Association Between 2 Angiographic Subtypes of Renal Artery Fibromuscular Dysplasia and Clinical Characteristics

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Association between two angiographic subtypes of renal artery fibromuscular dysplasia and clinical characteristics

Savard. Uni- and multifocal renal artery FMD

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Abstract

Background: Initially based on histology, the diagnosis of renal artery fibromuscular dysplasia (FMD) is now mostly based on angiographic appearance because arterial tissue samples are rarely available. This retrospective cross-sectional study aimed to assess clinical relevance of a binary angiographic classification of FMD lesions (unifocal or multifocal) based on computed tomographic or magnetic resonance angiography.

Methods and results: Adult patients diagnosed with FMD in a single tertiary care center for hypertension management were identified by screening electronic files. FMD lesions were reviewed and classified according to computed tomography or magnetic resonance angiography as multifocal if there were at least two stenoses in the same arterial segment; otherwise, they were classified as unifocal. Of 337 patients with established renal artery FMD, 276 (82%) were classified as multifocal. Patients with unifocal and multifocal lesions differed significantly in median age at diagnosis of FMD (30 and 49 years) and hypertension (26 and 40 years), sex distribution (female:male ratio 2:1 and 5:1), initial blood pressure (157/97 and 146/88 mmHg), current smoking (50 and 26%), prevalence of unilateral renal artery lesions (79 and 38%), presence of kidney asymmetry (33 and 10%), renal revascularization procedures (90% and 35%), and hypertension cure rates in patients who underwent revascularization (54% and 26%).

Conclusions: A binary angiographic classification into unifocal or multifocal renal artery FMD is straightforward and discriminates two groups of patients with different clinical phenotypes.

Key words: fibromuscular dysplasia; hypertension, renal; renal artery stenosis.

Introduction

Fibromuscular dysplasia (FMD) is a heterogeneous group of idiopathic, non-atherosclerotic, relatively rare vascular diseases, leading to the narrowing of medium-sized arteries, mostly the renal and internal carotid arteries [1, 2]. Renal artery FMD is the second most frequent cause of renovascular hypertension [3]. Pathologic classifications of FMD were proposed in the sixties [4-6] and consensus classifications were subsequently proposed by Harrison & McCormack [7] and Stanley *et al* [8]. They identified three main types of FMD according to the dominant arterial wall layer involved: intimal fibroplasia, present in less than 10% of cases; medial fibroplasia, the most frequent type of FMD (rarer medial FMD lesions are perimedial fibroplasia and medial hyperplasia) and adventitial or periarterial fibroplasia, which is the rarest FMD subtype [1, 7, 8].

Surgery for renal artery FMD makes pathologic specimens available and allows the use of pathologic classifications. In recent years, however, most patients with renal artery FMD needing intervention undergo percutaneous angioplasty rather than surgical reconstruction. A recent meta-analysis of interventions for renal artery FMD after 1995 identified only one published surgical series but 24 angioplasty series [9]. Consequently, contemporary classification needs to be based on the angiographic appearance of FMD lesions. Pathologic-angiographic correlation studies indicate that a string-of-beads appearance is associated with medial fibroplasia [4-8], whereas other angiographic aspects, either focal or tubular, are not associated with any specific type of FMD (Table 1).

In the present study, we investigated whether a binary angiographic classification of FMD into unifocal and multifocal types discriminated between distinct clinical phenotypes.

Methods

Patients

We screened our institution's electronic medical record database and the computerized collection of minutes of the multidisciplinary meetings for adult patients for whom the diagnosis of FMD was considered between January 1st 1986 and November 30th 2011. We also cross-checked research databases used in the Hypertension Unit and in the Department of Genetics. The weekly meetings are attended by hypertension specialists, vascular radiologists and vascular surgeons. We accepted cases as FMD without further verification if the diagnosis was confirmed at multidisciplinary meetings and if angiographic reports mentioned a typical string-of-beads appearance. Other records and imaging studies were reviewed by at least two of us (S.S., P.-F.P., A.A.) to ascertain FMD diagnosis. Our diagnostic pathway meets the recent recommendations of a European consensus panel [10]. Echo-Doppler is not specific enough to diagnose renal artery FMD and was only used for screening. Computed tomography angiography (CTA), magnetic resonance angiography (MRA) and catheter-based angiography were used for diagnostic confirmation. CTA and MRA are non-invasive and specific enough to rule in FMD, but not sensitive enough to rule it out in case of high clinical suspicion. Catheter-based angiography was performed: (i) when revascularization was medically justified; (ii) when the diagnosis remained uncertain after CTA or MRA. The procedure for the inclusion of patients was consistent with French institutional guidelines.

