CHAPTER 5

CARDIAC RISK ASSESSMENT USING AUGMENTATION INDEX

5.1 GENERAL

This chapter presents the methodologies that are usually adopted for the measurement of cardiac risk and the method presently proposed in this research and its special merits. At the beginning, initial studies of Photoplethysmography concept in-terms of measurement, techniques and related research is done and then a measurement method based on Augmentation Index is proposed for this work since it is cost effective.

The PPG signal is obtained from the subject using Photoplethysmograph. The photoplethysmograph (PPG) is a non-invasive electro-optical signal to measure pulsations associated with changes of blood volume. PPG sensor is used to obtain the pulse wave from the subject. Figure 5.1 presents the block diagram for PPG signal acquisition.

![Figure 5.1 Block Diagram for PPG signal acquisition](image-url)
5.2 **PPG SENSOR**

The PPG sensor used in the experimental set up is of reflective type. The Figure 5.2 shown below is the sensor that is used for PPG.

![Figure 5.2 PPG sensor](image)

It shows the PPG sensor, having an emitter and detector, wrapped around the finger. The photoplethysmographic sensor is placed below the tip of the finger and pressure is applied on the proximal phalanx. Since the cuff is wrapped on the proximal phalanx of the finger rather than on the arm, it makes less discomfort for prolonged usage. The blood volume changes on the finger are detected by the sensor. Non-invasive pressure measurement is an oscillometric method which applies the theory of sphygmomanometer (Dai Junwei and Wang Boliang 2006; Mohammad Alnaeb et al 2007)

5.3 **ARTERIAL STIFFNESS AND AUGMENTATION INDEX**

5.3.1 **Arterial Stiffness**

All arteries are composed of three layers, the intima, media and adventitia. The intima is the innermost layer, a single layer of endothelial cells and associated connective tissue. The middle layer is the media which is composed of a varying amount of elastic and smooth muscle tissue depending
on the size and location of the artery in the arterial tree. The outer layer is the adventitia which is fibrous connective tissue.

![Figure 5.3 Structure of normal artery and stiffened artery](image)

Figure 5.3 shows the structural difference between a normal artery and a stiffened artery. The lumen of the stiffened artery is narrowed by plaque deposition.

Large arteries are not just simple conduits for blood. They also act as a buffer to the pulsatile blood flow from the heart. This role is fulfilled via the elastic nature of the arterial walls. Detailed assessment of the arterial tree requires information about the form of the arterial pulse (i.e. the arterial pressure waveform) and information about how the arterial walls move in reaction to this waveform (i.e. the arterial distension waveform).

Arterial stiffness is a generic term that describes the rigidity of the arterial wall. The physiological reason for the elastic nature of the arterial wall is to buffer the pulsatile ejection of blood from the heart and to provide near
constant flow in the capillary beds. The mechanical principles behind arterial stiffness are complex but are based on the relationship between stress and strain. In the case of arterial stiffness, the stressing force is the pressure of pulsatile blood flow and the resulting strain is the change in length of the arterial wall.

5.3.2 Mechanical Principles of Arteries

Force (stress) acting on a solid body at rest causes parts of the body to move relative to each other (strain). At the end of the application of the force, if the body regains its original form, then it is said to be elastic. If the body retains the deformation caused by the force acting upon it then it is said to be plastic.

5.3.3 Strain

Strain is described as the ratio of the deformation of a body compared to its original form and thus has no units. Longitudinal strain is defined as the change in length of a body in response to stress. An increase in length is positive strain and a decrease in length is negative strain. Compressive strain causes a change in volume of a body and shear strain to angular deformation, a displacement of two points in parallel planes in a direction parallel to those planes. A body that is extended longitudinally (longitudinal strain) will at the same time get shorter transversely (transverse strain). The ratio of transverse to longitudinal strain is called the Poisson ratio ($\sigma$). $\sigma$ for a particular material is constant under small strain. The effective range for $\sigma$ is 0 to 0.5. In a small extension of a material with a ratio of 0.5, the volume of the material remains the same when stretched. This is known as iso-volumetric deformation, and it is exhibited by rubber like substances where $\sigma = 0.487$ for the arterial wall is believed to be close to 0.5. If the elastic properties are not the same the material is said to be anisotropic. If the elastic
properties in each direction are not the same but the material is iso-volumetric under strain then the average values of $\sigma$ must be equal to 0.5.

