https://doi.org/10.48047/AFJBS.6.15.2024.9992-10002

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

DETERMINANTS OF RENAL RESISTIVE INDEX IN INDIVIDUALS WITH DIABETES MELLITUS

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Volume 6, Issue 15, Oct 2024

Received: 05 Sep 2024

Accepted: 20 Sep 2024

Published: 15 Oct 2024

doi: 10.48047/AFJBS.6.15.2024.9992-10002

ABSTRACT

Background and aim: This study examined factors associated with elevated renal resistive index in patients with type 2 diabetes. RRI, measured using Doppler ultrasound, indicates renal vascular resistance. Increased RRI has been observed in this patient population. Factors linked to higher RRI include older age, female gender, high blood pressure, elevated heart rate, increased body mass index, smoking, dyslipidemia, and certain medical conditions or medications. The aim of this research was to investigate these factors to enhance clinical management of patients with type 2 diabetes.

Methods and Material: This was a cross-sectional study conducted at Wahidin Sudirohusodo hospital in Makassar. It included adult patients with type 2 diabetes mellitus who underwent Doppler ultrasonography. An elevated renal resistive index was defined as a value greater than 0.70. The researchers analyzed the renal resistive index values in relation to factors such as age, diabetes duration, blood pressure, heart rate, body mass index, dyslipidemia, medical history, smoking, and concurrent medications. The data were analyzed using logistic regression and chi-square statistical tests.

Results: The study found that age, heart rate, dyslipidemia (odd ratio 10.2), and over 10 years of diabetes (odd ratio 8.9) were factors influencing the renal resistive index. Patients with high blood pressure, obesity, beta-blocker use, and heart failure had a higher proportion of elevated renal resistive index.

Conclusions: RRI in patients with diabetes mellitus is influencedby heart rate, age, duration of diabetes and dyslipidemia. Dyslipidemia has a 10.2-fold higher risk of increased RRI.

Keywords: Renal resistive index, Diabetes mellitus, renal ultrasonography, renal resistive index in diabetic patients, renal resistance

Introduction

The International Diabetes Federation projects the number of diabetes mellitus (DM) patients will further rise from 10.7 million in 2019 to 13.7 million by 2030. Patients with diabetes mellitus frequently develop severe acute and chronic complications due to arterial stiffening within capillary, afferent and efferent arterioles.[1]

The renal resistive index (RRI) reflecting the status of the renal microvasculature. RRI has been found to be elevated in patients with type 2 diabetes mellitus and atherosclerosis.[2] The normal range for RRI in adults is 0.47 to 0.70, with less than a 5-8% difference between the two kidneys.[3] Numerous studies have associated an RRI value of ≥ 0.75 with microvascular complications.[4]

Research has identified various mechanisms that lead to an elevated renal resistive index in patients with type 2 diabetes mellitus.[5] Hypertension can lead to kidney scarring, increased stiffness of small renal blood vessels, ultimately increasing renal resistance.[6] A longer history of diabetes and dyslipidemia are linked to the development of atherosclerosis.[7] Autoimmune conditions, pregnancy, elevated body mass index, and menopausal status contribute to the higher RRI values observed in women.[8,9,10] Medication such as beta-blocker, angiotensin II receptor blocker, angiotensin converting enzyme inhibitor, calcium channel blocker, diuretic,[11] and comorbidities condition such as coronary heart disease, heart failure, chronic obstructive pulmonary disease (COPD)[11,12] contribute to the higher RRI.

Material And Methods

This was an analytical cross-sectional study conducted at Wahidin Sudirohusodo Hospital, where doppler ultrasonography was used to measure the renal resistive index. The study participants were type 2 diabetes mellitus patients aged 18 and above. A RRI greater than 0.70 is considered elevated. The observed RRI values were analyzed based on factors that can influence them. Data analysis was performed using SPSS version 25, including descriptive statistics, chi-square test, and multivariate analysis using multiple logistic regression. Statistical test results were considered significant if the p value was <0.05.

