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Magnetic resonance imaging of the kidney in Type 1 (insulin-dependent) diabetes mellitus

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Summary. Reductions in the physiological cortical to medullary signal intensity ratio are found in magnetic resonance scans of the kidney in non-diabetic glomerular disease. Whether this abnormality can also characterise patients with Type 1 (insulin-dependent) diabetes mellitus and nephropathy is not known. We measured the cortical to medullary signal intensity ratio in magnetic resonance images of the kidney in 34 patients with Type 1 diabetes (ten with either clinical proteinuria or raised serum creatinine or both, nine with microalbuminuria, seven with normal urinary albumin excretion and long duration of diabetes and eight with Type 1 diabetes of short duration). The cortical to medullary signal intensity ratio showed a trend to cluster at lower values in the normoalbuminuric patients with normal serum creatinine rather than in the nine healthy individuals, independent of Type 1 diabetes duration (1.47 ± 0.06 and 1.41 ± 0.13 vs 1.63 ± 0.16; five groups Scheffé F-test $p = 0.05$–0.1). Among the Type 1 diabetic patients, significant reductions in the cortical to medullary signal intensity ratio characterised overt nephropathy (1.19 ± 0.15, $p < 0.05$ vs all groups), but not microalbuminuria (1.47 ± 0.13, p = NS), concomitantly with low glomerular filtration rate and elevated fractional excretion of uric acid, but independent of glycaemic control. The determinants of the renal cortical to medullary signal intensity ratio in Type 1 diabetes are uncertain. Reductions in the cortical to medullary signal intensity ratio may be a late finding in diabetic nephropathy, and parallel the accompanying impairment in kidney haemodynamics. Magnetic resonance imaging of the kidney may not offer clues in the early diagnosis of diabetic nephropathy.

Key words: Type 1 (insulin-dependent) diabetes mellitus, diabetic nephropathy, microalbuminuria, magnetic resonance, chronic renal failure.

The development of magnetic resonance tomography has represented a major advance in the techniques of biological imaging. Scans of any organ can be acquired in any desired plane without the hazards of X-ray exposure, and computerised signal processing allows high-definition images to be obtained, where signal intensity can be easily measured. Magnetic resonance scans of the healthy kidney are characterised by a difference in signal intensity in the cortex compared with the medullary area [1], which can be quantified by calculating the cortical to medullary signal intensity ratio (CMR).

After the initial anecdotical reports [1], a number of studies consistently found that CMR may be reduced in chronic renal failure [2–6]. CMR was then found to be inversely related to serum creatinine, which suggested that reductions in CMR may be a sensitive, although aetiologically non-specific, sign of renal disease [5, 6]. However, most of this evidence relied upon observations in patients with clinically manifest, non-diabetic renal disease compared with healthy individuals [1, 3–6] and CMR was not always found to correlate with serum creatinine [7].

Diabetic nephropathy may represent a useful model with which to extend these observations. Clinically overt nephropathy eventually develops in 30–40% of patients with Type 1 (insulin-dependent) diabetes mellitus [8]. This long-term complication of diabetes is classically heralded by clinical proteinuria, rising blood pressure and falling glomerular filtration rate (GFR), slowly progressing to end-stage renal failure [9]. Elevated urinary albumin excretion in the range of microalbuminuria predicts clinical proteinuria [10–13], thereby identifying patients at a subclinical stage of diabetic kidney disease, when GFR is still normal or elevated [14, 15]. Thus, we explored CMR in Type 1 diabetes, and investigated whether reductions in CMR may be an early finding in diabetic kidney disease and characterise patients with microalbuminuria.

Table 1. General clinical features of healthy individuals and Type 1 (insulin-dependent) diabetic patients

