The relation between flow mediated dilatation of the Brachial artery and acute kidney injury in the patients admitted to the ICU

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Abstract: Back Ground: Assessment of functional vascular impairment is usually performed by using noninvasive vascular function tests. Impairment of vascular function is highly concomitant with the progress and maintenance of atherosclerotic conditions, ending with injury in the target organ. The introduction of ultrasounds as non-intensive technique for diagnosis of some disordered such as vascular diseases is important for measurement of conduit artery dilation consequent to post ischemic hyperemia, an arterial shear stress stimulus and assessment of temporary suprasystolic cuff inflation around the limbs. Ultrasounds (USs) is widely applicable in many scientific and medicinal fields due to its noninvasive nature and simplicity, therefore it is known as flow mediated dilation (FMD) approach. **Methods:** This was a case-control study. The study took place in intensive care unit (ICU) of the Faculty of medicine Cairo University. FMD of the brachial artery by B-mode SIEMENS ACUSON X300 ultrasonography was assessed. FMD was calculated with the formula: FMD = [(DF –Di)\ DI] x 100. **Results:** FMD of the brachial artery was significantly low (7.31% \pm 0.75%) in patients with AKI compared to (11.67 % \pm 1.26%) in control group which showed statistical significance (P<0.001). **Conclusion:** From this study, our present observations indicate that AKI is associated with endothelial dysfunction with significant lowering in the flow mediated dilatation of the Brachial artery case group.

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1. Introduction

Generally, the endothelium play an important role in vascular system such as, modifying the tone of blood vessels, keeping the vascular homeostasis, and structure, therefore it is known as an endocrine organ. The endothelial cells are responsible for synthesis of paracrine hormone e.g. nitric oxide (NO) (1), a potent vasodilator. which have influential antiatherogenic properties. (2).

The important role of NO liberated from endothelial cells is mainly for protection of vascular system such as, cell proliferation, platelet aggregation, to prevent migration and adhesion of leukocytes, expression of adhesion molecules, and encouraging smooth muscle cells relaxation. Differently, endothelial dysfunction are usually associated with several chronic diseases like hypertension, coronary artery disease, atherosclerosis, diabetes mellitus and peripheral artery disease, all these disordered are described by decreased bioavailability of NO.

Introduction of ultrasonography in many medicinal and scientific fields as a non-invasive vascular function method have been settled and implemented for evaluation of functional vascular impairment and for assessment of atherosclerosis severity. (3-5). Damage of vascular function, like dysfunction of endothelial cells and augmented arterial toughness, is related greatly to the advance and neglect of atherosclerotic situations, which will lead to injury in the target organ and cardiovascular disorders (6). In 1992, Celermajer and his collogues (7), commenced an ultrasonography (US) images involving temporary suprasystolic cuff inflation around the limbs and estimated the degree of arterial dilation on sequential to post ischemic hyperemia and an arterial shear stress trigger because of its simplicity, easy to use, noninvasive method and as prognostic research tools tat can be applied in many clinical and research purposes (8-14). Scientists and physicians nowadays are interested in applying broadly this non-invasive methods e.g. flow mediated dilation (FMD) in their practice. In chronic kidney disease patients, a compromised response in the physiologic vascular reactivity, indicating that endothelial dysfunction, was found using BAFMD (15).

Study design

This was a case-control study. The study carried out in the medical intensive care unit (ICU) of the Faculty of medicine Cairo University. Control normal cases which participating in this study was engaged from the resident community, stratified by gender and age to approximate the sepsis cohort. Prospectively defined exclusion criteria.

2. Methodology

Included patients were subjected to the following: Written consent (by the patient or his relatives).

Detailed History.

Full clinical assessment.

Laboratory tests on admission and follow up including urea, creatinine, sodium, potassium, random blood sugar, complete blood count, coagulation profile, liver function tests.

FMD of the brachial artery by B-mode SIEMENS ACUSON X300 ultrasonography was assessed. The diameter of the brachial artery was measured at rest initially (Di). Then, ischemia was induced by inflating the pneumatic cuff to a pressure 50 mmHg above systolic one, in order to obliterate the brachial artery and induce ischaemia. After 1 minute, the cuff was deflated, and the diameter was measured after 60 seconds post deflation (DF). FMD was calculated with the formula: FMD = [(Df –Di)\ DI] x 100

Data Management and Analysis:

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 25). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

i. Descriptive statistics:

1. Mean, Standard deviation $(\pm SD)$ and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data. 2. Frequency and percentage of non-numerical data.

ii. Analytical statistics:

1. Student T Test was used to assess the statistical significance of the difference between two study group means.

2. *Mann Whitney Test (U test)* was used to assess the statistical significance of the difference of a non-parametric variable between two study groups.