Our protocols has been approved by Ethics Committee of Biomedical Research on Human, Faculty of Medicine, Universitas Hasanuddin, Makassar, South Sulawesi.

Result

The study determined that 45 participants exhibited an elevated renal resistive index, whereas 43 participants displayed normal renal resistive index values.

Table 1. Characteristics of the study population **(n:88)**

Variabel	cathegory	n	%	Min	Max	Mean	SD
Gender	Female	48	54,5				
	Male	40	45,5				
Age	<60 year	43	48,9	26	80	58,2	11,1
	>=60 year	45	51,1				
Body mass index	Obese	41	46,6	16,2	38,7	25,7	4,6
	Non Obese	47	53,4				
Smoking habit	Yes	14	15,9				
	No	74	84,1				
Duration of DM	<5 year	35	39,8				
	5-10 year	34	38,6				
	>10 year	19	21,6				
Dyslipidemia	Increase	26	86,7%				
	Normal	4	13,3%				
Heart Rate	Bradycardia	7	8,0	56	100	79,1	12,0
	Normal	81	92,0				
Hypertension	Yes	59	67,0				
	No	29	33,0				
RRI	Increase	45	51,1	0,56	0,92	0,71	0,08
	Normal	43	48,9				

n=number of samples; SD=standard deviation; DM=diabetes mellitus; min=minimal; max=maximal

The Impact of Age, Gender, Hypertension, Pulse, Body Mass Index, Dyslipidemia, Smoking habit, and Duration of Diabetes Mellitus on Renal Resistive Index

Table 2. The Impact of Age on Renal Resistive Index

Age cathegory			RRI cathegory		
			Increase	Normal	Total
	<60 years old	n	15	28	43
		%	34,9%	65,1%	100,0%
	>=60 years old	n	30	15	45
		%	66,7%	33,3%	100,0%
Total		n	45	43	88
		%	51,1%	48,9%	100,0%

Chi Square test (p=0.003)

Table 3. The Impact of Gender on RRI

Gender			RRI category		Total
			Increase	Normal	
	Woman	n	25	23	48
		%	52.1%	47.9%	100.0%
	Man	n	20	20	40
		%	50.0%	50.0%	100.0%
Total		n	45	43	88
		%	51.1%	48.9%	100.0%

Chi Square test (p=0.846)

Table 4. The Impact of Hypertension on RRI

Hypertension			RRI category		
			Increase	Normal	Total
	Yes	n	33	26	59
		%	55.9%	44.1%	100.0%
	No	n	12	17	29
		%	41.4%	58.6%	100.0%
Total		n	45	43	88
		%	51.1%	48.9%	100.0%

Chi Square test (p=0.199)

Table 5. The Impact of Pulse on RRI

Pulse			RRI category		Total
			Increase	Normal	
	Bradycardia		13	2	15
		%	86.7%	13.3%	100.0%
	Normal	n	32	41	73
		%	43.8%	56.2%	100.0%
Total		n	45	43	88
		%	51.1%	48.9%	100.0%

Chi Square test (p=0.003)

Table 6. The Impact of BMI on RRI

BMI category			RRI category		
			Increase	Normal	Total
	Obese	n	22	19	41
		%	53.7%	46.3%	100.0%
	Non Obese	n	23	24	47
		%	48.9%	51.1%	100.0%
Total		n	45	43	88
		%	51.1%	48.9%	100.0%

Chi Square test (p=0.658)

Tabel 7. The Impact of Dyslipidemia on Renal Resistive Index

Dyslipidemia			RRI Cathegory		Total
			Increase	Normal	
	Yes	n	26	4	30
		%	86,7%	13,3%	100,0%
	No	n	19	39	58
		%	32,8%	67,2%	100,0%
Total		n	45	43	88
		%	51,1%	48,9%	100,0%

Chi Square test (p=0,000)

Table 8. The The Impact of smoking on RRI

Smoke			RRI category		
			Increase	Normal	Total
	Yes	n	4	10	14
		%	28.6%	71.4%	100.0%
	No	n	41	33	74
		%	55.4%	44.6%	100.0%
Total		n	45	43	88
		%	51.1%	48.9%	100.0%

Chi Square test (p=0.065)

Table 9. The duration of diabetes mellitus affects the renal resistive index.