5.3.4 Elastic Theory

Elastic theory attempts to explain the relationship between the force applied to a body and its consequent change of deformation. The behaviour of a body in response to a stress distinguishes solid from liquid, as a liquid will undergo viscous flow whereas a solid will not. However a large number of bodies are termed viscoelastic as they exhibit qualities attributable to both an elastic solid and a viscous liquid; their behaviour in any given situation depends on the size of the stressing force and the rate at which it is applied. Arterial walls are viscoelastic. Arterial walls retain large deformations. The arterial walls are composed principally of collagen, elastin and smooth muscle which all have different elastic properties.

5.3.5 Stress

Stress is the intensity of force acting over a given area of a body and thus the units of stress are force per unit area. The effect of stress on a point in a plane can be described by forces acting in parallel to the axis and acting tangentially to the axis. These forces can be resolved into six independent components of stress. Given that Hooke's law demonstrates that strain is proportional to stress, in an anisotropic material there are 36 constants of proportionality as there are six components of strain and six components of stress acting at any one point on a body. Fifteen of these constants can be shown to be interrelated. Thus in an isotropic material, 21 constants need to be considered. An isotropic material however has the same elastic behaviour in all three axes and thus the number of constants of proportionality becomes 2 instead of 21. It is immediately apparent therefore why arterial walls are assumed to be isotropic even though structural analysis demonstrates different macro- and microscopic components.
5.3.6 Indices of Arterial Stiffness


Table 5.1 indicates the various indices of arterial stiffness and their mode of measurement.

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Mode of measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse pressure</td>
<td>The difference between systolic and diastolic pressure</td>
<td>Sphygmomanometry</td>
</tr>
<tr>
<td>Arterial compliance</td>
<td>Absolute diameter(or area) change for a given pressure step</td>
<td>Ultrasound, MRI</td>
</tr>
<tr>
<td>Arterial distensibility</td>
<td>Relative change in diameter (or area) for a given pressure change, the inverse of elastic modulus.</td>
<td>Ultrasound, MRI</td>
</tr>
<tr>
<td>Elastic modulus</td>
<td>The pressure change required for theoretical 100% stretch from resting diameter</td>
<td>Ultrasound, MRI</td>
</tr>
<tr>
<td>Augmentation index</td>
<td>Difference between the second and first systolic peaks as a percentage of pulse pressure</td>
<td>Pressure waveform</td>
</tr>
<tr>
<td>Stiffness index</td>
<td>Ratio of the log of systolic/diastolic pressures to relative change in diameter</td>
<td>Ultrasound</td>
</tr>
<tr>
<td>Pulse wave velocity</td>
<td>Velocity of travel of the pulse along a length of artery</td>
<td>Pressure waveform</td>
</tr>
</tbody>
</table>

Ultrasound, MRI
There are many indices of arterial stiffness. All require information about simultaneous change in arterial size and arterial pressure in order to quantify the change in arterial stiffness. The change in arterial size may be calculated as the change in diameter or change in volume. Both of these parameters should be measured at the same site in the arterial tree due to discrepancy in values across the arterial tree. As in most cases of equipoise, the existence of multiple indices for quantifying arterial stiffness reflects the fact that none of them are superior to one another; all have inherent advantages and disadvantages.

5.3.7 **Augmentation Index**

The augmentation index is defined as the ratio of augmented ascending aortic pressure and pulse pressure and can be calculated from the formula given in Equation 5.1 (Michael Rourke and Wilmer Nichols 2002).

\[
\text{Augmentation Index (Ai)} = \frac{Ps - Pi}{Ps - Pd}
\]  

(5.1)

Where,

Ps $\rightarrow$ systolic pressure point.

