Peripheral Arterial Compliance and Atherosclerotic Burden

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Summary

We have developed a new method for rapidly measuring peripheral arterial compliance (Vasogram™), applicable in the primary care setting. In an observational multi-center study, 342 subjects were recruited over a broad range of cardiovascular risk and anticipated atherosclerotic burden. Study data included demographics, cardiovascular risk factor assessment, measurement of peripheral arterial compliance at the thigh and calf levels, and a novel multi-slice MRI of the abdominal aorta. Mean Percent Wall Area (% Wall) of the abdominal aorta was the measurement for generalized atherosclerotic burden. Statistical analyses were performed to determine whether Vasogram™ measures were predictive of atherosclerotic burden (%Wall). The gender adjusted R^2 for the Vasogram™ was 0.199. The gender adjust R^2 for a standard set of cardiovascular risk factors was 0.171, suggesting Vasogram™ measurements are more predictive of atherosclerotic burden than multiple combinations of conventional risk factors.

Introduction

Primary prevention of coronary heart disease may require starting preventive measures, such as lipid-lowering drugs, at a significantly younger age than the majority of subjects selected in published clinical trials [1-4]. However, it is not cost-effective to treat an entire population long term. Therefore, the introduction of diagnostic methodologies that target patients at high enough risk of future atherosclerotic vascular disease to warrant the expense and hazards of treatment, years to decades before symptoms or flow limiting stenoses develop, is a priority [5]. Although controversial, standard risk assessment using clinical and biochemical parameters, such as the Framingham CHD Risk Profile, may not adequately stratify risk [6]. There is intense interest in techniques that focus on arterial function and structure [7].

Decreased arterial compliance may be used as an early marker of vascular disease; it may also be associated with progression of atherosclerosis [8]. A new non-invasive method for directly measuring local arterial compliance at the calf and thigh using air plethysmography, Vasogram™, has been studied [9,10]. Unlike other methods used to evaluate arterial stiffness, the measurement of compliance by air plethysmography, is not confounded by blood pressure, peripheral vascular resistance, or changes in the aorta. It may therefore be a purer measure of atherosclerotic burden.

Arterial compliance in the lower extremities, measured by air plethysmography has been shown to correlate with the extent of coronary artery disease in patients undergoing diagnostic coronary angiography [9] and conventional risk factors in patients without vascular disease [10]. The clinical value of advanced risk assessment tools depends on providing prognostic information that is incremental to conventional clinical risk evaluation. In order to further evaluate arterial compliance measured by air plethysmography as a risk stratification tool, we studied the relationship between arterial compliance, standard cardiovascular risk factors and a novel measure of atherosclerotic burden using multi-slice Magnetic Resonance Imaging (MRI) of the aorta in patients with a broad range of atherosclerotic risk as determined by NCEP/ATPIII guidelines [11].

Materials and Methods

Subjects

The study was conducted at four clinical centers from December 2001 to July 2002. Males 35-69 years old and females 45-79 years old, meeting established inclusion/exclusion criteria, were enrolled. Patients were divided equally into four subgroups (low risk, moderate risk, equivalent CAD, and documented CAD).

Cardiovascular Risk Factors

Cardiovascular risk factors and demographics were collected by questionnaire and clinical measurement. Cardiovascular risks included the following variables: history of tobacco use, hypertension, diabetes mellitus, hyperlipidemia and obesity status.

Determination of Peripheral Arterial Compliance

The Vasogram™ was used to measure arterial compliance at the thigh and calf levels. Each subjects had four repeat Vasogram measurements. The Vasogram™ system is a computer-controlled air plethysmograph designed for clinical use. This device has an air pump, calibration chamber, and high-resolution pressure transducer. The patient interface is via standard blood pressure cuffs placed at the thigh and calf levels (**Figure 1**). Measurements were taken independently at each level. For this study, cuff pressures (Pc) were changed from 30 to 130 mm Hg in 10 mm Hg increments. The Pc range was individualized as a function of the subject's brachial arterial pressure. At each pressure, the Vasogram™ measured maximum segmental limb volume change as a function of time during the cardiac cycle. During the early stages of diastole, a calibration volume (Vcal) of 0.65 ml rapidly expands the system volume. This introduction of volume produces an abrupt change in pressure (Pcal). With the measurement of the maximum pressure change (Pm) during the cardiac cycle of interest and Pcal, it is possible to determine the local maximum volume change (Vm) during the cycle (**Figure 2**). This procedure is performed over the Pc range previously mentioned. With this information, Vm at each cuff pressure is plotted; this is illustrated in **Figure 3**.

