Long-Term Outcome of Atherosclerotic Renovascular Disease in Patients Submitted to Angioplasty

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SUMMARY

Background

The current increase in the diagnosis of atherosclerotic renovascular disease (ARD) befalls from the progressive recognition of its clinical impact. The role of percutaneous renal angioplasty as an alternative treatment has motivated, and continuous doing it, mainfold clinical trials.

Objective

To analyze a population submitted to percutaneous renal angioplasty and assess the safety of the procedure and the long-term clinical response.

Material and Methods

There were retrospectively and consecutively included 100 patients treated percutaneously. It was carried out a follow up by telephone calls or visits (median 1.7 years, interquartile range 25-75, 1.2 to 2.7 years) during which clinical and laboratory data was collected.

Results

A total of 100 patients were analyzed, mostly male (72%), mean age of 67.3 ± 9.9 years, with multiple cardiovascular risk factors (HBP 95%, DLP 74%, tobaccoism 63%, DM 28%) and extensive atherosclerotic vascular involvement (coronary disease 56%, peripheral vascular disease 39%). Stent angioplasty was carried out in 98% of cases, 22% bilaterally, with a success rate of 99%. It was observed a significant decrease in systolic blood pressure (SBP) at long-term follow-up (preprocedural SBT 139.7 ± 24.2mm Hg - postprocedural SBT 129.7 ± 13.9mm Hg, P <0.05), as well as a reduction in the number of indicated drugs (2.8 ± 1.03 - 1.7 ± 0.9, p = 0.02). These beneficial results were even higher in patients with bilateral involvement. Regarding renal function, 49% of patients showed sustained improvement (creatinine clearance: 53.6 ± 18.4 ml / min basal versus. 60.8 ± 19.5 ml / min at follow up, P = 0.011), whereas 20.4% showed a significant impairment in glomerular filtration. The improvement in glomerular filtration was more common in patients with advanced chronic impairment . (70.5% stages ≥III versus 13.5% stages 0-II; p=0.01) and with bilateral renal angioplasty (creatinine clearance: 52.8 ± 25.3 ml / min basal versus 66.1 ± 15.1 ml / min at follow-up; p = 0.032). In multivariate analysis, renal disease degree ≥III (OR29.6, CI95% 8.3 -105.8; p >0.001) and male sex (OR 16.2, CI 95% 4.3-105. 8: P> 0.001) were independent predictors of improvement in glomerular filtration rate at follow up.

Conclusions

Percutaneous treatment of renovascular disease is an additional therapeutic option of high security and good long-term outcomes in high-risk patients. Likewise it highlights the benefit of the TRA in patients with significant basal renal impairment, despite a late revascularization.

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Key words > Renal Artery - Atherosclerosis - Balloon Angioplasty - Renal Failure - Renovascular Hypertension

Abbreviations >

TRA	Transluminal Renal Angioplasty	**ARD**	Atherosclerotic Renal Disease
BNP	Brain Natriuretic Peptide	**HBP**	High Blood Pressure
DLP	Dyslipidemia	**DBP**	Diastolic Blood Pressure
DM	Diabetes Mellitus	**SBP**	SystolicBlood Pressure

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BACKGROUND

The current increase in the diagnosis of atherosclerotic renovascular disease (ARD) befalls from the growing recognition of its clinical impact. Epidemiological studies inform the progressive nature of this entity and consider that ARD affects 6.5% of the population older than 65 years. (1-3) This prevalence has tripled in the context of disease in other vascular territories. (4, 5)

The goal of the treatment is to control its clinical manifestations such as refractory hypertension (HT), impaired renal function and episodes of pulmonary edema. (6-8) These manifestations, as well as ARD per se, are associated with an increased cardiovascular morbidity.(7, 9, 10)

The role of percutaneous renal angioplasty as an alternative treatment has motivated, and continuous doing it, mainfold clinical trials. In spite of the fact that there are guidelines and recommendations, there is still uncertainty about the safety and the expected clinical outcome. (11-14)

The purpose of this study was to analyze the population undergoing a percutaneous renal angioplasty, evalute the procedure safety and the long-term clinical response.