	Healthy individuals	Type 1 diabetic patients				*p*
		Short DD	NA	μA	DN	
Group	1	2	3	4	5	
Age (years)	31.9 ± 7.07	25.9 ± 3.2	36.0 ± 10.6	31.7 ± 9.6	29.8 ± 3.5	NS
Gender (male/female)	5/4	4/4	1/6	5/4	2/8	NS
Duration of diabetes (years)	–	3.2 ± 2.0[a]	16.9 ± 6.6	20.5 ± 6.7	19.2 ± 4.3	0.0001
Retinopathy (A/B/P)	–	8/0/0[a]	2/1/2	1/4/4	1/2/7	0.0013
median AER (range), μg/min	3.8 (1.0–7.2)	4.8 (2.9–6.9)	8.5 (5.7–17.0)	42 (35–159)	1,447 (6.8–3,627)	0.0001
HbA_{1c} (%)	–	6.7 ± 2.3[b]	8.1 ± 0.57	9.7 ± 1.3	10.1 ± 3.5	0.020
Daily insulin dose (IU/kg)	–	0.48 ± 0.18	0.68 ± 0.12	0.69 ± 0.23	0.65 ± 0.15	NS
Body mass index (kg/m^2)	24.0 ± 3.0	21.9 ± 2.8	22.1 ± 2.0	24.1 ± 2.2	22.7 ± 2.3	NS
Mean blood pressure (mm Hg)	91.3 ± 4.2	83.7 ± 8.1	88.8 ± 8.6	97.6 ± 8.3[c]	104.3 ± 11.2[d]	0.0001

All values are mean ± SD except where indicated.
p overall significance by one-way ANOVA or by contingency table analysis.
DD, Duration of diabetes; NA, normoalbuminuria; μA, microalbuminuria; DN, (clinically overt) diabetic nephropathy.
A/B/P, absent/background/proliferative.

Scheffé F-test:
[a] $p < 0.05$ vs Groups 3, 4 and 5
[b] $p < 0.05$ vs Group 5 and $0.05 < p < 0.1$ vs Group 3
[c] $0.05 < p < 0.1$ vs Groups 2 and 3
[d] $p < 0.05$ vs Groups 1, 2, 3 and 4

Patients and methods

All Type 1 diabetic patients were selected at the Diabetes Outpatient Clinic of our Institute. The diagnosis of Type 1 diabetes relied only upon clinical criteria. Age at diagnosis was always less than 35 years, requirement of exogenous insulin was continuous since diagnosis, and all patients had a history of ketonuria associated with episodes of poor glycaemic control. A total of five diagnostic categories were considered for this pilot study. One group of patients was selected for the presence of overt diabetic nephropathy, which was considered when urinary albumin excretion rate (AER) persistently exceeded 200 μg/min in at least two out of three timed overnight urine samples collected over the preceding year, or when serum creatinine concentration was greater than 133 μmol/l or both, independent of AER. Patients with microalbuminuria formed a second group. The diagnosis of microalbuminuria was in agreement with the international consensus [16], with AER persistently in the range of 20–200 μg/min in at least two of three sterile (nitrite dipstick negative), timed overnight urine collections over at least 2–6 months prior to the study. Normoalbuminuria was thus considered with a finding of AER less than 20 μg/min, and patients with normal AER and duration of diabetes in a range comparable to that of patients with micro- and macroalbuminuria formed a third group. The fourth group included patients with Type 1 diabetes of short duration (1–6 years). Finally, nine healthy members of Hospital Staff with no history of renal disease volunteered for control purposes.

Seven out of 10 patients with overt renal disease were receiving anti-hypertensive medication, which was not discontinued for the study. The morning dose was, however, postponed until after the measurement of CMR on the day of the investigation. Treatment included angiotensin converting enzyme (ACE) inhibitors, calcium channel blockers and, in two cases, furosemide. All of the remaining patients were only receiving insulin.

The study protocol complied with the Helsinki declaration. All participating individuals verbally gave their informed consent, and attended a special visit, which included physical examination and magnetic resonance of the kidney. Body weight was taken in light indoor clothing, and height was measured with no shoes. Retinal detail was qualitatively evaluated by ophthalmoscopic examination through dilated pupils. Blood pressure was measured with a standard mercury sphygmomanometer on the right arm, after 5-min rest in the sitting position; systolic and diastolic recordings (Korotkoff phases I/V) were taken at the nearest 5 mm Hg. The prescribed daily insulin requirement was recorded. Patients were then asked to submit a single timed overnight urine collection within one month of the first visit, in order to check AER and measure urinary creatinine and uric acid; on that occasion a fasting blood sample for routine clinical chemistry was taken, and ^{51}Cr-EDTA GFR was measured.