To determine the local arterial compliance, the maximum volume change (MaxVm) is identified from this curve and divided by the subject's brachial pulse pressure. This value is normalized to a 50 mm Hg pulse pressure to facilitate comparison among patients and quote the compliance as MaxV50 in millimeters. Higher scores for MaxV50 correspond to more compliant arteries. Testing, which takes approximately 20 minutes can be performed in virtually any examining room (**Figure 4**).

Thoracic and Abdominal Aortic Magnetic Resonance Imaging (MRI)

All subjects enrolled in the study had a novel multi-slice MRI of their thoracic/abdominal aorta to evaluate aortic distensibility and wall thickness. The Mean % Wall Area in the abdominal aorta was used as a measure of atherosclerotic burden (**Figure 5**). To maintain consistency, all images were transferred to a central MRI Core Laboratory for image analysis and interpretation.

Results

The primary objective of the statistical analysis using SAS Version 8.02 was to evaluate whether the Vasogram™ measures were predictive of atherosclerotic burden, as determined by Mean % Wall. The secondary objective was to compare the predictive ability of the Vasogram™, to a set of standard cardiovascular risks factors. The primary measure of model predictive ability was gender adjusted R^2, a measure of the fractional reduction in the variance of Mean % Wall obtained by predictors. The R^2 for the Vasogram™ alone was 0.199; the R^2 for a comprehensive combination of cardiovascular risk factors as defined above was 0.171.

Conclusions

Reduction in arterial compliance is an early marker of atherosclerosis (burden and cardiovascular mortality) and can be seen in patients with hypertension, diabetes, and elevated blood lipids. The measurement of arterial compliance in the lower extremities using the Vasogram™ is more predictive of atherosclerotic burden, as measured by aortic MRI, than a combination of conventional risk factors. The method is rapid and inexpensive; it may find a place in the primary care setting for cardiovascular risk assessment. Although, MRI is also non-invasive and offers the opportunity to visualize and quantify atherosclerotic plaque, it is expensive and its reproducibility has not been reported [12].

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Captions

Figure 1 Schematic of the Vasogram™ components, which include standard blood pressure cuffs, pump, valving, calibration chamber and high-resolution pressure transducer.

Figure 2 Cuff pressure (Pc) as function of time during the cardiac cycle. Introduction of 0.65ml (Vcal) in early diastole causes a pressure change (Pcal) that, along with the maximum pressure change (Pm) is used to calculate maximum local volume change (Vm).

Figure 3 Maximum Volume change (Vm) as a function of mean cuff pressure (Pc). The maximum volume change (MaxV) occurs when mean cuff pressure is just above the diastolic pressure (Pd).

Figure 4 Vasogram™ System.

Figure 5 Mean Percent Wall Area (% Wall) of the abdominal aorta used as a measure of atherosclerotic burden.