MATERIAL AND METHODS

From January 1999 to October 2007, the database of Interventionist Cardiology Service they were retrospectively reviewed, consecutive carrying patients of unilateral or bilateral renal artery stenosis who were submitted to a renal angioplasty. Treated patients showed a severe injury that compromised lumen in ≥70% unilaterally or bilaterally and/or a gradient of translesional systolic pressure ≥20mm Hg. All patients were routinely medicated with aspirin 100 mg / day and clopidogrel 75 mg / day or ticlopidine, in addition to their antihypertensive treatment and cardiovascular prevention. Immediately prior to the beginning of the intervention it was administered intraarterially 100 IU / kg heparin.

All had a follow up by visits and / or telephone calls, in which clinical (blood pressure, current treatment, new admissions) and laboratory (renal function) information were collected.

HBP was defined and evaluated according to the latest guidelines published by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC). (15) After the procedure it was carried out a follow up of the numbers of blood pressure and renal function. The impact of revascularization on HBT was classified as cured, improved or failed. (16) The renal function was assessed by creatinine (mg / dl) and glomerular filtration rate calculated with the modified equation of diet in renal disease by the National Kidney Foundation. (17) Chronic kidney failure was defined as the impairment of renal function for three months or more and it was classified according to the National Kidney Foundation in its five stages (stage 1: Kidney damage with normal or increased renal filtration (> 90 ml / min) , Stage 2: Kidney damage with mild impairment (60-89 ml / min), stage 3: Glomerular filtration 30-59 ml / min), stage 4: 15-29 ml / min, stage 5: <15 ml / min or dialysis). (18) It was defined as improvement in secondary renal function to revascularization to an increase ≥20% of glomerular filtration rate at follow up. (19)

Statistical analysis

Continuous variables are presented as mean and standard deviation or median and interquartile range accordind to the distribution were Gaussian or not. In the comparison of two groups were used t test or the Wilcoxon test according to the distribution were parametric or not, respectively.

Categorical variables were expressed as percentages and compared with Chi-square test. It was carried out an analysis of multivariate logistic regression entering variables which obtained a value of $p<0.20$ in simple logistic regression to identify predictors of improvement in glomerular filtration rate at follow up as a dichotomic variable. It was considered statistically significant a value of $p<0.05$. It was used the two-tailed t test for paired samples to assess the development of blood pressure and creatinine clearance at follow-up compared to basal values.

RESULTS

Population and procedural characteristics

Of a total of 100 patients studied, most of them were male (n = 72). The mean age of the population was 67.3 ± 9.9 years. Many of the patients had multiple cardiovascular risk factors (95% HBP, 74% DLP, 63% Tobaccoism, 28% DM) and extensive atherosclerotic vascular compromise (56% coronary disease, 39% peripheral vascular disease). The clinical presentation of patients has been mixed, mostly secondary to (43%) refractory HBP, (30%) new impariment of renal function without other objective cause and 3% with repeated episodes of heart failure. 8% of patients required hospitalization in the context of unstable conditions (5 patients due to hypertensive crisis, 3 patients because of episode of heart failure).

The remaining population was asymptomatic. It highlights the presence of two patients with single functioning kidney and 11% had reduced renal size (less than 8cm) in relation to the contralateral in association with significant renal artery stenosis.

It was obtained a 99% of success in the procedure. Stent angioplasty was carried out in 98% of cases, of which 62% it was introduced directly. In 22% bilateral renal angioplasty was carried out (Table 1).

