

ASSESSMENT OF FLOW MEDIATED DILATATION OF BRACHIAL ARTERY BY ANGIODEFENDER DEVICE AS COMPARED TO BRACHIAL ARTERY ULTRASOUND IMAGING.

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Abstract

Aims & Objectives: To demonstrate, Angiodefender device, is comparable to “Brachial artery ultrasound imaging” (BAUI) in their abilities to quantify percentage flow mediated vasodilation (FMD) of the brachial artery.

Methods: Study was conducted on 100 patients, flow mediated vasodilation was measured by BAUI as well as by the Angiodefender device and the results were compared.

Results: The mean %FMD measured by the BAUI was found to be 7.46 ± 4.21 whereas mean %FMD measured by the Angiodefender was 8.24 ± 2.46 , (p value 0.113). Positive correlation was found between both the tests with correlation coefficient of 0.65, p value < 0.0001 which is highly significant.

Conclusion: Results obtained by both the methods were comparable, there was no significant statistical difference. Positive correlation was highly significant between both the tests with correlation coefficient of 0.65.

Keywords: Brachial artery ultrasound imaging, Angiodefender, Flow mediated vasodilation

Introduction

The endothelium plays multiple pathologic and physiologic roles including the regulation of smooth muscle tone, control of thrombosis, inhibition of leukocyte and platelet cell adhesion, and promotion of intra-arterial permeability^{1,2,3}. Endothelial dysfunction is an imbalance between the chemical species which regulate vessel tone, thomboresistance, cellular proliferation and mitosis. It is the first step in atherosclerosis and is associated with coronary artery disease, peripheral artery disease, heart failure, hypertension^{4,5} and hyperlipidemia⁶. It follows that the assessment of endothelial function has become an area of considerable interest to the medical and research communities.

There are many techniques for assessing endothelial function. These techniques can be either invasive or non-invasive, and assess different aspects of pathobiology. Invasive methods include imaging of

vasomotor responses of epicardial coronary arteries via quantitative coronary angiography or intravascular ultrasound and changes in vessel diameters and cross-sectional areas in response to endothelium-dependent interventions are documented⁷.

Non-invasive methods of measuring endothelial function include ultrasound FMD, salbutamol-mediated endothelial function measured by pulse wave analysis (PWA) or pulse contour analysis (PCA), flow-mediated magnetic resonance imaging (MRI), laser Doppler flowmetry, and flow-mediated pulse amplitude tonometry (PAT)⁷.

For the assessment of pre-clinical disease, the ideal technique for measuring endothelial function must be non-invasive, reliable, reproducible, cheap, and easy to perform⁸.

Developed in 1992 by Celermajer and colleagues, the flow-mediated dilation test is now the most commonly utilized non-invasive assessment of vascular endothelial function in humans⁹. FMD, an

endothelium dependent function in the brachial artery is assessed by Brachial artery ultrasound imaging (BAUI) ^{10,11,12}. This technique stimulates the endothelium to release nitric oxide (NO) with subsequent vasodilation that can be imaged and quantitated as an index of vasomotor function ¹². Peripheral endothelial function as assessed by FMD correlates with coronary artery endothelial function ^{13, 14}.

However, although the principle of this technique seems simple, its application is technically challenging and requires extensive training and standardization ^{15,16,17,18,19}. Study preparation, image acquisition and site selection, sphygmomanometer probe position, cuff occlusion time, accurate use of edge-detection software, and correct characterization of the FMD response are crucial, as recently outlined in detail in guidelines by Charakida et al ¹⁷, Thijssen et al ¹⁸ and Harris et al ¹⁹.

Angiodefender device (Everist Genomics) which is CE certified and has been proven to be equivalent to gold standard BAUI for measuring % FMD ²⁰, uses a novel, proprietary software algorithm to analyse pulse wave amplitude data collected before and after brachial artery occlusion by a standard upper arm sphygmomanometric blood pressure cuff. The procedure is non-invasive and employs neither ultrasound nor Doppler flow analysis and do not require any expertise ²¹.

MATERIAL & METHODS

The present study was conducted in the Department Of Cardiology, RNT Medical College & MB Hospital from Aug 2015 to Nov 2016.