3. *Chi-Square test* was used to examine the relationship between two qualitative variables.

4. *Fisher's exact test* was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells

5. Correlation analysis (using Pearson's method) to assess the strength of association between two quantitative variables. The correlation coefficient denoted symbolically "r" defines the strength (magnitude) and direction (positive or negative) of the linear relationship between two variables.

• r=0-0.19 is regarded as very weak correlation

- r=0.2-0.39 as weak correlation
- r=0.40-0.59 as moderate correlation
- r=0.6-0.79 as strong correlation
- r= 0.8-1 as very strong correlation

6. *Kaplan-Meier Survival Analysis* is a descriptive procedure for examining the distribution of time-to-event variables. Additionally, you can compare the distribution by levels of a factor variable or produce separate analyses by levels of a stratification variable

P- value: level of significance. -P>0.05: Non significant (NS). -P< 0.05: Significant (S).

-P<0.01: Highly significant (HS).

3. Results:

		Mean / N	SD / %	Median (IQR)
Group	Control	100	31.3%	
	Case	219	68.7%	
Gender	Male	121	37.9%	
	Female	198	62.1%	
Age		46.15	19.44	48 (27 - 63)
Smoking	No	252	79.0%	
	Yes	67	21.0%	

	Group					tost
	Control		Case	Student t-test		
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	P-value	Sig.
Urea	13.19 ± 2.44	13 (11 - 15.5)	157.45 ± 89.49	140 (100 - 200)	< 0.001 ^(M)	
Creatinine	0.75 ± 0.09	0.7 (0.7 - 0.8)	5.42 ± 3.43	4.7 (2.8 - 6.6)	< 0.001 ^(M)	
Uric acid	4.67 ± 0.52	4.5 (4.1 - 5.2)	9.75 ± 8.56	8 (6.8 - 11.55)	< 0.001 ^(M)	
ALT	19.15 ± 2.51	18 (17 - 23)	92.85 ± 209.27	28 (15 - 73)		
AST	19.92 ± 5.32	20 (15 - 23)	119.41 ± 258.76	37 (23 - 98)	< 0.001 ^(M)	S
Hb	12.84 ± 0.69		9.4 ± 2.62		< 0.001	S
WBCs (x10 \square)	5.91 ± 1	6.4 (5.4 - 6.7)	14.46 ± 16.44	12.5 (8.2 - 17.2)		
Platelet (x10 \Box)	349.73 ± 55.85	341 (312 - 399)	206.16 ± 130.21	184 (103 - 290)	< 0.001 ^(M)	S
Flow mediated dilatation of the Brachial artery	11.67 ± 1.26		7.31 ± 0.75		< 0.001	S

		APACHE SCORE	APACHE Mortality %	SOFA 0	SOFA 48 hrs	SOFA 96 hrs
Flow mediated	Pearson Correlation	0.098	0.089	0.074	0.023	0.036
dilatation of the	P-value	0.150	0.189	0.279	0.734	0.650
Brachial artery	Sig.	NS	NS	NS	NS	NS

4. Discussion

Our study design was observational case-control study conducted on 329 patients (219 cases, 100 control patients).

Our hypothesis was endothelial dysfunction measured by FMD of the brachial artery was evident in patients with CKD (15), so it may be also evident in patients with AKI.

To our knowledge this is the first study done to prove this hypothesis.

In our study FMD of the brachial artery was significantly low $(7.31\% \pm 0.75\%)$ in patients with AKI compared to $(11.67\% \pm 1.26\%)$ in control group which showed statistical significance (P<0.001).

Other studies showed significant lower FMD aft ha brachial artery in patients with Chronic kidney disease, Verbeke et al. 2011 showed that the high correlation between ESRD and _BA can be used as an indicator for dropping of FMD in ESRD diseased subjects. (16).

Limitations of the study

The main limitation is that the arterial system is non-homogenous and obtained data from the brachial artery by ultrasonography images cannot be systematically generalized to other arterial regions.

Conclusion

Our present observations indicate that AKI is associated with endothelial dysfunction the Flow mediated dilatation of the Brachial artery was low significantly in studied diseased patients. In our stud ether was insignificant correlation between Flow mediated dilatation of the Brachial artery and mortality, APACHI score and SOFA score.

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