During the procedure three dissections were found to implant the stent over the renal artery at the distal edge, in one of them it was required the placement of a new stent due to an alteration of distal flow. During hospitalization, there were not greater cardiovascular events associated with the procedure. 11.4% of the treated patients underwent with acute renal impairment, without the need of hemodialysis. This impairment occurred more frequently in patients with chronic renal failure (28.6% versus 8.1%, p = 0.049). The median follow-up was 1.7 years (25-75, 1.2 to 2.7 years interquartile range)

Blood pressure outcome

43% of the studied patients were derived to the hemodynamic service with a diagnosis of refractory HBP, in 13% of them associated with acute concomitant

basal renal impairment. The total population showed a reduction in systolic blood pressure (SBP) at long term follow up of 10mm Hg after surgery (preprocedural SBP 139.7 ± 24.2mm Hg; postprocedural SBP 129.7± 13.9mmHg p<0.05); mean of reduction of 10 ± 3mm Hg, without changes in relation with diastolic blood pressure (DBP). Also, HBP was classified as cured, improved and failed after revascularization, It was objectified a favourable tendency towards cured-improved versus failed (3% cured, 59% improved, 38% failed; p = 0.09).

It was analyzed the difference in the number of drugs indicated preprocedure and postprocedure and it was found a significant reduction in antihypertensive drugs used after surgery. Prior to renal angioplasty it was confirmed an use of 2.8 ± 1.03 drugs per patient, which were reduced to 1.7 ± 0.9 (p = 0.02). Patients undergoing bilateral renal angioplasty before surgery were medicated with a greater number of antihypertensive drugs (Table 1). In this subgroup was evident at follow up a clear reduction in the number of indicated drugs (3 ± 1.04 presurgery versus 1.6 ± 0.9 postsurgery, p = 0.008) as well as a tendency to reduction in numbers of systolic blood pressure (preprocedural SBP 142.1 ± 25.3mm Hg versus postprocedural SBP 128 ± 11; p = 0.06, mean reduction of 14 ± 7mm Hg).

Renal function outcome

More than half of the population had advanced basal chronic renal impairment (stages III-V, 61%). Mean blood creatinine in the total of patients was of 1.58± 1mg/dl. The indication for percutaneous secondary renal revascularization to new impairment in renal function was of 30%.

AT long-term follow up of all treated patients, 49% showed sustained improvement in creatinine clearance (53.6 ± 18.4 ml / min basal versus 60.8 ± 19.5 ml / min at follow up; p = 0.011) (Figure 1A). However, 20.4% showed a significant impairment in glomerular filtration.

The improvement in glomerular filtration was more common in patients with advanced chronic impairment .(70.5% stages ≥III versus 13.5% stages 0-II, P = 0.01) and less common in women (18.5 % vs. 49%, p = 0.01). Among basal characteristics, women had a lower percentage of comorbid conditions (DM, coronary artery and peripheral disease). The basal creatinine was significantly lower in women, however, both glomerular filtration rate as prevalence of advanced chronic renal failure were similar in women and men (Table 2, Figure 1 B and C).

In patients undergoing bilateral renal angioplasty, 64% showed a significant improvement in creatinine clearance (52.8 ± 25.3 ml / min basal versus 66.1 ± 15.1 ml / min at follow-up; p = 0.032).

In order to identify predictors of improvement in glomerular filtration rate, it was carried out a multivariate logistic analysis with different clinical variables (sex, grade ≥ 3 renal disease, basal DM, SBP and DBP, number of antihypertensive drugs). The presence of grade III renal disease (OR 29.6, CI 95% 8.3-105.8; p<0.001) and male sex (OR16.2, CI 95% 4.3-105.8; p> 0.001) were independent predictors of improvement in glomerular filtration rate at follow up (see Figure 1).

Long-term follow up

At long term follow up there were multiple vascular events: CVA (n = 2), acute coronary syndrome (n = 5), surgical revascularization (n = 4), coronary angioplasty (n = 6) and peripheral angioplasty (n = 6) and 11 percutaneous renal re surgery, which were secondary to clinical manifestations. In eight of these were found restenosis and in three, progression of significant contralateral disease. Within the first six were objectified diffuse stent restenosis, in their majority treated with balloon (5 with balloon, 1 with pharmacologic stent) and two on lesions treated with balloon, in which metal stent was implanted.