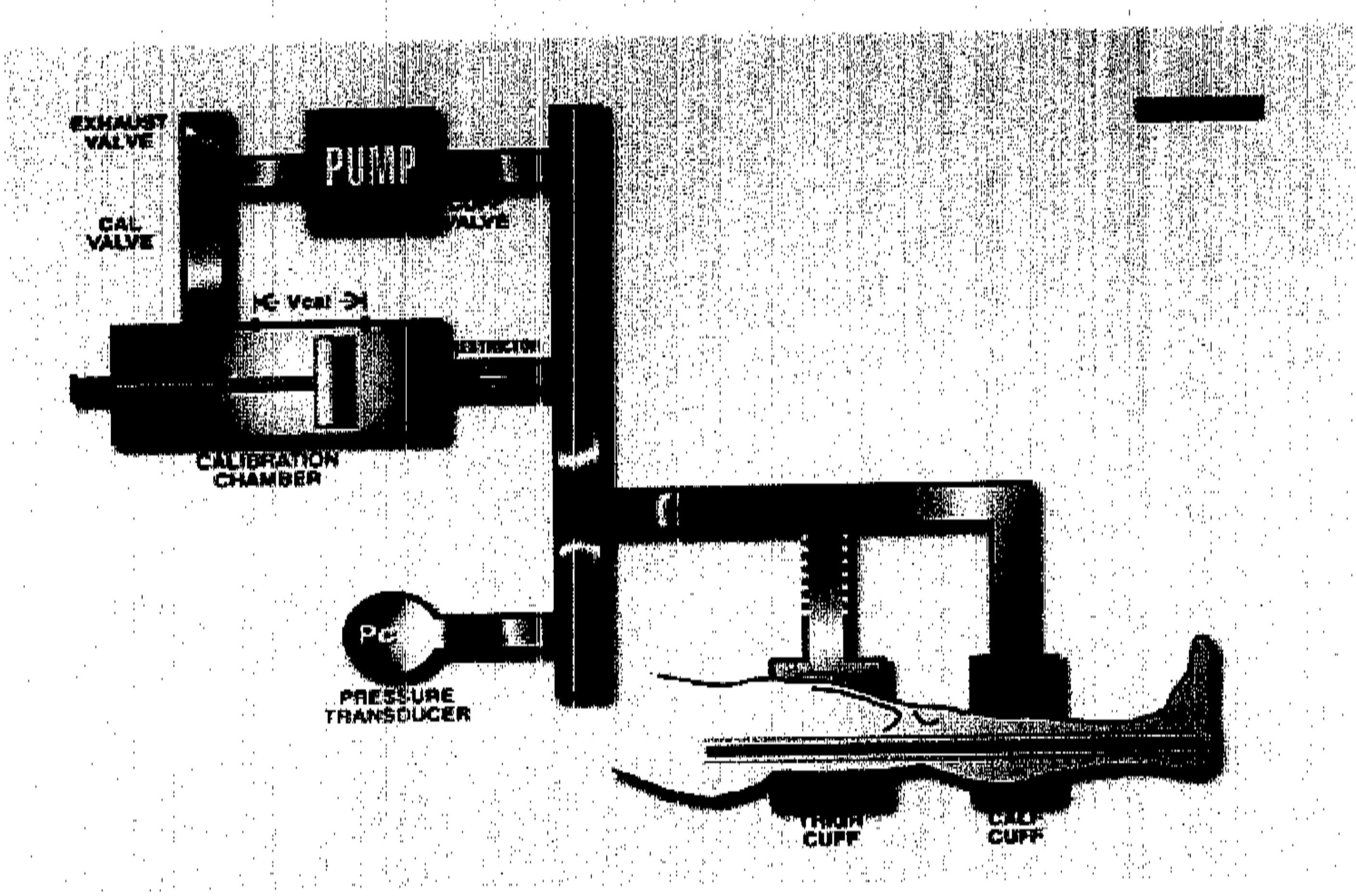
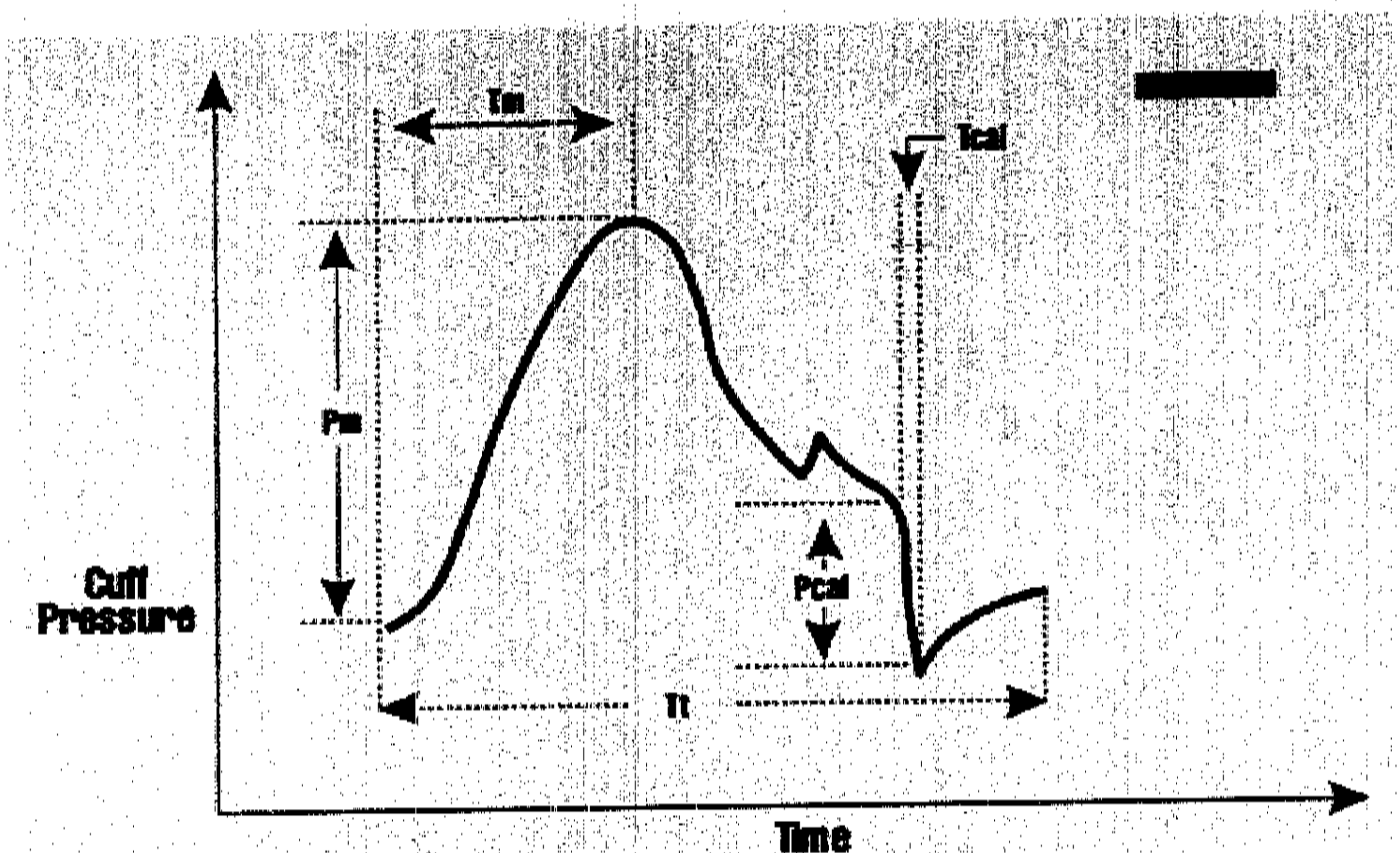