Diagnostic Criteria

In accordance with current definitions [1, 7, 8], we considered the diagnosis of renal artery FMD in patients with non-atherosclerotic stenosing lesions affecting the trunk or branches of the renal arteries in the absence of aortic wall thickening or biochemical evidence of inflammation and in the absence of known syndromic arterial disease, such as type-1 neurofibromatosis, pseudo-xanthoma elasticum, vascular Ehlers-Danlos, Williams or Alagille syndromes [10].

Angiographic classification was based on imaging studies performed before any renal artery intervention. Cases with confirmatory CTA or MRA performed before 1990 were not retained to ensure the quality and availability of imaging studies.

CTA of the renal arteries and aorta were performed up to 2005 on a 4-row multislice CT scanner (Somatom, Siemens AG, Erlangen, Germany) with a slice thickness of 1 mm, and subsequently on a GE LightSpeed VCT 64-slice scanner (GE Medical Systems, Milwaukee, Wisconsin) with a slice thickness of 0.625 mm. Non-ionic contrast medium (100 mL of Xenetix, 350 mg of iodine/mL; Guerbet, Roissy, France) was injected with a power injector into a peripheral vein at a rate of 4-5 mL/s followed by a 30-mL saline flush. The helical acquisition was initiated after the bolus reached the abdominal aorta using a triggering system. MRA examinations were performed on a 1.5 T scanner (Excite up to 2005, currently Excite HDx, General Electric Medical Systems, Waukesha, Wisconsin) with multichannel body array coil. Bolus tracking was used to monitor the arrival of contrast agent to the abdominal aorta. Gadoterate meglumine (Dotarem; Guerbet, Roissy, France) was injected at 1.8 mL/s followed by a 30-mL saline flush, using an automated power injector (Optistar, Mallinckrodt). The sequence parameters for the image acquisition varied as follows: For coronal orientation, parameters included repetition time msec/echo time msec, 3–6/1–2; flip angle, 25°–35°; number of signals acquired, 0.5–1; section thickness, 1.8–2.2 mm; pixel size, 1.2–0.8 & 1.5–1.1 mm; and overall acquisition time, 25 seconds or less. The vascular field of view was tailored to each patient to include the kidneys, celiac trunk, superior and inferior mesenteric arteries, common and external iliac arteries. CTA and MRA data were analyzed on a computer workstation (Advantage Workstation, AW4.4, GE Medical Systems).

We limited inclusion to cases with renal artery FMD, with or without FMD lesions in other vascular beds. FMD lesions were classified according to their radiological appearance as either unifocal (presence of a single focal or tubular stenosis, Figure 1 A and B) or multifocal

(presence of two or more stenoses on a given vessel segment, with or without the typical string-of-beads appearance, Figure 1 C, D, E and F) [5, 6, 8, 11]. Patients who had unifocal FMD lesions on a segment of renal arteries but multifocal FMD lesions on another segment or another vascular bed were classified as having multifocal FMD. The presence of renal artery dissections or aneurysms without direct evidence of an FMD stenosing lesion was not considered sufficient to diagnose FMD [12]. The extent of renal artery FMD lesions was scored 1 to 4 depending on the presence of unilateral or bilateral lesions involving renal artery trunk, branches, or both as previously published [13]: 1, trunk or branch(es), but not both, affected on one side; 2, trunk and branch(es) affected on one side; 3, trunk or branch(es), but not both, affected on both sides; 4, trunk and branch(es) affected on both sides. Renal asymmetry was defined as a difference >20 mm in the bipolar length between the two kidneys on ultrasound [14]. Hypertension cure was defined as a blood pressure <140/90 mmHg in the absence of any antihypertensive drug.

