolic blood pressure was measured in each limb and the ABI was calculated as the ratio between the blood pressure of the ankle and the blood pressure of the arm. PAD was considered to be present when this index was ≤0.9, in accordance with the recommendations of experts in this field.[7]

– A search for carotid atherosclerosis by means of Doppler ultrasound of the supra-aortic trunk with an ATL-HDI 3500 Doppler ultrasound device with multifrequency heads of 5-2 and 7-4 MHz. Examination was made for the presence of carotid plaques (defined areas of thickness), and measurements were made of the intima-media wall thickness (mean wall thickness after 3 measurements at 2, 4, and 6 cm proximal to the common carotid bifurcation), and carotid stenosis in accordance with the criteria of the University of South Florida.[8]

– Measurement of the maximum diameter of the infrarenal aorta by means of abdominal aorta ultrasound. The presence of an aneurysm was diagnosed when the diameter was >3 cm.

Evaluation of cardiovascular risk factors. The following traditional CRF were studied:

1. Dyslipidemia. The lipid profile was calculated after a 12 hour fast and measurements made of total cholesterol and its subfractions, and triglycerides. Dyslipidemia was considered to be present when the patient was receiving treatment with lipid lowering drugs or in the presence of any of the following criteria: total cholesterol ≥240 mg/dL, triglycerides ≥150 mg/dL, or high density lipoprotein (HDL) cholesterol <40 mg/dL.

2. Smoking. Each patient was classified as a non-smoker, active smoker, or ex-smoker (if the patient had ceased smoking at least six months previously). The smokers were also evaluated as to their exposure, calculating this as the packet-year index and the number of years as a smoker.

3. Diabetes. Patients were considered to have diabetes if they were receiving treatment with antidiabetic agents or if two measurements of fasting glucose were ≥125 mg/dL.

4. Hypertension. Patients were considered to have hypertension if they were being treated with antihypertensive drugs or if their resting blood pressure was ≥140/90 mm Hg. The data analysis considered the casual blood pressure and the pulse pressure, defined as the difference between the systolic blood pressure and the diastolic blood pressure.

Laboratory measurements relating to cardiovascular risk factors.

1. Traditional CRF. Full lipid profile workup: total cholesterol, HDL cholesterol and LDL cholesterol, triglycerides, and blood glucose. In the diabetic patients, the glycosylated hemoglobin was also measured.

2. Emergent CRF. Fibrinogen, lipoprotein (a), apolipoproteins A1 and B, ultrasensitive C reactive protein, homocysteine, type A serum amyloid and microalbuminuria (previously validated techniques).[9]

Other cardiovascular risk factors. The following genetic markers were genotyped: apo E (E2E3, E2E4, E3E3, E3E4, E4E4), angiotensin converting enzyme (ACE: DD, II, ID), glycoprotein IIB-III (PIA: A1A1, A2A2, A1A2), and plasminogen activator inhibitor-1 (PAI-1: 4G4G, 5G5G, 4G5G).[10]

Statistical Analysis

We used the χ^2 test and the Student *t* test to compare the clinical and analytical characteristics between the 2 groups when the values followed a normal distribution. For abnormal distributions, the values were transformed logarithmically beforehand. Multivariate logistic regression analysis was used to assess the association between the different variables and the PAD. Those variables associated ($P<.1$) with the presence of PAD were included in a forward stepwise logistic regression analysis, in order to determine those variables having an independent association with PAD.

RESULTS

Detection of Unknown Peripheral Arterial Disease

The ABI was ≤0.9 in 37 patients, who were thus by definition considered to have PAD. These 37 patients formed the group with both ACS and PAD (the ACS-PAD group). The remaining patients (n=104) composed the group of patients with ACS but no evidence of PAD (the ACS group).

Accordingly, the prevalence of PAD in the study population of patients admitted with ACS was 26%, with a 95% confidence interval (CI) of 18.7%-33.2%, calculated in accordance with the sample size.

A total of 20 patients in the ACS-PAD group reported a history of intermittent claudication and 2 had undergone a peripheral vessel bypass operation.

Detection of Atherosclerosis in Other Vascular Territories

1. Carotid intima-media index. The intima-media index was significantly greater in the ACS-PAD group (0.119±0.04 vs 0.0905±0.02; $P=.007$).

2. Presence of carotid plaque. Of the patients with PAD, 64.9% had carotid plaques. This percentage was significantly greater ($P<.001$) than that of the persons with just ACS (24%).