Magnetic resonance imaging and CMR calculation

Magnetic resonance imaging was performed with a 0.5-T superconducting magnet (MRT 50-A; Toshiba System, Tokyo, Japan). Data were obtained by the use of a 256 × 256 matrix and were displayed in a 512 × 512 matrix. The thickness of each section was 7.5 mm with an intersection gap of 1 mm. The spin-Echo technique was used with a relaxation time of 500 ms and an echo time of 20 ms (T1-weighed images). At least four images were taken both in sagittal and paracoronal planes in all patients. Signal intensity (SI) was measured without knowledge of the renal diagnosis, in two independent sections of the right and left kidney, which were chosen as those with the largest kidney surface among the four images obtained per organ. Ten regions of interest, each of 4 mm^2, were considered in the cortex and 10 in the medullary area of each section. Mean cortical SI (cSI) and medullary SI (mSI) were then independently calculated in both kidneys of every patient and were finally used to calculate CMR by two independent equations:

- $CMR_{(I)} = cSI/mSI$ (I)
- $CMR_{(II)} = (cSI - mSI)\,(cSI + mSI)$ (II)

The identity of measurements in the left and in the right kidney was then tested in order to justify the eventual use of the arithmetic mean of CMR in the left and the right kidney as the outcome biological variable.

Other measurements

Urinary albumin concentration was measured with a commercially available radioimmunoassay (Pharmacia, Uppsala, Sweden) [17].

Serum and urinary creatinine were measured by autoanalyser (COBAS FARA II; Roche, Basel, Switzerland) using a suitably modified Jaffé reaction [18]. Serum and urinary uric acid were measured with an enzymatic-colorimetric technique on the same autoanalyser [19]. Glycosylated haemoglobin was measured by HPLC (Diamat; Bio-Rad, Richmond, Va., USA; normal range: 4.0–6.0%) [20]. GFR was measured by the ^{51}Cr-EDTA technique (single bolus injection) according to a previously published method [21]. Results were normalised by correcting for body surface area, and expressed in ml per min.

Table 2. Renal function measurements in healthy individuals and Type 1 (insulin-dependent) diabetic patients

	Healthy individuals	Type 1 diabetic patients				p
		Short DD	NA	μA	DN	
Group	1	2	3	4	5	
^{51}Cr-EDTA GFR, ml/min *(n)*	ND	131 ± 14 (4)	84 ± 29 (3)[a]	104 ± 31 (8)	36 ± 23 (6)[b]	0.0002
Serum creatinine (μmol/l)	65 ± 13	59 ± 7	79 ± 24	79 ± 13	217 ± 164[c]	0.001
Creatinine clearance (ml/min)	140 ± 55	155 ± 40	120 ± 58	130 ± 64	53 ± 34[c]	0.0012
Serum uric acid (mmol/l)	0.252 ± 0.090	0.216 ± 0.060	0.264 ± 0.084	0.216 ± 0.072	0.312 ± 0.060[d]	0.05
Uric acid clearance (ml/min)	7.4 ± 6.8	9.1 ± 6.2	7.9 ± 3.9	9.8 ± 5.7	6.7 ± 4.98	NS
FE uric acid (%)	5.0 ± 2.8	5.8 ± 3.6	7.4 ± 5.4	8.6 ± 4.3	15.7 ± 10.4[e]	0.009

All values are mean ± SD.
p overall significance by one-way ANOVA.
DD, Duration of diabetes; NA, normoalbuminuria; μA, microalbuminuria; DN, (clinically overt) diabetic nephropathy.
FE, fractional excretion; ND, not done

Scheffé F-test:
[a] $0.05 < p < 0.1$ vs Groups 2 and 5
[b] $p < 0.05$ vs Groups 2, 3 and 4
[c] $p < 0.05$ vs Groups 1, 2, 3 and 4
[d] $p < 0.05$ vs Groups 2 and 4
[e] $p < 0.05$ vs Group 1 and $0.05 < p < 0.1$ vs Groups 2 and 3

Calculated variables

Body mass index was calculated from weight and height, and expressed in kg/m^2. Daily insulin dose was corrected for body weight and expressed as IU/kg. Mean blood pressure was calculated as diastolic blood pressure plus one third pulse pressure. Diuresis was calculated and expressed in ml/min from the volume and duration of each urine collection. Creatinine and uric acid clearances were calculated as usual from their urinary excretion rate and serum concentration; results were expressed in ml/min after normalisation to 1.73 m^2 of body surface area. The fractional excretion of uric acid was calculated by dividing each value by the corresponding GFR as measured with creatinine clearance, and was expressed in percent values.