Clinical data retrieval

We extracted clinical and biological data collected at the first visit in our unit. For patients referred after FMD had been diagnosed elsewhere, we considered clinical and biochemical data collected at the first visit to our unit if it occurred within 1 year of the diagnosis of FMD and if there had been no renal artery intervention during this period. We estimated creatinine clearance using the Cockcroft-Gault formula [15] normalized for body surface area considering intrinsic limits of each equation [16] and the fact that most creatinine measurements were not done with current standards.

Statistical methods

Comparisons were performed between unifocal and multifocal FMD. Quantitative variables are reported as medians, 25^{th} and 75^{th} centiles and were compared with the Mann Whitney test. Nominal and ordinal variables are reported as numbers and percentages and were compared

with Fisher's exact test and the trend Chi² test, respectively. Due to the large difference in distribution of age and sex between the two groups, we tested if p-values < 0.05 for unadjusted comparisons remained < 0.05 after adjusting for age and sex. Adjusted comparisons were performed with ANOVA for continuous variables and with the Mantel-Haenzel test for binary variables. Age at evaluation (FMD diagnosis) was dichotomized into ≤ 40-year old or > 40-year old for these adjustments. Reported p-values are two-sided and, due to the exploratory nature of the study, no adjustment was made for multiple comparisons. Stata 9.2 (Stata-Corp, College Station, Texas, USA) was used for statistical analyses.

Results

Patient screening and selection

Querying databases found 700 patient records in which the diagnosis of FMD was mentioned at least once. Among all these potential FMD patients, 363 were excluded for the reasons shown in Figure 2, and 337 were considered to have conclusive diagnosis of renal artery FMD. Overall, 56 of these patients (7 with unifocal and 49 with multifocal FMD) had been diagnosed elsewhere within the year preceding the first visit to our unit, without undergoing any renal artery intervention in the meantime.

Characteristics of FMD patients at first visit

There were less than 20% missing data for all baseline variables except estimated creatinine clearance (21% missing data), renal asymmetry (28% missing data) and other vascular bed imaging. Indeed, we systematically assess extra-renal arteries in patients with renal artery FMD since 2009. Before that, extra-renal vascular beds were mostly assessed in patients with neurological symptoms or complications, or in patients with digestive symptoms or intermittent claudication. Cervical arteries were assessed in 24/61 patients with unifocal FMD and in

127/276 patients with multifocal FMD; digestive arteries were assessed in 16 and 97 patients respectively, and ilio-femoral arteries in 22 and 123 patients, respectively.

Table 2 reports characteristics at presentation of patients with unifocal and multifocal FMD. Multifocal FMD was the most frequent type (82%). Almost all patients were referred for hypertension, including twenty-two patients following a recent neurological event (stroke, vertebral or carotid artery dissection, or intracranial aneurysm rupture) related to cervical artery FMD (19 with multifocal FMD, 3 with unifocal FMD). Patients with unifocal FMD were younger (age distribution is shown in Figure 3), were more frequently current smokers and had higher blood pressure levels at presentation than patients with multifocal FMD. Kidney asymmetry was more frequent in patients with unifocal FMD. FMD more frequently affected the right renal artery in both subtypes. Patients with multifocal FMD more frequently had bilateral lesions and had a higher renal artery score than patients with unifocal FMD. P-values adjusted for sex and age at FMD diagnosis remained < 0.05 for the following variables: diastolic BP ($p=0.04$), kidney asymmetry ($p=0.03$), unilateral disease ($p<0.001$), renal artery score ($p<0.001$). Although cervical FMD lesions were sought in less than one patient in two, they tended to be more frequently diagnosed in patients with multifocal renal artery FMD than in those with unifocal FMD.