Duration of DM			RRI category		
			Increase	Normal	Total
	<5 years	n	7	28	35
		%	20.0%	80.0%	100.0%
	5-10 years	n	24	10	34
		%	70.6%	29.4%	100.0%
	>10 years	n	14	5	19
		%	73.7%	26.3%	100.0%
Total		n	45	43	88
		%	51.1%	48.9%	100.0%

Chi Square test (p=0.000)

Table 10 . The distribution of renal resistive index categories in relation to drug utilization among the patients.

Drug Utilization			RRI category	
			Increase	Normal
	Beta Blockers	n	9	3
		%	75.0%	25.0%
	CCB	n	23	19
		%	54.8%	45.2%
	ARB	n	6	7
		%	46.2%	53.8%
	ACEi	n	11	6
		%	64.7%	35.3%
	Diuretic	n	4	0
		%	100.0%	0.0%

Table 11. Distribution of Renal Resistive Index Categories Across Comorbidities in Patients with Diabetes Mellitus

Comorbidities		RRI category	
		Increase	Normal
Coronary heart disease	n	4	2
	%	66.7%	33.3%
Heart failure	n	5	3
	%	62.5%	37.5%
COPD	n	0	1
	%	0.0%	100.0%

Multivariate Analysis

Tabel 12. A Multivariate Analysis Investigating the Effects of Age, Dyslipidemia, and Duration of Diabetes Mellitus on the Renal Resistive Index

Variable	B	S.E.	Wald	p	OR	95% Lower	95% Upper
Age Cathegory	-0,506	0,594	0,727	0,394	0,6	0,19	1,93
Dyslipidemia	2,322	0,675	11,834	0,001	10,2	2,72	38,29
Duration of DM			11,582	0,003			
Duration of DM(1)	2,187	0,785	7,765	0,005	8,9	1,91	41,49
Duration of DM(2)	0,168	0,724	0,054	0,816	1,2	0,29	4,89

Discussion

Diabetes mellitus can lead to metabolic changes, such as the formation of advanced glycation end-products and increased aldose reductase activity, which cause interstitial fibrosis and elevated intrarenal resistance. Additionally, hemodynamic factors, including vasoconstrictors like angiotensin II, endothelin, and nitric oxide, contribute to the development and progression of microvascular complications.[13] Furthermore, increase in renal resistance due to factors such as pulse pressure and atherosclerosis may influence the renal resistive index.[8]

Several studies have described the influence of age on changes in the renal resistive index. [4,6] Consistent with these findings, our study found that the proportion of subjects with an increased RRI was significantly higher in those aged ≥60 years. The increase in RRI in older age is attributed to factors such as arteriosclerosis, which leads to elevated renal vascular resistance,

as well as focal interstitial fibrosis, glomerulosclerosis, and arteriolar sclerosis.[14] The duration of diabetes itself is associated with atherosclerosis.[7] Our research also showed a significant influence of the duration of diabetes on RRI, with the proportion of subjects with an increased RRI being highest among those with a diabetes duration exceeding 10 years.

While prior studies have reported that female gender may influence renal resistive index, our findings did not demonstrate a significant effect of gender on RRI. Furthermore, our study did not include participants with autoimmune conditions or pregnancy, and only a small number were postmenopausal, with 52% of the female subjects being obese. Importantly, we also did not observe a significant impact of body mass index on RRI.

Obesity can have direct and indirect impacts on the kidneys, including increased renal workload, inflammation, oxidative stress, and hormonal imbalances.[15, 16, 17] The study by Moriconi et al. incorporated the renal resistive index in the clinical risk assessment of obese patients, as it found a significant correlation between renal hemodynamic dynamics and microcirculatory abnormalities.[10] While we did not find a significant influence of BMI on RRI, the proportion of subjects with increased RRI was higher in the obese group.