Statistical analysis

Results are expressed as arithmetic mean with standard deviation or as median with range. Student's t-test was considered for paired observations. Correlation between variables was evaluated by Spearman's or Pearson's test as appropriate. Comparisons in categorical variables were tested by contingency table analysis. Comparisons in continuously distributed variables were made by one-way analysis of variance. The null hypothesis was rejected as usual for p values lower than 5%. The level of significance was appropriately set in context with multiple comparisons by the Scheffé F-test.

Results

Clinical features of patients

The general clinical features of patients are shown in Table 1. AER was found to be normal in all patients with Type 1 diabetes of short duration, and was in the non-proteinuric range (6.8 and 87 μg/min) in two patients with raised serum creatinine (160 and 240 μmol/l), who were receiving anti-hypertensive medication. Mean age was slightly, but not significantly, younger in patients with Type 1 diabetes of short duration than in the other groups. Gender was well matched in patients with microalbuminuria and in those with short-term Type 1 diabetes comparable with healthy individuals, but a relevant though non-significant female gender predominance was present both in normoalbuminuric patients with long-term Type 1 diabetes and patients with overt nephropathy. Duration of diabetes was comparable in both groups of patients with elevated AER and patients with normal AER but long duration of diabetes. Mean blood pressure and glycosylated haemoglobin values were higher in both groups with renal disease compared with normoalbuminuric patients, though statistical significance was reached only in patients with overt nephropathy. No differences in daily insulin dose and body mass index were found among Type 1 diabetic patients. Serum creatinine was also elevated only in patients with overt nephropathy, and parallel differences were found in serum uric acid. Consistently, creatinine clearance was only reduced in patients with clinical nephropathy (Table 2). ^{51}Cr-EDTA GFR was only measured in a subset of Type 1 diabetic patients, as women of childbearing potential were not considered for this test when urinary albumin was known to be normal, and a few patients did not comply (Table 2). GFR ranged through values corresponding to advanced renal disease in patients with nephropathy. Though ^{51}Cr-EDTA GFR largely predicted creatinine clearance ($n = 21$; $y = 1.017x + 11.906$, $r = 0.721$, $p = 0.0002$), the latter was almost significantly associated with a 15% mean GFR overestimation in pooled observations (100.4 ± 61.1 vs 87.0 ± 43.3 ml·min^{-1}·1.73 m$^{2\,-1}$, $p = 0.16$). Mean uric acid clearance was comparable in all groups. The fractional excretion of uric acid was elevated only in patients with clinical nephropathy (Table 2).

Renal imaging and validation of SI and CMR measurements

No macroscopic structural abnormalities of the kidneys could be detected in any patient by magnetic resonance scans. Figure 1 shows two typical images obtained in Type 1 diabetic patients. The demarcation between cortical and medullary area could be seen in all but one patient with extremely low GFR.

Individual, within-kidney coefficients of variation in signal intensity ranged between 11% and 17% in the cortex and between 10% and 15% in the medullary area. Validation analyses showed that cSI and mSI were very