Renal artery interventions and characteristics at follow-up

Most (53/61; 87%) patients with unifocal FMD, but fewer than half (105/276; 38%) of those with multifocal FMD had undergone a renal artery intervention at any time (nephrectomy, surgical reconstruction or percutaneous angioplasty) (unadjusted and adjusted $p<0.001$). For those patients who had at least one intervention, the median number of interventions was 1 [1, 2] for both FMD subtypes ($p = 0.49$ for the difference).

Among patients who had a clinical follow-up visit in our unit more than 365 days after the diagnosis of FMD, 28/31 (90%) with unifocal FMD and 50/141 (35%) with multifocal FMD

had undergone renal artery intervention (Table 3, adjusted and unadjusted p<0.001). The decreases from baseline to follow-up in systolic blood pressure and in the number of antihypertensive agents administered were larger for patients with unifocal FMD than with multifocal FMD. When the comparison was restricted to patients who had undergone renal artery interventions, those with unifocal and multifocal FMD had similar drops in systolic blood pressure (–29 [–51, –14] and –29 [–48, –19], p = 0.86). However, the proportion of patients cured of hypertension was 15/28 (54%) for unifocal FMD and 13/50 (26%) for multifocal FMD (p = 0.03). This difference remained significant after adjusting for sex and age (p = 0.02).

Discussion

Since the advent of renal artery percutaneous angioplasty, few patients with FMD undergo primary surgical revascularization [9]; furthermore, any surgery usually follows one or more attempts at percutaneous angioplasty [10]. Consequently, unaltered pathologic samples are rarely available so the diagnosis and classification of FMD has to be based on the angiographic appearance of stenoses and exclusion criteria (the disease affects medium-sized arteries, is neither atherosclerotic nor inflammatory, and there is no known syndromic vascular disease).

Previous and current angiographic classifications

Several series published in the sixties and seventies described comparisons of pathology and catheter-based angiography. These studies led to an angiographic classification, in which the beaded aspect was a specific but not sensitive correlate of the medial-type FMD (see Table 1). Several later series used a pathologic terminology (e.g. intimal, medial or subadventitial fibroplasia), although pathologic specimens were not available [17-21]. More recent series dichotomized renal artery FMD into two subtypes according to various criteria: multifocal or unifocal, medial or non-medial, or FMD with or without a ‘beaded’ or ‘string-of-pearls’

appearance [13, 22-24]. Other series considered FMD to be present only where angiography showed "beads" or a "string-of-pearls" [25-27]. Twenty-four of the 47 studies reporting percutaneous angioplasty in patients with FMD did not indicate the criteria used for diagnosing FMD [9]. To avoid these confusing considerations, we propose a binary angiographic classification into multifocal or unifocal disease. This classification is possible from CTA or MRA, which are minimally invasive imaging tests. In the present angiographic classification, unifocal FMD includes focal or tubular FMD, sometimes called non-medial FMD. Multifocal FMD is defined by the presence of multiple stenoses on a given vessel segment with or without the string-of-beads appearance. Patients with or without the typical string-of-beads pattern did not differ in clinical presentation, distribution of lesions, or number of interventions and we therefore considered them altogether (Supplemental Table 1). This finding strengthens the view that patients with multifocal FMD stenoses represent a relatively homogeneous subgroup, whether stenoses alternate with arterial dilatations or not. Our data show that this binary angiographic classification, at least at the renal artery level, distinguishes patients who also differ by several clinical traits, making them two distinct entities.

Comparison between unifocal and multifocal FMD

In our series of adult patients with established renal artery FMD, 61 of the 337 (18%) patients showed the unifocal pattern. This proportion is similar to that reported in the angiographic/pathologic series by McCormack et al [6] (31%), Kincaid et al [5] (11%) and Stanley [8] (16%) (See Table 1), and in a recent meta-analysis of angioplasty in FMD [9] (30%). However, non-medial FMD accounted for only 8.6% of 302 cases in the US registry for FMD [2]. The difference between the proportion of unifocal FMD in the present series and the proportion of non-medial FMD in the US registry may have several explanations: The spectrum of patients differs since the US registry dealt with FMD at any vascular bed whereas patient with cervical artery FMD only (without renal artery FMD) were excluded from the present series;

angiographic criteria used to define medial-type and non-medial-type FMD across the 9 participating US centers were not reported; and the type of FMD was not recorded in 145 patients from this registry. Using a similar terminology and similar diagnostic methods should help to compare observations across centers and conclude whether the observed difference in the prevalence of unifocal (or non-medial) FMD is linked to diagnostic criteria, patient presentation or the vascular beds involved.