Pd $\rightarrow$ diastolic pressure point.

Pi $\rightarrow$ point of inflection.

The points of interest Ps, Pi and Pd of a pulse wave are presented in Figure 2.3. The early part of the aortic pressure wave, with amplitude (Pi - Pd), is generated by the left ventricular ejection wave. This forward-traveling pressure wave is dependent upon peak flow and central artery stiffness and is not influenced by wave reflections. The latter part of the pressure wave, with amplitude (Ps-Pi), is generated by the reflected wave...
arriving during systole and adding to the forward pressure wave. Therefore, pulse pressure = (Pi - Pd) + (Ps-Pi) = (Ps - Pd) and augmentation index = (Ps - Pi)/ (Ps- Pd). This augmentation of the pressure wave is dependent upon the elastic properties of the entire arterial tree, the velocity of the reflected wave, and distance to the major reflecting site. From the formula for augmentation index and the theory behind PPG signal it is clear that when the arteries becomes stiffer, AI becomes lesser.

This method of estimating arterial elasticity has been used in several studies. The augmentation index may therefore provide a more composite index of arterial compliance and hence be a better surrogate marker of whole body compliance than exclusively large artery measures, such as central PWV. Furthermore, increased arterial stiffness has been consistently demonstrated in type 2 diabetes and has also been proposed as independent risk factor for vascular disease.

5.4 CURRENTLY USED TECHNOLOGY

5.4.1 Peripheral Arterial Tonometry (PAT-AIX)

Peripheral Arterial Tonometry (PAT) is a noninvasive method to measure endothelial dysfunction and potentially identify patients with early-stage coronary artery disease. Endothelial dysfunction is measured by the PAT signal which is obtained using the Endo-PAT 2000 System and proprietary software. The test involves the measurement of blood flow in the fingertips following compression of the upper arm with an inflatable cuff. Figure 5.4 shows the peripheral arterial tonometry system having a finger PPG sensor attached to a wrist unit.
Figure 5.4 Peripheral Arterial Tonometry

The formula used to measure Augmentation index using the above mentioned instrument is given in Equation 5.2

\[
PAT – AIX = (P2 - P1) \times 100 / P1
\]  \hspace{1cm} (5.2)

P1- Pulse pressure

P2- Pressure corresponding to inflection point.

5.4.2 Atcor Medical Sphygmocor

Figure 5.5 shows an advanced tonometer instrument. AtCort launched a new tonometer sleeve that can be retro-fitted to existing tonometers to make the capture of high quality peripheral artery blood pressure waveforms much easier and quicker. There has been a strong positive response to the new tonometer, particularly from new Sphygmocor users.
5.4.3 CV Profiler Device

This product offers the physician the ability to quickly evaluate patient cardiovascular systems in the office or in medical clinic.

Figure 5.6 CV Profiler device

Figure 5.6 shows the CV profiler device used for hypertension diagnostics. Inchave developed a method for non-invasively measuring the elasticity of large and small arteries, providing early assessment of vascular disease designed for use by U.S. physicians only.
5.5 PROPOSED ALGORITHM FOR CARDIAC RISK PREDICTION

All the above mentioned instruments are not affordable by all. Therefore to help the society to access this facility at a lower cost, an algorithm is implemented to calculate the augmentation index by using PPG signal. This algorithm is as efficient as the above mentioned instruments.

In the proposed technique PPG signals are obtained from the patients. From the PPG signals the baseline drift is removed by smoothening filter. For this signal, the global and local maxima and minima values are obtained. The points of interest, Ps, Pi and Pd are obtained from the maxima and minima. For patients to whom the point of interest is not present in the signal the second derivative of the signal is taken and the point at which it crosses zero is considered as the Pi value. Using these values Augmentation Index is calculated using the formula. By assessing the augmentation index that is measured the cardiac risk of a patient can be predicted. Following are the steps done in calculating the Augmentation Index.