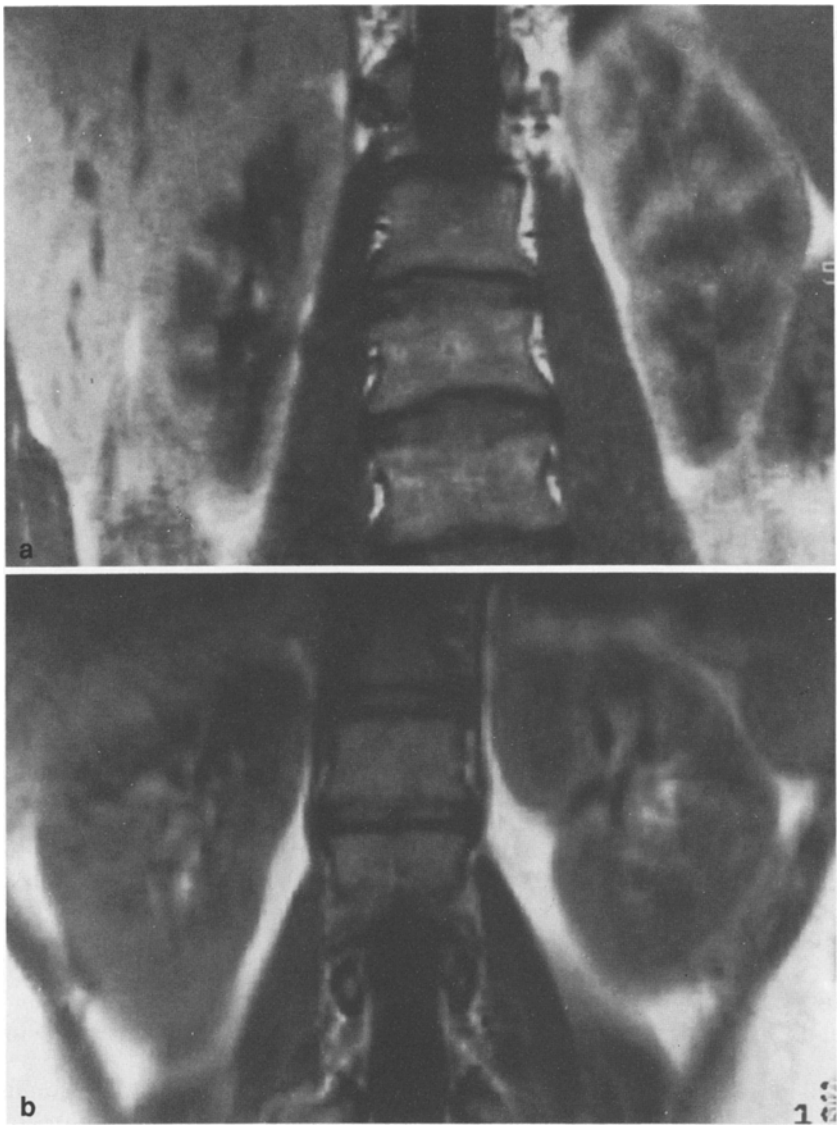

Fig. 1a, b. Magnetic resonance images of the kidney in Type 1 (insulin-dependent) diabetes mellitus. **a** Patient with normal urinary albumin excretion and serum creatinine; the visual contrast between the cortical and the medullary (darker) area can be readily identified. **b** Patient with overt nephropathy. The visual contrast between the cortical and the medullary area is not easily recognised

similar in the right and in the left kidney ($n = 43$; cSI: 499 ± 179 vs 506 ± 180 signal intensity units, $p = 0.5$; mSI: 355 ± 129 vs 358 ± 129, $p = 0.5$), consistent with the presence of significant correlations between the values obtained in the left kidney and those of the right kidney, with regression lines approaching the identity line (cSI: *r:* 0.92, $p < 0.0001$, 95% confidence limits of slope = 0.80–1.05; mSI: $r = 0.90$, $p < 0.0001$, 95% confidence limits of slope = 0.76–1.04). Similar findings characterised calculated CMR, in that no differences in $CMR_{(I)}$ were found between the left and the right kidney ($n = 43$; 1.433 ± 0.196 vs 1.425 ± 0.212, $p = 0.6$), and the regression line also approached the identity line ($CMR_{(I)r} = 0.954\ CMR_{(I)l} + 0.057$, $r = 0.882$, $p < 0.0001$; 95% confidence limits of slope: 0.79–1.11).

A strong linear correlation between CMR values as independently calculated by equations (I) and (II) was found ($r = 0.987$); the finding of a similarly strong rank correlation (Spearman's rho = 0.993) suggested that the visual contrast was identically scored by the values obtained with either equation, albeit expressed by arithmetically different scales. Taken together, these observations justified considering the arithmetic means of left and right $CMR_{(I)}$ values as the outcome biological variable for the further analysis of results. $CMR_{(I)}$ is heretofore simply referred to as CMR.

Concomitants of CMR

The distribution of CMR in each group of patients is shown in Figure 2. CMR clustered around lower mean values in both groups of patients with normoalbuminuria rather than in healthy individuals, but statistical significance was missed when accounting for multiple comparisons (Scheffé F-test $p = 0.05$–0.1). CMR was similarly distributed in Type 1 diabetic patients with microalbuminuria and in normoalbuminuric patients. Patients with overt nephropathy were characterised by a larger reduction in CMR, which remained strongly significant when the comparison was restricted to Type 1 diabetic patients (analysis of variance $p < 0.0001$).