In addition to the angiographic appearance, various clinical characteristics differed between unifocal and multifocal FMD patients. A higher proportion of unifocal than multifocal FMD patients were men, and unifocal FMD was diagnosed almost 20 years earlier than multifocal FMD. Bilateral lesions were less frequent in unifocal than multifocal FMD patients. At referral, blood pressure was higher and renal asymmetry more frequent for unifocal FMD than multifocal FMD patients. Among patients with a follow-up over 365 days, unifocal FMD patients more frequently underwent renal artery intervention but this may be because the degree of unifocal stenosis is more easily evaluated by non-invasive angiography and unifocal lesions are more amenable to angioplasty. There was also a larger drop in blood pressure and in the number of antihypertensive agents in patients with unifocal FMD; this was explained by a higher proportion of renal artery interventions because the blood pressure drop was similar in both subgroups if only revascularized patients are considered. The overall cure rate was 36% after angioplasty, entirely consistent with published results [9]. However, our results suggest that hypertension cure rates are higher in patients with unifocal FMD (54%) than in those with multifocal FMD (26%). Patients with unifocal FMD were younger, had a shorter duration of hypertension at diagnosis of FMD, and displayed renal asymmetry more frequently than patients with multifocal FMD. All these findings increase the probability of true renovascular hypertension rather than associated essential hypertension. Moreover quantifying stenosis grade is notoriously difficult in multifocal FMD [24]. Consequently, patients with non

hemodynamically significant multifocal FMD and associated essential hypertension may be advised to undergo angioplasty, resulting in a disappointing BP outcome.

The few previous papers comparing clinical characteristics between FMD subtypes are consistent with our results. McCormack *et al* [6] reported that 9 of 14 patients with intimal FMD and 3 of 15 patients with medial FMD were male. Stewart *et al* [21] and Stanley *et al* [8] stated that intimal fibroplasia (with a non-beaded aspect) occurs more frequently in children and young adults. Meaney *et al* [19] and Goncharenko *et al* [17] reported that patients with non-beaded renal artery FMD more frequently had progressive stenoses. In a previous study of sporadic and apparently familial FMD [13], we found the same age and sex difference between unifocal and multifocal FMD as in the present study. These various findings suggest that unifocal and multifocal FMD are distinct entities. The unifocal FMD type (with no predictable histological substrate) appears to be a precocious, severe and progressive form of FMD, whereas the multifocal type (mostly reflecting medial fibroplasia) presents as a relatively diffuse but milder arterial disease. Our data concerning extra-renal FMD should be considered with caution however, because until recently, we did not systematically investigate cervical arteries in patients with renal artery FMD.

Strengths and weaknesses of the study

Our study is based on a large number of carefully selected and well-characterized patients with FMD. It relies on contemporary, easily available imaging tests, CTA and MRA. We performed multiple comparisons so some of the p values of <0.05 may have been due to chance alone. However, most differences were highly significant ($p < 0.001$) and can therefore be regarded with confidence. Our study is retrospective and exposed to referral biases. The retrospective design entails limitations, including missing data, especially for extra-renal vascular imaging. Consequently, robust conclusions cannot be drawn about the prevalence of concomitant FMD lesions on other vascular beds. Recent data show that the prevalence of cervical arteries lesions

in patients with FMD has been underestimated [2] and this is probably also the case in this series. Indeed, only hypertensive patients are referred to our center, leaving out those who present with signs or symptoms suggesting cervical artery FMD but who do not have high blood pressure. By contrast, the computerized and structured data recording for clinical care resulted in there being very few missing data for other variables. All our patients had renal artery FMD and most were referred on the basis of resistant hypertension or hypertension diagnosed at a young age. This may explain why the median age at referral for the present series was lower than those for series that included patients with cervical artery FMD [28]. Finally, CTA and MRA allow FMD to be diagnosed reliably but not to quantify stenosis grade. Therefore, we did not attempt to relate blood pressure levels or renal asymmetry to the severity of renal artery stenosis. Studying such relationships requires either well-standardized renal artery duplex Doppler studies or invasive angiographies with intravascular ultrasound investigations or transtenotic pressure gradient determination.