5.5.1 Calculating the Extremas

The following is the concept of calculating the extrema of the given signal. The steps involved are as follows,

(i) To find the points of Local maxima:

x=a is a point of maxima value of f, if

• f(a) = 0 and,

• f(x) changes sign from positive to negative as x increases through a, i.e. f(x)>0 at every point sufficiently close to and to the left of a and f(x)<0 at every point sufficiently close to and to the right of a.
(ii) To find the Global maxima:

The maximum value among the points of local maxima is given as the global maxima.

(iii) To find the points of Local minima:

\( x = a \) is a point of minima value of \( f \), if

- \( f(a) = 0 \) and,
- \( f(x) \) changes sign from negative to positive as \( x \) increases through \( a \), i.e. \( f(x) < 0 \) at every point sufficiently close to and to the left of \( a \), and \( f(x) > 0 \) at every point sufficiently close to and to the right of \( a \).

(iv) To find the Global minima:

The maximum value among the points of local minima is given as the global minima.

The global maxima is referred as the \( Ps \) (systolic pressure point) value. Local minima is the \( Pi \) (point of inflection) value and the global minima is referred as \( Pd \) (diastolic pressure point) value (Figure 2.3).

5.5.2 Identification of the type of the Signal

The signal has to be studied in advance so as to identify if the point of Inflection is noticeable or not. If the point of inflection is present then the value can be taken from the extrema points and directly substituted in the formula for calculation of Augmentation Index. If the point of inflection is unnoticeable then the derivative of the signal is taken and the point of inflection is found using the derivative.
5.5.3 Extraction of Single Cycle

The maximum point is detected, for every peak, a minimum point to the left and two minimum points to the right are calculated, and this comprises a single cycle. For each cycle the Augmentation Index is calculated and the average is taken.

5.5.4 Calculation of Augmentation Index

The formula used to calculate Augmentation Index is given as follows.

\[
Ai = \frac{Ps - Pi}{Ps - Pd}
\]  

(5.1)

Where,

\hspace{1cm}Ps \rightarrow \text{systolic pressure point.}

\hspace{1cm}Pd \rightarrow \text{diastolic pressure point.}

\hspace{1cm}Pi \rightarrow \text{point of inflection.}

Using Equation 5.1 the augmentation index has been calculated. PPG signals are obtained from a group of patients in a private hospital. The normal patients were within the age of 40. The signals were obtained for about a minute after the patient completely relaxes. The abnormal patients were with various degrees of cardiac risk, the abnormal signals were taken from patients admitted for complications that lead to cardiac risk like diabetes and kidney problems. These patients were above the age of 40.
5.6 RESULTS OF MATLAB IMPLEMENTATION

i) Normal Signal

a) First Subject

Figure 5.7 presents the PPG obtained from the normal signal and the detected peak and valley points or in other words the maxima and minima points of the entire signal calculated from the proposed algorithm. Figure 5.8 presents the global maxima or maxima, global and local maxima and minima of PPG signal which refers the points of interest Ps, Pd and Pi. Figure 5.9 shows the extraction of a single cycle with maxima, a minimum point to its left and two minimum points to its right from which the Augmentation Index is calculated for each cycle.

Figure 5.7 Normal PPG Signal with extremas
b) Second Subject

Figure 5.9 presents the local maxima and minima of PPG signal obtained from the second normal patient/subject.
Figure 5.10 Maxima and minima of normal PPG signal

ii) Abnormal Signal

a) First Subject

Figures 5.10 to 5.12 present the PPG signal obtained from two normal and two abnormal patients from which the peak and valley points (maxima and minima point) are calculated. In every cycle global maxima (Ps), global minima (Pd) and local minima (Pi) are calculated. Using these values AI is calculated and presented in Table 5.2. But in Figure 5.12 the signal used is without Pi. For this case, the second derivative is taken and the point at which it crosses zero is taken as the point of inflection.