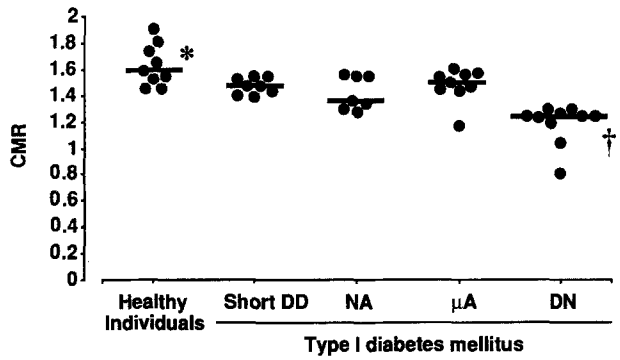

Fig. 2. Distribution of the cortical to medullary signal intensity ratio (CMR) in healthy individuals and in patients with Type 1 (insulin-dependent) diabetes mellitus of short duration (short DD), long-term diabetic patients with normal AER (NA), patients with microalbuminuria (μA) and patients with overt diabetic nephropathy (DN). One-way ANOVA $p < 0.0001$. Scheffé F-test: ✶ $0.05 < p < 0.1$ vs short DD, NA and μA; and † $p < 0.05$ vs all groups

CMR was positively associated with creatinine clearance among patients with nephropathy (rho = 0.707, $p = 0.033$), but not in any other group. Consistently, a similar relationship was found with the reciprocal of serum creatinine ($n = 10$; Spearman's rho = 0.776; $p = 0.020$) and with ^{51}Cr-EDTA GFR ($n = 6$; rho = 0.929; $p = 0.038$).

CMR was not related either with AER (rho = 0.367; $p = 0.3$) or with ^{51}Cr-EDTA GFR ($n = 8$; rho = 0.595; $p = 0.12$) among patients with microalbuminuria.

The fractional excretion of uric acid appeared to be negatively related with CMR only among patients with overt nephropathy, though statistical significance was just missed (rho = −0.585, $p = 0.07$), and a parallel negative correlation with creatinine clearance was found in the same group of patients (rho = −0.624; $p = 0.061$).

CMR did not appear to be significantly correlated with any other variable among those considered here, namely age, gender and duration of diabetes, HbA_{Ic}, daily insulin dose, body mass index and arterial blood pressure in any group of patients.

Discussion

This study describes kidney imaging in Type 1 diabetes by magnetic resonance for the first time. The finding that CMR is reduced in the kidneys of Type 1 diabetic patients with clinically overt nephropathy extends similar observations in other chronic renal parenchymal diseases [3–6], further supporting the view that this sign may non-specifically occur in concomitance with chronic renal failure, and may be partly independent of the primary nature of kidney disease. Furthermore, CMR was, by and large, similar among patients without overt nephropathy, independent of urinary albumin excretion in the range of microalbuminuria. Thus, reductions in CMR may only characterise diabetic nephropathy at a late stage, suggesting either that CMR is relatively insensitive at detecting kidney disease or that the determinants of this phenomenon may rather parallel those of clinically reduced GFR and chronic renal failure. Indeed, the presence of a positive relationship between CMR and GFR among patients with overt diabetic kidney disease supports the hypothesis that impaired kidney haemodynamics and/or their determinants or concomitants may be involved in producing this visual abnormality [5, 6]. Though the pathophysiology of this phenomenon remains poorly understood, the physical basis of magnetic resonance may be consistent with this view.

Magnetic resonance imaging represents the composite effect of the alignment of odd atoms conveniently stimulated by a sufficiently strong magnetic field, largely represented by hydrogen atoms in the human body [22]. Thus, changes in the biodistribution of hydrogen atoms, which are predominantly although not totally relevant to water molecules, result in changes in SI. Studies in the rat, where the percentage of tissue water could be directly measured, showed an inverse relationship between SI, as measured in T1-weighed images, and percent water in a number of normal and pathologic tissues [23]. Thus, the almost invariable normal finding of higher SI in the cortex of the kidney than in the medulla may only reflect a relatively larger water content in the latter. In line with these observations, changes in the intrarenal biodistribution of water and ions are known to induce changes in CMR. Ureteral ligation and chronic hydronephrosis disproportionately increase the percent of tissue water in the renal cortex of the obstructed kidney, producing a reduction in CMR in the dog [24]. Similar changes in CMR have been acutely reproduced in man by inducing water/furosemide diuresis, which may increase renal cortical water content and reduce cSI by increasing the delivery of urine to the distal convoluted tubule [1]. These observations suggest that reductions in CMR can be interpreted as relative increases in the cortical to medullary water content in diabetes and chronic renal failure.