Perspectives

An essential step towards collaborative studies on rare diseases is to establish a consensus for definition and classification. Our results indicate that minimally invasive angiography reliably distinguishes two types of FMD. Collecting prospective data from a large number of patients with FMD in international databases should help elucidate the pathophysiology of FMD and confirm whether the natural history correlates with the angiographic phenotype.

Conclusion

Our analysis suggests that a binary angiographic classification into unifocal and multifocal types of FMD is clinically relevant. Unifocal and multifocal types of FMD have differing non-angiographic phenotypes. Unlike histological classifications that can only be applied to

operated patients, the angiographic classification may be used for all FMD patients. It should facilitate future pathophysiological, epidemiological, clinical, and genetic studies.

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Disclosures

None.

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Figure legends

Figure 1

Images of renal artery fibromuscular dysplasia lesions.

Multislice computed tomography angiographies (A, C, E) and digital substracted angiographies (B, D, F) of renal arteries with unifocal (A, B) and multifocal (C, D, E, F) FMD lesions. On panel (E), irregularities (arrow) of the arterial wall suggested multifocal FMD that was confirmed by selective angiography (F) clearly showing at least three diaphragms (heads of arrow). FMD, fibromuscular dysplasia.

Figure 2

Flow chart showing the selection of patients with fibromuscular dysplasia.

*Takayasu arteritis, 8; Alagille syndrome, 4; renal artery spasm related to pheochromocytoma, 3; pseudo-xanthoma elasticum, 2; Ehlers-Danlos syndrome, 2; Williams syndrome, 1.

FMD, fibromuscular dysplasia; CTA, computed tomography angiography; MRA, magnetic resonance angiography.

Figure 3

Age distribution at diagnosis of renal artery fibromuscular dysplasia.

Table 1. Pathologic classifications of renal artery fibromuscular dysplasia and corresponding angiographic appearance

	No. of patients	Classification	Frequency, %	Angiographic appearance
McCormack [6]	67	Intimal fibroplasia, 14	21	Focal
1966		Medial fibroplasia, 15	22	String of beads
		Fibromuscular hyperplasia, 7	10	Focal
		Subadventitial fibroplasia, 31	46	Focal or beaded
Harrison [4]	60, excluding patients	Medial thickening, 44	73	Multifocal beaded pattern, 31/44
1967	with aneurysms only	Perimural, 16	27	Focal, tubular or multifocal
Kincaid [5]	60 with pathologic	Intimal, 5	8	Focal or tubular, 5/5
1968	examination	Medial, 53	88	Multifocal, 38/53
		Periarterial, 2	3	Tubular, 2/2
Harrison &	NR (consensus	Intimal fibroplasia	1-2	NR
McCormack [7]	document)	Secondary intimal fibroplasia	NR	NR
1971		Medial fibroplasia with mural aneurysm	60-70	String of beads
		Medial hyperplasia	5-15	NR

		Perimedial fibroplasia	15-25	May be beaded
		Periarterial fibroplasia	<1	NR
Stanley [8]	177 (25 children), 86	Intimal fibroplasia	~5	Focal or tubular
1975	specimens suitable for	Medial hyperplasia	~1	Focal
	classification	Medial fibroplasia	~85	A continuum of disease angiographically
		Perimedial dysplasia	~10	Focal, occasionally multiple constrictions

NR, not reported

Table 2. Past history and characteristics at diagnosis of fibromuscular dysplasia in patients with unifocal or multifocal renal artery lesions

