



Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx



Review

Increased renal resistive index in type 2 diabetes: Clinical relevance, mechanisms and future directions

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ARTICLE INFO

Article history:
Available online xxx

Keywords:

Albuminuria
Creatinine clearance
Microvascular
Macrovascular
Renal resistive index
Type 2 diabetes

ABSTRACT

Type 2 diabetes is a global health challenge. In type 2 diabetes both microvascular (nephropathy, retinopathy, neuropathy) and macrovascular complications arise. In kidney, renal pathological changes leading to diabetic nephropathy are mainly secondary to atherosclerosis of the intra and extra renal arteries together with microangiopathy of the glomerular capillaries, afferent arterioles and efferent arterioles. Renal resistive index (RRI) is defined as a ratio of the difference between maximum and minimum (end-diastolic) flow velocity to maximum flow velocity derived from the Doppler measurements of main renal and intrarenal (segmental/interlobar) arteries. Renal resistive index is tightly related to renal arteriosclerosis, and represents an integrated index of arterial compliance, pulsatility and downstream microvascular impedance. In meantime, growing suggest that RRI has also been closely related with atherosclerosis. Most studies performed in type 2 diabetes showed RRI is increased in type 2 diabetes. In this review, we summarize the data regarding RRI with regard to performed studies, pathogenesis and prognosis, especially focusing on type 2 diabetes (T2D). We also review the data regarding the development of metabolic syndrome (MetS) and RRI.

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1. Introduction

Diabetes mellitus (DM) affects the whole vascular system leading to both micro and macrovascular complications. In kidney, renal pathological changes leading to diabetic nephropathy (DN)

are mainly secondary to atherosclerosis of the intra and extra renal arteries together with microangiopathy of the glomerular capillaries, afferent arterioles and efferent arterioles. Diabetic nephropathy is a well-known microvascular complication of diabetes [1].

Classically, DN is first characterized by glomerular hyperfiltration, followed by microalbuminuria and then macroalbuminuria and lastly decreased glomerular filtration rate (GFR). However, recent evidence suggest that albuminuria does not always correlate with impairment of renal function and, in turn, renal failure is not associated with albuminuric nephropathy is

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<http://dx.doi.org/10.1016/j.dsx.2016.08.019>

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Table 1

Major studies examining renal resistive index in type 2 diabetes.

Study	N	Place of RRI measurement	Design	RRI and albuminuria	RRI, age, DM duration, glucose and HbA1c	RRI and creatinine clearance	Other findings
Ref [9]	37 type 1 and 61 type 2 DM patients	Arcuate, interlobar arteries	Cross-sectional	RRI >0.70 associated with higher proteinuria	RRI >0.70 associated with older age and longer DM duration –No specific mention regarding RRI, glucose and HbA1c	RRI negatively correlated with creatinine clearance	RRI significantly higher in clinically established diabetic nephropathy groups.
Ref [10]	34 type 2 DM patients, 50 controls	Arcuate, interlobar arteries	Cross-sectional	No relationship between RRI and albuminuria	RRI associated with age and DM duration –No specific mention regarding RRI, glucose and HbA1c	RRI negatively correlated with creatinine clearance	RRI was 0.56 ± 0.23 in controls, 0.61 ± 0.04 in type 2 DM patients with creatinine <1.4 mg/dl, and 0.79 ± 0.07 in type 2 DM patients with creatinine >1.4 mg/dl
Ref [11]	85 type 2 DM patients and 42 controls	Interlobar arteries	Cross-sectional	No relationship between RRI and microalbuminuria	RRI positively correlated with age No relationship between RRI and glucose & DM duration	No data regarding RRI and creatinine clearance	RRI significantly higher in type 2 DM patients RRI negatively correlated with renal volume No relationship between RRI and blood pressure
Ref [12]	112 type 2 DM patients, 37 controls	Interlobar arteries	Cross-sectional	Patients divided into four groups; group I, UAE < 20 mcg/min (N=42); group II, $20 \leq$ UAE < 200 mcg/min (N=28); group III, $UAE \geq$ 200 mcg/min (N=25); group IV, serum creatinine \geq 1.5 mg/dl (N=17). RRI and PI in groups II, III, and IV were significantly higher than those in the controls (P<0.001) RRI and PI were significantly higher in group IV than in groups I, II and III (P<0.0001)	RRI positively and independently associated with age and DM duration No association between RRI and glucose & HbA1c	RRI negatively and independently associated with creatinine clearance	RRI correlated with femoral and carotid intima-media thickness –No relationship between RRI and mean blood pressure
Ref [13]	36 type 2 DM patients, 10 controls	Interlobar arteries	Cross-sectional	No relationship between RRI and albumin/creatinine ratio	RRI correlated with age No relationship between RRI and glucose & HbA1c	RRI positively correlated with creatinine clearance	RRI significantly higher in DM patients than in controls (P<0.002) BMI correlated with RRI and mean blood pressure RRI independently associated with GFR
Ref [14]	61 type 2 DM patients	Interlobar arteries	Cross-sectional	No relationship between RRI and albuminuria	No specific mention regarding RRI, age, DM duration, glucose and HbA1c	RRI negatively correlated with GFR	
Ref [15]	48 type 2 diabetic-CKD patients, 48 nondiabetic-CKD patients, 29 controls	Interlobar arteries	Cross-sectional	No specific data	RRI correlated with age–No specific mention regarding RRI and glucose & HbA1c	RRI negatively correlated with creatinine clearance	RRI higher in CKD patients than in controls RRI higher in diabetic-CKD patients than in non-diabetic CKD patients RRI positively and independently correlated with DM and age, and negatively and independently with creatinine clearance
Ref [16]	155 type 2 DM patients	Interlobar artery	Cross-sectional	Patients divided into four groups; group I, UAE <30 mg/day (N=69); group 2, $30 \leq$ UAE < 300 mg/day (N=44), group 3, $UAE \geq$ 300 mg/day and serum creatinine <1.5 mg/dl (N=22); group 4 serum creatinine >1.5 mg/dl (N=20)	RRI positively correlated with age and DM duration No relationship between RRI and HbA1c–No specific mention regarding RRI and glucose	RRI negatively correlated with creatinine clearance	RRI significantly higher in group 4 than in groups 1, 2, and 3 RRI similar among groups 1, 2 and 3 RRI correlated positively with systolic and negatively with diastolic blood pressure
Ref [17]	325 type 2 DM patients	Interlobar arteries	Cross-sectional	No relationship between RRI and albuminuria	RRI independently and positively associated with age RRI positively correlated with DM duration No association between RRI and HbA1c–No specific mention regarding RRI and glucose	RRI independently and negatively correlated with GFR	RRI is positively and independently correlated with BMI, and negatively and independently with diastolic blood pressure

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