Metabolic factors such as dyslipidemia have been associated with an increased risk of atherosclerosis, which can lead to elevated renal vascular resistance and the renal resistive index.[18] Our study found a significant influence of dyslipidemia on the renal resistive index.

Hemodynamic factors also play a role in the renal resistive index values. The study by Sveceny et al. on hypertensive patients over two years found an inverse relationship between the renal resistive index and the ratio of 24-hour diastolic to systolic blood pressure as well as changes in pulse pressure.[19] In contrast, our study did not find a significant influence of hypertension on RRI, although the proportion of subjects with increased RRI was higher in the hypertensive group compared to the non-hypertensive group. This may be related to the fact that the majority of hypertensive subjects in our study were under 60 years of age, did not have dyslipidemia, and were not bradycardic.

The study found a significant influence of heart rate on the renal resistive index, with the proportion of subjects with increased RRI being significantly higher in those with bradycardia compared to those with normal heart rate. According to the literature, the increase in RRI among subjects with bradycardia is attributed to prolonged diastole and reduced end-diastolic velocity.[20]

The study by Chen et al. demonstrated that patients with COPD exhibited a greater decline in renal functional reserve, which was associated with inflammation.[12] In our study, we did not find a significant influence of smoking on the renal resistive index. However, the proportion of subjects with increased RRI was lower among smokers compared to non-smokers. This finding may be influenced by the longer duration of diabetes mellitus in the non-smoking group, as well as the older age observed in this group.

Our study found that the proportion of subjects with increased renal resistive index was highest among those with comorbid heart failure. Prior studies have linked increased renal resistive index to impaired cardiac function, potentially due to the effects of reduced cardiac output and venous congestion on renal blood flow.[3]

Certain medications that affect the vasomotor properties of arterioles, such as nitroglycerin and captopril, have been reported to influence the renal resistive index.[20] Similarly, diuretics, beta-blockers[5,6,9] and calcium channel blockers[8] have been found to impact the renal resistive index as well. In our study, the proportion of subjects with an increased renal resistive index was highest among those using beta-blockers and lowest among those using angiotensin II receptor blockers.

The multivariate analysis revealed that dyslipidemia was the most significant factor influencing the renal resistive index. Subjects with dyslipidemia had a 10.2-fold greater risk of having an increased RRI. Subjects with DM duration exceeding 10 years had an 8.9-fold higher risk of having an increased RRI.

This study had several limitations. A prospective study would be required to evaluate interventions in high-risk subjects. Additionally, some subjects presented with multiple comorbidities and were taking multiple medications concurrently, which added complexity to the analysis.

Conclusion

The renal resistive index in patients with diabetes mellitus is influenced by factors such as heart rate, age, duration of diabetes, and dyslipidemia. Patients with dyslipidemia have a 10.2-fold higher risk of having an increased renal resistive index.

Acknowledgments:

This research was supported by the Department of Internal Medicine, Faculty of Medicine, Hasanuddin University, Makassar, South Celebes, Indonesia.

Funding:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics Committee Approval

This research was approved by the Ethics Committee for Biomedical Research on Humans, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia. Based on recommendation letter Number: 441/UN4.6.4.5.31/ PP36/ 2024, June 13rd, 2024, and duration of the study approval from June 13rd, 2024 to June 13rd, 2025, protocol number: UH24050373.

Conflict of Interest statement*:*

Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interests, patent/licensing arrangements, etc.) that might give rise to a conflict of interest concerning the submitted article

Author's Contributions:

WM (concept, design, resources, materials, data collection and processing, analysis and interpretation, literature search, manuscript writing). HK (concept, design, supervision, analysis and interpretation, literature search). MA (concept, design, supervision, analysis and interpretation, literature search). SB (concept, design, critical review). KH (concept, design, critical review). AF (concept, design, critical review). AS (Concept, Design, Analysis and Interpretation, Critical Review). All authors were involved in drafting the manuscript, revising it, and evaluating its content. They have all read and approved the manuscript, confirming the accuracy and integrity of the research details.

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