3. Detection of abdominal aorta aneurysms. Overall, aortic aneurysms were detected in 8 patients. Six of these 8 belonged to the ACS-PAD group ($P=.0011$).

Study of the Prevalence of Cardiovascular Risk Factors According to the Presence of Peripheral Arterial Disease

1. Age and sex. The age of the patients in the ACS-PAD group was significantly older than the ACS group (62±6 vs 58±9 years; *P*=.022). There were no significant differences regarding the presence of men (83.8% in the ACS-PAD group as compared with 84.6% in the ACS group).

2. Traditional CRF:

– Hyperlipidemia. No significant differences were detected between the two groups for the prevalence of dyslipidemia (75.7% in the ACS-PAD group as compared with 86.5% in the ACS group). Neither were any significant differences detected in cholesterol and triglyceride concentrations (Table 1).

– Smoking. No significant differences were detected between the 2 groups regarding history of smoking, with 31 patients in the ACS-PAD group (83.8%) being smokers or ex-smokers and 80 patients in the ACS group (76.9%). However, it was of note that among those patients with a history of smoking, the patients in the ACS-PAD group had been smokers for significantly longer than the patients in the ACS group. Moreover, the former had smoked more cigarettes than the latter, the difference being almost significant (Table 2).

– Diabetes. The prevalence of diabetes was significantly greater in the ACS-PAD group (35.1%) as compared with the ACS group (19.2%). Furthermore, we measured the glycosylated hemoglobin (HbA_{1c}) of the diabetic patients in both groups, and found that it was significantly higher in the ACS-PAD group (Table 2). Likewise, the percentage of diabetic patients with HbA_{1c}>7% was also greater in this group (Table 2).

– Blood pressure. We noted a significantly greater prevalence of hypertension in the group of patients with ACS-PAD as compared with the group with ACS (81% vs 53%). Moreover, the casual systolic blood pressure was significantly higher in the former group, as was the pulse pressure, though not the diastolic blood pressure (Table 2).

TABLE 1. **Lipid Parameters in the 2 Groups***

	ACS Group	ACS-PAD Group	*P*
TC, mg/dL	176.9±35.4	183.5±33.6	NS
LDL-C, mg/dL	106.4±27.9	112.9±29.7	NS
HDL-C, mg/dL	43.6±11.2	43.8±10.8	NS
Triglycerides, mg/dL	111†	170†	NS

*TC indicates total cholesterol; LD-C low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; ACS group, group of patients with acute coronary syndrome; ACS-PAD group, group of patients with acute coronary syndrome and associated peripheral arterial disease.
†Median, given in the values that do not follow a normal distribution.

TABLE 2. **Other Parameters in Relation With the Cardiovascular Risk Factors***

	ACS Group	ACS-PAD Group	*P*
Smoking, years	34.7±10.9	41.4±9.8	.004
Packets-year	46.3±29	58.2±30.5	.063
HbA_{1c}, mg/dL	5.9±1.5 (n=31)	6.8±0.6 (n=13)	.05
Microalbuminuria	3.1†	4.9t	.028
HbA_{1c}>7%	3.8%	13.5%	.039
Casual SBP, mm Hg	123±18	132±23	.025
Casual DBP, mm Hg	77±11	77±11	NS
Pulse pressure, mm Hg	45±14	55±19	.007

*SBP indicates systolic blood pressure; DBP, diastolic blood pressure; ACS group, group of patients with acute coronary syndrome; ACS-PAD group, group of patients with acute coronary syndrome and associated peripheral arterial disease.
†Median, given in the values that do not follow a normal distribution.

Emergent Cardiovascular Risk Factors

1. Lipids. We found no significant differences between the two groups in the concentrations of lipoprotein (a), apo A1, or apo B (Table 3).

2. Inflammatory markers and homocysteine. We detected significantly higher values of C reactive protein and amyloid in the ACS-PAD group (Table 4). The values of both fibrinogen and homocysteine were also higher in this group, although the differences were not quite significant.

3. Genetic study. After determining the genotypes, we then studied the alleles and the genotypes associated with cardiovascular disease. According to the literature, these are the *E4*, *PIA2* allele, and the DD genotype. We also studied the presence of the 4G allele, which appears to be protective. However, we found no significant differences in any of these genotypes in patients with or without PAD (Table 5).

Multivariate Analysis

The logistic regression analysis showed that poorly controlled diabetes (defined as a HbA_{1c}<7%), time-dependent smoking (evaluated by decades) and an increased pulse pressure (for each 10 mm Hg increase) were independent predictors for the presence of PAD (Table 6).