Likewise, it was found two episodes of acute kidney failure, both related to surgery in patients with chronic renal impairment and two episodes of heart failure, associated with acute coronary events. There were observed 6 deaths during follow-up, 4 of vascular causes (2 acute myocardial infarction, 2 postoperative, myocardial resvacularization surgery) and the rest of oncological cause.

DISCUSSION

Our analysis of consecutive patients with renovascular renal disease submitted to renal angioplasty allows us to know the characteristics of this population and showed the safety and potential benefit of this therapeutic alternative.

Renal atherosclerosis is a prevalent entity, especially in patients with involvement of other vascular beds, (20) as it could be objectified in this study. Despite the continued advance in interventional treatment, it is still controversial in the context of renovascular disease. (21) That is why different additional parameters have recently been assessed (renal angiographic blush, BNP levels, fractional flow reserve, Doppler resistance index) in order to identify patients who could obtain the greatest clinical benefit. (22-24) However, current scientific evidence is insufficient to standardize the role of renal angioplasty. (25) Prior randomized studies had important limitations, including the big move of patients from the medical treatment branch to TRA (44% in the DRASTIC study), the complicated definition of inclusion of patients or the low cutoff point of significant stenosis in the ASTRAL study. This, together with the small number of patients enrolled in the STAR study, limits the real conclusions of benefit of this treatment. (26-28)

Despite the return flow to renal level, treatment of this entity represents a more complex challenge. Concomitant factors of this disease, as HBP, dyslipidemia and diabetes, are associated independently

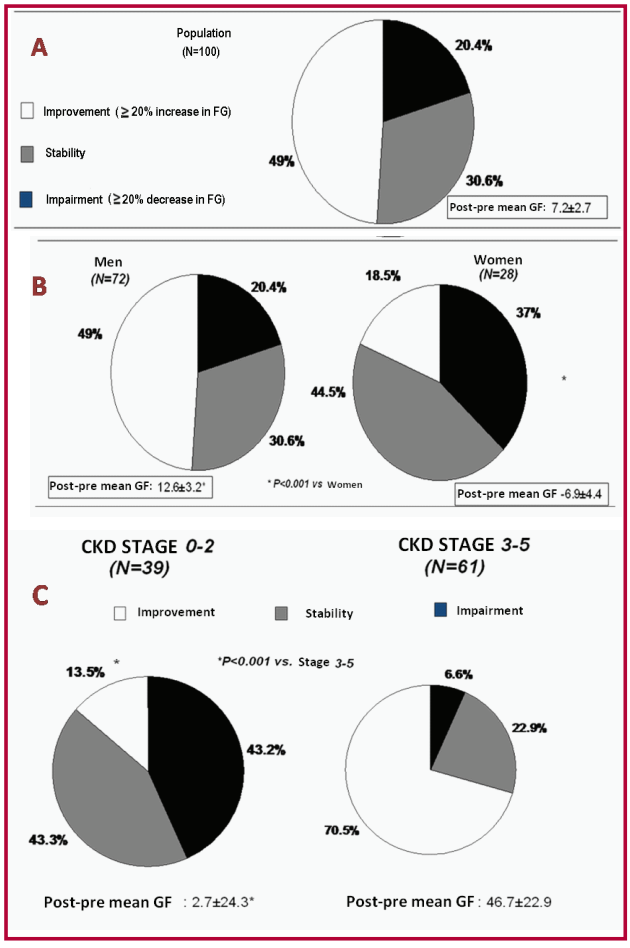

Fig 1. Long term evolution of renal function after transluminal renal angioplasty. Discrimination of subgroups. GF: Glomerular filtration rate. CKD: chronic kidney disease.