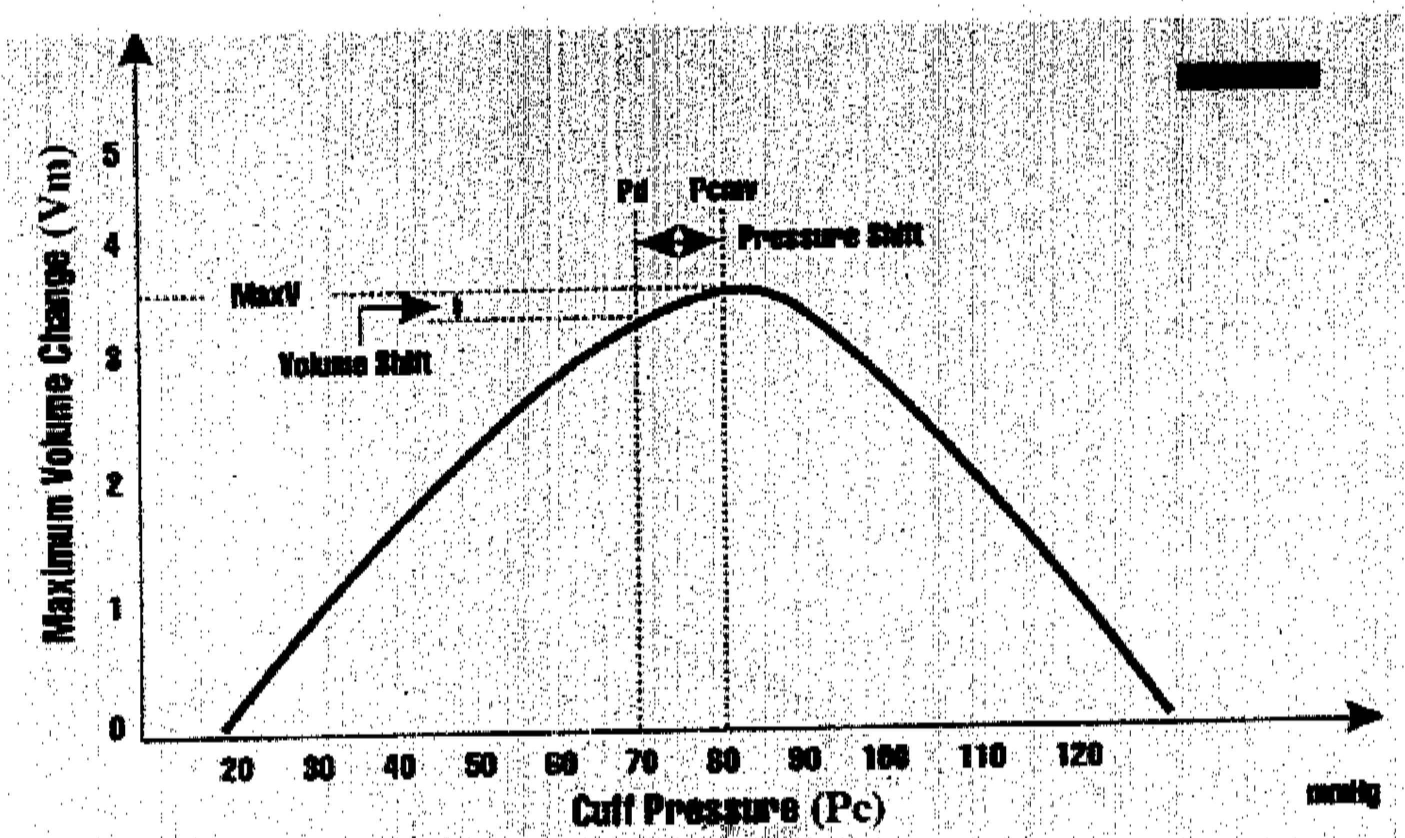