A total of 100 cases were studied. All stable patients of either sex consecutively selected from the outdoor department of M B Hospital who were ready to participate, were included in this observational study. Written informed consent of each patient were obtained after explaining details of the study. % FMD were calculated by BAUI and Angiodefender randomly with a gap of one hour between the two tests. Exclusion criteria were patients undergoing coronary catheterization for acute coronary syndrome or for other reasons like hypertensive crisis associated with troponin elevation, valvular heart disease, congenital heart disease, cardiomyopathy, patients with baseline ECG rhythm abnormalities. FMD through BAUI were measured according to the guidelines by Thijssen DH et al ¹⁸.

All subjects were instructed not to eat for at least 6 hours before the procedure or consume alcohol, or

caffeine-containing drinks for at least 24 hours prior to the procedure. Patients were laid in supine position in a quiet temperature-controlled room for 10 minutes before the examination. The diameter of the brachial artery was measured by 2D ultrasound images using a commercially available system (vivid 7 GE) and images were recorded. A baseline image was obtained at rest 2 to 10 cm above the antecubital fossa incident with the R-wave on the electrocardiogram. To create a flow stimulus in the brachial artery, a blood pressure cuff was placed on the forearm and inflated to at least 50 mm Hg above systolic pressure to occlude arterial flow for 5 minutes. A second measurement was performed 60 to 80 seconds after cuff release to endothelial-dependent flow-mediated vasodilatation of the brachial artery (FMD). For each measurement, average of a minimum of three cardiac cycles were recorded. FMD was calculated as the percentage change in diameter compared with the baseline resting diameter.

The Angiodefender device uses a novel, proprietary software algorithm to analyse pulse wave data collected before and after Brachial Artery (BA) occlusion by an upper arm sphygmomanometric cuff. At the end, of the testing procedure (~15 min), the maximal relative post-occlusion change in the diameter of the BA relative to baseline is calculated and expressed as a percentage of flow mediated dilation (%FMD). Angiodefender test results are not dependent on user technique or operator proficiency ²¹

STATISTICAL ANALYSIS

Unpaired t-test was used to compare the mean values of the two tests. The agreement between the two methods were evaluated with passing-bablock regression analysis and correlation coefficients. P value less than 0.05 was considered statistically significant.

RESULTS:

Present study was conducted on a total of 100 patients out of which 90 were male and 10 female. Mean age was found to be 50.4 years. 90 out of 100 patients were less than 60 years of age and the remaining 10 patients were more than 60 years of age. Total no. of individuals free from all risk factor were 13. Mean age (in years) of population free from all risk factor was 42.46 ± 4.52 , in Diabetic Population 45.75 ± 3.96 , in Hypertensive population 57.34 ± 5.37 , in Smoker 51.85 ± 8.09 and in SIHD 54.54 ± 9.22 .

The mean %FMD measured by the BAUI was found to be 7.46 ± 4.21 whereas mean %FMD measured by the Angiodefender was 8.24 ± 2.46 , p value being 0.113 as shown in table 1.

Table 1:

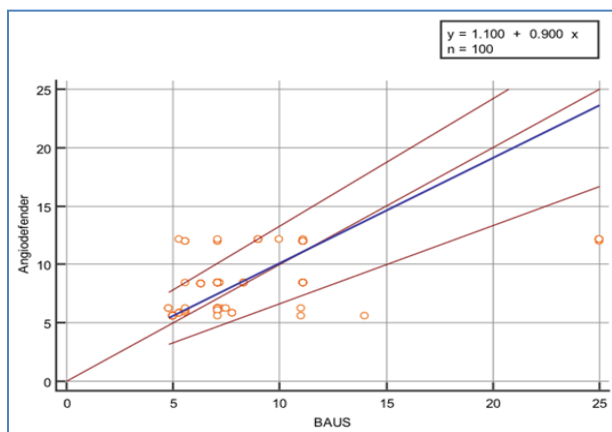
	Mean \pm SD	P Value
BAUI	7.46 \pm 4.21	0.113
Angiodefender	8.24 \pm 2.46	