Table 1. Basal Caracteristics according to the type of compromise

	Bilateral (n = 22)	Unilateral (n = 78)	p
Age (Years ± SD)	66.8 ± 10	66.7 ± 5	0.89
Body mass index (kg/m2 ± SD)	22.2 ± 10.1	24.5 ± 3.1	0.72
Hypertension, %	100	87.1	0.65
Dyslipidemia, %	68.1	64.1	0.56
Diabetes mellitus, %	50	25.6	0.04
Basal Creatinine (mg/dl ± SD)	1.54 ± 1	1.59 ± 0.9	0.52
Antihypeertensive drugs (number ± SD)	3 ± 1.04	1.9 ± 1.05	0.01
Systolic blood pressure (mm Hg ± SD)	142.1 ± 25.3	128.1 ± 15	0.06
Creatinine clearance (ml/min ± SD)	52.8 ± 25.3	58.5 ± 20.1	0.54

Table 2. Basal Caracteristics according to gender

	Male (n = 72)	Female (n = 28)	p
Age, (years ± SD)	67.8 ± 8,6	66 ± 12.8	0.89
Body mass index (kg/m2 ± SD)	26.8 ± 4.1	25.5 ± 3.9	0.56
Hypertension, %	93	100	0.61
Diabetes mellitus, %	37.4	10.7	0.01
Coronary disease, %	68	25	0.01
Peripheral vascular disease, %	44.4	25	0.07
Basal creatinine, (mg/dl ± SD)	1.66 ± 0.8	1.22 ± 1	0.05
Kidney failure> stage 3, %	61.1	60.7	0.52
Glomerular filtration (ml/min/1.73 m2)	53.2	54.7	0.65

and directly associated with renal impairment. (29) Likewise, variable linked to surgery, such as contrast-induced nephropathy or atheroembolization, have a preponderant role in the renal outcome of these patients. According to it, our study showed a high prevalence of hypertensive and diabetic patients with target-organ damage prior to clinical renal manifestation. This reality could be manifested in patients (20.4%) who continued with impaired renal function despite successful treatment. This impairment is congruent with which is referred in the current bibliography. (8, 30, 31) However, it is noteworthy that patients with a greater impairment (kidney failure in stage III) have been benefited even more, because in them there was only 6.6% of latter significant impairment. (31, 32) Likewise, taking into account the limitation of glomerular filtration rate as a variable to compare between groups with renal impairment in 0-II and advanced stages, it was showed a high percentage of stability (43.3%) among patients in the first group.

With regard to the differences concerning gender, previous studies show that men would have a greater number of glomeruli and increased production of prostaglandins, which provides greater protection against nephrotoxicity induced by contrast, secondary injury to ischemic and hyperfiltration. (30, 33) Moreover, women experience a worsening of renal function after contrast exposure. (34, 35)

Adequate control of HBP in the context of atherosclerotic and / or peripheral coronary compromise is very useful, as it prevents the progression of vascular disease. (29) In our record we have a population of high cardiovascular risk patients in whom we obtained a better control of blood pressure at long-term of follow up. This benefit was greater in patients with severe bilateral compromise. In this subgroup, renal atherosclerosis is a clear trigger for clinical expression, as the microvascular renal injury by significant renal artery stenosis and vascular remodeling by

uncontrolled systemic hypertension are at a similar outcome. These findings are comparable to the results obtained by Webster and et al., who certify the greatest benefit in controlling blood pressure in patients with bilateral compromise. (36)

Study Limitations

Our paper presents some limitations that we consider convenient to highlight.

First, the retrospective nature of this study constitutes a limitation, since in some cases it makes difficult to establish indication criteria, implementation of preventive treatment of contrast nephropathy or discontinuation of nephrotoxic drugs before surgery. Second, the sample size is small, which limits the assessment of the number of events in the long term. Third, it has not been able to collect in a systematic way complementary studies postintervention as a form of objective follow up in order to assess restenosis.