TABLE 3. **Other Parameters in Relation With the Lipids***

	ACS Group	ACS-PAD Group	*P*
Lipoprotein (a)	21.2†	35.6†	NS
apo A1	132.1±30.6	136.1±26.9	NS
apo B	88.8±20.4	95.2±21	NS

*ACS group indicates group of patients with acute coronary syndrome; ACS-PAD group, group of patients with acute coronary syndrome and associated peripheral arterial disease.
†Median, given in the values that do not follow a normal distribution.

TABLE 4. **Parameters in Relation to Markers of Cardiovascular Risk***

	ACS Group	ACS-PAD Group	*P*
CRP, mg/L†	2.18	3.1	.016
Amyloid, mg/mL†	3.7	5.2	.043
Fibrinogen	340.3±73.3	369.3±91.2	.057
Homocysteine, mmol/L†	9.4	11.45	.067

*CRP indicates C reactive protein; ACS group, group of patients with acute coronary syndrome; ACS-PAD group, group of patients with acute coronary syndrome and associated peripheral arterial disease.
†Median, given in the values that do not follow a normal distribution.

TABLE 5. **Genetic Factors in Relation With Cardiovascular Risk***

	ACS Group	ACS-PAD Group	*P*
Allele *E4*†	24.3%	13.9%	NS
Allele *PIA2*‡	31.1%	41.7%	NS
Genotype *DD*$	45.6%	27.8%	NS
Allele *4GII*	74.7%	75%	NS

*ACS group indicates group of patients with acute coronary syndrome; ACS-PAD group, group of patients with acute coronary syndrome and associated peripheral arterial disease.
†apo E gene. ‡Glycoprotein IIB/III gene. $Angiotensin converting enzyme gene. IIPlasminogen activator inhibitor 1 gene.

TABLE 6. **Predictive Factors of Peripheral Arterial Disease in Patients With the Acute Coronary Syndrome***

	Peripheral Arterial Disease
	OR (95% CI)
Poorly controlled diabetes	6.3 (1.1-66.7)
Smoking exposure time	1.5 (1.2-2.0)
Pulse pressure	1.9 (1.3-2.7)

*OR indicates odds ratio; CI, confidence interval.

DISCUSSION

One of the most important results of this study is the finding of a greater prevalence of the new and emergent CRF in patients with ischemic heart disease and asymptomatic or undiagnosed PAD as compared with patients with just ischemic heart disease alone.

Numerous studies have appeared over recent years examining these new CRF in groups of patients with CAD.[11,12] Just as certain traditional CRF are more prevalent in patients with CAD and PAD, it is to be expected that some of these new factors are also more prevalent. Very few studies have focused on coronary patients, making an active search for those with associated undiagnosed or subclinical PAD, and later studying the possible existence of differences in the CRF studied.

In our series of patients we found a prevalence of PAD, as determined by the ABI, of 26%. Of these 37 patients, 15 were asymptomatic, thus showing a high percentage of cases that escape clinical evaluation.

The prevalence of PAD in patients with CAD varies widely (15%-35%), depending on the method of detection of the peripheral disease and the population studied. For instance, it is not the same to detect the clinically manifest disease as to detect the disease that is still either subclinical or asymptomatic. Nikolsky et al[13] found a prevalence of 18.9% of symptomatic PAD. Narins et al,[14] in a study undertaken in 1045 patients admitted with acute myocardial infarction, found that 7.5% reported intermittent claudication. With reference to the study population itself, age and severity of the CAD are determinants of the prevalence.[15-17] Ness et al[15] found that 26% of patients with CAD who were aged around 80 years old also had PAD. Depending on the severity of the CAD, Atmer et al[16] found a prevalence of 14% in patients with either no or only minimal atheromatous lesions and 32% in patients with severe disease.

A similar study to ours, regarding the detection of PAD from the ABI, is the PIPS study (Detection of Peripheral Arterial Disease in Patients Presenting for Coronary Angiography and/or Intervention Patients Study). The preliminary results of this study, designed by Moussa et al, were presented for 88 patients at the 2003 Congress of the American College of Cardiology.[18] The prevalence of PAD was 26%, which coincides with that found by us.