	Unifocal FMD (n = 61)		Multifocal FMD (n = 276)		
	No.*	Values	No.*	Values	*p*
Male sex	61	19 (31)	276	47 (17)	0.02
Personal history of hypertension	61	60 (98)	276	258 (93)	0.22
Age at diagnosis of hypertension, years	60	26 [21, 36]	256	40 [32, 49]	<0.001
Age at diagnosis of FMD, years	61	30 [25, 39]	276	49 [42, 58]	<0.001
History of diabetes	59	1 (2)	269	12 (4)	0.48
History of hypercholesterolemia	59	10 (17)	270	78 (29)	0.07
Current smoker	58	29 (50)	268	69 (26)	<0.001
Systolic blood pressure, mmHg	55	157 [137, 174]	234	146 [128, 162]	0.006
Diastolic blood pressure, mmHg	55	97 [87, 110]	234	88 [76, 100]	<0.001
No. of antihypertensive agents	55	1 [1, 2]	234	2 [1, 3]	0.74
Body mass index, kg/m²	54	22 [20, 24]	232	23 [21, 27]	<0.001
Estimated creatinine clearance,† ml/min/1.73m^2	49	91 [83, 109]	218	86 [73, 100]	0.07

Renal asymmetry >20 mm	48	16 (33)	195	19 (10)	<0.001
FMD site: right, unilateral	61	29 (48)	276	85 (31)	
left, unilateral	61	19 (31)	276	20 (7)	<0.001
bilateral	61	13 (21)	276	171 (62)	
Median renal artery score	61	1 [1, 2]	276	3 [1, 3]	<0.001
Presence of renal artery aneurysms	61	7 (11)	276	31 (11)	1
Presence of renal artery dissections	61	4 (7)	276	12 (4)	0.50
Presence of cervical arteries FMD	24	6 (25)	127	65 (51)	0.03
Presence of ilio-femoral arteries FMD	22	2 (9)	123	30 (24)	0.16
Presence of digestive arteries FMD	16	5 (31)	97	50 (52)	0.18

The number of patients available for analysis is shown for each variable. Values are numbers of patients (percentage) for binary variables and median [25th centile, 75th centile] for quantitative variables. FMD, fibromuscular dysplasia. * Missing data mostly concern patients referred more than one year after the diagnosis of FMD; †using the Cockcroft-Gault formula

Table 3. Characteristics at follow-up over 365 days for patients with unifocal or multifocal renal artery FMD with first visit before October 1st 2010

	Unifocal (n = 52)		Multifocal (n = 213)		
	No.	Values	No.	Values	*p*
Patients with clinical follow-up >365 days	52	31 (60)	213	141 (66)	0.42
Follow-up duration, years	31	4 [2, 8]	141	4 [3, 9]	0.39
Renal artery intervention during follow-up	31	28 (90)	141	50 (35)	<0.001
Current smoker, at last follow-up	31	9 (29)	139	24 (17)	0.14
Body mass index at last follow up, kg/m²	30	23 [22, 26]	130	25 [22, 28]	0.25
Systolic blood pressure at last follow-up, mmHg	31	123 [114, 130]	139	124 [114, 135]	0.54
Change in systolic blood pressure, mmHg	31	-30 [-53, -14]	138	-20 [-37, -5]	0.03
Diastolic blood pressure at last follow-up, mmHg	31	77 [74, 85]	139	74 [67, 82]	0.06
Change in diastolic blood pressure, mmHg	31	-19 [-35, -3]	138	-14 [-27, -2]	0.14
Number of antihypertensive agents at last follow-up	31	0 [0, 1]	140	2 [1, 3]	<0.001
Change in number of antihypertensive agents	31	-1 [-1, 0]	139	0 [-1, 1]	0.006
Estimated creatinine clearance at last follow-up,*	25	130 [109, 153]	106	124 [108, 146]	0.45

m/min/1.73m²						
Change in estimated creatinine clearance,* ml/min/1.73m²	25	42 [24, 53]	98	41 [27, 56]	0.96	

The number of patients available for analysis (No.) is shown for each variable. Values are numbers of patients (percentage) for binary variables and median [25th centile, 75th centile] for quantitative variables. FMD, fibromuscular dysplasia. *Using the Cockcroft-Gault formula