Figure 5.11 Maxima and minima of abnormal PPG signal
5.7 CALCULATION OF AI FOR PPG SIGNALS WITHOUT PI

The normal and the abnormal waveforms were different in their patterns. The point of inflection was present in few abnormal signals and was unpredictable in most of the abnormal signals. This appearance of the wave is mainly due to the damping effect and thereby the point of inflection becomes difficult to be detected. This is mainly due to aging, diabetes, atherosclerosis or arterial stiffness. For signals of this type the second derivative of the signal is taken to detect the point of inflection. The point at which the second derivative crosses zero denotes the point of inflection (Gonzalez et al 2008).

5.7.1 Calculation of AI for signals with no Pi, by derivative method

Figure 5.13 presents a PPG signal without Pi. Figure 5.14 shows the method used to calculate the point of inflection. The second derivative of the signal is taken to detect the point of inflection. The point at which the second derivative crosses zero denotes the point of inflection.
Figure 5.13 Signal with no Pi

Figure 5.14 Calculation of Pi using second derivative method
<table>
<thead>
<tr>
<th>Subject</th>
<th>Ps</th>
<th>Pi</th>
<th>Pd</th>
<th>AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Subjects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 1</td>
<td>1.86</td>
<td>1.36</td>
<td>1.42</td>
<td>0.88</td>
</tr>
<tr>
<td>Patient 2</td>
<td>1.88</td>
<td>1.14</td>
<td>1.32</td>
<td>0.73</td>
</tr>
<tr>
<td>Patient 3</td>
<td>1.69</td>
<td>1.38</td>
<td>1.23</td>
<td>0.68</td>
</tr>
<tr>
<td>Patient 4</td>
<td>1.82</td>
<td>1.42</td>
<td>1.20</td>
<td>0.62</td>
</tr>
<tr>
<td>Patient 5</td>
<td>1.70</td>
<td>1.38</td>
<td>1.22</td>
<td>0.66</td>
</tr>
<tr>
<td>Abnormal Subjects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 1</td>
<td>1.98</td>
<td>1.38</td>
<td>0.14</td>
<td>0.32</td>
</tr>
<tr>
<td>Patient 2</td>
<td>1.90</td>
<td>1.48</td>
<td>0.18</td>
<td>0.25</td>
</tr>
<tr>
<td>Patient 3</td>
<td>1.95</td>
<td>1.47</td>
<td>0.29</td>
<td>0.28</td>
</tr>
<tr>
<td>Patient 4</td>
<td>1.92</td>
<td>1.29</td>
<td>0.16</td>
<td>0.35</td>
</tr>
<tr>
<td>Patient 5</td>
<td>1.85</td>
<td>0.88</td>
<td>0.17</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Table 5.2 shows the calculated Augmentation Index of 10 patients in a private hospital. The Augmentation index calculated from 5 normal patients ranges above 0.6. Remaining patients have diabetes and kidney problems, for these patients the Augmentation Index was found to be below 0.6 according to our algorithm. The doctors also endorsed our estimation with the patient’s medical report. Moreover our technique was used to obtain Augmentation Index for more than 20 of our colleagues of age below 35 with normal health as per the statement given by them. The Augmentation Index of all of them
was found to be in the range of 0.63 to 0.95. Since for patients having arterial stiffness AI decreases, the patients having less AI value can be categorised under cardiac risk category. So from the above study it is confirmed that this technique can be applied in hospitals for the prediction of cardiac risk.

5.8 SIMULATION RESULTS USING Lab VIEW

Figure 5.15 is the block diagram showing the application of the Lab VIEW software. In this case PPG signal is sent as input. The algorithm used in Lab VIEW detects the peak and valley points. Using these values the points of interest Ps (systolic pressure point), Pi (point of inflection) and Pd (diastolic pressure point) are obtained. Using the obtained points of interest the Augmentation Index is calculated by the formula and the calculated AI value is sent out as output by Lab VIEW.