Identification of patients with PAD on top of their CAD is interesting. In patients whose main diagnosis is PAD (with or without symptoms), long-term survival is worse than that of controls.[19,20] When the PAD is associated with coronary disease, the prognosis is considerably worse.[14,21,22]

Of interest was the finding that the patients with PAD had a greater prevalence of carotid plaques (65% vs 24%), which reveals the more generalized involvement of atherosclerotic disease in these patients and may explain the worse prognosis. Carotid involvement in patients with CAD is common, although the figures vary.[23,24] A recent study published by our group showed the high incidence of asymptomatic lesions in other vascular territories apart from the territory that was clinically involved.[25]

When we analyzed the presence of traditional CRF, we found a greater prevalence of hypertension and diabetes in the patients with associated PAD. It is difficult to compare our results with those of other authors, because of the few studies using the same design, although diabetes seems to play an important role.[14,18,26] Our results concerning traditional CRF and their implication as independent predictors of the onset of PAD are concordant with those of other studies already undertaken. Just like Narins et al,[14] we

too found no differences regarding the lipid profile between the 2 groups of patients.

With regard to the inflammatory markers, we found a significant increase in C reactive protein, amyloid and fibrinogen in the patients with both CAD and PAD. An extensive review of the literature has revealed just a few studies of similar design that have investigated these or similar markers. One such study, recently published by Brevetti et al,[27] compared 134 patients with isolated CAD with 40 patients with associated PAD. The markers of inflammation in the latter group of patients were significantly higher. Additionally, a greater percentage of the patients who also presented PAD had multivessel disease. Narins et al[14] reported similar findings. This finding concerning the inflammarory markers is of great relevance. Our study, as others, was unable to determine whether this inflammatory and prothrombotic state in patients with CAD predisposes to the development of PAD or whether it simply reflects more diffuse atherosclerotic involvement. A reasonable doubt remains as to whether the rise in these inflammatory markers occurs first in certain patients susceptible to more severe atherosclerotic disease that, with time, affects several vascular territories, or whether it concerns peripheral vascular involvement that leads to an increase in the markers.

Numerous studies over recent years have examined the markers of inflammation as predictors of recurrent cardiac events and of death after a coronary episode.[28-30] They have even been researched in the setting of primary prevention. The strongest association with prognosis was seen with fibrinogen and C reactive protein. Most studies were undertaken over the long term, though some examined intrahospital survival.[31,32] Recent data also suggest that the C reactive protein may be a marker for the risk of restenosis after percutaneous revascularization,[33,34] though not all the studies agree with these results.[35] High levels of elevated C reactive protein levels predict prognosis and recurrent events in patients with stroke and PAD.[36-39] The working groups of the American College of Cardiology/American Heart Association have recently undertaken a review of the subject and have included a classification of the recommendations.[40]

The homocysteine values were higher in the patients with PAD, though the difference was not quite significant. Multiple studies have detected an association between hyperhomocysteinemia and cardiovascular disease.[41,42] Darius et al[43] saw that hyperhomocysteinemia was only slightly more associated with PAD, but not with coronary and cerebrovascular disease.

The genotype study showed no greater prevalence of any particular genotype in the patients who also had PAD. Some studies have found a greater prevalence of certain genotypes in patients with PAD as the main diagnosis and of other genotypes in patients with coronary disease.[44,45] However, we were unable to find any relevant study with a similar design to that employed by us. Beilby et al found that polymorphism (I/D) of the *ACE* and *PIA1/A2* genes was not associated with PAD.[46]

Limitations of the Study

One limitation of this study concerns the small size of the study population. Although the results are highly concordant with those of the few other studies that have used a similar design, some of the findings of this study should be interpreted with caution. In particular, a few of the trends detected in our study might have reached statistical significance if a larger sample had been included. Thus, the small sample size reduces the ability to detect associations between those CRF included in the study and PAD. In fact, we found important differences in the concentration of triglycerides between the 2 groups (Table 1); nevertheless, these differences were not statistically significant. Similar situations were found with lipoprotein (a) (Table 3) and the genotype distribution (Table 5). In these cases, it is not possible to know whether the association does not exist or whether the study lacked the statistical power to detect the differences.

CONCLUSIONS

Peripheral arterial disease is not only relatively common in patients with ACS, but in a high percentage of cases it is not detected during the clinical evaluation. Various traditional and emerging CRF are more prevalent in patients with both ACS and PAD, and some of these factors are independent predictors of the disease.

Clinical Implications

Although no direct clinical implications can be deduced from this study, we believe that it provides a series of useful consequences in clinical practice. The search for unknown PAD in patients with coronary disease by means of relatively easy, noninvasive methods may be very useful because it identifies a subgroup of patients who fail to be recognized during the conventional clinical examination, and who have a worse prognosis and who will require more aggressive treatment of their CRF.

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