Enhanced handling of water and sodium may occur at cortical nephron structures both in diabetes and in chronic renal failure, thus representing one possible mechanism of reduced CMR in patients with clinically overt diabetic nephropathy. Elevated single-nephron glomerular filtration rate and proximal tubular sodium and water reabsorption are common compensatory changes in healthy nephrons surviving primary renal injury in the rat [25]. Excess proximal reabsorption, associated with reduced natriuresis and an expanded sodium pool are widely recognised features of Type 1 diabetic patients [26–28], seem more prominent in patients with overt kidney disease [29], and are likely to induce some degree of interstitial oedema which may play a functional role in the reduction of CMR. These hypotheses are theoretically consistent with the distribution pattern of CMR in our groups of patients, but remain largely speculative and await direct and more extensive investigation with relevant techniques, such as simultaneous inulin and lithium clearance [30], or indirect quantitation of kidney tissue water by the use of alternative magnetic resonance equipment allowing the measurement of relaxation time by quenching technique.

Another factor of possible relevance to functional changes in CMR could be represented by anti-hypertensive treatment. Our study does not allow the singling out

of a possible independent effect of treatment for hypertension upon CMR in patients with overt nephropathy. The effect of ACE-inhibitors and calcium channel blockers upon CMR is not known, but two of our patients with nephropathy were receiving daily doses of furosemide, which is known to affect CMR as previously discussed [1]. However, after both cases were excluded from analysis, CMR remained significantly low in patients with overt nephropathy. Though disturbed kidney haemodynamics are the most widely accepted explanation for reduced CMR in renal disease, this abnormality may not be entirely functional in origin. For example, CMR seems unrelated with serum creatinine in sickle-cell nephropathy, and excess renal iron deposition has been suggested as a possible factor confounding reductions in cortico-medullary contrast in these patients [7]. Furthermore, renal histological changes *per se* have been suggested as being associated with low CMR, and apparently more strongly than GFR. This hypothesis has been pursued after finding a negative correlation of CMR with the degree of interstitial fibrosis in the setting of kidney allografts [31], but no histologically controlled studies of CMR in native kidneys are currently available. Indeed, the quantitative inverse relation between glomerular sclerosis and kidney function late in the course of diabetic nephropathy [32] may render difficult the isolation of an independent contribution to CMR of progressing structural lesions vs functional compensatory changes in surviving nephron function. Glomerular sclerosis is quantitatively more represented in histological sections of the kidney from patients with overt nephropathy than in patients with normoalbuminuria but a similarly long duration of diabetes [33, 34]. Glomerular lesions are protean in microalbuminuria, and can barely be distinguished from those found in normoalbuminuric patients only when hypertension and/or reduced creatinine clearance are concomitant [35]. Thus, the degree of glomerular involvement of the kidney in diabetes may be consistent with the differences in CMR we observed among Type 1 diabetic patients, but only properly controlled studies may help to answer this question.

Taking together our results and previous observations, we would like to suggest that the measurement of CMR in the setting of conventionally diagnosed and prospectively followed diabetic nephropathy may questionably add little clinical information to the measurement of albuminuria and GFR. Though our hypotheses may apparently encourage further investigation of the functional and structural determinants of CMR in diabetes, failure to associate significant reductions in CMR with microalbuminuria also seems to restrict any pragmatic interest in the pathophysiology of this phenomenon to an academic speculation. Of course these comments are not relevant to magnetic resonance imaging of the kidney *per se,* nor to other perspective applications of this technique in the study of renal pathophysiology in Type 1 diabetes. For example, the availability of this non-invasive technique might find useful application in the measurement of kidney volume early in the course of Type 1 diabetes. Large kidneys more often seem to be associated with glomerular hyperfiltration [36], an intriguing abnormality controversially associated with the subsequent development of overt nephropathy [12, 37], and magnetic resonance imaging of the kidney may offer the possibility of integrated volume calculation after geometrically precise scans.

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