Figure 5.16 presents the front panel showing the output of results after AI calculation. Figure 5.15 presents the block diagram used for calculation of Augmentation Index from PPG signal.
Figure 5.15 Block diagram for AI calculation from PPG signals
Figure 5.16 Front panel of AI calculation using Lab VIEW
Table 5.3 Augmentation Index of Healthy Subjects

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>Ps</th>
<th>Pd</th>
<th>Pi</th>
<th>AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>1.72</td>
<td>1.36</td>
<td>1.14</td>
<td>0.62</td>
</tr>
<tr>
<td>Patient 2</td>
<td>1.86</td>
<td>1.42</td>
<td>1.36</td>
<td>0.88</td>
</tr>
<tr>
<td>Patient 3</td>
<td>1.78</td>
<td>1.23</td>
<td>1.36</td>
<td>0.76</td>
</tr>
<tr>
<td>Patient 4</td>
<td>1.68</td>
<td>1.13</td>
<td>1.28</td>
<td>0.72</td>
</tr>
<tr>
<td>Patient 5</td>
<td>1.77</td>
<td>1.20</td>
<td>1.31</td>
<td>0.82</td>
</tr>
<tr>
<td>Patient 6</td>
<td>1.80</td>
<td>1.22</td>
<td>1.41</td>
<td>0.67</td>
</tr>
<tr>
<td>Patient 7</td>
<td>1.82</td>
<td>1.20</td>
<td>1.43</td>
<td>0.62</td>
</tr>
<tr>
<td>Patient 8</td>
<td>1.89</td>
<td>1.35</td>
<td>1.15</td>
<td>0.72</td>
</tr>
<tr>
<td>Patient 9</td>
<td>1.78</td>
<td>1.16</td>
<td>1.47</td>
<td>0.84</td>
</tr>
<tr>
<td>Patient 10</td>
<td>1.71</td>
<td>1.23</td>
<td>1.36</td>
<td>0.72</td>
</tr>
<tr>
<td>Patient 11</td>
<td>1.79</td>
<td>1.17</td>
<td>1.40</td>
<td>0.62</td>
</tr>
<tr>
<td>Patient 12</td>
<td>1.70</td>
<td>1.24</td>
<td>1.38</td>
<td>0.69</td>
</tr>
<tr>
<td>Patient 13</td>
<td>1.70</td>
<td>1.22</td>
<td>1.38</td>
<td>0.66</td>
</tr>
<tr>
<td>Patient 14</td>
<td>1.76</td>
<td>1.19</td>
<td>1.30</td>
<td>0.80</td>
</tr>
<tr>
<td>Patient 15</td>
<td>1.76</td>
<td>1.19</td>
<td>1.32</td>
<td>0.77</td>
</tr>
</tbody>
</table>

Table 5.3 presents the augmentation values obtained from few of our colleagues. And it is found that, the AI values are above 0.6 which is in good agreement with their health condition as per the statement given by them.
Figure 5.17 Front panel of AI calculation for signals without Pi

Figure 5.17 is respectively similar to Figure 5.16, but in the second case the input to the Lab VIEW is the PPG signal without Pi. Here to calculate Pi value the second derivative is taken and the point at which it crosses zero is taken as Pi.
5.9 CONCLUSION

In this research arterial stiffness is assessed by using the values obtained using augmentation index. To validate this, major hospitals were approached. It is found that equipment to measure arterial stiffness using AI is not available. Hence our results could not be validated using experimental values. However results of the proposed work could be justified with the following:

1. PPG signals of renal and diabetes patients from a hospital were obtained. The data of the patients is given as input to the proposed algorithm and AI is calculated. It is found that the AI values (below 0.6) are in good agreement with the results. The doctors also endorsed our estimation with the patient’s medical report and health condition.

2. From physionet database, PPG signals of a few aged patients with renal and diabetes problems were collected. For these signals using the proposed algorithm AI is calculated. AI value for these patients is found to be in good agreement with the results (below 0.6). So with the above information, the results in this research are found to be reliable.

From this study the demarcation of AI between normal and abnormal patient is found to be about 0.6. When AI is less than 0.6, the patient can be classified under cardiac risk category. When AI is above 0.6, the patient can be classified into normal category. Since augmentation index which measures the degree of arterial stiffness decreases when the artery is stiffened, lesser AI values are categorized into cardiac risk category.