The mean %FMD measured by BAUI and the Angiodefender, were similar in various subgroups with no significant statistical difference. (Table 2)

Table 2:

Age group	BAUI	Angiodefender	P Value
≤ 60 year(90)	7.63 \pm 5.04	7.68 \pm 2.44	0.9326
>60 Years (10)	9.71 \pm 2.36	8.18 \pm 0.69	0.0647
Female(10)	6.94 \pm 2.36	6.74 \pm 1.15	0.8123
Male (90)	7.94 \pm 5.07	7.84 \pm 2.40	0.8659
HTN (44)	6.68 \pm 2.18	6.91 \pm 1.29	0.5486
Smoker(68)	7.27 \pm 5.04	8.26 \pm 2.11	0.1375
Diabetic (68)	6.43 \pm 1.93	7.03 \pm 1.26	0.0842
IHD (44)	6.42 \pm 2.33	6.65 \pm 1.16	0.698
Normal (13)	11.74 \pm 9.34	11.81 \pm 1.03	0.979

Passing bablock regression analysis showed statistical equivalence and there was positive correlation ($r = 0.65$) between Angiodefender and BAUI as depicted in Graph 1.



Graph 1: Passing Bablock Regression Analysis

Spearman rank correlation coefficient

Table 2:

Correlation coefficient	0.655
Significance level	P<0.0001
95% CI	0.527 to 0.755

DISCUSSION:

The primary objective of the present study was to assess flow mediated dilatation of brachial artery by Angiodefender device and compare it with BAUI. In our study, the results obtained by both the methods were comparable without any significant statistical difference. Similar findings were found in the study conducted by Thakrar N et al²².

In our study positive correlation was found between BAUI and Angiodefender with correlation coefficient of 0.65, p value being highly significant (p value < 0.0001) which was analogous to the study done by Kalsiwal in Medanta Heart Institute, New Delhi, India in 2011, with correlation of 0.67²³ and Moscow Medical Academy, Moscow, Russia in 2010 with Pearson correlation coefficient of 0.84, p value < 0.0001²³. Our study enrolled a larger cohort (N=100) compared to the above mentioned study.

As a marker for preclinical disease, it has been suggested that FMD may be more closely correlated with the non-Framingham (i.e, low or medium) risk factors than Framingham (high) risk factors²⁴. In a recent study, Matsushima and colleagues claim that brachial artery FMD can diagnose the presence of coronary stenosis in high-risk individuals with similar accuracy to treadmill testing²⁵. Also, in small scale clinical studies, FMD has been found to be an independent predictor for further cardiac events in patients, post myocardial infarction^{13,26}.

Conventional risk factors for atherosclerosis can be increasingly identified in the general population but targeting those who are likely to develop the disease as well as maximizing the benefits of any intervention has not been realized yet. Risk factors associated with the development of atherosclerosis include age, smoking, hypertension, diabetes and family history, but despite large scale epidemiological studies, approximately half the burden of atherosclerotic cardiovascular disease is unexplained by conventional risk factors. Patients who manifest complications of atherosclerosis and those who are at higher risk of future cardiovascular events require aggressive treatment of risk factors. Risk factor modification is associated with improved outcome²⁷.

Brachial ultrasound FMD allows the early detection of patients who would not be eligible for medical therapy under current guidelines, but who are at increased risk for cardiovascular events. There is no

doubt that a test which detects otherwise (silent) cardiovascular risk would allow early intervention by lifestyle change, or drug therapy, and primary prevention could start as early as childhood²⁸. This in the long-term could dramatically reduce the mushrooming burden of cardiovascular disease on the healthcare system. However as % FMD measured by BAUI is technically demanding and has many logistic issues therefore, Angiodefender could emerge as a potential alternative.

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Conflict of interest: The authors declare that there is no conflict of interests regarding the publication of this paper.

CONCLUSION:

Angiodefender is a CE Mark-certified device equivalent to BAUI. It accurately and reproducibly quantifies FMD without the need of expensive ultrasound equipment or operator expertise and, therefore, is the most promising available instrument of its type for prospectively assessing CVD risk and has the potential for replacing BAUI as it is cost-effective tool and well-suited for quickly enhancing primary medical care in any location where it is used.

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