EXHAUST VALVE
PUMP
CAL VALVE
VALVE
Vcal
CALIBRATION CHAMBER
Pc
PRESSURE TRANSDUCER
CUFF
CUFF

Figure 1



INSTANTANEOUS CUFF PRESSURE vs TIME CURVE

Figure 2



MAXIMUM VOLUME vs CUFF PRESSURE

figure 3

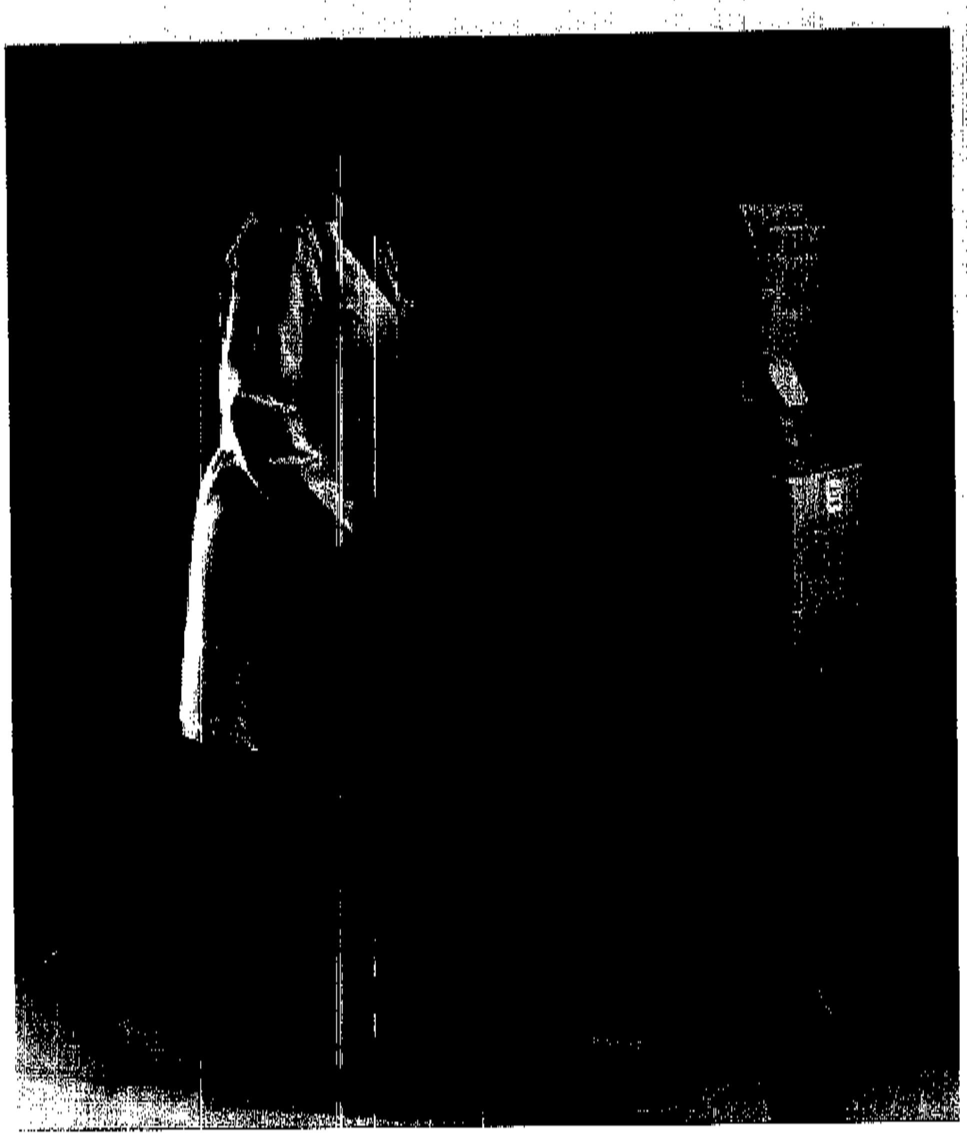
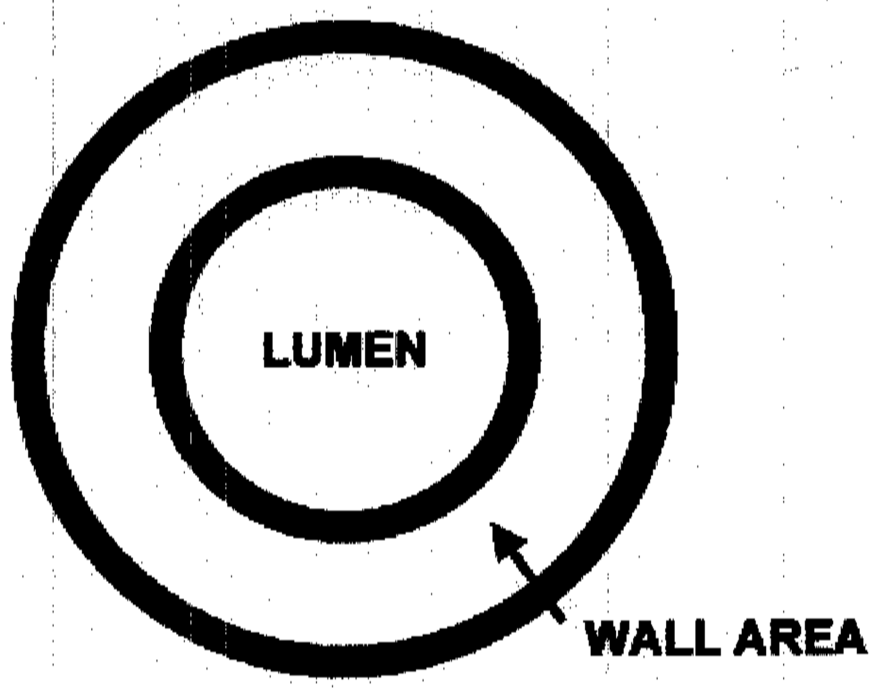


Figure 4



$$\% \text{ Wall} = \frac{\text{Wall Area}}{\text{Wall Area} + \text{Lumenal Area}} \times 100\%$$

Figure 5

Noicely, Karlene

From: Raines, Jeffrey
Sent: Thursday, February 19, 2004 8:23 AM
To: Noicely, Karlene
Cc: 'gregory.grimaldi@csfb.com'
Subject: FW: Proceedings of the 3rd Intl Congress on Heart Disease (Washington DC, USA, July 12-15, 2003)

Dear Karlene:

Attached is the latest information regarding the Third World Congress and the associated paper on the Vasogram. Please file.

Sincerely,

Jeff

Greg: FYI (this will be helpful) jr

-----Original Message-----
From: Editorial Secretariat [mailto:secretariat@monduzzi.com]
Sent: Thursday, February 19, 2004 4:35 AM
To: Raines, Jeffrey
Subject: Proceedings of the 3rd Intl Congress on Heart Disease (Washington DC, USA, July 12-15, 2003)

Email: jraines@med.miami.edu
Workcode: D712C0182

Dear Dr . Jeff Raines,

Thank you for sending us your paper for publication in the proceedings of
the 3rd International Congress on Heart Disease (Washington DC, USA, July
12-15, 2003).

The publication is now being edited by Dr. Kimchi, and we plan to have it
available to the printers in about 3 weeks. As soon as the editing is completed, we will speed the printing process up and notify you the exact
publication and order shipping date.

Thanking you for your precious collaboration.

Sincerely,

The Editorial Secretariat
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