Because of these limitations, we are aware that our study does not allow us to define the undisputed therapeutic behaviours in patients with this pathology so controversial.

CONCLUSIONS

The findings of this current study suggest that percutaneous treatment of renovascular disease is a complementary therapeutic alternative of high safety and good long-term outcomes. Likewise, it is also highlighted the benefir of TRA in patients with significant basal renal impairment, despite a late revascularization. However, the surgery is part of a comprehensive treatment that requires the correct selection of patients and the subsequent strict medical control.

RESUMEN

Evolución alejada de la enfermedad renovascular aterosclerótica en pacientes sometidos a angioplastia

Introducción

El actual incremento en el diagnóstico de la enfermedad renovascular aterosclerótica (ERA) deviene del progresivo reconocimiento de su impacto clínico. El papel de la angioplastia renal percutánea como tratamiento alternativo ha motivado, y continúa haciéndolo, múltiples ensayos clínicos.

Objetivo

Analizar una población sometida a angioplastia renal percutánea y evaluar la seguridad del procedimiento y la respuesta clínica alejada.

Material y métodos

Se incluyeron en forma retrospectiva y consecutiva 100 pacientes intervenidos percutáneamente. Se realizó un seguimiento telefónico o por visitas (mediana 1,7 años; rango intercuartil 25-75, 1,2-2,7 años) durante el cual se recolectaron los datos clínicos y de laboratorio.

Resultados

Se analizaron 100 pacientes, la mayoría de sexo masculino (72%), edad media de 67,3 ± 9,9 años, con múltiples factores de riesgo cardiovascular (HTA 95%, DLP 74%, TBQ 63%, DM 28%) y amplio compromiso vascular aterosclerótico (enfermedad coronaria 56%, enfermedad vascular periférica 39%). Se realizó angioplastia con stent en el 98% de los casos, el 22% en forma bilateral, con un éxito del 99%. Se observó un descenso significativo de la tensión arterial sistólica (TAS) en el seguimiento alejado (TAS preprocedimiento 139,7 ± 24,2 mm Hg - TAS posprocedimiento 129,7 ± 13,9 mm Hg; $p < 0,05$), así como una reducción del número de drogas indicadas (2,8 ± 1,03 - 1,7 ± 0,9; $p = 0,02$). Estos resultados beneficiosos fueron incluso mayores en pacientes con compromiso bilateral. En relación con la función renal, el 49% de los pacientes evidenciaron una mejoría sostenida (depuración de creatinina: 53,6 ± 18,4 ml/min basal vs. 60,8 ± 19,5 ml/min al seguimiento; $p = 0,011$), mientras que el 20,4% presentó un deterioro importante en el filtrado glomerular. La mejoría en el filtrado glomerular fue más frecuente en pacientes con deterioro crónico avanzado (70,5% estadios ≥ III vs. 13,5% estadios 0-II; $p = 0,01$) y con angioplastia renal bilateral (depuración de creatinina: 52,8 ± 25,3 ml/min basal vs. 66,1 ± 15,1 ml/min al seguimiento; $p = 0,032$). En el análisis multivariado, la enfermedad renal grado ≥ III (OR 29,6, IC 95% 8,3-105,8; $p > 0,001$) y el sexo masculino (OR 16,2, IC 95% 4,3-105,8; $p > 0,001$) fueron predictores independientes de mejoría del filtrado glomerular en el seguimiento.

Conclusiones

El tratamiento percutáneo de la enfermedad renovascular es una alternativa terapéutica complementaria de elevada seguridad y buena evolución alejada en pacientes de riesgo alto. Se destaca asimismo el beneficio de la ATR en pacientes con deterioro renal basal importante, a pesar de una revascularización tardía.

Palabras clave > Arteria renal - Aterosclerosis - Angioplastia - Insuficiencia renal - Hipertensión renovascular

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